New-onset urticaria

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INTRODUCTION

Urticaria, or hives (sometimes referred to as welts or wheals), is a common disorder, with a lifetime prevalence of approximately 20 percent in the general population [1]. A typical urticarial lesion is an intensely pruritic, erythematous plaque (picture 1). Urticaria is sometimes accompanied by angioedema, which is swelling deeper in the skin. A presumptive trigger, such as a drug, food ingestion, insect sting, or infection, may be identifiable in patients with new-onset urticaria, although no specific cause is found in many cases, particularly when the condition persists for weeks or months. (See 'Etiologies' below.)

The epidemiology, clinical manifestations, etiologies, diagnosis, and management of new-onset urticaria will be reviewed here. Chronic urticaria and isolated angioedema are discussed separately.

- (See "Chronic spontaneous urticaria: Clinical manifestations, diagnosis, pathogenesis, and natural history".)
- (See "Chronic spontaneous urticaria: Standard management and patient education".)
- (See "An overview of angioedema: Clinical features, diagnosis, and management".)

CATEGORIZATION OF URTICARIA

Urticaria (with or without angioedema) is commonly categorized by its chronicity:

Acute urticaria — Urticaria is considered acute when it has been present for less than six weeks.

Chronic urticaria — Urticaria is considered chronic when it is recurrent, with signs and symptoms recurring most days of the week, for six weeks or longer.

The period of six weeks is somewhat arbitrary and simply represents a timeframe in which new cases of urticaria usually resolve. More than two-thirds of cases of new-onset urticaria prove to be self-limited (acute) [2]. The lesions of acute and chronic urticaria are identical in appearance, so when the problem first develops, it is not possible to differentiate the two disorders [3].

EPIDEMIOLOGY

Urticaria affects up to 20 percent of the population at some point in their lives and occurs across the age spectrum [1].

CLINICAL MANIFESTATIONS

Urticarial lesions are circumscribed, raised, erythematous plaques, often with central pallor (picture 2). Lesions may be round, oval, or serpiginous in shape and vary in size from less than 1 centimeter to several centimeters in diameter. They are intensely itchy. Pruritus may disrupt work, school, or sleep. Symptoms often seem most severe at night.

Individual lesions are transient, usually appearing and enlarging over the course of minutes to hours and then disappearing within 24 hours. Lesions may coalesce as they enlarge (picture 3A-B). Urticarial lesions are not normally painful and resolve without leaving residual ecchymotic marks on the skin, unless there is trauma from scratching. If lesions are long-lasting, painful, or leave residual bruising, the diagnosis of urticarial vasculitis should be considered. (See 'Differential diagnosis' below.)

Any area of the body may be affected, although areas in which clothing compresses the skin (eg, under waistbands) or skin rubs together (axillae) are sometimes affected more dramatically. Typically, compressed areas become more severely affected once the restricting clothing has been removed.

Angioedema, when associated with urticaria, usually affects the face and lips, extremities, and/or genitals. Angioedema **without** urticaria should prompt consideration of other

angioedema disorders, such as drug-induced angioedema (eg, angiotensin-converting enzyme [ACE] inhibitors), idiopathic angioedema, and hereditary and acquired C1 inhibitor deficiency. (See "ACE inhibitor-induced angioedema" and "An overview of angioedema: Pathogenesis and causes".)

PATHOPHYSIOLOGY

Urticaria is mediated by cutaneous mast cells in the superficial dermis. Basophils have also been identified in lesional biopsies [4]. Mast cells and basophils release multiple mediators upon activation including histamine (which causes itching) and vasodilatory mediators (which cause localized swelling in the uppermost layers of the skin). The same process gives rise to angioedema when mast cells deeper in the dermis and subcutaneous tissues are activated. (See "Mast cells: Development, identification, and physiologic roles".)

ETIOLOGIES

The potential causes of new-onset urticaria are numerous, although no specific etiology can be identified in many patients. Acute urticaria is more likely to have an identifiable etiology compared with chronic urticaria. The different etiologies activate mast cells through various mechanisms.

Common causes — Common causes of new-onset urticaria include infections; allergic reactions to medications, foods, or insect stings and bites; reactions to medications that cause nonallergic mast cell activation (eg, narcotics); and ingestion of nonsteroidal anti-inflammatory drugs (NSAIDs) (table 1).

Infections — Viral, bacterial, and parasitic infections are associated with new-onset urticaria.

- **Viral and bacterial infections** – Acute urticaria may develop during or following a viral or bacterial infection, particularly in children. Infections are associated with over 80 percent of cases of acute urticaria in some pediatric series [2,5-8]. Immune activation, involving immune complex formation and/or complement activation, is a proposed mechanism, although the exact pathogenesis is unclear.

  - In one study, common viral illnesses and bacterial infections (eg, urinary tract infections) were the leading identifiable trigger for acute urticaria in 57 children between the ages of one and three years who presented to an emergency department

[5]. Many of these children had also received antibiotics, so it was not clear in these patients if the infection, the drug, or the combination had triggered urticaria.

- In another study, 88 children presenting to an emergency department with delayed cutaneous reactions while taking beta-lactam antibiotics were evaluated. Of these, 47 of 88 had urticarial eruptions. All were tested for common childhood viral infections and then later evaluated for drug allergy with testing followed by drug challenge (regardless of test results) [9]. Two-thirds had one or more positive viral studies, demonstrating infections with picornavirus (most common), coronavirus, respiratory syncytial virus, and several others. When the children were later challenged with the culprit antibiotic, only 4 had recurrent urticaria. Thus, urticaria was related to the viral infection or the combination of the viral infection and the antibiotic in most, and only 4 of 88 had a drug allergy. (See "Penicillin allergy: Delayed hypersensitivity reactions", section on 'Delayed urticarial eruptions'.)

- Acute urticaria, refractory to antihistamines but responsive to azithromycin, has been associated with documented *Mycoplasma pneumoniae* infection in children [10,11].

- Acute urticaria can occur in the prodromic, preicteric phase of hepatitis A or B infection and less commonly with hepatitis C [12]. Urticaria may be an initial manifestation of human immunodeficiency virus (HIV) infection [13]. (See "Acute and early HIV infection: Pathogenesis and epidemiology".)

- Episodes of acute urticaria, as well as of reactivation of chronic spontaneous urticaria that was in a remission state, have been observed following severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection during the pandemic period both in children [14] and in adults [15]. In addition, short-lived episodes of acute urticaria have been recorded following SARS-CoV-2 vaccination both in subjects with prior chronic urticaria and in normal subjects [16].

- **Parasitic infections** – Parasitic infections generally cause acute, self-limited urticaria in association with prominent eosinophilia [17].

  - Infections with *Ancylostoma*, *Strongyloides*, *Filaria*, *Echinococcus*, *Trichinella*, *Toxocara*, *Fasciola*, *Schistosoma mansoni*, and *Blastocystis hominis* have all been associated with urticaria. Stool examination is probably only indicated in travelers to endemic areas and in patients with peripheral blood eosinophilia. (See "Approach to the patient with unexplained eosinophilia".)

- Ingestion of fish contaminated with the parasite *Anisakis simplex* can also cause urticaria. *Anisakis* can be transmitted through the ingestion of sushi [18]. (See "Seafood allergies: Fish and shellfish", section on 'Anisakis'.)

