

Clinical practice guideline for diagnosis and management of urticaria

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Abstract

Urticaria is a common skin condition that can compromise quality of life and may affect individual performance at work or school. Remission is common in majority of patients with acute spontaneous urticaria (ASU); however, in chronic cases, less than 50% had remission. Angioedema either alone or with urticaria is associated with a much lower remission rate. Proper investigation and treatment is thus required. This guideline, a joint development of the Dermatological Society of Thailand, the Allergy, Asthma, and Immunology Association of Thailand and the Pediatric Dermatological Society of Thailand, is graded and recommended based on published evidence and expert opinion. With simple algorithms, it is aimed to help guiding both adult and pediatric physicians to better managing patients who have urticaria with/without angioedema. Like other recent guideline, urticaria is classified into spontaneous versus inducible types. Patients present with angioedema or angioedema alone, drug association should be excluded, acetyl esterase inhibitors (ACEIs) and non-steroidal anti-inflammatory drugs (NSAIDs) in particular. Routine laboratory investigation is not cost-effective in chronic spontaneous urticaria (CSU), unless patients have clinical suggesting autoimmune diseases. Non-sedating H₁-antihistamine is the first-line treatment for 2-4 weeks; if urticaria was not controlled, increasing the dose up to 4 times is recommended. Sedating first-generation antihistamines have not been proven more advantage than non-sedating antihistamines. The only strong evidence-based alternative regimen for CSU is an anti-IgE: omalizumab; due to very high cost it however might not be accessible in low-middle income countries. Non-pharmacotherapeutic means to minimize hyper-responsive skin are also important and recommended, such as prevention skin from drying, avoidance of hot shower, scrubbing, and excessive sun exposure.

Keywords: urticaria, Thai, guideline, diagnosis, management

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Introduction

This clinical practice guideline was developed in collaboration with the Dermatological Society of Thailand, the Allergy, Asthma, and Immunology Association of Thailand and the Pediatric Dermatological Society of Thailand. The aim of this endeavor was to develop a guideline that would provide helpful and practical advice to general practitioners and specialty physicians regarding how to effectively manage patients with spontaneous urticaria.

Definition

Urticaria, a heterogeneous group of diseases, is characterized by wheals and flares that sometimes concomitantly present with angioedema (edema in the deep dermis and subcutaneous tissue). Urticaria can be caused by several factors, including physical stimuli, immunological response to foods, drugs, and infectious agents, or as a part of inflammatory or malignancy conditions. However, the most common cause is idiopathic in nature.

Signs and symptoms

Pruritus is the most predominate symptom. Other characteristic signs include wheals and flares that vary in size, with individual wheals usually resolving within 24 hours without residual hyperpigmentation. In some cases, urticaria can occur concomitantly with angioedema that typically involves deep dermis and subcutaneous fat, such as in the periorbital tissues, lips, tongue, and hands. Angioedema can persist for up to 72 hours and is often accompanied by burning sensation and/or mild pain. Itching is not common in angioedema.

Urticaria with or without angioedema can be a manifestation of anaphylaxis. Other manifestations of anaphylaxis include chest discomfort, hoarseness, wheezing, abdominal pain, and diarrhea. Respiratory difficulty and circulation collapse in anaphylaxis can lead to anaphylactic

shock, which is a serious and life-threatening condition. The criteria for anaphylaxis diagnosis is shown in **Table 1**.¹

Classification

Urticaria is classified into 2 types (**Table 2**):^{2,3}

1. **Spontaneous urticaria**, which is classified according to its duration into 2 subtypes:
 - 1) **Acute urticaria (AU)** is characterized by spontaneously occurring wheals for less than 6 weeks
 - 2) **Chronic urticaria (CU)** is characterized by spontaneously occurring wheals at least 2 days per week for a period of 6 weeks or more
2. **Inducible urticaria** (also known as physical urticaria) occur when triggered by specific physical stimuli

Diagnostic approach for urticaria

History taking and physical examination to identify causes and precipitating factors are important for diagnosis. The diagnostic approach for urticaria is shown in **Figure 1**.⁴ In addition to diagnosis and severity assessment, laboratory investigations indicated by history and physical examination are sometimes necessary to identify causes (**Table 3**).^{2,5}

It should be noted that even in a clinical setting where history review, physical examination, and investigations have been undertaken, the cause(s) of acute and chronic urticaria often remain elusive. Spontaneous wheals in chronic spontaneous urticaria (CSU), previously called chronic idiopathic urticaria or CIU,⁶ are proposed to be caused by various mechanisms, including:

1. Reaction of autoantibodies (IgG) to high-affinity IgE receptors (FcεRI) or to IgE on the surface of mast cells or basophils, accounting for 30-50% of CSU patients and may define autoimmune urticaria.^{7,8}
2. Activation of coagulation pathway occurs in some CSU patients, which results in increased plasma D-dimer levels.⁹

