Chapter 23
Urticaria

Marcus Maurer, Markus Magerl, Torsten Zuberbier, and Karsten Weller

Abstract Urticaria is a heterogeneous group of diseases and highly frequent. Wheals and angioedema are the signature signs and itch is the key symptom. Most cases of urticaria resolve within days. Those that do not tend to be of long duration and associated with severely impaired quality of life. Some patients with chronic urticaria develop wheals and angioedema exclusively in response to specific triggers (inducible urticaria), but most do not (spontaneous urticaria). The aim of chronic urticaria management is complete relief of signs and symptoms, which is often achieved by symptomatic rather than curative treatment. Modern, second generation H1-antihistamines are the first-line therapy.

Keywords Urticaria • Hives • Wheals • Angioedema • Itch • Mast cells • Histamine

23.1 Definition

Urticaria is a heterogeneous group of mast cell-mediated diseases characterized by itchy wheals, angioedema, or both [42]. Urticaria wheals are short-lived superficial itchy skin swellings. As they develop, these wheals are initially whitish in color (Fig. 23.1). They then develop a surrounding flare (erythema) before they resolve completely over the course of minutes to hours without showing subsequent skin changes. Urticaria wheals are usually itchy but may also come with a burning or stinging sensation. Angioedema is defined as a rapid swelling (edema) of the dermis and subcutaneous tissue or of the mucosa and submucosal tissue (Fig. 23.2). In contrast to wheals, angioedema is not usually itchy but sometimes painful, and it lasts longer. In urticaria, angioedema most commonly occurs in the face (lips, around the eyes) but may also affect the extremities and other skin sites.

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K. Kabashima (ed.), *Immunology of the Skin*, DOI 10.1007/978-4-431-55855-2_23

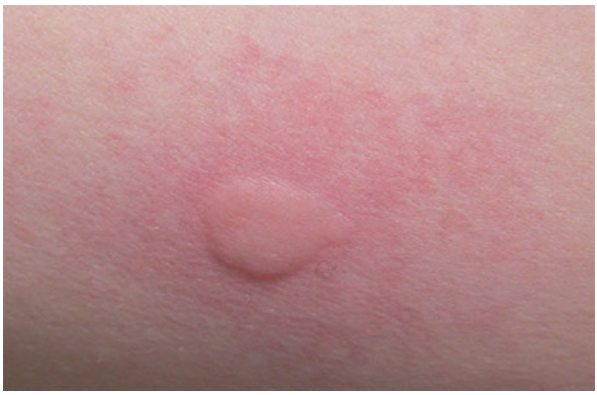

Fig. 23.1 Newly developing wheal

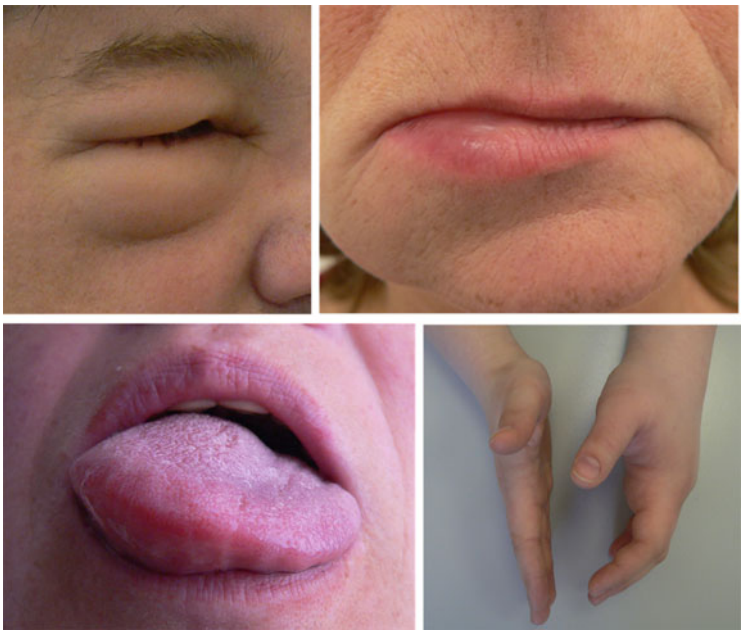

Fig. 23.2 Angioedema

23.2 Classification

Urticaria is classified according to (1) its duration and (2) its triggers of exacerbation (Table 23.1). In acute urticaria, the signs and symptoms occur for less than 6 weeks, whereas chronic urticaria is of more than 6 weeks duration [42]. The development of wheals and angioedema in urticaria patients can either be

