

Urticaria (Hives) — Definition and Treatment

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Urticaria is a very common dermatological condition, which is classified into acute urticaria and chronic urticaria based on the duration of the symptoms. The etiology is different for acute and chronic urticaria. Diagnosis requires a thorough history-taking and physical examination, and a laboratory evaluation may be helpful depending upon the underlying etiology. In this article, etiology, pathophysiology, clinical features, diagnosis, differential diagnosis, and management of urticaria will be discussed.



Definition and Epidemiology of Urticaria

Wheals (hives or “nettle rash”) are the hallmark lesions in urticaria. Wheals are self-limiting, superficial, erythematous or pale, raised lesions due to edema of **dermis** and **epidermis**. Urticaria lasting up to six weeks is called **acute urticaria**, while that lasting for more than six weeks is called **chronic urticaria**.

Urticaria is the most common dermatologic disorder seen in the emergency department. About 15 to 20% of the general population experience acute urticaria during their lifetime, while a lifetime incidence of chronic urticaria is 2-3%. Chronic urticaria is more common in **females**.

Signs and Symptoms of Urticaria

Information regarding a history of previous urticaria and duration of rash and itching is useful for categorizing urticaria as acute, recurrent, or chronic.

For chronic or recurrent urticaria, important considerations include previous **causative factors and the effectiveness of various treatments, as follows:**

Precipitants, such as heat, cold, pressure, exercise, sunlight, emotional stress, or chronic medical conditions.

Other medical conditions that can cause pruritus (usually without rash), such as diabetes mellitus, chronic renal insufficiency, primary biliary cirrhosis, or other non-urticarial dermatologic disorders.

Family and a personal medical history of angioedema – characteristics of angioedema include vasodilation and exudation of plasma into the deeper tissues, more so than with simple urticaria; angioedema can occur with and without the wheals of simple urticaria and presents clinically as subcutaneous swelling that is generally non-pitting and non-pruritic; it can affect the mouth as well as the mucosal surfaces of the respiratory and GI tracts, manifesting as hoarseness and GI upset. It can be a feature of anaphylaxis if the throat is involved, leading to airway compromise.

Etiology of Urticaria

Etiology of acute and chronic urticaria is different.

Acute urticaria

- **Allergy**
 - Foods: Fish, shellfish, eggs, nuts, milk, soy
 - Drugs: Penicillins, cephalosporins
 - Insect venom: Bee stings, wasp stings
 - Inhalants: House dust mites, pollens, molds, animal danders
 - Miscellaneous: Blood products, implants, contactants
 - As part of anaphylaxis
- **Infections**
 - [Upper respiratory tract infections](#), pharyngitis, [urinary tract infections](#), gastrointestinal infections
 - Viral infections (Epstein-Barr virus, hepatitis B virus, [HIV](#), coxsackievirus)
 - [Fungal infections](#)
 - [Bacterial infections](#) (streptococcal infections, campylobacter jejuni, mycoplasma)
 - Parasitic infections (anisakiasis, ascariasis, strongyloidiasis)
 - Post-infectious (following non-specific viral infections)
- **Non-allergic**
 - Non-IgE-mediated **histamine** release: Polymyxin, vancomycin, opioids, atracurium, radiocontrast media, dextrans
 - **Pseudoallergic reactions:** Aspirin, other NSAIDs, alcohol, foods rich in vasoactive amines (cheese, fish, tomatoes, pineapples, etc), food additives (tartrazine, other azo dyes, benzoates, sulphites, monosodium glutamate, aspartate, etc.)
- Physical urticarias

- Hormonal changes: Pregnancy, menstrual or pre-menstrual period
- Emotional stress
- Idiopathic