Table 1. Criteria for diagnosis of anaphylaxis¹

<p>Anaphylaxis condition diagnosis is made when any 1 of the following 3 criteria is fulfilled:</p> <ol style="list-style-type: none"> 1. Acute onset of symptoms (within minutes or several hours) with skin and/or mucosal tissue involvement such as generalized hives, pruritus, flushing, swollen lips, tongue, or uvula and at least one of the following: <ol style="list-style-type: none"> 1.1 Respiratory symptoms, such as rhinitis, hoarseness, dyspnea, wheezing breath sound from bronchospasm, stridor, decreased lung function, such as decreased peak expiratory flow (PEF), or decreased blood oxygen levels 1.2 Reduced blood pressure or multi-organ system failure, such as hypotonia (collapse), syncope, or incontinence 2. Two or more of the following symptoms that occur after contact with a suspected allergen (within minutes or several hours) <ol style="list-style-type: none"> 2.1 Skin and submucosal membrane involvement, such as generalized hives, pruritus, flushing, swollen lips, tongue, or uvula 2.2 Respiratory symptoms, such as rhinitis, hoarseness, dyspnea, wheezing breath sound from bronchospasm, stridor, decreased peak expiratory flow (PEF), or decreased blood oxygen levels 2.3 Reduced blood pressure or multi-organ system failure, such as hypotonia (collapse), syncope, or incontinence 2.4 Gastrointestinal tract involvement, such as abdominal pain, nausea, or vomiting 3. Reduced blood pressure that occurs after contact with a known allergen (within minutes or several hours) <ol style="list-style-type: none"> 3.1 For infants and children, systolic blood pressure lower than normal value according to age or decrease in systolic blood pressure of more than 30 percent of baseline 3.2 For adults, systolic blood pressure less than 90 mmHg or decrease in systolic blood pressure more than 30 percent of baseline
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Notes:

Low systolic blood pressure in children is defined, as follows:

- <60 mmHg (0 day to 28 days of age)
- <70 mmHg (1 month to 1 year of age)
- <70 mmHg + (2 x age) (1 year to 10 years of age)
- <90 mmHg (11 to 17 years of age)

Table 2. Classification of urticaria^{2,3}

Type	Subtype	Definition
Spontaneous urticaria	Acute spontaneous urticaria	Spontaneously occurring wheals and/or angioedema for <6 weeks
	Chronic spontaneous urticaria	Spontaneously occurring wheals and/or angioedema for 6 weeks or longer
Type	Subtype	Precipitating factors
Inducible urticaria or physical urticaria	Cold urticaria	Cold objects, air, fluids, wind
	Delayed pressure urticaria	Vertical pressure (stimulates wheal reaction within 3-12 hours)
	Heat urticaria	Localized heat
	Solar urticaria	Radiation from ultraviolet and/or visible light
	Symptomatic dermographism	Mechanical shearing forces (stimulates wheal reaction within 1-5 minutes)
	Vibratory angioedema	Vibratory forces such as pneumatic hammer (stimulates wheal reaction within 1-2 hours)
	Aquagenic urticaria	Water
	Cholinergic urticaria	Increasing core body temperature
	Contact urticaria	Contact with substance that predisposes patient to wheal reaction

Guidelines for management of patients with urticaria (Figure 2,3)^{2,10-15}

1. Treating the underlying causes: If the cause can be identified, eliminate the cause. For example, in drug-induced urticaria, discontinuation of the causative drug will resolve the hives. Avoid aggravating factors, such as consumption of alcoholic beverages.¹⁶

2. Non-pharmacotherapy to minimize skin hyper-responsiveness

2.1 Prevention of and care for dry skin

It is recommended to regularly apply cream or lotion without perfume to keep the skin moist and reduce skin sensitivity.

2.2 Avoidance of skin stimulation

Precipitating factors, such as scratching, wearing tight clothes, carrying heavy objects, friction massage, steam and hot vapor, body scrub, using perfume, heavy sun exposure, and exposure to too hot or too cold temperatures should be avoided.

3. Medical treatment

3.1 Antihistamines

H₁-antihistamines are commonly used to control the symptoms of urticaria. There are 2 generations of antihistamines, including:

A. Second-generation (non-sedating) antihistamines (Table 4)^{2,3,17}

Non-sedating antihistamines are long-acting drugs. Adverse effects, such as sedation and dry mouth, are less likely. This type of antihistamines should be considered as first-line treatment, especially in patients who are machine controllers, drivers, students, and the elderly. Response rates of non-sedating H₁-antihistamines were 40-50%, however, increasing dose (up to 4-fold) of evidence-based drugs, such as levocetirizine,^{11,12} desloratadine,¹¹ rupatadine,¹³ and bilastine,¹⁴ could increase the efficacy of treatment without increasing adverse effects. For fexofenadine up dosing to 4-fold, there was no data of randomized controlled trial. However, in vitro study, increasing concentration of fexofenadine could limit chronic eosinophil inflammation by stimulating apoptosis pathway.¹⁵ A randomized, double-blinded, placebo-controlled trial reported treatment with