Table 23.1 Classification of urticaria

Acute urticaria	*Acute spontaneous urticaria*	Spontaneous appearance of wheals, angioedema, or both <6 weeks due to known or unknown causes
	Chronic spontaneous urticaria	Spontaneous appearance of wheals, angioedema, or both ≥6 weeks due to known or unknown causes
Chronic urticaria	*Chronic inducible urticaria*	*Physical urticarias*
		Symptomatic dermographism[a]
		Cold (contact) urticaria
		(Delayed) pressure urticaria
		Solar urticaria
		Heat (contact) urticaria
		Vibratory angioedema
		Cholinergic urticaria
		Contact urticaria
		Aquagenic urticaria

From Zuberbier et al. [42]
[a]Also called *urticaria factitia*, dermographic urticaria

unpredictable and unprompted, in spontaneous urticaria, or it can occur only in response to specific triggers and eliciting situations, in inducible urticarias. In the inducible urticarias, specific triggers, which can be exogenous and acting on the skin directly (physical urticarias, contact urticaria, aquagenic urticaria) or not (cholinergic urticaria), are responsible and required for the induction of signs and symptoms. Triggers of physical urticaria are skin contact with cold and heat (cold urticaria, heat urticaria), mechanical triggers such as friction, pressure and vibration (symptomatic dermographism, pressure urticaria, vibratory urticaria, respectively), or ultraviolet or visible light (solar urticaria) [42]. Triggers of symptoms in contact urticaria are skin contact with urticariogenic substances, and in the case of aquagenic urticaria exposure to water. In cholinergic urticaria, symptoms are brought about by exercise or passive warming (sauna, hot showers, spicy food). Frequently, patients show more than one urticaria type, for example chronic spontaneous urticaria and symptomatic dermographism.

23.3 Epidemiology

Urticaria is a very common disease and usually of short duration (acute urticaria). Virtually everyone, at one point during his or her life, develops acute urticaria. Most commonly, this is acute contact urticaria, caused by skin contact with urticariogenic substances derived, for example, from stinging nettles or jellyfish (Fig. 23.3). Acute spontaneous urticaria is also very common, and it is estimated that its lifetime prevalence is up to 20 % [25]. Acute spontaneous urticaria rarely progresses to chronic spontaneous urticaria. Nonetheless, chronic spontaneous urticaria, which is thought to be twice as frequent as chronic inducible urticaria, is estimated to have a

Fig. 23.3 Contact urticaria induced by stinging nettle

point prevalence of 0.5–1 % [25]. Chronic spontaneous urticaria can affect all age groups with a peak incidence between the twentieth and the fortieth year of life; that is, patients are primarily affected during important years of their working age [25]. Women are affected about twice as often as men [25].

23.4 Pathogenesis

The signs and symptoms of urticaria, both spontaneous and inducible, are due to the activation and degranulation of skin mast cells and the effects of pro-inflammatory mediators released in the process. Mast cells are long-lived resident cutaneous cells that predominantly localize around blood vessels and sensory nerves [26] as well as in the upper papillary dermis. They contain cytoplasmic granules in which preformed mediators are stored that are released into the cell's vicinity by degranulation in response to activation [36]. These preformed mast cell mediators include histamine, heparin, and proteases (e.g., tryptase, chymase) [7] as well as several cytokines. Upon activation and degranulation, skin mast cells also rapidly produce and secrete prostaglandins, leukotrienes, and platelet activating factor [36]. Mast cells are thought to function as sentinel cells of the skin and a first line of defense against bacteria and other pathogens [27]. The inflammatory effects of their mediators include the activation of sensory skin nerves (itch, burning sensation, pain), the dilatation of skin blood vessels (erythema, hyperthermia) and the induction of plasma extravasation (wheals and angioedema). Histamine plays a critical role in skin mast cell-mediated vasodilation and extravasation, by acting on H1 receptors [8]. The degranulation of skin mast cells in urticaria patients also results in the

recruitment of basophils, neutrophils, eosinophils, and other immune cells to the site of activation [41]. The mechanisms of mast cell activation in urticaria are largely unclear. In chronic urticarias, mast cells are typically not activated by the binding of environmental allergens to specific IgE bound to cell surface IgE receptors [42], as is the case in allergies such as allergic rhinitis and anaphylaxis. Reported candidates for relevant signals involved in mast cell activation in chronic spontaneous urticaria include autoantibodies to IgE [11] or the IgE receptor [15], IgE autoantibodies directed against autoantigens (autoallergens) such as thyreoperoxidase [2], complement components such as C5a [10], as well as neuropeptides [4], for example, substance P.

23.5 Clinical Picture

23.5.1 Acute Spontaneous Urticaria

Acute spontaneous urticaria usually resolves within a few days to weeks. Viral infections of the upper airways as well as nonsteroidal antiphlogistics (e.g., ibuprofen, diclofenac, acetylsalicylic acid) and other drugs are common causes. But in many acute spontaneous urticaria patients no relevant cause can be identified. The spectrum of signs and symptoms ranges from a few short-lived wheals to severe angioedema attacks with persistently reoccurring multiple and confluent wheals that affect large body areas.