COVID-19 vaccines and boosters — Urticaria with or without angioedema has been reported in association with coronavirus disease 2019 (COVID-19) messenger ribonucleic acid (mRNA) vaccines and boosters, particularly the Moderna mRNA booster. In a study of over 800 patients in two cohorts with newly diagnosed urticaria that had occurred most days of the week and persisted for weeks to months, 92 and 94 percent of cases were temporally associated with receiving the Moderna vaccine or booster [19]. Onset of urticaria was between 8 and 13 days after vaccination. In those patients with subsequent resolution, the duration of symptoms ranged from two to six months. The author and editors of this topic have also observed reactivation of chronic urticaria that had been quiescent for years.

IgE-mediated allergic reactions — Immunoglobulin E (IgE)-mediated, type I immediate allergic reactions often involve urticaria. Urticaria that is caused by an allergic reaction usually occurs within minutes to two hours of exposure to the culprit allergen. Causes include medications, foods and food additives, insect stings and bites, latex, and blood products.

Allergic reactions may be limited to the skin or part of a systemic allergic reaction (eg, anaphylaxis) (table 2 and table 3). Generalized urticaria or angioedema following exposure to a potential allergen should be interpreted as a systemic reaction with an attendant risk of anaphylaxis upon subsequent exposure, and patients should be advised to avoid the potential cause until further evaluated. (See 'Referral' below.)

- **Medications** – The antibiotics most frequently implicated in causing IgE-mediated urticaria include beta-lactams (penicillins and cephalosporins), although antibiotics from virtually all classes have been reported (picture 4). (See "Penicillin allergy: Immediate reactions".)

- **Stinging and biting insects** – Stinging insects that can cause true urticarial lesions as part of an allergic reaction include Hymenoptera (eg, bees, wasps, hornets, and imported fire ants) and *Triatoma* (eg, kissing bugs).

  Bedbugs, fleas, and mites can cause papular urticaria, usually on the lower extremities. The lesions of papular urticaria resolve over the course of weeks. (See "Bee, yellow jacket, wasp, and other Hymenoptera stings: Reaction types and acute management" and "Reactions to bites from kissing bugs (primarily genus *Triatoma*)" and "Bedbugs".)

- **Latex** – Occupational, recreational, dental, or surgical exposure to latex may cause urticaria, angioedema, asthma, or anaphylaxis in susceptible individuals [20]. Everyday scenarios in which patients may be exposed to significant amounts of latex include inflation of balloons and use of latex gloves. Penile and vulvar/vaginal urticaria and angioedema are seen upon exposure to latex condoms, with vulvar/vaginal symptoms resembling acute vaginitis. (See "Latex allergy: Epidemiology, clinical manifestations, and diagnosis".)

- **Foods and certain food additives** – Allergic reactions to foods can cause urticaria, typically within 30 minutes of ingestion. Milk, eggs, peanuts, tree nuts, soy, and wheat are the most common foods to cause generalized urticaria in children. In adults, fish, shellfish, tree nuts, and peanuts are most often implicated [21]. In Mediterranean areas, the most frequent cause of food-induced urticaria is the peach, due to sensitization to lipid transfer protein [22]. (See "Clinical manifestations of food allergy: An overview".)

  Synthetic additives in commercially prepared foods are believed to be a relatively rare cause of urticarial reactions. In contrast, certain natural compounds, such as the yellow food dye annatto and the red dye carmine red, have been well-documented causes of urticaria and anaphylaxis. Adverse reactions to food additives are discussed in detail elsewhere. (See "Allergic and asthmatic reactions to food additives".)

- **Contact with allergens** – Physical contact with a number of agents may result in urticaria, including plant products and resins, raw fruits and vegetables, or raw seafood. People employed in food processing can develop contact urticaria from various exposures [23]. Children sometimes develop urticaria upon contact with animal saliva, if allergic to those allergens. In contrast, detergents, soaps, and lotions are more likely to cause contact dermatitis than urticaria. (See "Clinical features and diagnosis of allergic contact dermatitis" and "Allergic contact dermatitis in children".)

- **Urticarial transfusion reactions** – Acute urticaria in the setting of transfusion may arise from several mechanisms, including IgE-mediated allergic reactions, complement-mediated reactions, and other immunologic events. These reactions are discussed elsewhere. (See "Immunologic transfusion reactions".)

Direct mast cell activation — Certain drugs and plants can cause urticaria due to mast cell degranulation through a non-IgE-mediated mechanism. The most frequently implicated are narcotics, muscle relaxants, vancomycin, and radiocontrast media. Nettle plants are examples of plants that cause direct mast cell activation. Some years ago "pseudoallergens" contained in certain foods were considered as a possible co-factor in patients with chronic urticaria, and this

concept appeared in the European Academy of Allergy and Clinical Immunology (EAACI) Guidelines for a while, but the lack of any convincing evidence has led to the exclusion of this hypothesis in the most recent, revised versions of this document [24]. In these cases, urticaria may develop variably within minutes to some hours after contact; in the case of drugs, this may sometimes depend on the route of administration of a drug (eg, oral versus intramuscular/intravenous). The wheal-and-flare response to stinging nettle is practically immediate (a few seconds).

- **Narcotics** – Opiate analgesics, such as morphine and codeine, cause direct mast cell activation. Dextromethorphan, an opiate derivative ingredient in cough suppressant syrups, can also cause urticaria [25].

- **Muscle relaxants** – Anesthetic muscle relaxants, including atracurium, vecuronium, succinylcholine, and curare, may cause urticaria. Muscle relaxants can also cause IgE-mediated anaphylaxis. Allergic reactions to these medications are reviewed in greater detail elsewhere. (See "Perioperative anaphylaxis: Clinical manifestations, etiology, and management".)

- **Vancomycin** – Vancomycin infusion reaction is seen after rapid vancomycin infusion and presents as diffuse erythema or flushing, sometimes with accompanying urticaria. The concomitant use of opiates and vancomycin may increase the likelihood of a reaction. (See "Vancomycin hypersensitivity".)

- **Radiocontrast medium** – Radiocontrast agents are associated with urticaria and angioedema. (See "Diagnosis and treatment of an acute reaction to a radiologic contrast agent".)

- **Stinging nettle** – The nettle plant (*Urtica dioica*), after which the disorder "urticaria" was named, is a common weed found in Europe, North and South America, and parts of Africa that causes hives and a stinging sensation immediately following contact with the skin [26-28]. These symptoms may be due to histamine in the nettle plant itself, in addition to mediators that cause pain [29].

Nonsteroidal anti-inflammatory drugs — Nonsteroidal anti-inflammatory drugs (NSAIDs), such as aspirin, ibuprofen, naproxen sodium, and others, can trigger urticaria and/or angioedema by two distinct mechanisms:

- **Pseudoallergic/pharmacologic** – NSAIDs cause urticaria in some individuals, presumably due to underlying abnormalities in arachidonic acid metabolism. This form of NSAID reaction is called a pseudoallergic reaction because the mechanism is nonimmunologic.

NSAID pseudoallergy can be seen with any agent (eg, aspirin, ibuprofen) that inhibits the cyclooxygenase 1 (COX-1) enzyme and rarely occurs with agents that are very weak inhibitors of COX-1. Patients with pseudoallergy usually tolerate acetaminophen and the selective cyclooxygenase 2 (COX-2) inhibitors. Pseudoallergic reactions attributed to NSAIDs are discussed in more detail separately. (See "NSAIDs (including aspirin): Allergic and pseudoallergic reactions", section on 'Pseudoallergic reactions'.)