240 mg/day fexofenadine significantly decreased visual analog scale score of pruritus and severity index when compared to treatment with 120 mg/day fexofenadine.¹⁸ Finn *et al.* reported minimal adverse effects from using 480 mg/day of fexofenadine.¹⁹ Accordingly, increasing dose of fexofenadine is also included in the EAACI guideline 2013.²

B. First-generation (sedating) antihistamines (Table 5)^{2,3,17}

The common side effects of this generation of antihistamines are drowsiness, sedation, and dry mouth. As such, these antihistamines should be avoided in elderly patients and in patients with contraindications like benign prostate hypertrophy, glaucoma, or asthma. With regard to side effects, EAACI/GA2LEN/DEF/WAO Guideline 2013 recommends the use of first-generation (sedating) -antihistamines only when second-generation non-sedating antihistamines are not available. In addition, previous study reported that sedating antihistamines at bedtime combined with non-sedating antihistamines did not improve treatment efficacy in CSU. In fact, that combination taken at bedtime appeared to enhance adverse reactions due to the sedating effect during the daytime.²⁰

3.2 Alternative treatment with other drugs

a. Corticosteroids^{21,22}

Oral corticosteroids, such as prednisolone, should be considered in cases of severe AU, severe serum sickness, urticarial vasculitis, and delayed pressure urticaria that are not responsive to other treatments. It should be noted that oral corticosteroids are not likely to be effective in treating other types of physical urticaria. In CU patients, prednisolone should not be prescribed regularly or continued for a long period of time. It should be used only in recalcitrant disease or in disease exacerbation for a short period of time.

b. Combination of H₁- and H₂-antihistamines

Treatment using H₂-antihistamines in combination with H₁-antihistamines has low quality of evidence and its efficacy is still unclear. However, some experts recommend this combination therapy due to its low cost and high safety profile.²³ This combination treatment likely improves symptoms better than using H₁-antihistamines alone.

Table 3. Additional investigations for diagnosis of urticaria, especially in cases that are not responsive to treatment^{2,5}

Types and subtypes	Investigations
Spontaneous urticaria	
Acute spontaneous urticaria	No routine diagnostic test (unless patient history is strongly suggestive)
Chronic spontaneous urticaria	Differential blood count*, ESR* Discontinue suspicious drugs, such as NSAIDs Additional diagnostic tests, including autologous serum skin test**, test for <i>Helicobacter</i> *, gastroscopy*, ANA*, D-dimer**, [†] stool examination for parasites*, skin test including physical test*, specific IgE*, thyroid hormone, and autoantibodies* (In patients younger than 15 years, thyroid antibody test is not necessary in some cases)
Inducible or physical urticaria	
1. Cold urticaria	Cold provocation test (ice cube, cold water)**, differential blood count*, ESR*, cryoglobulins*
2. Delayed pressure urticaria	Pressure test** - A rod with a 0.2-1.5 kg/cm ² weight placed on the patient's thigh or back for 10 minutes and 20 minutes; or - A shoulder strap with 6.8 kg (15 pound) sandbags on each side placed upon patient's shoulder in sitting position for 15 minutes
3. Heat urticaria	Warm arm bath**
4. Solar urticaria	Expose patient to ultraviolet and multi-wavelength visible light**
5. Symptomatic dermographism	Test for dermographism**, differential blood count*, and ESR*
6. Vibratory angioedema	Apply vortex vibration to forearm or fingers for 1-5 minutes**
7. Aquagenic urticaria	Apply wet room temperature clothing to forearm for 15-20 minutes
8. Cholinergic urticaria	Provocation by exercise or hot bath for 15-20 minutes**
9. Contact urticaria	Immunologic and non-immunologic reactions can be the cause. Diagnostic tests include patch test and skin prick testing. Dermatologic or/and specialist consultations are recommended.

*Investigations to identify causes; **Investigations for diagnosis

[†]Some CSU patients can have increased levels of plasma D-dimer resulting from activation of coagulation pathway

Abbreviations: ESR, erythrocyte sedimentation rate; NSAID, non-steroidal anti-inflammatory drug; ANA, antinuclear antibodies; CSU, chronic spontaneous urticaria

Accordingly, combined H₁ and H₂-antihistamine therapy may be considered in some recalcitrant CSU patients who do not respond well to H₁-antihistamines alone.^{24,25} Discontinuation of H₂-antihistamines should be considered if clinical symptoms are not improved within 2-4 weeks after initiation.²⁶

c. Leukotriene receptor antagonists

Montelukast was reported to be useful in treatment of CU patients who were not responsive to initial antihistamine treatment and in urticaria patients with aspirin-sensitive condition.²⁷ Although the quality of evidence supporting the efficacy of montelukast combined with antihistamines is low, some patients responded well to this combination. If there is no response after adding montelukast for 2-4 weeks, the medication should be discontinued.

d. Ciclosporin

The optimal dose is 2.5-5 mg/kg/day.^{28,29} Ciclosporin should not be used for longer than 3-6 months due to its adverse effects. There is not enough evidence to support the use of ciclosporin in children under 18 years of age.

e. Omalizumab

The reported findings from many studies support the effectiveness of omalizumab in CSU patients.^{30,31} Omalizumab has been approved by the Thai Food and Drug Administration for the treatment of recalcitrant CSU patients who are older than 12 years of age. However, the cost of omalizumab is high, relative to the cost of

conventional therapy. Specialist referral is recommended if the use of omalizumab is indicated (Appendix III. Omalizumab treatment guidelines).