23.5.2 Chronic Spontaneous Urticaria

The symptoms of chronic spontaneous urticaria are generally the same as in acute spontaneous urticaria, but in contrast, chronic spontaneous urticaria is characterized by a long duration with up to 50 % of patients affected for more than 10 years [35]. The mean length of chronic spontaneous urticaria seems to be around 4–7 years. In up to half of all patients both wheals and angioedema occur, and in about one in ten patients only angioedema develops [25]. The remaining patients solely show wheals. Most patients with moderate or severe disease activity have symptoms every day or almost every day [37]. Disease activity may change markedly over time in the same patient, but the natural course also varies considerably between different subjects.

23.5.3 Chronic Inducible Urticaria

In chronic inducible urticaria, the development of wheals and angioedema is always provoked by the exposure to specific triggers. These conditions are, therefore, more predictable than spontaneous urticaria and disease activity depends on the frequency (and avoidance) of exposure to the relevant trigger at above threshold strength. The sensitivity to symptom-inducing triggers tends to be stable in individual patients over time. Triggers of inducible urticaria include the exposure to low or high temperatures, UV or visible light, as well as pressure and other mechanical forces for the physical urticarias and exposure to urticariogenic substances (contact urticaria), water (aquagenic urticaria), or situations associated with an increase in body temperature (cholinergic urticaria). Skin sites exposed to inducible urticaria triggers such as the hands are therefore more commonly affected. The only exception to this rule is cholinergic urticaria, where triggers (exercise, hot bath, spicy food) do not act directly on the skin but by increasing the body temperature [19]. Similar to chronic spontaneous urticaria, skin lesions in chronic inducible urticaria patients can be accompanied by systemic problems (e.g., hypotension in cold urticaria, malaise in delayed pressure urticaria). These extracutaneous symptoms are thought to be due to the effects of histamine and other pro-inflammatory mediators released at skin sites of trigger exposure and wheal and angioedema development. Chronic inducible urticarias show spontaneous remission in the vast majority of patients, but there are currently no biomarkers or other indicators that allow us to predict, for individual patients, when this will occur. Chronic inducible urticaria usually persists for several years before resolving spontaneously [25].

23.6 Diagnostics

23.6.1 Acute Urticaria

Acute urticaria usually does not require a diagnostic workup, because it is self-limited. The one exception to this rule is suspicion of acute urticaria due to an allergy (i.e., exposure to an allergen in a sensitized patient) or the existence of other eliciting factors such as nonsteroidal antiphlogistics. In this case, allergy tests as well as educating the patients may be useful to allow patients to avoid re-exposure to relevant causing factors.

23.6.2 Chronic Spontaneous Urticaria

The diagnostic workup in patients with chronic spontaneous urticaria should (1) exclude the presence of severe inflammatory conditions, (2) identify the causes in patients with severe and/or longstanding disease, (3) assess disease activity and impact, and (4) exclude differential diagnoses if indicated.

In all patients with chronic spontaneous urticaria, the correct diagnosis should be confirmed by a thorough history, and severe inflammatory conditions should be ruled out by assessing erythrocyte sedimentation rates/C-reactive protein levels and a differential blood count. A physical examination should be performed and all nonsteroidal antiphlogistics should be discontinued and avoided in the future [42].

In patients with long-standing disease and/or high disease activity, underlying causes should be looked for. The search for underlying causes in chronic spontaneous urticaria should be based on clues from the history. Common causes are autoreactivity, autoallergy, chronic infections, and intolerance to food components.

Autoreactivity, that is, a harmful response of the body to itself, is thought to be the relevant cause in one third to half of chronic spontaneous urticaria patients [16]. High disease activity, the development of angioedema, the lack of benefit from antihistamine therapy and autoimmune comorbidities should all prompt the search for autoreactivity.

In addition, most patients with chronic spontaneous urticaria have been found to exhibit IgE antibodies to autoantigen (autoallergens) such as thyreoperoxidase [2] or double-stranded DNA [13], and anti-IgE therapy effectively controls disease activity in these patients [23].

Chronic spontaneous urticaria can also be caused by bacterial infections [42], for example, of the gastrointestinal tract by *Helicobacter pylori* or chronic ear, nose, or throat infections, especially of the teeth, as well as by parasitic infections and, rarely, viral infections. The spectrum of relevant infections varies across geographical regions [42]. Underlying infections may be asymptomatic or associated with mild symptoms. In many patients no systemic signs of inflammation and infections can be detected. It is, therefore, recommended to investigate patients thoroughly when checking for common chronic spontaneous urticaria causing infections.

