Last revised: 06/2020
Next expected review: 12/2020

Urticaria

Goal: Provide PCPs with initial workup algorithm for urticaria, including when to refer.

Diagnostic Workup

Inclusion Criteria
Raised, red, itchy, pruritic, fleeting plaques

! All urticaria is caused by release of histamine, but histamine release is not always IgE-mediated (type I allergic reaction).

Does the patient truly have urticaria? This includes 3 components:
1) Area of central swelling, usually with surrounding erythema
2) Itchiness
3) Fleeting/migrating individual wheals (usually lasting 30 mins-24 hrs)

No →

Consider these alternative conditions that may be mistaken for urticaria.

Non pruritic:
- Auriculotemporal syndrome
- Sweet syndrome

Pruritic:
- Eczema
- Contact dermatitis
- Drug eruptions
- Insect bites
- Bullous pemphigoid
- Erythema multiforme minor
- Plant-induced reactions (e.g. poison ivy, poison oak)
- Viral exanthem

Yes ↓

Signs/symptoms concerning for anaphylaxis (involvement of at least 2 organ systems)?

Yes → Administer epinephrine, send to ER. Use ASAP score to guide decision making if diagnosis of anaphylaxis is unclear. After ER visit, refer to allergist.

No ↓

Urticaria preceded by exposure to potential identifiable trigger* within 2 hours of onset?

Yes → Refer to allergist for workup of IgE-mediated allergic reaction or non-IgE mediated mechanism (through direct mast cell activation).

No ↓

Symptoms of acute viral or bacterial infection? (e.g. respiratory illness, UTI, otitis media)

Yes → Diagnostic workup for infections targeted to current symptoms, treat accordingly.
- Infections are associated with over 60% of pediatric acute urticaria cases. Mechanism is through autoimmune response to the infection, in which IgG develops against mast cells and triggers degranulation.[5]
- If urticaria develops multiple days into antibiotic course, it is very unlikely an IgE-mediated drug allergy.[5] Do not label the patient with an allergy to the drug! When child is well, either adminster an observed dose in the office and watch for 1 hour, or refer to allergist for definitive allergy testing.

No ↓

Travel to endemic area for parasitic infections, or found to have peripheral blood eosinophilia?

Yes → Order stool O&P.
- Infections with *Ancylostoma*, *Strongyloides*, *Filaria*, *Echinococcus*, *Trichinella*, *Toxocara*, *Fasciola*, *Schistosoma mansoni*, and *Blastocystis hominis* have all been associated with urticaria.

No → Continue to next page

* Consider the following categories of potential culprits of IgE-mediated allergic reactions:
- Medications
- Foods & food additives
- Insect bites and stings
- Latex
- Blood products