4. Other treatment modalities

4.1 Calamine lotion application

Calamine lotion, cooling powder, and a refreshing towel can be applied to the hives-affected area for symptomatic relief of itching.

4.2 Patient education regarding etiology, process of disease, prognosis, and psychosocial support

Disease symptoms can cause psychological stress to patients, which may exacerbate disease activity.³² As part of a holistic approach to patient management, psychosocial support should be considered. Knowledge regarding disease severity, natural course of the disease, and stress reduction should be provided to patients to help them participate in the effective management of the disease.

Specialist referral:

Referral to a specialist is recommended if disease symptoms cannot be controlled with the treatment protocols recommended in this guideline.

Disease prognosis

1. Acute spontaneous urticaria

A majority of cases may develop spontaneous regression within 3 weeks.³³ One university hospital-based study in Thai people reported that 21% of acute spontaneous urticaria cases progressed to CU.³⁴

2. Chronic spontaneous urticaria

Adults: Approximately 50% of adult CU patients without angioedema had spontaneous remission within 1 year, with 20% having had intermittent exacerbations over a 2-year period. Seventy-five percent of patients with angioedema alone or CU with concomitant angioedema had persistent disease longer than 1 year while 20% had persistent disease over 20 years.³⁵ In Thai CSU patients, 34% and 84% had disease remission within 1 year and 5 years, respectively, with an average remission duration of 390 days.³⁶ Aging patients tended to have shorter duration than non-aging patients.³⁷

Children: Approximately 50% of pediatric CU patients had disease that persisted for longer than 1 year (median duration 16 months)³⁸ and 19% of patients had disease remission within 1 year.³⁹

Appendix I. Grades of evidence and strength of recommendation for this clinical practice guideline¹⁷

• Grades of evidence

- 1a Meta-analysis of RCTs
- 1b Single RCT
- 2a Systematic review of cohort studies
- 2b Single cohort studies and RCTs of limited quality
- 3a Systematic review of case-control studies
- 3b Single case-control study
- 4 Case series, case-cohort series or cohort studies of limited quality, expert committee opinion

Abbreviation: RCT, randomized controlled trial

Table 4. Second-generation (non-sedating) antihistamines^{3,17}

Drug	Pediatric dosage		Approved age	Adult dosage	Dose adjustment	Pregnancy category	Grades of evidence	Strength of recommendation
	Age	Dose						
Cetirizine	2-6 years	2.5 mg twice daily or 5 mg once daily	>2 years	10 mg once daily	Hepatic or renal function impairment (CrCl<30 ml/min/1.73m ²)	B	1a	A
	>6 years	10 mg once daily						
Desloratadine	6-11 months	1 mg once daily	>6 months	5 mg once daily	Severe renal function impairment (CrCl<30 ml/min/1.73m ²)	C	1a	A
	1-5 years	1.25 mg once daily						
	6-11 years	2.5 mg once daily						
	≥12 years	5 mg once daily						
Fexofenadine	6 months to <2 years	15 mg twice daily	>6 months	180 mg once daily or 60 mg twice daily	Renal function impairment (CrCl<80 ml/min/1.73m ²)	C	1a	A
	2-11 years	30 mg twice daily						
	≥12 years	60 mg twice daily or 180 mg once daily						
Levocetirizine	>6 years	5 mg once daily	>6 years	5 mg once daily	Dose adjustment is not necessary for patients with only hepatic impairment, but it should be considered in patients with both hepatic and renal impairment (CrCl<50 ml/min/1.73m ²)	B	1a	A
Loratadine	2-12 years	5 mg once daily	>2 years	10 mg once daily	Hepatic function impairment	B	1a	A
	>12 years, >30 kg	10 mg once daily						
Rupatadine	6-11 years (≥25 kg)	5 mg once daily	>12 years (tablet) >6 years (oral solution)	10 mg once daily	Hepatic or renal function impairment (CrCl<30 ml/min/1.73m ²)	B	1a	A
Bilastine	>12 years	20 mg once daily	>12 years	20 mg once daily	Dose adjustment is not necessary for patients with both hepatic and renal impairments	B	1a	A

Table 5. First-generation (sedating) antihistamines^{3,17}

Drug	Pediatric dosage (mg/kg/day)	Approved age	Adult dosage	Pregnancy category	Dose adjustment	Grades of evidence	Strength of recommendation
Chlorpheniramine*	0.35-2	1 year	PO 4 mg q 4-6 hrs	B	-		
Cyproheptadine	0.25	2 years	PO 4 mg q 6-8 hrs	B	Hepatic function impairment	4	C
Diphenhydramine	5	2 years	PO 25-50 mg q 4-6 hrs	B	Hepatic function impairment		
Hydroxyzine*	1-2	6 months	PO 10 mg q 6 hrs	C	Hepatic function impairment		