- **Allergic** – A specific NSAID can also cause acute urticaria in patients who are allergic to that one agent. These reactions are presumed to represent true, immunologic allergy. (See "NSAIDs (including aspirin): Allergic and pseudoallergic reactions", section on 'Allergic reactions (presumed IgE-mediated)'.)

Both allergic and pharmacologic reactions to NSAIDs may occur within minutes after taking the drug, although pharmacologic reaction may frequently take longer (up to one to two hours). Both pharmacologic and allergic reactions to NSAIDs can be severe. However, the management differs. (See "NSAIDs (including aspirin): Allergic and pseudoallergic reactions", section on 'Management'.)

Scombroid syndrome — The ingestion of poorly preserved fish (tuna in most cases, but sometimes mackerel or sardines) containing large amounts of histamine may cause acute symptoms that resemble those of an IgE-mediated allergic reaction characterized by flushing, urticaria, diarrhea, headache, and sometimes bronchospasm. In this case also, symptoms may appear from a few minutes up to one to two hours after ingestion depending on the concentration of histamine in the fish, the quantity ingested, and the association with other foods. (See "Scombroid (histamine) poisoning".)

Uncommon causes — Uncommon causes of new-onset urticaria include various physical factors, serum sickness, and hormone-associated disorders.

- **Physical stimuli** – Physical urticarial syndromes are forms of chronic urticaria that are triggered by specific physical factors, such as cold exposure, sudden changes in body temperature, pressure or vibration against the skin, exercise, exposure to sunlight, or other stimuli. These disorders are reviewed separately. (See "Physical (inducible) forms of urticaria" and "Cold urticaria".)

- **Serum sickness** – Serum sickness and serum sickness-like reactions to exogenous proteins or medications may present with an urticarial rash accompanied by fever, polyarthralgias, polyarthritis, and/or lymphadenopathy. This typically develops within one to three weeks after administration of the causative agent. Proteinuria, edema, and

abdominal pain may also be present. These reactions are discussed elsewhere. (See "Serum sickness and serum sickness-like reactions".)

- **Progesterone-associated urticaria** – There are rare reports of progesterone-containing oral contraceptives, hormone replacement therapy, or endogenous progesterone associated with cyclic urticaria [30,31]. The disorder is sometimes called autoimmune progesterone dermatitis [32-35]. Lesions usually appear during the second half of the menstrual cycle and resolve with menstruation.

SYSTEMIC DISORDERS THAT MAY INCLUDE URTICARIA

Uncommonly, urticaria or urticaria-like lesions may be an early feature of a systemic disorder, including the following:

- **Urticarial vasculitis** – Urticarial vasculitis should be suspected when individual lesions are painful, are long-lasting (longer than 24 to 36 hours), appear purpuric or ecchymotic, or leave residual ecchymosis or hyperpigmentation upon resolution (in the absence of trauma from scratching) (picture 5 and picture 6 and picture 7). Vasculitis should also be suspected in patients with urticaria accompanied by fever, arthralgias, arthritis, weight changes, bone pain, or lymphadenopathy. Urticarial vasculitis may be a cutaneous or systemic disease, and it may occur in the setting of another rheumatologic disorder or rarely, a malignancy. (See "Urticarial vasculitis" and "Cutaneous manifestations of internal malignancy".)

- **Mastocytosis** – Mastocytosis and mast cell disorders are rare conditions in which patients present with apparent allergic reactions and anaphylaxis to a variety of triggers. Characteristic skin findings are helpful in diagnosis. These disorders are reviewed separately. (See "Mastocytosis (cutaneous and systemic) in adults: Epidemiology, pathogenesis, clinical manifestations, and diagnosis".)

- **Systemic lupus erythematosus, rheumatoid arthritis, Sjögren's disease, celiac disease, autoimmune thyroid disease, and other autoimmune diseases** – Urticaria may be a presenting manifestation or occur sporadically over time in patients with autoimmune conditions [36]. The etiology of this remains unclear but may be due to direct mast cell activation via complement receptors or due to the generation of autoantibodies that may result in anaphylactoid degranulation. Screening for these disorders in the setting of an acute episode of urticaria is not indicated, unless there are other preceding symptoms that suggest that one of these disorders may be present.

- **Cutaneous small vessel vasculitis** – Some forms of cutaneous small vessel vasculitis can appear urticarial during early stages. Urticarial lesions that are persistent in a single location for >24 hours, have bruising, are painful, or are accompanied by systemic symptoms (eg, fever) should raise a concern for vasculitis.

  - Urticarial vasculitis is a disorder characterized by urticarial lesions with vasculitic findings on skin biopsy (picture 6). The disorder may be systemic or limited to the skin. (See "Urticarial vasculitis".)

  - Immunoglobulin A (IgA) vasculitis (Henoch-Schönlein purpura) is a systemic vasculitis with a prominent cutaneous component characterized by purpuric lesions, particularly involving the lower extremities. The skin lesions can be urticarial initially, although the development of systemic disease with arthralgias, abdominal pain, and renal involvement should prompt investigation for this condition. (See "IgA vasculitis (Henoch-Schönlein purpura): Clinical manifestations and diagnosis", section on 'Skin manifestations'.)

  - Patients with lupus may also develop urticarial lesions that persist and become vasculitic. Skin biopsy may show evidence of vasculitis. (See "Overview of cutaneous lupus erythematosus".)

- **Malignancies** – Urticaria may also be seen with malignancies, especially immunoglobulin M (IgM) and sometimes immunoglobulin G (IgG) paraproteinemias. The etiology is also unclear but may be due to complement-mediated pathways. In these cases, the urticaria is persistent and becomes chronic. (See "Chronic spontaneous urticaria: Clinical manifestations, diagnosis, pathogenesis, and natural history", section on 'Unclear association with malignancy'.)

The urticaria associated with systemic disorders is usually recurrent, persistent, and relatively difficult to treat, so patients with these disorders typically present with chronic urticaria. Clinical features that can help distinguish these disorders from uncomplicated chronic urticaria are reviewed separately. (See "Chronic spontaneous urticaria: Clinical manifestations, diagnosis, pathogenesis, and natural history", section on 'Differential diagnosis'.)

EVALUATION AND DIAGNOSIS

Urticaria is diagnosed clinically, based upon a detailed history and physical examination confirming the presence of characteristic skin lesions [37-40].

Clinical history — The clinical history should determine the following:

- Were there other signs and symptoms of a generalized allergic reaction or anaphylaxis? Patients may fail to report more subtle symptoms unless specifically asked. The clinician should ask about chest tightness or difficulty breathing, hoarse voice or throat tightness, nausea, vomiting, crampy abdominal pain, lightheadedness, and other symptoms of anaphylaxis (table 2). (See "Anaphylaxis: Emergency treatment".)

- Has the patient had hives previously in the past? Some children develop acute urticaria repeatedly with infections. Adults may develop urticaria following nonsteroidal anti-inflammatory drug (NSAID) ingestion but may not recognize the association until it has occurred several times. Does the patient have other allergic disorders?

- Were there any symptoms or signs to suggest an underlying systemic disorder? Specifically, has the patient recently had unexplained fever, weight loss, arthralgias, arthritis, or bone pain [41,42]? Diseases that may include hives as part of the clinical presentation are reviewed separately. (See 'Systemic disorders that may include urticaria' above.)