Many patients suspect that their chronic spontaneous urticaria is due to what they eat and drink. Whereas food allergies are rarely found to be the cause of chronic spontaneous urticaria [43], many patients exhibit food intolerance [6, 21, 44], for example, to taste intensifiers, preservatives, or to naturally occurring aromatic compounds, biogenic amines, and salicylic acid. Chronic spontaneous urticaria due to food intolerance is confirmed by a documented decrease in disease activity after a 4-week diet that is virtually devoid of potentially relevant food components (sometimes called pseudoallergens) and by an increase in disease activity after oral provocation with these food components. Independent studies found beneficial effects of a pseudoallergen-low diet in one third to three quarters of chronic spontaneous urticaria patients [6, 21, 44].

Less frequent causes of chronic spontaneous urticaria include other chronic inflammatory conditions such as gastritis or inflammation of the bile duct, systemic *Lupus erythematosus*, and other autoimmune disorders as well as sensitizations to type I allergens (in less than 1 %).

All patients with chronic spontaneous urticaria should be investigated and monitored for their disease activity, disease impact on quality of life, and disease control. The gold standard for measuring disease activity in spontaneous urticaria is the urticaria activity score (UAS) [29]. To obtain UAS values, patients are usually asked to document every day for seven consecutive days (UAS7) the numbers of wheals and the intensity of pruritus they experienced over the last 24 h using a 0–3 point scale for wheals (0 for none, 1 for <20, 2 for 20–50, and 3 for >50) and pruritus (0 for none, 1 for mild: present but not annoying or troublesome, 2 for moderate: troublesome, but does not interfere with normal daily life activity or sleep, and 3 for intense: interferes with normal daily life or sleep). The UAS7 (minimum = 0, maximum = 42) is then calculated as the sum of the daily totals of the wheal and the itch scores. In chronic spontaneous urticaria patients who develop angioedema, but not wheals, the angioedema activity score (AAS) should be used [40] which is also a validated, prospective diary-type instrument assessing the frequency and severity of angioedema symptoms. Patients with wheals and angioedema should be assessed with both scores, the UAS7 and the AAS.

Disease activity and quality of life impairment are poorly correlated in many patients with chronic spontaneous urticaria. Thus, the UAS7 and/or the AAS should be used together with the disease-specific quality of life questionnaires, that is, the CU-Q_2oL [3] (for patients with wheals), the AE-QoL [38] (for patients with angioedema), or both (for patients with wheals and angioedema).

The urticaria control test (UCT) is a novel and validated tool for assessing disease control in all patients with chronic urticaria (spontaneous or inducible) [39]. The UCT has only four items and a clearly defined cut-off for patients with "well-controlled" versus "poorly controlled" disease, and it is thus ideally suited for the management of patients in routine clinical practice. An overview on available instruments for patients with chronic urticaria is depicted in Table 23.2.

Table 23.2 Tools for assessing disease activity, disease control, and disease impact on quality of life in patients with chronic urticaria

	Chronic spontaneous urticaria			
	Patients with wheals	Patients with wheals and angioedema	Patients with angioedema	Inducible urticaria
Disease activity	UAS	UAS and AAS	AAS	Determination of trigger threshold with specific provocation test
Disease control	UCT	UCT	UCT	UCT
Quality of life	CU-Q_2oL	CU-Q_2oL and AE-QoL	AE-QoL	No instrument available yet

UAS Urticaria Activity Score, *AAS* Angioedema Activity Score, *UCT* Urticaria Control Test, *CU-Q_2oL* Chronic Urticaria Quality of Life Questionnaire, *AE-QoL* Angioedema Quality of Life Questionnaire

Finally, the diagnostic workup in chronic spontaneous urticaria patients should include the consideration of differential diagnoses, especially in patients resistant to standard treatment. Patients with recurrent wheals who do not develop angioedema may have urticaria vasculitis or an autoinflammatory condition such as Schnitzler syndrome or cryopyrin-associated periodic syndromes [17]. Patients with recurrent angioedema who do not develop wheals may have hereditary angioedema or another form of bradykinin-mediated angioedema. A thorough history that includes the right questions and, if indicated, a limited set of investigations is sufficient to confirm or exclude the most common differential diagnoses of chronic spontaneous (and inducible) urticaria (Fig. 23.4) [24].

23.6.3 Inducible Urticarias

The underlying causes of chronic inducible urticarias with the exception of contact urticaria are unknown and routine investigations for underlying causes are therefore not recommended [42]. An exception may occur if there are compelling clues from the history. The diagnostic workup in inducible urticaria patients is aimed at the identification of the relevant elicitation triggers and at measuring trigger thresholds [19].