*Although both chlorpheniramine and hydroxyzine have low grades of evidence and weak strength of recommendation due to a small number of comparison studies, both drugs should be considered for treatment of acute spontaneous urticaria in children

• Classification of strength of recommendation

Recommendation strength	Evidence grade
A	1a, 1b
B	2a, 2b, 3a, 3b
C	4
D	Expert opinion

Appendix II. Laboratory testing

Laboratory testing should be routinely performed. Clinical settings that may be justified for laboratory investigation, including: (i) history and physical examination are suggestive of precipitating causes; and, (ii) patient symptoms resist first-line antihistamine treatment. (Figure 4)^{40,41}

1. Laboratory investigations^{2,42,43} (tests selection should be considered on clinical indication and an individual justification basis)

- Complete blood count (CBC)
- Erythrocyte sedimentation rate
- Stool examination
- Chest X-ray
- Sinus X-ray
- Antinuclear antibodies (ANA)
- D-dimer
- Helicobacter testing
- Gastroscopy
- Thyroid antibodies and/or thyroid function test (should be conducted in suspected thyroid disease, especially when autoimmune urticaria is suspected)

2. Skin prick testing (SPT)

SPT is an allergy testing method that is used for diagnosis of IgE-mediated allergy. Positive SPT indicates allergen-specific IgE in serum; however, positive allergens are not always the cause of symptoms. For food allergy, SPT has a highly-reliable negative predictive value of 95%; however, the positive predictive accuracy is less than 50%, when compared to double-blind placebo-controlled food challenge test.⁴⁴ Accordingly, a positive SPT result should be carefully interpreted and evaluated.

Of note, SPT plays a limited role in CU. SPT is commonly used in suspected cases and is used to confirm diagnosis of food or drug allergy identified by IgE-mediated hypersensitivity reaction in allergic AU patients.

3. Diagnosis of food allergy

Food intolerance can develop from either IgE- or non-IgE-mediated reactions.⁴⁵ In IgE-mediated food allergy, either SPT or specific serum IgE testing can be used to diagnose, but its interpretation should be carefully conducted. Specific serum IgG is neither reliable nor helpful in diagnosing food allergy. Double-blind placebo-controlled food challenge test is the gold standard for diagnosis of food allergy.⁴⁶

4. Serum autoantibodies for diagnosis of chronic autoimmune urticaria⁴⁷⁻⁴⁹

4.1. In vivo testing

- **Autologous serum skin testing (ASST)** ASST is a screening test used to detect autoreactivity. Sensitivity is approximately 70% and specificity is 80%. Positive ASST was found in 30-60% of CU patients; however, it does not affect patient management.

4.2. In vitro testing (These tests are currently available in some countries and are expensive)

- **Basophil histamine release assay** Basophil histamine release assay is used for serum functional autoantibodies detection. Obtaining fresh basophils from healthy individuals is necessary for accurate laboratory testing.
- **Direct immunoassays** These laboratory methods, including Western blotting, immunoprecipitation, enzyme-linked immunosorbent assay, and flow cytometry (which uses chimeric cell lines expressing human FcεRI α), are able to detect non-functional and functional anti-FcεRI autoantibodies.

Appendix III. Omalizumab treatment guidelines^{30,31}

Omalizumab is an additional drug that can be used to treat treatment-resistant CSU in adults or adolescents older than 12 years of age. Omalizumab is an add-on therapy to H₁-antihistamine treatment.

Patients should fulfill all of the following criteria in order to be considered for omalizumab treatment:

1. Patients are under specialist care, including dermatologists and/or immunologists;
2. Patients are older than 12 years of age;
3. Cause of urticaria is not identifiable by further investigations and CBC, ANA, and urine analysis results are normal;

4. Patients are diagnosed by specialists as moderate to severe CSU that is not responsive to conventional treatment; and,
5. Disease duration is longer than 3 months and the symptoms remain persistent despite the use of guideline-based treatment (Figure 5).

