The clinical presentations of urticaria

Anne Kobza Black

Urticaria is a common skin condition. Although an episode may be mild and last only a few days, chronic urticaria can significantly affect the quality of life. The condition is frequently misunderstood by patients who believe the condition is always the result of an allergy and is dangerous.

Urticaria (nettle rash, hives, weals) and angio-oedema are a group of disorders characterized by short-lived swellings that can occur anywhere on the body (Greaves, 1995).

CLINICAL FEATURES

The weal is a pale, raised oedematous cutaneous lesion which is usually surrounded by erythema. Weals are often itchy, particularly when they first appear, and can be single or multiple, and of any size and shape, including rounded, annular and bizarre serpiginous patterns (*Figure 1*). Except for certain subsets of urticaria, they last for less than 24 hours fading through an erythematous macular stage to leave normal appearing skin without residual scaling or pigmentation. New lesions then usually occur elsewhere.

Angio-oedema (previously called angioneurotic oedema) is generally considered to be a form of transient swelling occurring in the deeper dermal, subcutaneous and submucosal tissues. Angio-oedema often affects loose tissue such as eyelids, lips (*Figure 2*), sometimes within the mouth, including tongue, pharynx

Figure 1. Weals of different sizes and shapes, lasting for less than 24 hours.

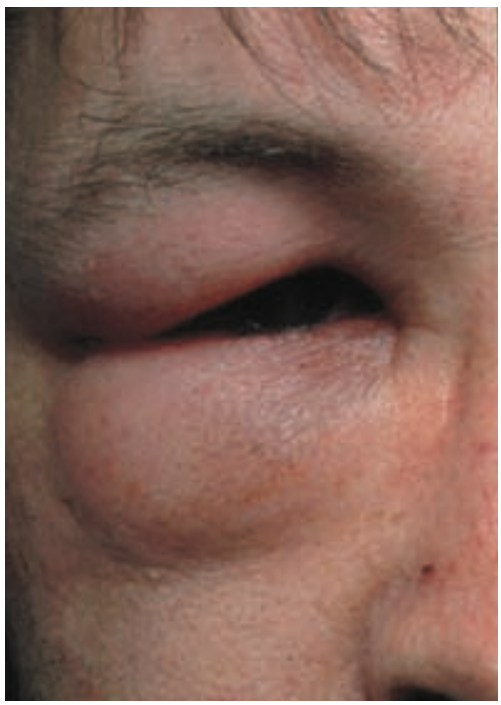

Figure 2. Angio-oedema of eyelids with sudden onset and resolving in 2 days.

Dr Anne Kobza Black is Senior Lecturer and Consultant Dermatologist, St John's Institute of Dermatology, Guys, Kings and St Thomas' School of Medicine, St Thomas Hospital, London SE1 7EH

and larynx, and sometimes mucous membranes. Lesions of angio-oedema may be skin-coloured or red, may itch and resolve within a few days. Urticaria and angio-oedema are essentially the same process, and coexist at some time in up to 50% of patients, with urticaria alone occuring in 40% and angio-oedema alone in 10%.

Patients with some forms of urticaria have associated systemic symptoms of flushing, arthralgia and gastrointestinal symptoms and lethargy. Occasionally in the most acute forms of urticaria, particularly from an allergic cause, there may be progression to anaphylaxis with respiratory embarrassment and syncope.

INCIDENCE

The majority of urticarias are probably not seen by doctors but several studies suggest that up to 15% of the population will have an episode of urticaria at some stage of their lives. The ratio of male to female sufferers is approximately 1.5:1.

QUALITY OF LIFE

The itching and wealing are often most severe at night, interfering with sleep. The onset of the swellings may be unpredictable and sometimes painful, leading to embarrassment and distress. Chronic urticaria patients in a specialist clinic perceived their quality of life to be similar to those with severe coronary disease awaiting a triple coronary bypass (O'Donnell et al, 1997).

DIAGNOSIS AND CLASSIFICATION

Patients will often present at a time when they have no visible lesions, so a diagnosis and classification of urticaria is dependent on a thorough history (Kozel et al, 1998) (*Table 1*), physical examination and investigations as appropriate.