In symptomatic dermographism, also called urticaria factitia or dermographic urticaria, wheals are induced by scratching. Provocation testing should be done by stroking the skin of the volar forearm or the upper back with a smooth and blunt object such as a closed ballpoint pen or a dermographometer [1], for example, the FricTest (Moxie GmbH, Berlin, Germany, Fig. 23.5), which allows for simultaneous testing of four different trigger strengths, or a pen-shaped dermographic tester with a spring-loaded tip that can be adjusted to exert different strengths of shear force (HTZ Limited, Vulcan Way, New Addington, Croydon, Surrey, UK). Provocation tests with dermographometers are done by placing them vertically on the skin and then moving them across the skin with a defined pressure. The test is positive when a wheal occurs at the provocation site within 10 min. When the test is positive, threshold tests should be performed (Fig. 23.6).

Delayed pressure urticaria patients develop erythematous angioedema-like swellings at skin sites exposed to pressure. These swellings are induced by vertical pressure, for example, by shoulder straps of bags, tight shoes, or prolonged sitting (e.g., bicycle ride). Swellings occur with a delay of four to eight hours and typically persist for several hours, in some patients for several days. Weighted rods or dermographometers are used to test for delayed pressure urticaria. The result is positive when a red palpable swelling is present 6 h after testing.

In patients with vibratory angioedema cutaneous swellings occur within minutes after exposure to vibration at skin contact sites. This can be tested with a laboratory vortex mixer.

In cold urticaria, itchy wheal and flare-type skin reactions or angioedema are induced by exposure to cold, typically within minutes after cold contact (cold air,