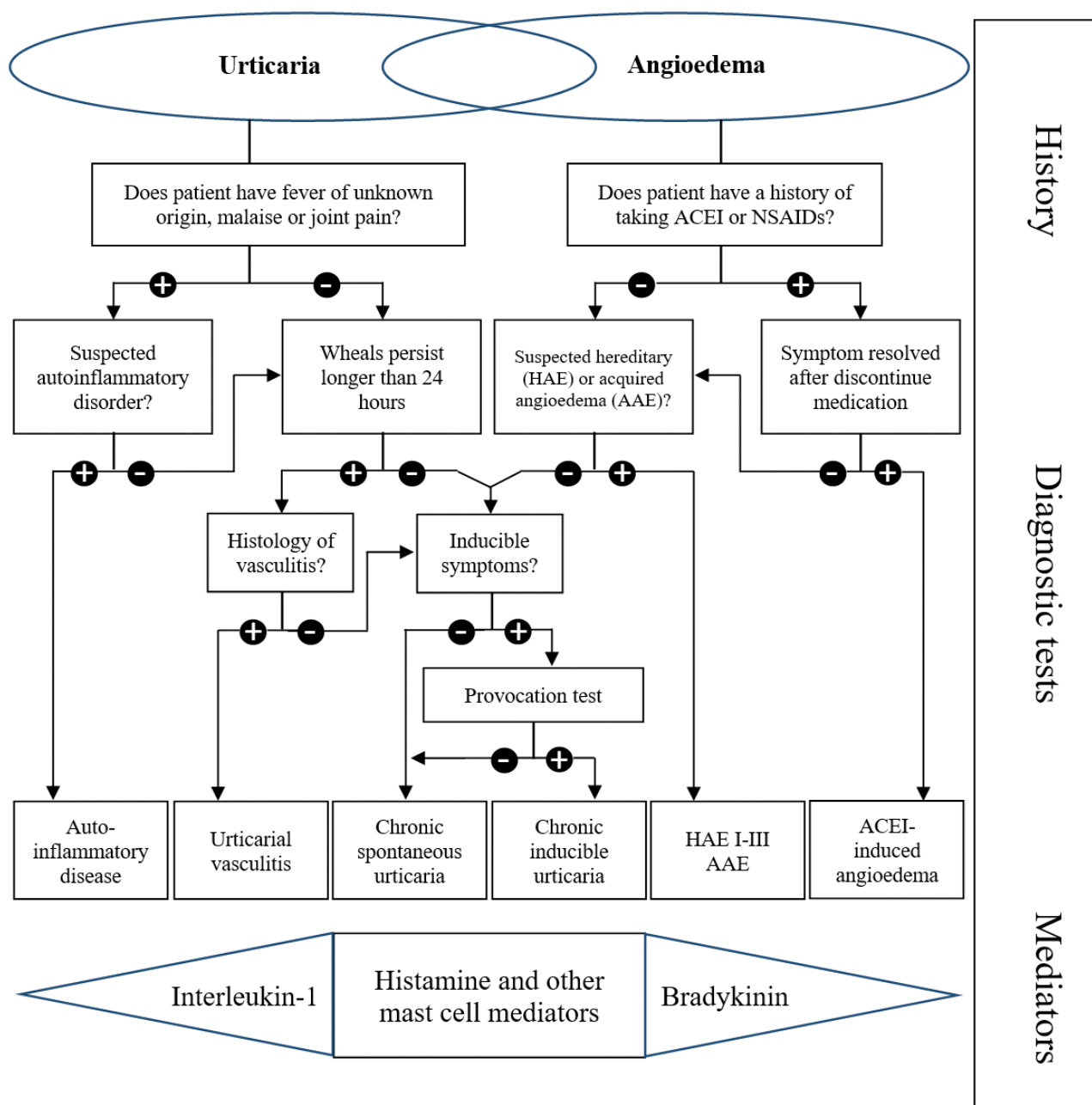
Omalizumab dosage and evaluation

The initial recommended dose of omalizumab is 150 mg by subcutaneous injection every 4 weeks.⁵⁰ Treatment response will be evaluated 4 weeks after the first injection using weekly urticaria activity score (UAS7). UAS7 score will be recorded over a 7-day period by patients before each visit. If UAS7 score decreases by more than 30% from the baseline score, the same dosage (150 mg every 4 weeks) should be continued. If no

significant improvement is observed after 4 weeks of treatment (UAS7 decrease less than 30% from baseline score), an increase in dose to 300 mg every 4 weeks is recommended. If no significant improvement is once again observed after the second 4-week period, then omalizumab discontinuation should be considered.

If the patient responds well to omalizumab treatment and is able to reduce other conventional drugs, decreasing the dose of omalizumab or extending the dosage interval should be considered. Omalizumab discontinuation should be considered every 3-6 months. Re-administration of omalizumab after discontinuation is based on changes in clinical factors and physician's discretion.

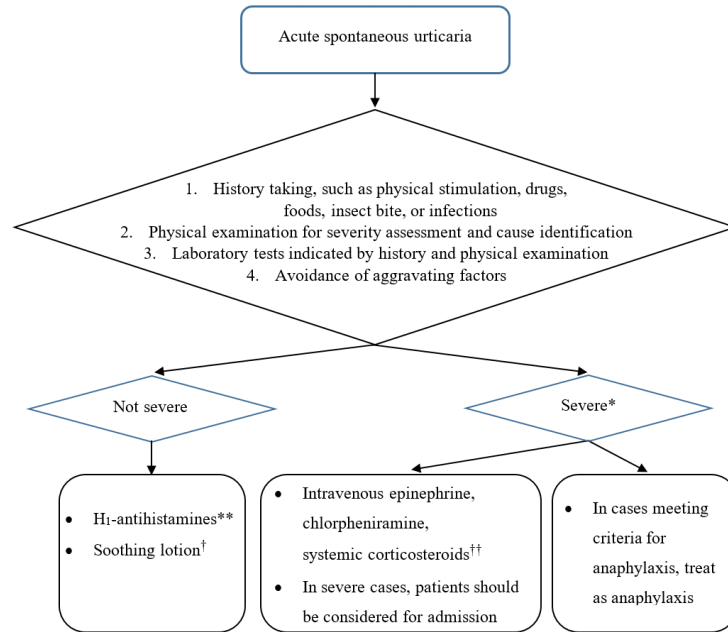
Figure 1. Diagnostic approach for urticaria⁴