Conventionally urticaria is classified by its duration and trigger factors (*Table 2*). In acute urticaria the disorder has been present for less than 6 weeks and in chronic urticaria for longer. Urticaria can also be intermittent, present at irregular intervals. This classification is of limited value, for although in acute urticaria a cause such as infection, medication or allergy may sometimes be detected, in the vast majority of urticarias no cause can be found.

Different forms of urticaria frequently coexist in the same patient, for example ordinary and physical urticaria or several types of physical urticaria.

Ordinary urticaria

This is the most common form, accounting for 75% of urticaria seen in dermatological practice. It is the term used when other forms of urticaria such as predominantly physical, contact and immune complex ones are excluded.

Although swelling of the lips and tongue can occur in ordinary urticaria it is rarely life threatening, except occasionally in acute allergic conditions following some foods (e.g. peanuts) and medications (e.g. penicillin).

The prognosis is variable but in a series of patients with chronic urticaria, resolution occurred in 50% in 1–2 years, although 20 years later 20% were still affected (Champion et al, 1969).

Predominantly physical urticarias

These account for up to 20% of all urticarias, and can be diagnosed from history and con-

TABLE 1.
Patient history

Pattern of episode(s)	Frequency and severity of episodes
	Any precipitating factor in the precious 2 weeks, e.g. febrile illness, ingestion of drugs, or any suspected food or alcohol, any physical factors (such as friction/pressure on the skin, heat, cold, exercise, sunlight)
History of individual lesions	Appearance — what are they like, are they itchy, painful or bruised
	How long do they last? If they persist for over 24 hours suspect urticarial vasculitis and delayed pressure urticaria
	Sites affected, e.g. pressure areas, exposed areas only (e.g. cold or solar urticaria)
	Any angiooedema especially of mouth/throat/tongue with respiratory embarrassment,
Other symptoms	Associated with swellings, e.g. fainting, wheezing, abdominal or joint pain
	Any other symptoms generally
	Any other medical problems?
Therapy	Treatments used and response
Family history	Urticaria, angiooedema or recurrent abdominal pain (hereditary angiooedema): atopy

firmed by appropriate challenge. Weals appear predictably on the skin after a specific stimulus. This usually occurs within minutes at the site of challenge and usually resolve within 2 hours, except for cases of delayed pressure urticaria or rare forms of cold urticaria. Angio-oedema and systemic symptoms including flushing, palpitations, headache, wheezing and syncope can occur in any physical urticaria if the condition is severe or the challenge extreme.

Dermographism (literally skin writing): This is the commonest physical urticaria and can affect up to 5% of the population. In