Chronic urticaria

- **Autoimmune**
 - Autoantibodies against α -subunit of Fc ϵ RI (most common)
 - Anti-IgE antibodies
- **Infections**
 - [Helicobacter pylori](#)
 - [Candida infections](#)
 - Intestinal helminth, dental sepsis, sinusitis, urinary tract infections, cholecystitis, toxocara canis, urticarial vasculitis
 - Parenteral antisera, penicillins, radiocontrast media, hepatitis B
 - Associated with other medical disorders
 - [Autoimmune disorders](#) ([systemic lupus erythematosus](#), thyroiditis, [rheumatoid arthritis](#), vitiligo, pernicious anemia, [celiac disease](#), etc.)
 - [Hypo-](#) or [hyperthyroidism](#)
 - Malignancies, lymphoma

Amyloidosis

- **Mastocytosis, urticaria pigmentosa** (cutaneous mastocytosis)
- Idiopathic - also called chronic spontaneous urticaria (CSU)

Note: In more than half of chronic urticaria, the exact etiology cannot be identified.

Pathology and Pathophysiology of Urticaria

Basic pathophysiology for the development of urticaria involves **extravasation of fluid in dermis and epidermis** due to the release of vasoactive substances from cells, most commonly mast cells and basophils.

Histamine is the most important vasoactive substance; stimulation of H₁ receptors on endothelial and smooth muscle results in increased capillary permeability, while that of H₂ receptors dilatation of arterioles and venules. Other vasoactive substances include **bradykinin, leukotriene C4**, and **prostaglandin D2**.

Typical allergic urticarias involve **IgE-mediated histamine release** (type I hypersensitivity), while urticarial vasculitis involve **cytotoxic T cell-mediated responses** (type II hypersensitivity).

Urticarias associated with autoimmune conditions involve **immune complex-mediated reactions** (type III hypersensitivity); while urticarias associated with some infections and transfusion reactions involve complement system.

Symptoms of Urticaria

Duration of urticarial lesion (> 24 hours in urticarial vasculitis and delayed pressure urticaria), and a **detailed history of triggers** (allergic, pseudoallergic, and physical urticaria) are most important characteristics that give clues towards etiology. Although cholinergic urticarias are typically **papular urticaria**, the shape or size of lesions are not

always suggestive of etiology.



Image: "Hives on back." by DLdoubleE - Own work. License: Public Domain

Urticarias occur as **erythematous macules** developing into edematous raised skin lesions, usually accompanied by **significant itching** and are self-limiting (usually < 24 hours).

The lesions classically have **central pallor** with surrounding **red flare**. Lesions can be **single or multiple**, can be of **variable size** (tiny to large lesions) **and shapes** (linear, annular, serpiginous, or irregular), and can occur **anywhere on the body's surface**. They are usually **transient**, may be **migratory or coalescent**, typically **blanch with pressure**, and leave normal skin after resolution.

Angioedema is simultaneously present in half of the patients with urticaria. Urticaria may be accompanied by systemic symptoms, such as malaise, feelings of heat or cold, **headache**, pain in abdomen, vomiting, **diarrhea**, arthralgia, dizziness, etc.

Acute allergic urticaria develops within minutes (not more than one hour) after exposure to food, drug, insect sting, or other substance causing IgE-mediated allergic reaction. Acute urticaria due to inhalant allergy is rare.

Acute urticaria may occur as a **symptom of anaphylaxis** due to a severe allergic reaction to an allergen. **Food-dependent exercise-induced anaphylaxis (FDEIA)** is a condition when an allergic reaction occurs only if an intake of a food allergen is followed by exercise.

Acute urticaria due to **pseudoallergic reaction** or **non-IgE-mediated histamine release** clinically resembles acute allergic urticaria, but the mechanism does not involve IgE antibodies.

Clinically, wheals in chronic urticaria are similar to those seen in acute urticaria. Features of underlying autoimmune or other medical disorder may be present. Physical urticarias are also simultaneously present in many patients with **idiopathic** or **autoimmune chronic urticaria**.

Chronic urticaria may be aggravated by non-specific viral infections, upper respiratory tract infections, drugs (aspirin, other NSAIDs, ACE inhibitors), alcohol, dietary

pseudoallergens, physical factors, emotional stress, and hormonal changes.