- Is a possible etiology apparent from the patient's history (table 1)? (See 'Etiologies' above.)

  - Was the patient in his/her usual state of health when the hives appeared or has the patient been ill recently with viral or bacterial infections? Has the patient experienced any recent health events, such as musculoskeletal injuries for which he/she was taking NSAIDs or new diagnoses requiring unfamiliar medications or treatments?

  - The patient should be asked to review events in the hours before the urticaria appeared. What had the patient ingested (foods, beverages, candy)? Was the patient involved in exercise or physical exertion? Was the patient exposed to extremes of temperature or stung by an insect? The answers may reveal clues to allergic or physical causes of urticaria.

  - Patients should be questioned about any new medications or supplements in the preceding days or weeks [43,44]. Were any medications taken in the hours before the urticaria appeared?

  - Inquiries should be made about recent travel (and symptoms of parasitic infection) and sexual history. (See 'Infections' above.)

  - A complete review of systems is valuable in the patient with new-onset urticaria.

Physical examination — Lesions should be visualized directly in order to make the diagnosis with certainty, since the term "hives" is used nonspecifically by patients. If the patient has no lesions at the time of evaluation, showing patients photographs of urticaria and asking if their lesions look similar can be helpful, although the diagnosis will need to be confirmed at some point in the future (picture 2).

Individual urticarial lesions usually appear and resolve completely within 24 hours. If the patient is unsure of the duration of the lesions, a lesion can be circled with a pen and time to resolution noted.

Laboratory studies — Laboratory studies are typically normal in patients who lack any history or physical findings to suggest an underlying disease process [3].

- For patients presenting with new-onset urticaria (with or without angioedema) in whom the clinical history and physical exam do **not** suggest an underlying disorder or urticarial vasculitis, international, European, and British practice parameters state that laboratory testing is not indicated [45-47]. American practice parameters state that a limited evaluation "may be considered" in such patients, primarily for the purpose of detecting underlying disorders earlier in the one-third of patients in whom urticaria will prove persistent (ie, initial presentation of chronic urticaria) [48]. In this setting, complete blood count with differential, urinalysis, erythrocyte sedimentation rate, and liver function tests are suggested. However, the author's approach is to obtain these tests in patients with persistent symptoms.

- In patients in whom a specific etiology is suspected, laboratory studies and further evaluation should be directed at establishing or excluding that cause. (See 'Etiologies' above.)

Tests for allergic causes — An allergic cause is possible if the clinical history reveals a specific trigger to which the patient was exposed shortly before the onset of symptoms (usually within one to two hours). If the history does suggest a possible allergy, serum tests for allergen-specific immunoglobulin E (IgE) antibodies are appropriate, if commercially available. For example, if a patient who does not normally eat seafood but did so at a special occasion develops hives within 10 minutes of eating a crab cake, it would be reasonable to obtain a crab-specific IgE test, particularly if there were no other new foods ingested and the patient is avoiding seafood for fear of a repeat reaction. However, the interpretation of allergy tests can require some expertise. A positive result is suggestive, although not diagnostic, of allergy, and a negative result does not exclude allergy. Because of this, we suggest that patients suspected of having an allergy be referred to an allergist/immunologist for further evaluation when possible.

Skin tests with fresh food, which should be performed by an allergy specialist, is probably the most convenient, inexpensive, and sensitive way to detect food hypersensitivity. (See 'Referral' below and "Overview of in vitro allergy tests".)

DIFFERENTIAL DIAGNOSIS

The conditions discussed in this section are those that may mimic various features of urticaria [49]. The presence or absence of pruritus is a helpful clinical feature that can be used to narrow the differential.

Pruritic conditions — Pruritic conditions that are more likely to be confused with urticaria are discussed here. An overview of the causes of pruritic dermatoses is found separately. (See "Pruritus: Etiology and patient evaluation".)

- **Atopic dermatitis** – Atopic dermatitis is a common disorder that presents initially as intensely pruritic erythematous patches with papules and some scaling. In children, the face, scalp, extremities, or trunk are typically involved, while the diaper area is spared. In older children and adults, the flexural areas (neck, antecubital fossae, and popliteal fossae) are most commonly involved. Other sites include the face, wrists, and forearms (picture 8). Erythematous areas of involvement last for days or weeks and have ill-defined borders. Scaling and xerosis develop with time. (See "Atopic dermatitis (eczema): Pathogenesis, clinical manifestations, and diagnosis".)

- **Contact dermatitis** – Contact dermatitis refers to any dermatitis arising from direct skin exposure to a substance. The dermatitis may either be allergic or irritant-induced. The latter is more common. Contact dermatitis is an erythematous, papular dermatitis, often with areas of vesiculation (picture 9). It is distributed in the areas of direct contact. (See "Allergic contact dermatitis in children" and "Irritant contact dermatitis in adults" and "Common allergens in allergic contact dermatitis".)

- **Drug eruptions** – Drug eruptions, also called morbilliform or exanthematous drug eruptions, are cutaneous drug reactions that closely mimic viral exanthems but occur in association with a medication. These dermatoses may or may not be pruritic and begin as small macules and/or papules that become larger and confluent with time (picture 10). The individual lesions are persistent, unlike urticaria. (See "Drug eruptions".)

- **Insect bites** – Insect bites produce individual lesions that persist for days in most cases (see "Insect and other arthropod bites"). However, the stings of some insects can cause

true urticaria as part of a systemic allergic reaction. (See 'IgE-mediated allergic reactions' above.)

- **Bullous pemphigoid** – In older adults, bullous pemphigoid may start with pruritus, with or without urticarial lesions. Blistering usually becomes evident eventually. (See "Clinical features and diagnosis of bullous pemphigoid and mucous membrane pemphigoid", section on 'Clinical features of bullous pemphigoid'.)

- **Erythema multiforme minor** – Erythema multiforme minor is a syndrome characterized by erythematous, iris-shaped macules and vesiculobullous lesions with a target appearance (picture 11). The lesions may be painful or pruritic and distributed symmetrically on the extensor surfaces of the extremities (particularly the palms and soles). Individual lesions last several days, unlike urticaria. There may be accompanying fever and malaise. (See "Erythema multiforme: Pathogenesis, clinical features, and diagnosis".)

- **Plant-induced reactions** – Poison ivy and poison oak can present with urticaria-like lesions initially that evolve into vesicular lesions. (See "Poison ivy (*Toxicodendron*) dermatitis".)

Nonpruritic conditions — Nonpruritic conditions that may resemble acute urticaria include viral exanthems, the skin changes of auriculotemporal syndrome, and Sweet syndrome.

- **Viral exanthems** – Viral exanthems are common in children and can occur with many different infections, including erythema infectiosum (fifth disease), Epstein-Barr virus, enteroviruses, and measles. However, viral exanthems are generally not pruritic and usually consist of erythematous maculopapular eruptions that persist for days. Fever is often present. The macules are relatively fixed compared with urticarial lesions, which continually change, with new lesions appearing as older lesions resolve. (See topic reviews on specific infections.)

- **Auriculotemporal syndrome** – Auriculotemporal syndrome is a nonpruritic flushing and/or sweating of the skin over the cheeks or jawline (the areas supplied by the auriculotemporal nerve) that occurs transiently after eating and may be mistaken for urticaria associated with food allergy [50]. It can be seen in children or adults and may develop following damage to the nerve secondary to forceps delivery, viral infection, surgery, or other local trauma. Unilateral distribution is typical, although bilateral cases have been reported [51].