Abbreviations: ACEI, angiotensin converting enzyme inhibitors; NSAIDs, nonsteroidal anti-inflammatory drugs; HAE, hereditary angioedema; AAE, acquired angioedema

Figure courtesy of Marcus Maurer, Markus Magerl, Martin Metz, and Torsten Zuberbier, used with permission from John Wiley and Sons

Figure 2. Management algorithm for children and adult patients with acute spontaneous urticaria

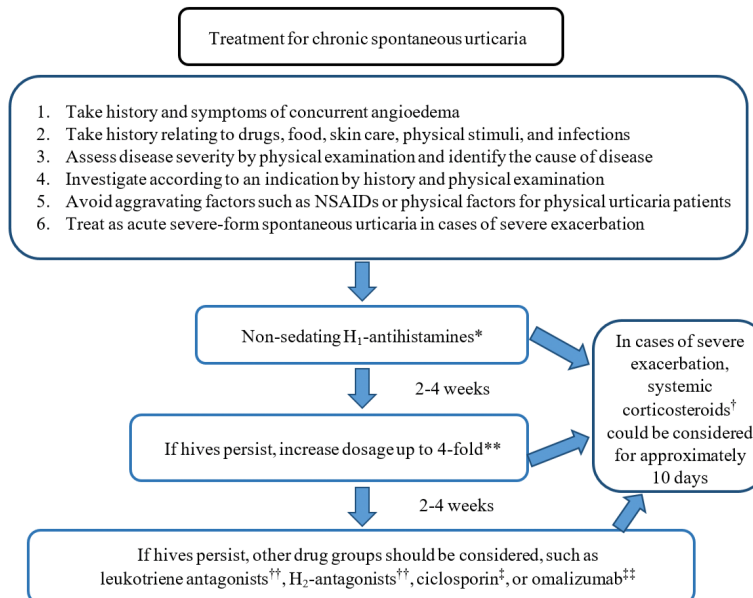


Notes:

- Patients with generalized rash may be considered for oral corticosteroids (e.g., prednisolone 20-30 mg/day) for no longer than 10 days.
- Drugs or substances that can aggravate urticaria, such as aspirin, non-steroidal anti-inflammatory drugs, codeine, morphine or ACEI, should be avoided.

*Edema and erythema of the face and neck, chest discomfort, generalized rash
 **Evidence grade 1a, recommendation strength A †Evidence grade 4, recommendation strength D
 ††Evidence grade 2b, recommendation strength B

Figure 3. Algorithm for treatment of chronic spontaneous urticaria



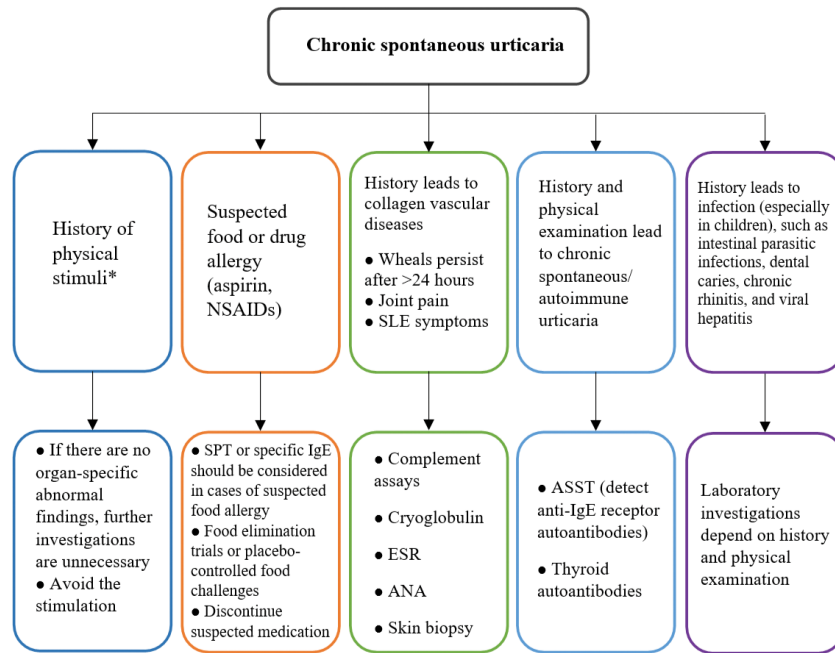
Notes:

Response rates of H₁-antihistamines were 40-50%, while low-dose corticosteroids, ciclosporin, and omalizumab had response rates of 70-80% in each treatment.