Physical urticarias occur as both acute and chronic urticaria. In this group, wheals develop within minutes of exposure to physical factors, such as cold temperature, heat, vibration (vibratory urticaria), pressure (pressure urticaria), water (aquagenic urticaria), or sunlight (solar urticaria).

Among cold urticarias, **idiopathic immediate cold contact urticaria** is most common, which is characterized by the development of wheals immediately on the exposure of skin to cold stimuli, such as cold objects, cold winds, or cold rain. **Systemic symptoms** like flushing, palpitation, headache, wheezing, and loss of consciousness may be present; edema of the mouth or pharynx can develop after exposure to cold drinks/foods.

Other cold urticarias include **delayed cold contact urticaria** (development of wheals after a few hours after contact with the cold), **familial cold urticaria**, **localized cold contact urticaria**, **acquired cold contact erythema** (painful erythema without whealing), and **generalized reflex cold urticaria** (widespread wheals in response to reduced core body temperature).

Cold urticaria may also be seen in some patients with **cryoglobulinemia**, **collagen vascular disease**, **chronic lymphatic leukemia**, **myeloma**, **infectious mononucleosis**.



[Image](#): "Eruption of Cholinergic Urticaria Welts on the Trunk." by Klope62 - Own work. License: [CC BY 3.0](#)

Cholinergic urticaria is a physical urticaria characterized by the development of typical small wheals in association with sweating or raised core body temperature. It is more common in adolescents, during winter months, and is aggravated by emotional stress and spicy foods. Heat contact urticaria develops in response to localized warming of the skin.

Delayed pressure urticaria is characterized by the development of wheals at sites of sustained pressure after 30 minutes to a few hours of delay. Unlike other types of urticarias, wheals last longer (up to 72 hours) and are painful or tender than itchy.

Immediate symptomatic dermographism, the most common form of dermographism, is characterized by the development of exaggerated wheal-and-flare reaction, along with itching in response to firm stroking of the skin. It is more common in young adults.

Other forms of dermographism include **red dermographism** (the development of punctate wheals in response to repeated rubbing), **cholinergic dermographism** (the development of erythematous line containing punctate wheals after firm stroking of skin),

and **delayed dermographism** (return of wheal after fading of normal **wheal-and-flare response**, persisting up to 48 hours).

The development of wheals following friction is called "**Darier's sign**", seen in **urticaria pigmentosa** (cutaneous mastocytosis).

Urticular vasculitis is characterized by urticarial lesions that last for > 24 hours that may be painful, tender, or burning and may resolve with residual hyperpigmentation.

Systemic symptoms like **migratory arthralgia**, gastrointestinal symptoms (nausea, vomiting, abdominal pain), pulmonary involvement (**cough, wheezing**), renal involvement (proteinuria, hematuria, nephritis), fever, lymphadenopathy, splenomegaly, are usually present. The syndrome develops as a **serum sickness-like syndrome** after 1-3 weeks of exposure to the etiologic agent and lasts for 1-4 weeks.

Diagnosis of Urticaria

Due to variable etiology, a **thorough history** and **complete physical examination** are necessary for the diagnosis of urticaria. In addition to details of urticaria and symptoms related to different systems, the history must also include **possible triggers, drug history**, and **family history**.

Clinical history and examination is usually sufficient to diagnose acute urticaria and laboratory investigations may not be necessary.

Challenge tests for physical urticaria



- **Image:** "Dermatographic urticaria ("skin writing"). Done by writing the "invisible" letters with an empty ball-point pen and waiting for a couple of minutes." by Mysid - Own hand, own photo. License: Public Domain

Dermographism: The development of wheals within minutes in response to the stroking of skin with a blunt object or with a calibrated **dermographometer** at $\leq 36 \text{ g/mm}^2$

- **Cholinergic urticaria:** The development of wheals within minutes in response to increasing core body temperature by 0.7-1.0°C by either exercising in warm environment or after taking a hot (42°C) bath for 15 minutes.
- **Cold urticaria (contact):** The development of urticaria within minutes after

application of an ice-containing plastic bag for up to 20 minutes.