- **Sweet syndrome** – Sweet syndrome is an uncommon disease characterized by recurrent episodes of painful, long-lasting inflammatory papules and plaques associated with fever, arthralgias, and peripheral leukocytosis (picture 12). There may be a history of a febrile illness one to three weeks before the onset of skin lesions in some cases. (See "Sweet syndrome (acute febrile neutrophilic dermatosis): Pathogenesis, clinical manifestations, and diagnosis".)

TREATMENT

Initial treatment of new-onset urticaria (with or without angioedema) should focus on the short-term relief of pruritus and angioedema, if present. Approximately two-thirds of cases of new-onset urticaria will be self-limited and resolve spontaneously. The literature on management of acute urticaria is sparse, probably because the condition is so often self-limited [52]. The agents discussed below have mostly been evaluated in the treatment of chronic urticaria, and in some cases, their use in acute urticaria is extrapolated from those studies, which are presented separately. (See "Chronic spontaneous urticaria: Standard management and patient education".)

H1 antihistamines — H1 antihistamines may be divided into older, first-generation agents (eg, diphenhydramine, chlorpheniramine, hydroxyzine) and newer, second-generation agents (eg, cetirizine, loratadine, fexofenadine, others). Second-generation agents are preferred for both adults and children.

Second-generation agents — The newer, second-generation H1 antihistamines are recommended as first-line therapy by published guidelines from both allergy and dermatology expert panels [53,54]. These drugs are minimally sedating, are essentially free of the anticholinergic effects that can complicate use of first-generation agents, have few significant drug-drug interactions, and require less frequent dosing compared with first-generation agents [55-59]. Second-generation agents can be sedating if combined with alcohol, so this should be avoided. Interactions with food are noted below. We know of no data demonstrating that any specific agent is more effective than another for the treatment of acute urticaria, although a few studies in patients with chronic urticaria suggest that cetirizine and levocetirizine may be modestly more effective than other agents. (See "Chronic spontaneous urticaria: Standard management and patient education", section on 'Agents and efficacy studies'.)

Some patients require higher than standard doses (shown below in parentheses) for control of urticarial symptoms and may experience drowsiness at these higher doses. Caution is therefore warranted until effects upon the individual are understood. The higher doses may have better

efficacy in some adults, although this has not been conclusively demonstrated. Studies of higher-dose antihistamines for chronic urticaria are reviewed separately. (See "Chronic spontaneous urticaria: Standard management and patient education", section on 'H1 antihistamines'.)

Treatment with H1 antihistamines results in clearance of the lesions in some patients, but in others, treatment may only achieve flattening of the lesions and reduction in pruritus, with persistence of erythematous macules. Patients in the latter group can begin to reduce medications after the erythematous lesions clear.

Second-generation H1 antihistamines include the following:

- **Cetirizine** – Cetirizine demonstrates a rapid onset of action and some mast cell-stabilizing activity. It can be mildly sedating, in a dose-dependent manner, although less so than first-generation agents. It is available in both intravenous (in some countries) and oral formulations, and the dosing is similar for either route of administration. Intravenous doses should be administered over one to two minutes. The standard oral or intravenous dose of 10 mg once daily is appropriate for adults and children aged 12 years and older (and may be increased to 10 mg twice daily in adults if needed).

  Children six years of age and older can receive 5 mg or 10 mg. The usual dose for children aged two to five years is 5 mg once daily. Smaller children aged six months to two years may be given 2.5 mg once daily (can be increased to 2.5 mg twice daily in children one year and older if needed). The maintenance dose for patients with significant renal and/or hepatic insufficiency should be reduced by one-half.

- **Levocetirizine** – Levocetirizine is an active enantiomer of cetirizine that produces effects equivalent to cetirizine at about one-half of the dose. For adults and children 12 years and older, the standard dose is 5 mg once daily in the evening (or up to 5 mg twice daily in adults if needed) or 2.5 mg once daily in the evening for children aged 6 to 11 years. Levocetirizine is unlikely to be effective as an alternative for patients who did not have an adequate response to cetirizine, and its sedative effects are similar to those of other second-generation antihistamines [60]. Dose reductions are necessary in renal insufficiency.

- **Loratadine** – Loratadine is a long-acting, selective H1 antihistamine. The standard dose is 10 mg once daily for ages six years and older, which is minimally sedating. It can be increased up to 10 mg twice daily in adults if needed. For children aged two to five years, the usual dose is 5 mg once daily. For patients with significant renal and/or hepatic insufficiency, the usual dose is administered every other day.

- **Desloratadine** – Desloratadine is the major active metabolite of loratadine and produces effects equivalent to loratadine at about one-half the dose. For adults and children 12 years and older, the standard dose is 5 mg once daily (or up to 5 mg twice daily in adults if needed).

  For children aged 6 to 11 years, the dose is 2.5 mg once daily, and for those aged 1 to 5 years, the dose is 1.25 mg once daily. A lower dose of 1 mg once daily is approved in the United States for small children aged 6 months to 1 year. For patients with significant renal and/or hepatic insufficiency, the usual dose is administered every other day.

- **Fexofenadine** – Fexofenadine is minimally sedating. The suggested dose is 180 mg daily for ages 12 years and older (or up to twice daily in adults if needed) or 30 mg twice daily for children aged 2 to 11 years. A lower dose of 15 mg twice daily is approved in the United States for small children aged six months to two years. For patients with significant renal insufficiency, the adult dose should be reduced to 60 mg once daily. It is best taken without food and specifically not with fruit juices.

There are additional nonsedating antihistamines that are available in many countries, although not in the United States:

- **Ebastine** – Ebastine is a nonsedating antihistamine that is licensed for use in children older than 12 years of age and adults. The usual dose is 10 mg daily, but it can be doubled to 20 mg daily if needed, although not in patients with liver insufficiency. One study of patients with acute urticaria found that 20 mg of ebastine was similar in efficacy to 5 mg of levocetirizine and caused fewer adverse effects [61].

- **Bilastine** – Bilastine is a nonsedating antihistamine with efficacy similar to cetirizine and higher than that of fexofenadine [62]. The initial dose is 20 mg daily for children older than 12 years of age and adults. Bioavailability is reduced approximately 30 percent by grapefruit juice, ketoconazole, or erythromycin, and it should not be taken with food. The drug minimally crosses the blood-brain barrier (because it is a zwitterion), does not cause somnolence, and is not affected by alcoholic beverages [63].

- **Rupatadine** – Rupatadine antagonizes both histamine and platelet-activating factor (PAF) receptors [64]. It is licensed at a dose of 10 mg daily for patients older than 12 years of age, although it is safe in patients older than 2 years of age [65]. As is the case for bilastine, the drug should not be taken with grapefruit juice, ketoconazole, or erythromycin, but (unlike bilastine) it is not affected by food.

First-generation agents — The first-generation antihistamines include diphenhydramine, chlorpheniramine, hydroxyzine, and others [66]. These agents are lipophilic and readily cross the blood-brain barrier, causing sedating and anticholinergic side effects that may be dose-limiting in some patients. Significant sedation and impairment of performance (eg, fine motor skills, driving skills, and reaction times) occur in more than 20 percent of patients [67]. Anticholinergic side effects include dry mouth, diplopia, blurred vision, urinary retention, or vaginal dryness. Patients should be warned specifically about these adverse effects. Despite these adverse effects, patients at low risk of complications (eg, young, healthy patients) may find a sedating H1 antihistamine at bedtime helpful, especially when combined with a nonsedating H1 antihistamine during the day.