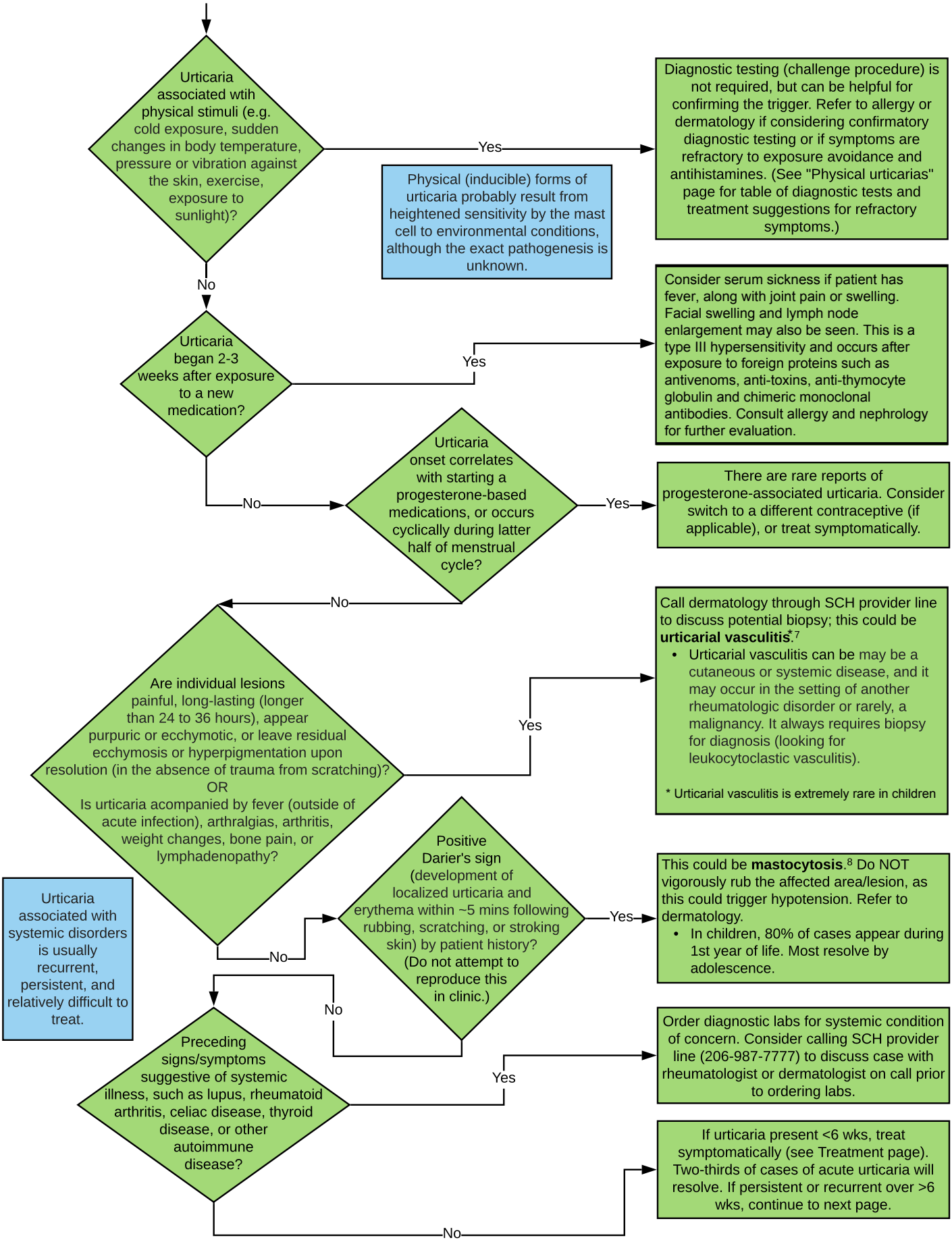
Consider the following categories of potential culprits of direct mast cell activation (non-IgE mediated):
- Narcotics (including codeine and dextromethorphan)
- Anesthetic muscle relaxants
- Vancomycin
- Radiocontrast medium
- Foods (tomatoes and strawberries especially)
- Stinging nettle plant

NSAIDS (e.g. aspirin, naproxen, ibuprofen) can cause urticaria due to IgE-medicated allergic reactions or due to non-allergic mechanism (due to underlying abnormalities in arachidonic acid metabolism).

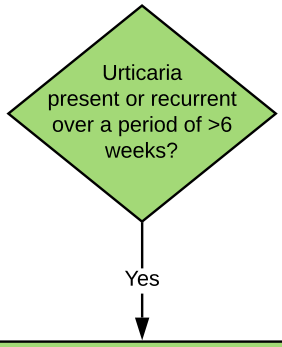
Acute urticaria: present <6 weeks.
Chronic urticaria: present most days of the week for >6 weeks.

In many patients, no specific etiology for urticaria can be identified. Acute urticaria is more likely to have an identifiable etiology than chronic urticaria.

Diagnostic Workup Cont. (Less Common Causes)



Diagnostic Workup Cont. (Chronic Urticaria)



Routine lab tests are unlikely to be revealing when the clinical history does not suggest an underlying allergic etiology or the presence of systemic disease. Guidelines suggest initially obtaining a limited set of laboratories to screen for the systemic disorders that may involve urticaria[3]:

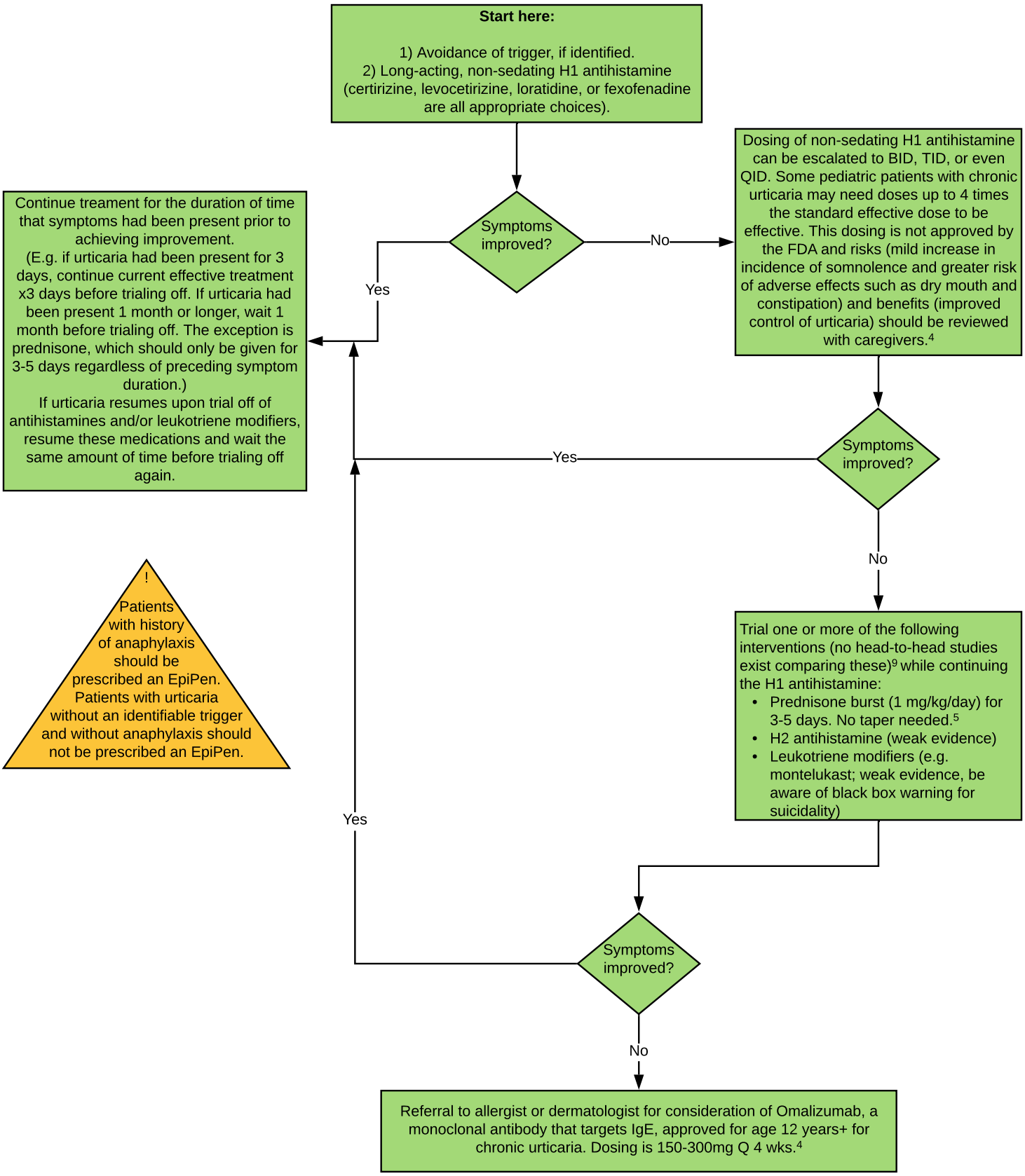
1. **CBC with diff**
   - Eosinophilia should prompt evaluation for an atopic disorder or parasitic infection.
2. **ESR or CRP**
   - Significant elevations in ESR or CRP should prompt further investigation for systemic diseases, such as autoimmune, rheumatologic, infectious, or neoplastic diseases. Such an evaluation may include measurement of antinuclear antibodies, cryoglobulins, hepatitis B and C serologies, total hemolytic complement, and a serum protein electrophoresis. If high ESR or CRP, refer to rheumatology or dermatology rather than ordering these subsequent labs in the primary care setting.
3. **Consider TSH +/- antithyroglobulin and antimicrosomal antibodies**
   - Autoimmiune thyroid disease is uncommon in children with chronic urticaria, and thyroid testing is not recommended by international guidelines as part of workup. However, urticaria can rarely be associated with autoimmune thyroid disease, so some clinicans choose to check these labs as part of the workup.