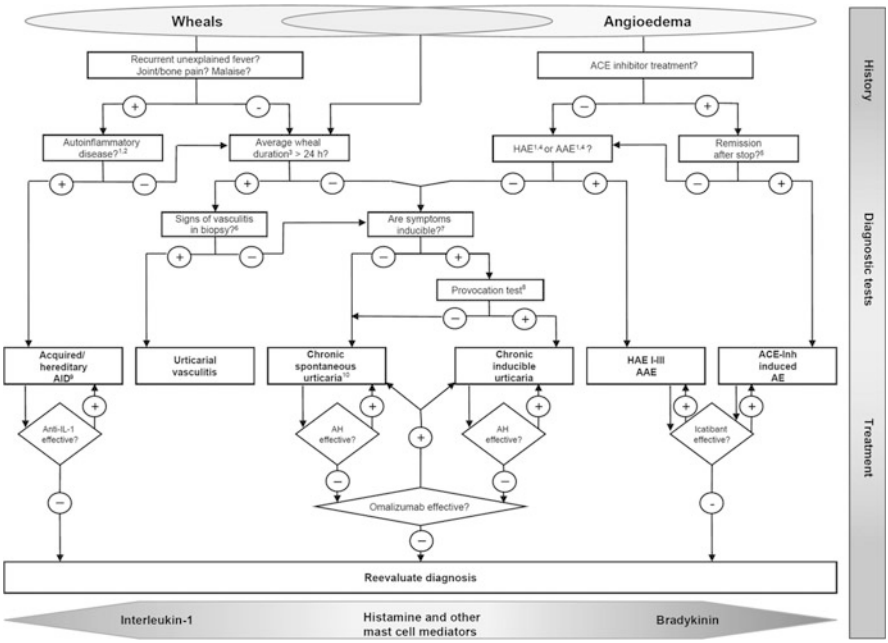

Fig. 23.4 Algorithm for diagnostic workup in patients with recurrent wheals, angioedema, or both (from Maurer et al. [24]). *AAE* Acquired angioedema due to C1-inhibitor deficiency, *ACE-Inh* angiotensin converting enzyme inhibitor, *AE* angioedema, *AH* H1-Antihistamine, *AID* Autoinflammatory disease, *HAE* Hereditary angioedema, *IL-1* Interleukin-1. (*1*) Patients should be asked for a detailed family history and age of disease onset. (*2*) Test for elevated inflammation markers (C-reactive protein, erythrocyte sedimentation rate), test for paraproteinemia in adults, look for signs of neutrophil-rich infiltrates in skin biopsy; perform gene mutation analysis of hereditary periodic fever syndromes (e.g., Cryopyrin-associated periodic syndrome), if strongly suspected. (*3*) Patients should be asked: "How long do your wheals last?" (*4*) Test for Complement C4, C1-INH levels, and function; in addition test for C1q and C1-INH antibodies if AAE is suspected; do gene mutation analysis, if former tests are unremarkable but patient's history suggests hereditary angioedema. (*5*) Wait for up to 6 months for remission; additional diagnostics to test for C1-inhibitor deficiency should only be performed if the family history suggests hereditary angioedema. (*6*) Does the biopsy of lesional skin show damage of the small vessels in the papillary and reticular dermis and/or fibrinoid deposits in perivascular and interstitial locations suggestive of urticaria vasculitis? If yes, direct immunofluorescence should be performed to look for immune complexes (immunoglobulins or complement) in vessel walls. Also, if suggested by the history, systemic vasculitic diseases which may present with urticaria vasculitis (e.g., lupus erythematosus or Sjögren's syndrome) should be ruled out and patients should be screened for antinuclear and extranuclear antibodies where indicated. (*7*) Patients should be asked: "Can you make your wheals appear?" (*8*) In patients with a history suggestive of inducible urticaria standardized provocation testing according to international consensus recommendations should be performed. (*9*) Acquired AIDs include Schnitzler's syndrome as well as systemic-onset juvenile idiopathic arthritis (sJIA) and adult-onset Still's disease (AOSD);, hereditary AIDs include cryopyrin-associated periodic syndromes (CAPS) such as familial cold autoinflammatory syndromes (FCAS), Muckle–Wells syndrome (MWS) and neonatal onset multisystem inflammatory disease (NOMID), more rarely hyper-IgD syndrome (HIDS), and tumor necrosis factor receptor alpha-associated periodic syndrome (TRAPS). (*10*) In some rare cases recurrent angioedema is neither mast cell mediator-mediated nor bradykinin-mediated, and the underlying pathomechanisms remain unknown. These rare cases are referred to as "idiopathic angioedema" by some authors

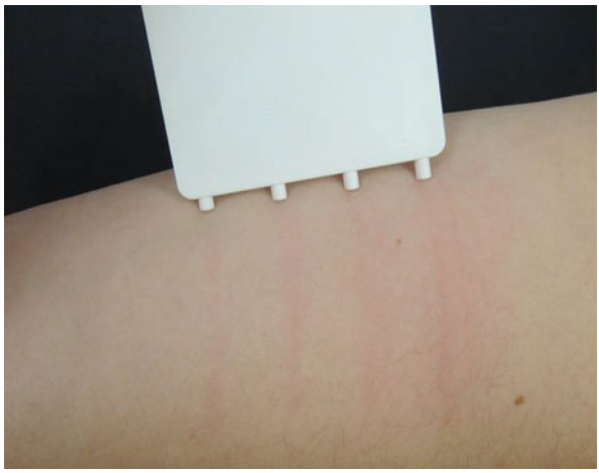

Fig. 23.5 FricTest, a dermographometer for diagnosing symptomatic dermographism and measuring trigger thresholds

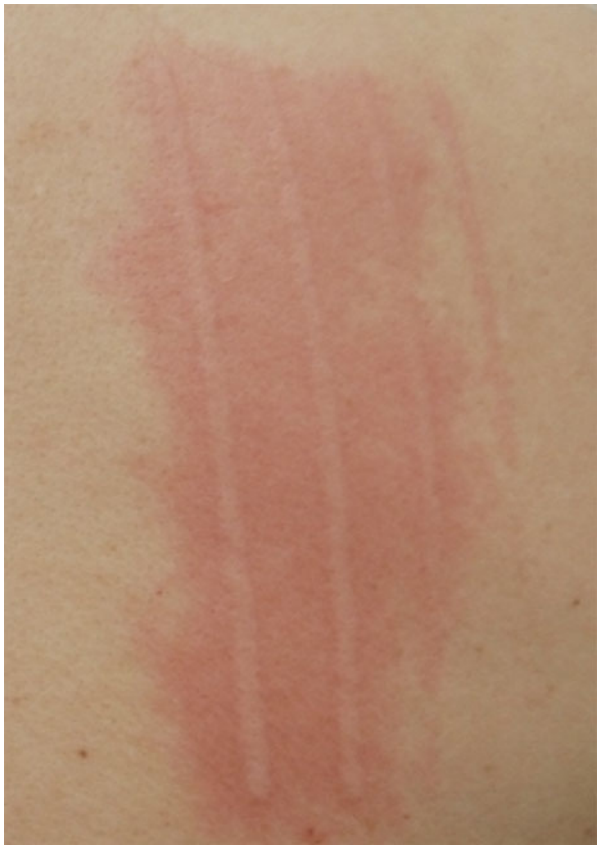

Fig. 23.6 Threshold test performed with the help of FricTest in a patient with symptomatic dermographism