- **Cold urticaria (generalized reflex):** The development of urticaria within minutes in response to exposure to a cold room (4°C) environment for 30 minutes.
- **Heat contact urticaria:** The development of urticaria within minutes after application of a heated (39-45°C) object for 2-5 minutes.
- **Solar urticaria:** The development of urticaria within minutes in response to exposure to sunlight or solar simulator.
- **Aquagenic urticaria:** The development of urticaria within minutes in response to an application of water or a water-soaked towel at body temperature for 15-30 minutes.
- **Vibratory urticaria:** The development of urticaria within minutes in response to an application of a laboratory vortex resting on the forearm or finger for 1-5 minutes.
- **Delayed pressure urticaria:** The development of urticaria within 24 hours after the application of sustained pressure over the back, shoulder, or thigh using a hanging weight or calibrated **dermographometer** at 100 g/mm²

In patients with chronic urticaria, after a thorough history and physical examination, basic laboratory evaluation includes **complete blood counts**, **erythrocyte sedimentation rate** (ESR), **thyroid function tests**, and **antinuclear antibodies** (ANA). Other useful investigations are as follows, which are performed depending upon clinical features:

- Evaluation for **serum cryoglobulins** in patients with cold urticaria.
- **Allergy evaluation** for patients with suspected allergies.
- Appropriate pathological and microbiological evaluation for suspected **infections**.
- Anti-IgE, anti-FcεRI antibodies and autologous serum skin test (**ASST**) for autoimmune urticaria.
- **Punch biopsy** from urticarial lesion in suspected urticarial vasculitis, which would suggest leukocytoclastic vasculitis.

Differential diagnoses

- Acute contact dermatitis
- Atopic dermatitis
- Urticarial drug reactions
- Drug eruptions/non-urticarial drug reactions
- Erythema multiforme
- **Henoch-Schonlein purpura** and other causes of purpura
- Pityriasis rosea

Therapy of Urticaria

H₁-antagonists are used as the first line treatment of urticaria. **Non-sedating second generation antihistamines** (levocetirizine, fexofenadine, loratadine, desloratadine) are preferred over sedating first generation antihistamines (diphenhydramine, hydroxyzine). To achieve symptom control, the dose of a non-sedating antihistamine is uptitrated to up to four-fold, after which a first generation antihistamine can be added to the treatment regimen.

If H₁-antagonists cannot control symptoms, second-line add-on drug options include **H₂-antagonists** (cimetidine, ranitidine, famotidine) and **leukotriene antagonists**

(montelukast). Doxepin is an **antidepressant** with combined H₁- and H₂-antagonist effects, used in the treatment of refractory urticarias.

Drugs with immunomodulatory effects like cyclosporin, mycophenolate mofetil, methotrexate, colchicine, dapsone, and hydroxychloroquine can be used in the treatment of refractory urticaria. Omalizumab has been found to be effective in some patients with chronic urticaria. Other drugs/therapies that can be tried are **ultraviolet B, PUVA, intravenous immunoglobulin (IVIG), plasmapheresis**, etc.

Oral glucocorticosteroids are effective, but should not be used in the treatment of urticaria except as short courses in the management of exacerbations.

Topical cooling moisturizing applications are helpful to reduce itching. Topical corticosteroids have no role.

H₁-antihistamines are usually effective in the treatment of physical urticarias. **Ultraviolet B therapy** at suberythrogenic doses may additionally improve symptomatic dermatographism. Danazol, stanazolol, **beta blockers**, and omalizumab have been used in the treatment of cholinergic urticaria. A short course of prednisolone is effective in severe delayed pressure urticaria.

Tolerance can be induced by **repeated controlled exposure to a physical factor** like cold, heat, or ultraviolet light (solar urticaria). **Intravenous immunoglobulin and cyclosporin** have been found useful in solar urticaria.