Identifiable causes of urticaria

Infections
Viral
Parasitic
Bacterial
IgE-mediated allergic cases
Medications
Insects
Stinging (yellow jackets, bees, wasps, hornets, fire ants)
Biting (*Triatoma* [kissing bugs])
Foods
Blood products (urticarial transfusion reaction)
Latex (contact or inhaled)
Contact allergens (animal saliva, raw foods)
Aeroallergens (rare)
Food additives
Direct mast cell activation
Narcotics/opiates
Muscle relaxants (eg, succinylcholine)
Radiocontrast agents
Vancomycin
Physical stimuli
Dermatographism
Delayed pressure
Cold
Cholinergic
Vibratory
Aquagenic
Solar
Exertion/exercise
Miscellaneous mechanisms
Nonsteroidal anti-inflammatory drugs
Serum sickness
Transfusion reactions (distinct from IgE-mediated reactions)
Hormone-associated (progesterone)
Stinging nettle

IgE: immunoglobulin E.

Symptomatic Treatment



ASAP Score

The algorithm below is copied from Seattle Children's Anaphylaxis clinical standard work pathway:
https://www.seattlechildrens.org/pdf/anaphylaxis-pathway.pdf

1. **If the patient is clearly in anaphylaxis:**
   GIVE EPINEPHRINE FIRST
   DO NOT WAIT TO SCORE THE PATIENT
2. **Use the score:**
   a) To aid in the diagnosis of anaphylaxis and need for epinephrine, for patients where the diagnosis is unclear.
   b) To obtain a symptom score, sometimes after treatment is initiated, in order to track symptom severity over time.

Actions based on Anaphylaxis Score:

SCORE 1 - 4 pt. **Acute anaphylaxis may still be developing.** Routine use of epinephrine Is not indicated, but may be appropriate if symptoms are recent and progressing rapidly, or if indicated per the patient's anaphylaxis action plan. Place on monitors, observe closely in an environment with staff trained to monitor and treat for anaphylaxis, prepare to treat if needed.

SCORE ≥ 5 pts. **Acute anaphylaxis is very likely.** In the appropriate clinical context, epinephrine is indicated.

This score is only a guide. The decision to give epinephrine is a clinical decision that may vary by patient

ANAPHYLAXIS SCORE ASSISTING PROVIDERS (ASAP) *** SCORE ONLY CURRENT SYMPTOMS AND SIGNS, UNLESS 1 HOUR TIME FRAME IS NOTED (SKIN, ABDOMINAL) ***		
SKIN & MUCOSA	❑ **0 Absent:** No signs or symptoms ❑ **1 Mild:** Mild itching; ≤3 hives; flushing, erythema or hives that resolved in past 1 hour after antihistamine ❑ **2 Moderate (Mod):** Severe itching; >3 hives; flushing, erythema or raised rash (patchy or onset over >1 hour); face or lip edema, angioedema, red eyes ❑ **3 Severe:** Rapid (WITHIN THE PAST 1 HOUR) whole body flushing, erythema or hives; tongue or intraoral edema	
RESPIRATORY	❑ **0 Absent:** No signs or symptoms ❑ **1 Mild:** Occasional sneeze or cough; mild nasal congestion or runny nose; throat tickle; hoarseness ❑ **2 Mod:** Frequent sneezing or cough; severe nasal congestion or runny nose; subjective trouble swallowing or breathing, throat or chest tightness; chest pain; coarse breath sounds ❑ **3 Severe:** Stridor, wheeze, drooling or not swallowing, sniff position, dyspnea, diminished breath sounds, hypoxia	
CARDIOVASCULAR	❑ **0 Absent:** No symptoms, normal pulse, no hypotension (MAP ≥ 5th %ile) ❑ **1 Mild:** Tired; lightheaded; mildly dizzy; unexplained tachycardia; delayed capillary refill. ❑ **2 Mod:** Very dizzy/near fainting; pallor; weak pulse; sweaty; somnolent. Infants: listless or lethargic ❑ **3 Severe:** Hypotension (MAP <5th %ile); cyanosis; confusion; fainting, loss of consciousness, bradycardia, arrest.	
ABDOMINAL & PELVIC	❑ **0 Absent:** No signs or symptoms ❑ **1 Mild:** Nausea without vomiting; mild abdominal cramps or pain; uterine cramps; urinary incontinence ❑ **2 Mod:** Mod-severe pain; or vomiting and/or diarrhea ≥3 total WITHIN THE PAST 1 HOUR (or since epinephrine if it was given in the past hour) ❑ 3 **Severe:** Vomiting and/or diarrhea >3 total WITHIN THE PAST 1 HOUR (or since epinephrine if it was given in past hour)	
NEUROLOGICAL	❑ **0 Absent:** No signs or symptoms ❑ **1 Mild:** Anxious (without explanation); headache In infants: persistent crying or irritability ❑ **2 Mod:** Feeling of impending doom (like something terrible is about to happen)	
RISK FACTORS	❑ **0 Absent:** No suspected exposure, no history of allergies ❑ **1 Moderate Risk:** Symptom onset 1-10 hours after possible exposure AND no allergy history; known allergies with no exposure ❑ **2 High Risk:** Rapid onset, e.g. ≤ 1 hour post exposure (food, drugs, contrast); OR known allergies with possible exposure	
	TOTAL SCORE	