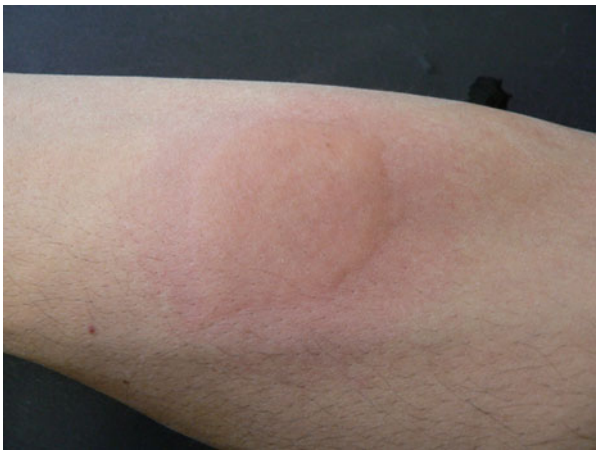

Fig. 23.7 Positive ice cube cold provocation test in cold urticaria patient

cold liquids, or objects). To perform a cold provocation test, a melting ice cube in a thin plastic bag (to avoid cold damage of the skin) is placed on the volar forearm for 5 min and the test response is assessed 10 min later. If the test site shows a palpable and visible wheal, the result is positive (Fig. 23.7). Cold urticaria patients should be evaluated for their individual temperature and/or stimulation time thresholds [1, 28] (Fig. 23.8), for example, by using a TempTest instrument [33]. The latest TempTest instrument (TempTest 4.0, Courage + Khazaka electronic GmbH, Köln, Germany, Fig. 23.9) simultaneously tests for skin responses to all temperatures from 4 to 44 °C (Fig. 23.10). Threshold measurements allow patients and physicians to monitor disease activity and responses to therapy.

In heat urticaria, wheals are usually well-defined and limited to the area of heat exposure. They develop within minutes after heat contact and usually resolve within 3 h. To test for heat urticaria, temperatures of up to 44 °C should be applied to the skin for 5 min (TempTest, metal/glass cylinders, filled with water, hot water bath), and responses should be assessed 10 min thereafter. Heat urticaria patients should also be tested for their temperature thresholds to determine disease status and treatment response.

Solar urticaria is characterized by itchy wheals that occur within minutes after skin exposure to UV and/or visible light. Solar urticaria is diagnosed by provocation tests done with solar simulators (with UV-A and UV-B filters) or monochromators (UV-A and UV-B, visible light). UV-A is tested at 6 J/cm^2 and UV-B at 60 mJ/cm^2 (buttocks). A palpable and clearly visible wheal at 10 min after testing confirms solar urticaria, in which case patients should be threshold tested for their minimal urticaria-triggering dose of radiation.

In cholinergic urticaria, itching and whealing occur in situations associated with a rise in body temperature. Wheals appear within minutes and typically last less than 1 h. To diagnose cholinergic urticaria, patients are first subjected to moderate physical exercise (treadmill or stationary bicycle) that makes them sweat. Patients with a positive result (wheals after 10 min) are then subjected, after a break of at

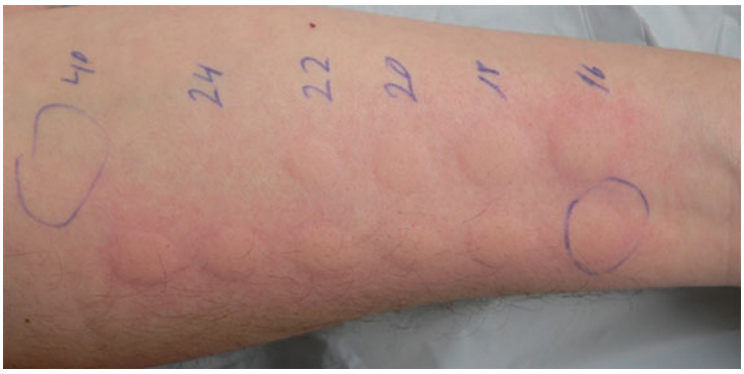

Fig. 23.8 Result of threshold testing performed with the help of TempTest 3.0 in patient with cold urticaria

Fig. 23.9 TempTest 4.0

least 24 h, to a warm bath (42 °C) for up to 15 min, which also usually leads to whealing in cholinergic urticaria patients.

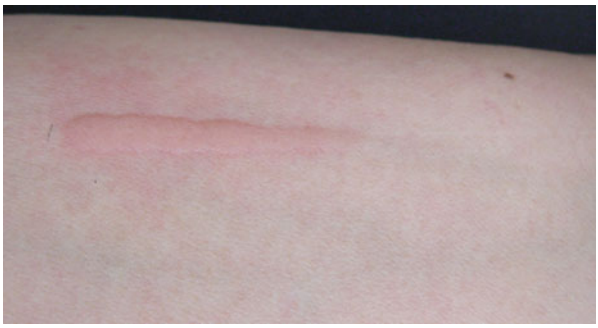

Fig. 23.10 Result of temperature threshold testing with TempTest 4.0

23.7 Therapy

23.7.1 Acute Spontaneous Urticaria

Patients with acute spontaneous urticaria should be advised to avoid eliciting factors, if they are known and avoidable. The therapeutic goal is to control and prevent the development of urticarial lesions until the condition resolves by itself. Mild cases may not require treatment or will respond to oral second generation H1-antihistamine treatment. In more severe cases, doses of nonsedating H1-antihistamines may have to be increased up to fourfold the licensed dose and oral steroids may also be necessary. Oral steroid intake should be limited to short-term treatment and should not be used as long-term treatment [42].