Some first-generation H1 antihistamines are available in parenteral preparations for use in patients in whom a more rapid onset of action is desired, such as those who have presented to the emergency department. Parenteral dosing of the first-generation agents is:

- **Diphenhydramine** – The dose in adults is 25 to 50 mg given by slow intravenous (IV) administration or intramuscular (IM) injection every four to six hours as needed. Children may receive 0.5 to 1.25 mg/kg (up to 50 mg per dose) IV/IM every six hours as needed.

- **Hydroxyzine** – The dose in adults is 25 to 50 mg deep IM administration in adults every six hours as needed. Do not administer intravenously. Children may receive 0.5 to 1 mg/kg (up to 50 mg per dose) IM every six hours as needed.

Pregnant and lactating patients — Pregnant patients may be treated initially with loratadine (10 mg once daily) or cetirizine (10 mg once daily). There are reassuring human data for each of these drugs in a large number of pregnant patients [68]. The first-generation agent chlorpheniramine, 4 mg orally every four to six hours, may also be safely used in pregnancy [69,70]. Safety issues surrounding the use of antihistamines in pregnancy are reviewed separately. (See "Recognition and management of allergic disease during pregnancy", section on 'Oral antihistamines'.)

Lactating patients may be treated with either cetirizine or loratadine (both are dosed at 10 mg once daily), which are minimally excreted in breast milk and should not cause sedation or poor feeding in the infant. (See "Pharmacotherapy of allergic rhinitis", section on 'Breastfeeding'.)

H2 antihistamines — There are very few data examining the use of H2 antihistamines for acute urticaria, but the practice is supported by one randomized trial of 91 adults presenting to an emergency department with acute allergic reactions [71]. Subjects received 50 mg IV diphenhydramine with either placebo or 50 mg IV ranitidine. At two hours, the number of patients in whom urticaria had resolved was statistically greater in the ranitidine group

compared with the placebo group (25 of 29 and 13 of 24, respectively). Options for H2 antihistamines include nizatidine, famotidine, ranitidine (no longer available in the US), and cimetidine, although caution should be used with cimetidine, since it can increase levels of other drugs. (See "Antiulcer medications: Mechanism of action, pharmacology, and side effects".)

Studies of the use of H2 antihistamines in chronic urticaria are conflicting and are reviewed elsewhere [72-74]. (See "Chronic spontaneous urticaria: Standard management and patient education", section on 'H2 antihistamines'.)

Glucocorticoids — Glucocorticoids do not appear to be necessary for isolated urticaria. However, a brief course (ie, usually a week or less) of systemic glucocorticoids may be added to antihistamine therapy for patients with prominent angioedema or if symptoms persist beyond a few days. Glucocorticoids do not inhibit mast cell degranulation but may act by suppressing a variety of contributing inflammatory mechanisms.

A small number of trials have examined the utility of glucocorticoids in the management of acute urticaria [75-77]. In the largest study, the addition of prednisone to levocetirizine did not speed resolution of acute urticaria. In this randomized trial, 100 adults presenting to the emergency department with urticaria of ≤24 hours duration without angioedema, anaphylaxis, or fever, were treated with the H1 antihistamine levocetirizine (5 mg once daily for five days) plus either placebo or prednisone (40 mg once daily for four days) and followed by phone for several days [77]. The primary endpoint was complete relief of itching two days after the start of therapy, and secondary endpoints included resolution of skin lesions, relapses, and adverse events. Most subjects had resolution of itch by day 2, with a slightly lower percentage itch-free in the prednisone group (79 versus 67 percent). Similarly, by day 2, skin lesions had resolved entirely in 78 and 70 percent of those in the placebo and prednisone groups, respectively. Thus, the addition of prednisone to levocetirizine did not speed resolution of acute urticaria. Between one-quarter and one-third of patients experienced relapse in both groups, generally within the first few days of therapy. Another smaller randomized trial found that glucocorticoids were helpful when added to antihistamines, although the antihistamine regimen used in that study (hydroxyzine 25 mg orally every four to eight hours) may have been more difficult to adhere to [75].

The optimal agent and dose have not been determined for acute urticaria, but we typically administer:

- In adults – Prednisone 30 to 60 mg daily, with tapering of the dose over five to seven days

- In children – Prednisolone 0.5 to 1 mg/kg/day (maximum 60 mg daily), with tapering of the dose over five to seven days

Antihistamine therapy should be continued during and after the course of glucocorticoids because some patients experience an exacerbation as the glucocorticoids are tapered or discontinued. If symptoms do not recur over several days after stopping glucocorticoids, then antihistamines can be discontinued also. For patients whose symptoms recur when medications are discontinued, antihistamines should be reinstituted and used at the lowest effective dose. Repeated courses of glucocorticoids should be avoided, as the risks of adverse effects outweigh the benefit for most patients (see 'Referral' below). The decision of prescribing gastrointestinal prophylaxis (eg, a proton pump inhibitor) during a systemic corticosteroid treatment depends essentially on the duration of therapy (that in this case should be as brief as possible) and the specific conditions of the patient (eg, prior chronic gastritis, gastric ulcers).

REFERRAL

Patients who are suspected of having an allergic etiology causing new-onset urticaria, such as a food or medication allergy, should be referred to an allergy specialist who will evaluated for possible causes and equip the patient with epinephrine for self-injection when indicated. These issues are discussed in detail separately. (See "Anaphylaxis: Emergency treatment", section on 'Discharge care'.)

PROGNOSIS

It should be explained to patients that about one-third of cases of new-onset urticaria will prove persistent and that if they continue to have ongoing symptoms after several weeks, they should seek re-evaluation in a primary care setting. Patients with difficult-to-control symptoms may also be referred to a dermatology or allergy specialist.

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Urticaria and angioedema (excluding hereditary angioedema)".)

INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topic (see "Patient education: Hives (The Basics)")
- Beyond the Basics topic (see "Patient education: Hives (urticaria) (Beyond the Basics)")

SUMMARY AND RECOMMENDATIONS

- **Prevalence and description** – Urticaria (also called hives or wheals) affect up to 20 percent of the population at some point in their lives. Urticarial lesions are intensely pruritic, circumscribed, raised, erythematous plaques, often with central pallor (picture 1). Morphology and size can vary (picture 2). Urticarial lesions typically develop over minutes to hours and resolve in hours to a day without residual markings. There may be accompanying angioedema, which is swelling deeper in the skin. (See 'Clinical manifestations' above and 'Epidemiology' above.)
- **Acute versus chronic** – Urticaria is classified as either acute or chronic. Acute urticaria is defined as periodic outbreaks of urticarial lesions that resolve within six weeks. Urticaria that persists beyond six weeks may represent the beginning of chronic urticaria, a disorder that is reviewed in detail separately. (See 'Categorization of urticaria' above and "Chronic spontaneous urticaria: Clinical manifestations, diagnosis, pathogenesis, and natural history".)
- **Possible triggers for new-onset urticaria** – A presumptive trigger, such as common viral and bacterial infections, medications, food ingestion, or insect sting, can sometimes be identified for new-onset urticaria. (See 'Etiologies' above.)