Physical Urticarias

This information is taken from the UpToDate article on "Physical (inducible) forms of urticaria".

Inciting factors and diagnostic tests for physical and other inducible urticarias

Disorder	Inciting trigger(s)	Diagnostic test
Symptomatic dermographism (urticaria factitia)	Firm stroking, scratching, pressure	Moderate stroking of the skin with a blunt, smooth object (eg, closed ballpoint pen tip, wooden tongue depressor) or dermographometer.
Delayed-pressure urticaria/angioedema	Application of pressure 0.5 to 12 hours before onset of symptoms	Sling with weights placed over arm or shoulder for 15 minutes (7 kg weight on 3 cm wide shoulder strap). Patient reports symptoms over next 24 hours. Dermographometers are used in research (100 grams/mm^2 for 70 seconds).
Cholinergic urticaria	Elevation of body temperature (exercise, hot water, strong emotion, hot or spicy food)	Exercise using a machine (stationary bicycle or treadmill) to the point of sweating. Then, continue for 15 minutes. If this test is positive, then passive heating of one/both arms in 42°C warm water bath to cause increase in body temperature of ≥1°C. Some patients may react to skin testing with own sweat.
Cold contact urticaria	Exposure of skin to cold air, cold liquids, or cold objects	Ice cube test - Melting ice cube in thin plastic bag for 5 minutes. TempTest where available to determine patient's threshold.
Heat contact urticaria	Warm object in direct contact with affected skin	Application of test tube containing 45°C water or metal cylinder heated to 45°C to skin for 5 minutes.
Exercise-induced urticaria/anaphylaxis	Physical exertion	Treadmill testing.
Aquagenic urticaria	Skin contact with water of any temperature Salinity of water important in some cases	Application of 35°C water in compress to upper body for 30 minutes.
Solar urticaria	Exposure of skin to sunlight (triggering wavelengths vary)	Exposure of normally covered skin to UVA (6 J/cm^2), UVB (60 mJ/cm^2), and visible light (projector).
Vibratory urticaria/angioedema	Lawn mowing, riding a motorcycle, horseback riding, mountain biking, exposure to vibrating machinery, holding some steering wheels	Vortex mixer is held against skin for 10 minutes.

UVA: ultraviolet A radiation therapy; UVB: ultraviolet B radiation therapy.

Consistent with the recommendations in: Magerl M, Altrichter S, Borzova E, et al. The definition, diagnostic testing, and management of chronic inducible urticarias - The EAACI/GA(2) LEN/EDF/UNEV consensus recommendations 2016 update and revision. Allergy 2016; 71:780.

Diagnostic considerations

It's generally best to defer administration of these tests to allergists or dermatologists: "During these challenges, physical stimuli are applied to the skin for a specified amount of time (usually a few minutes) and then removed. Urticaria typically develops **after** removal of the stimulus. Leaving the stimulus in contact with the skin until urticaria or angioedema actually appear can result in excessive exposure and systemic symptoms. Similarly, exposure time may need to be reduced in patients who describe unusual levels of sensitivity."

Treatment of refractory symptoms

"Patients who fail to respond to avoidance of the triggering stimulus combined with safe and practical doses of a second-generation antihistamine should be considered candidates for chronic therapy with omalizumab. Other therapies for refractory disease, depending upon the specific disorder, include phototherapy, physical desensitization protocols, and immunomodulatory agents."

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