*Evidence grade 1a, recommendation strength A
 **Evidence grade 2b, recommendation strength B. Increasing dose (up to 4-fold) of evidence-based drugs, such as desloratadine, levocetirizine, rupatadine, and bilastine, could increase the efficacy of treatment without increasing adverse effects. Alternatively, increasing the dose of other antihistamines may be ineffective.^{2,10-14} For fexofenadine up dosing to 4-fold, no data of randomized controlled trial supported, however, in vitro study, increasing concentration of fexofenadine could limit chronic eosinophil inflammation.¹⁵ If there are any reasons that cannot increase all above antihistamine dosage up to 4-fold, changing to or adding other different types of H₁-antihistamines are the alternative.

†Evidence grade 2b, recommendation strength B
 ††Evidence grade 2b, recommendation strength B. Low evidence of efficacy, but could be effective in some cases. If clinical symptoms do not improve after taking this medication for 2-4 weeks, discontinuation of this medication should be considered.
 ‡Evidence grade 1b, recommendation strength A
 ‡‡Evidence grade 1a, recommendation strength A. Should refer patient to specialized dermatologists or allergists; see Appendix III for omalizumab treatment guideline

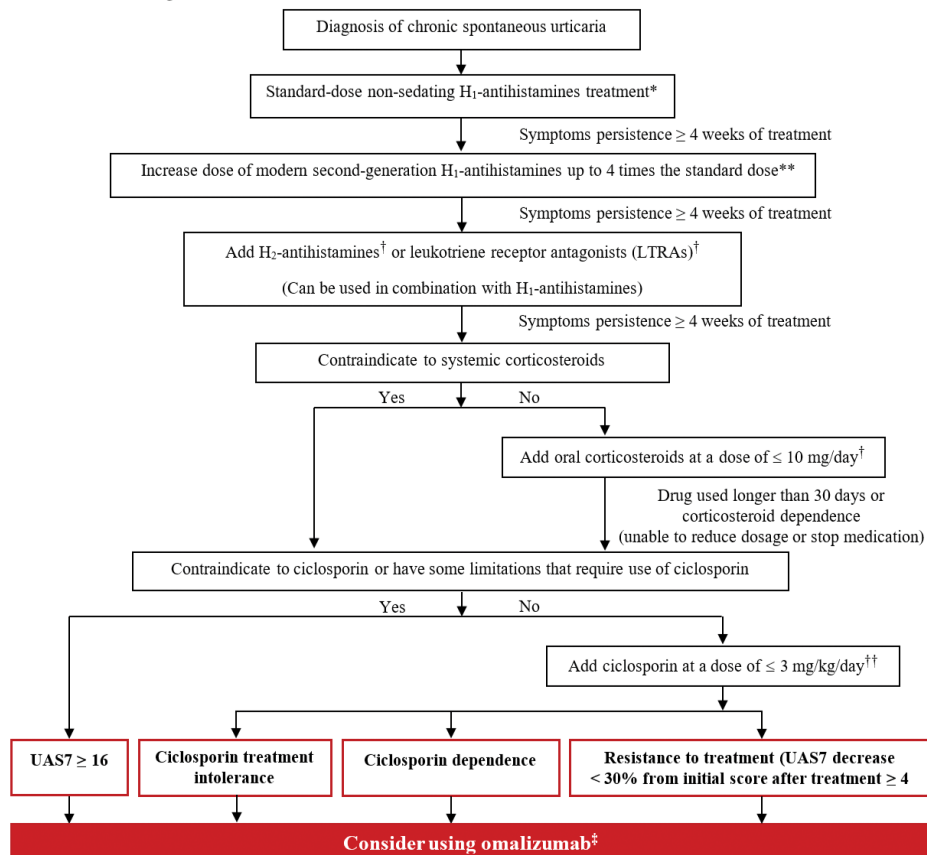
Figure 4. Algorithm for investigations of chronic spontaneous urticaria^{39,40}



*Should take history of physical stimuli, such as friction massage, steam, and hot vapor

Abbreviations: NSAIDs, nonsteroidal anti-inflammatory drugs; SLE, systemic lupus erythematosus; SPT, skin prick testing; ESR, erythrocyte sedimentation rate; ANA, antinuclear antibodies; ASST, autologous serum skin testing

Figure 5. Omalizumab treatment algorithm



*Evidence grade 1a, recommendation strength A

**Evidence grade 2b, recommendation strength B. If there are any reasons that cannot increase all above antihistamine dosage up to 4-fold, changing to or adding other different types of H1-antihistamines are the alternative.

†Evidence grade 2b, recommendation strength B

††Evidence grade 1b, recommendation strength A

‡Evidence grade 1a, recommendation strength A

Abbreviation: UAS7, weekly urticaria activity score

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