- **Systemic disorders that can involve urticaria** – Occasionally, urticaria may be the presenting feature of another systemic disorder, such as urticarial vasculitis, mastocytosis, or systemic lupus erythematous. There are specific clinical features that should prompt an evaluation for these conditions. (See 'Systemic disorders that may include urticaria' above.)

- **Diagnosis** – The diagnosis of urticaria is made clinically. A careful history should be performed to exclude possible anaphylaxis, identify a possible trigger, and determine if there are signs or symptoms to suggest urticarial vasculitis or an underlying systemic disorder. If the history does not suggest a specific trigger or underlying systemic illness, then laboratory tests are usually normal and not helpful. Some guidelines advocate obtaining a complete blood count with differential, urinalysis, erythrocyte sedimentation rate, and liver function tests at initial presentation, while others suggest no testing unless symptoms persist. (See 'Evaluation and diagnosis' above.)

- **Differential diagnosis** – Urticarial lesions are nearly always pruritic.

  - Other pruritic disorders that could be confused with urticaria include insect bites, atopic dermatitis, contact dermatitis, morbilliform drug eruptions, bullous pemphigoid, erythema multiforme minor, and plant-related dermatoses (eg, poison ivy). (See 'Pruritic conditions' above.)

  - Nonpruritic conditions that may resemble acute urticaria include viral exanthems, the skin changes of auriculotemporal syndrome, and Sweet syndrome. (See 'Nonpruritic conditions' above.)

- **Management** – The management of new-onset urticaria depends upon severity and associated angioedema.

  - In patients with mild symptoms of new-onset urticaria, we suggest treatment with a nonsedating H1 antihistamine alone (**Grade 2B**). Some patients may require higher than standard doses (eg, cetirizine 10 mg twice daily). In patients at low risk of complications from anticholinergic side effects (ie, healthy adults), use of a sedating H1 antihistamine at bedtime and a nonsedating H1 antihistamine during the day is a reasonable alternative. (See 'H1 antihistamines' above.)

  - In patients with persistent symptoms despite an H1 antihistamine or with prominent angioedema, we suggest adding a brief course of oral glucocorticoids (**Grade 2C**). We typically administer prednisone (30 to 60 mg daily) in adults or prednisolone (0.5 to 1 mg/kg/day) in children, tapered over five to seven days, while antihistamines are continued. (See 'Glucocorticoids' above.)

- **Prognosis** – Two-thirds of cases of urticaria (with or without angioedema) prove to be self-limited, resolving in days to a few weeks. Urticarial outbreaks that continue to occur after six weeks are classified as chronic. Patients with difficult to control symptoms that are persistent can be referred to an allergy or dermatology specialist.

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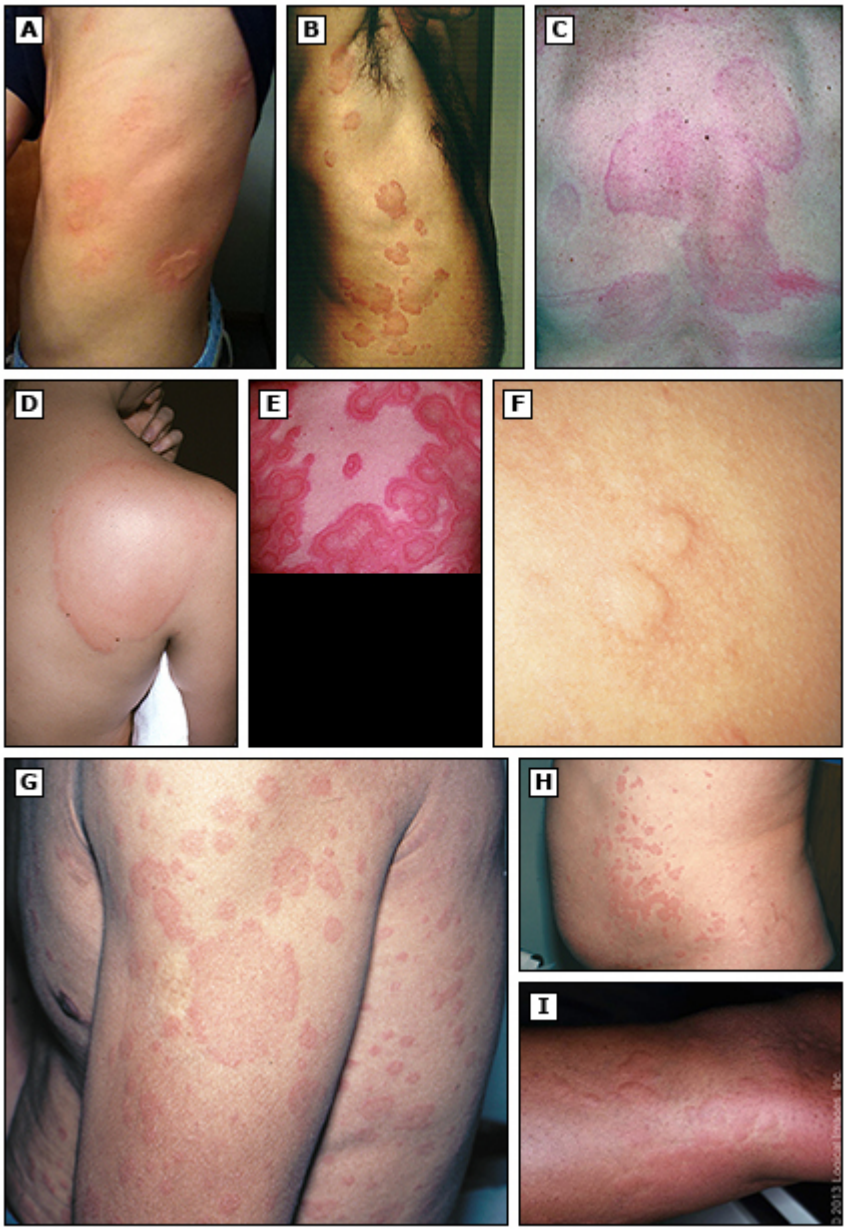
Topic 8101 Version 42.0

GRAPHICS

Acute urticaria on the trunk

Graphic 78544 Version 2.0

Urticaria - Multiple images



Multiple images of urticaria are shown. Urticarial lesions may be rounded (F) or irregular (A) in shape and uniform or mixed (G) in morphology. Individual lesions may be small (H) or large (D). Urticaria are raised plaques, although they may appear flattened in patients taking antihistamines (C). Although lesions are consistently erythematous, this may be difficult to appreciate on darkly pigmented skin (I). Some urticaria show central clearing (E).

Panel B courtesy of Andrew Samel, MD.

Panels C, F, G, and H reproduced with permission from: Goodheart HP. Goodheart's Photoguide of Common Skin Disorders, 2nd ed, Lippincott Williams & Wilkins, Philadelphia 2003. Copyright © 2003 Lippincott Williams & Wilkins.

Panel D courtesy of Lee T Nesbitt, Jr. The Skin and Infection: A Color Atlas and Text, Sanders CV, Nesbitt LT Jr (Eds), Williams & Wilkins, Baltimore, 1995.

Graphic 90166 Version 6.0

Confluent urticaria on child's abdomen

Urticaria often coalesce as individual lesions enlarge.

Graphic 115270 Version 1.0

Confluent urticaria on young child

Graphic 115231 Version 2.0

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.