23.7.2 Chronic Spontaneous Urticaria

The aim of treatment in patients with chronic spontaneous urticaria is to stop the reoccurrence of urticarial skin reactions. This can either be achieved by treating patients for underlying causes and triggers or by the prophylactic use of drugs that block the activation of mast cells or the effects of mast cell mediators. Some of the underlying causes of chronic spontaneous urticaria such as relevant infections can be treated and eradicated. In patients where no underlying causes are identified or where underlying causes are identified but cannot be treated, symptomatic treatment is required.

Second generation, nonsedating H1-antihistamines are the first-line symptomatic treatment for chronic spontaneous urticaria [42]. These should be taken as preventive therapy, on a daily basis. In patients who do not respond adequately to standard doses, nonsedating H1-antihistamines should be updosed (up to four times the standard dosage) after 2 weeks. Higher than standard doses have been shown to be safe and to be superior to standard dosages in chronic spontaneous urticaria [9, 34]. Patients who fail to respond adequately even to higher doses of second

generation H1-antihistamines should be treated with add-on omalizumab (anti-IgE), cyclosporin, or montelukast, a leukotriene antagonist (Fig. 23.11) [42]. With the exception of standard-dosed H1-antihistamines, all of these therapies are off-label. For any treatment that results in the complete control of symptoms, it is advisable to check patients for spontaneous remission every 6–12 months.

23.7.3 Chronic Inducible Urticaria

The treatment of inducible urticarias relies on the avoidance of eliciting stimuli and the prevention of symptoms by treatment with inhibitors of mast cell mediators. To completely avoid relevant triggers is often not possible for patients or associated with severe quality of life impairment. For symptomatic preventive therapy, the same treatment algorithm applies as for chronic spontaneous urticaria (Fig. 23.11) and second-generation nonsedating H1-antihistamines are recommended as the first-line treatment [42]. In many patients, higher than standard doses are more efficacious as compared to standard dose treatment and required to sufficiently control symptoms [18, 22, 32]. Patients who remain symptomatic on high-dose H1-antihistamine treatment are recommended to receive additional treatments such as omalizumab. Various treatment options appear to be especially effective in some inducible urticarias, but it is unclear why and controlled studies are missing. For example, UVB light therapy has been reported to be effective in patients with symptomatic dermographism [5], dapsone [12] and anti-TNF [20] in delayed pressure urticaria, antibiotic treatment with doxycycline or penicillin for several weeks in cold urticaria [30], afamelanotide in solar urticaria [14], and injections of botulinum toxin in cholinergic urticaria [31].

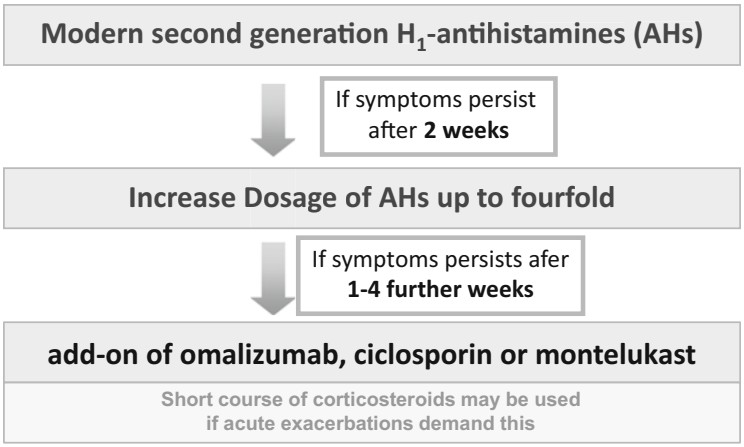

Fig. 23.11 Therapeutic algorithm for treating chronic spontaneous urticaria. (From Zuberbier et al. [42])

In principle, desensitization to eliciting triggers is possible in some types of inducible urticaria such as solar urticaria, cold urticaria, and cholinergic urticaria. However, this desensitization requires an ongoing self-provocation of the patients with their specific triggers to deplete urticaria-eliciting mediators, such as daily cold showers in cold urticaria or ongoing UV-treatment in solar urticaria, which is, for most patients, impossible to maintain over longer time periods.

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