When urticaria occurs as a symptom of **anaphylaxis**, the emergency management of anaphylaxis, including **intramuscular epinephrine**, is necessary. Etiological conditions underlying acute or chronic urticaria should be treated. The avoidance of allergens and avoidance of non-allergic triggers is important in patients when they are known or identified.

Prognosis of Urticaria

Prognosis depends upon the cause of urticaria. Idiopathic chronic urticarias and physical urticarias tend to undergo **remission** after a variable period ranging from a few months to 6-9 years.

The prognosis in acute urticaria is excellent. **Acute urticaria** is usually self-limited, and individual lesions commonly resolve within 24 hours; however, episodes may recur for up to 6 weeks.

The prognosis in chronic urticaria is more guarded and depends on the comorbid disease causing the urticaria, as well as the response to therapy. **Chronic urticaria** lasts more than 6 weeks.

Acute and chronic urticaria can result in a severely impaired quality of life from pruritus and associated sleeplessness, as well as anxiety and depression. The depression can be severe enough to lead to suicide in rare cases. Additionally, many of the diseases associated with chronic urticaria may cause significant morbidity and mortality.

Prevention

Patients with acute urticaria should avoid any medication, food, or other allergen that has precipitated urticaria or other serious allergic reaction previously. Chronic urticaria is seldom related to food allergens, and complicated elimination diets are seldom of benefit.

Long-Term Monitoring

Most patients with urticaria can be treated at home with first- or second-generation H1 antihistamines alone, or in combination with one another (i.e., cetirizine uptitrated to 20 mg twice daily, diphenhydramine 50 mg q6h or hydroxyzine 50 mg q6h for 24-48 h). In refractory cases, oral glucocorticoids can be added. Additional therapies likely warrant referral to a specialist.

If the patient has angioedema that is treated successfully in the ED, the patient should be sent home with an EpiPen prescription and told to keep it with him or her at all times and to use it if swelling of the lips, tongue, face develops, or if his or her voice acutely becomes hoarse.

Consultation with, or referral to, a dermatologist, allergist, immunologist, or rheumatologist may be appropriate in cases of suspected urticarial vasculitis and in cases of chronic or recurrent urticaria

Review Questions on Urticaria

The correct answers can be found below the references.

- 1. Which of the following physical urticarias are characterized by urticarial lesions that last longer than 24 hours?**
 - A. Idiopathic cold contact urticaria
 - B. Cholinergic urticaria
 - C. Delayed pressure urticaria
 - D. Solar urticaria
 - E. Vibratory urticaria
- 2. Which of the following infections is known to be associated with chronic urticaria?**
 - A. Epstein-Barr virus infection
 - B. Streptococcal pharyngitis
 - C. Campylobacter jejuni gastroenteritis
 - D. Staphylococcal skin infection
 - E. Helicobacter pylori gastritis
- 3. Urticarial lesions in which of the following conditions are most likely to resolve with residual hyperpigmentation?**
 - A. Acute drug allergy
 - B. Urticarial vasculitis
 - C. Chronic idiopathic urticaria
 - D. Solar urticaria
 - E. Chronic autoimmune urticaria

References

Grattan CEH, Black AK. **Urticaria and Mastocytosis**. In: Burns T, Breathnach S, Cox N, Griffiths C, editors. *Rook's Textbook of Dermatology*, 8th Edition. Blackwell Publishing, 2010, pp. 22.1-22.19.

Lazar AJF, Murphy GF. **The Skin**. In: Kumar V, Abbas AK, Aster JC, editors. *Robbins and Cotran Pathologic Basis of Disease*, 9th Edition. Elsevier Saunders, 2015, pp. 1162

Lawlor F, Black AK. **Urticaria**. In: Katsambas AD, et al, editors. *European Handbook of*

Dermatological Treatments. Springer-Verlag Berlin Heidelberg, 2015, pp. 997-1004.

[Urticaria](#) via medscape.com

Correct answers: 1C, 2E, 3B

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