Graphic 54872 Version 3.0

Symptoms and signs of anaphylaxis

Skin
Feeling of warmth, flushing (erythema), itching, urticaria, angioedema, and "hair standing on end" (pilo erection)
Oral
Itching or tingling of lips, tongue, or palate
Edema of lips, tongue, uvula, metallic taste
Respiratory
Nose - Itching, congestion, rhinorrhea, and sneezing
Laryngeal - Itching and "tightness" in the throat, dysphonia, hoarseness, stridor
Lower airways - Shortness of breath (dyspnea), chest tightness, cough, wheezing, and cyanosis
Gastrointestinal
Nausea, abdominal pain, vomiting, diarrhea, and dysphagia (difficulty swallowing)
Cardiovascular
Feeling of faintness or dizziness; syncope, altered mental status, chest pain, palpitations, tachycardia, bradycardia or other dysrhythmia, hypotension, tunnel vision, difficulty hearing, urinary or fecal incontinence, and cardiac arrest
Neurologic
Anxiety, apprehension, sense of impending doom, seizures, headache and confusion; young children may have sudden behavioral changes (cling, cry, become irritable, cease to play)
Ocular
Periorbital itching, erythema and edema, tearing, and conjunctival erythema
Other
Uterine cramps in women and girls

Original figure modified for this publication. Simons FER. Anaphylaxis. J Allergy Clin Immunol 2010; 125:S161. Table used with the permission of Elsevier Inc. All rights reserved.

Symptoms and signs of anaphylaxis in infants*

Anaphylaxis symptoms that infants cannot describe	Anaphylaxis signs that are potentially difficult to interpret in infants and why	Anaphylaxis signs in infants: Obvious but may be nonspecific
General		
Feeling of warmth, weakness, anxiety, apprehension, impending doom	Nonspecific behavioral changes, such as persistent crying, fussing, irritability, fright	
Skin/mucus membranes		
Itching of lips, tongue, palate, uvula, ears, throat, nose, eyes, and so forth; mouth-tingling or metallic taste	Flushing (may also occur with fever, hyperthermia, or crying spells)	Rapid onset of hives (potentially difficult to discern in infants with acute atopic dermatitis; scratching and excoriations, as such, will be absent in young infants); angioedema (face, tongue, oropharynx)
Respiratory		
Nasal congestion, throat tightness; chest tightness; shortness of breath	Hoarseness, dysphonia (common after a crying spell); drooling, increased secretions (common in infants)	Rapid onset of coughing, choking, stridor, wheezing, dyspnea, apnea, cyanosis
Gastrointestinal		
Dysphagia, nausea, abdominal pain/cramping	Spitting up/regurgitation (common after feeds), loose stools (normal in infants, especially if breastfed); colicky abdominal pain	Sudden, profuse vomiting
Cardiovascular		
Feeling faint, presyncope, dizziness, confusion, blurred vision, difficulty in hearing, palpitations	Hypotension; measured with an appropriate size blood pressure cuff, low systolic blood pressure for infants is defined as less than 70 mmHg from age 1 month to 1 year and less than (70 mmHg + [2 x age in years]) in the first and second years of life; tachycardia, defined as greater than 120 to	Weak pulse, arrhythmia, diaphoresis/sweating, pallor, collapse/unconsciousness

	130 beats per minute from the third month to second year of life inclusive; loss of bowel and bladder control (ubiquitous in infants)	
Central nervous system		
Headache	Drowsiness, somnolence (common in infants after feeds)	Rapid onset of unresponsiveness lethargy, or hypotonia; seizures

* More than one body system involved.

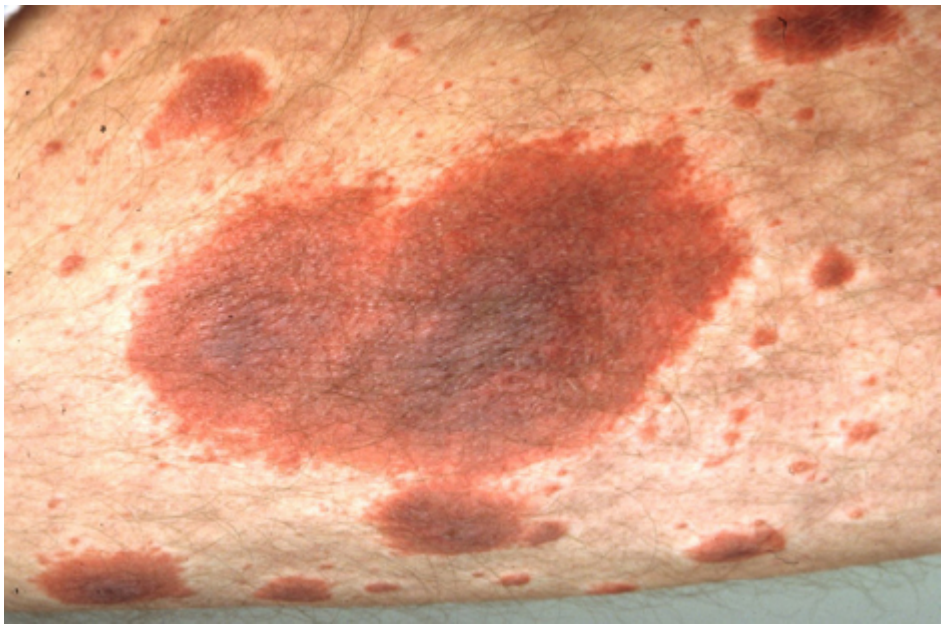
From: Simons FER. Anaphylaxis in infants: Can recognition and management be improved? J Allergy Clin Immunol 2007; 120:537.

Graphic 64957 Version 7.0

Urticarial drug eruption

Graphic 75230 Version 3.0

Urticarial vasculitis



Urticarial patch with central ecchymosis.

Graphic 54877 Version 3.0

Urticarial vasculitis

Annular patch with elevated borders.

Graphic 66203 Version 2.0

Urticarial vasculitis

Discrete and confluent urticarial patches with unusual annular and semi-annular features.

Graphic 77924 Version 3.0

Atopic dermatitis

Severe atopic dermatitis in a 12-year-old child showing in the typical location of the popliteal fossae. Note the oozing of serous fluid from the most involved areas plus the papular component and erythema.

Courtesy of Scott Walsh, MD, FRPCP.

Graphic 65407 Version 3.0

Allergic contact dermatitis

Allergic contact dermatitis is characterized by an erythematous, papular dermatitis with indistinct margins, distributed in areas of exposure.

Courtesy of James C Shaw, MD.

Graphic 71913 Version 1.0

Exanthematous (morbilliform) drug eruption

Drug-induced exanthems, such as this morbilliform eruption, often begin in dependent areas and generalize.

Courtesy of Andrew Samel, MD.

Graphic 70062 Version 5.0

Erythema multiforme

Characteristic target lesions of the palm in erythema multiforme begin with a central vesicle.

Courtesy of Nesbitt LT Jr. The Skin and Infection: A Color Atlas and Text, Sanders CV, Nesbitt LT Jr (Eds), Williams & Wilkins, Baltimore 1995.

Graphic 74095 Version 6.0

Sweet syndrome

A sudden, painful eruption that developed in a 50-year-old female who was febrile and had general malaise. There are multiple very edematous and erythematous papules and plaques, most of which appear vesicular or bullous on initial examination, but are firm with palpation (pseudovesiculation). However, the confluent lesions in the lower part of the picture are indeed bullous and here there is also exudation and crusting. Systems review in this patient revealed myelocytic leukemia.

Graphic 61290 Version 2.0