TABLE 2.
Classification and clinical features of urticaria and angioedema

Classification	Clinical features			
Ordinary urticaria (75%)	Acute (episode less than 6 weeks)	Weals, of any shape or size occur anywhere on the body, and resolve within 24 hours		
		Weals do not bruise or leave residual staining, pigmentation and scaling		
	Chronic	Clinical features as for acute		
		50% associated with angio-oedema		
		40% associated with delayed pressure urticaria		
	Intermittent			
Physical urticarias (20%)	These occur reproducibly following a specific physical stimulus			
	Dermographism (common)	Very itchy skin, weals within minutes at sites of trauma; often linear at sites of scratching, last less than 1 hour		
		Firm stroking of skin induces itchy weals at the site within minutes lasting less than an hour		
	Delayed pressure urticaria	Itching and sometimes painful weals occurring after a few hours at sites of sustained pressure from tight clothes or shoes or gripping tools, e.g. at waistline, on palms and soles, can last more than 24 hours		
		Associated nearly always with ordinary urticaria		
	Vibratory angioedema (very rare)	Vibration induces itchy red swellings at these sites lasting an hour		
		Application of a laboratory whorly mixer induces swellings at sites near stimulated site		
	Cholinergic urticaria	Small itchy symmetrical weals with flare predominantly on upper trunk but may be widespread within minutes following exercise, hot bath, emotional stress, and lasting less than 1 hour		
		Exercise till sweating or a hot bath induces characteristic weals within minutes		
	Localized contact heat urticaria (very rare)	Local heat application to the skin induces itching, redness, and wealing localized to the application sites		
	Cold urticaria	Itching erythema and weals within minutes of cold exposure usually on exposed areas		
		Application of an ice cube for 15 minutes or less to the skin induces wealing at the site		
	Solar urticaria	Itching erythema and weals on areas exposed to sunlight within minutes of exposure, lasting less than 1 hour; may occur with artificial light		
	Aquagenic urticaria (rare)	Sparse itching weals on areas exposed to water of any temperature: other physical urticarias to be excluded; weals occur after a bath at body temperature		
		Do not confuse with aquagenic pruritus without skin signs		
Contact urticaria	Immunological	Urticaria within minutes of contact of allergen at the site; more common in atopics.		
		Reaction IgE mediated and may be severe and become generalized, e.g. latex, nuts		
	Non-immunological	Often itching erythema only, sometimes wealing at site of contact, e.g. preservatives such as sorbic acid in food		
Urticarial vaculitis (5%)		Weals may last longer than 48 hours, may be painful and sometimes bruise. Confirm with biopsy. Systemic symptoms of arthralgia or abdominal pain may be present. There may be pulmonary involvement, renal, rarely eye and other organ involvement. The pathogenesis is thought to be immune complex mediated, but the antigen is usually unknown: rarely caused by lupus erythematosus or Sjögren's disease, infections		
Angiooedema	May be associated with any of the above groups of urticaria			
	If only/predominantly angio-oedema exclude C1 esterase inhibitor deficiency angio-oedema	C4 low and functional C1 esterase inhibitor low. C1 esterase inhibitor deficiency angio-oedema may be brought on by trauma such as surgery, dentistry and contact sport; may be associated with abdominal pain	Hereditary	Some may be new mutations and not have a family history, C1q normal
			Acquired (C1q usually low)	May be caused by consumption in lymphoreticular malignancy, lupus May be caused by an autoantibody directed against C1 esterase inhibitor

Combinations of different types of urticarias are common. IgE = immunoglobulin E

symptomatic dermographism the skin is very itchy and on application of moderate shearing force of the skin, such as scratching, wealing occurs at the site lasting for less than 1 hour (Breathnach et al, 1983) (*Figure 3*). It occasionally follows penicillin allergy or scabies infestation, but is nearly always idiopathic. Dermographism is not associated with any systemic disease. It commonly affects young healthy adults, and although there is a tendency to improvement the condition can last for many years.

Delayed pressure urticaria: This is a disabling disorder, characterized by the appearance of red painful swellings on the skin at the site of application of sustained pressure after a delay of several hours (Barlow et al, 1993). These commonly appear at sites of tight clothing such as at the waistline, on the soles of the feet after walking and on the hands after using tools. The swellings may take several days to subside and can be severe enough to inhibit walking or carrying out physical work. There may be associated flu-like symptoms and muscle ache. Up to 40% of patients with ordinary urticaria have an element of delayed pressure urticaria if questioned appropriately. The severity may vary with time and may be responsible for lack of improvement with antihistamine therapy. The prognosis of this condition is unpredictable, but it can last for many years.

Vibratory angio-oedema: This is extremely rare. There is a congenital and acquired form (Lawlor et al, 1989) which are clinically similar. Vibration of any sort such as jogging or rough towelling induces itching swellings within minutes at the skin site. It is generally not a severe condition or associated with any systemic disease.

Cholinergic urticaria: Cholinergic urticaria is a common physical urticaria, occurring up to 11% of young adults. It occurs in response to a rise in core body temperature, for example after exercise, a hot bath, immediately after emotional stress or eating spicy food. Itching erythematous macules and small monomorphic weals appear symmetrically on the trunk, but may be widespread and coalesce (Hirschmann et al, 1987) (*Figure 4*). Occasionally there may be associated angio-oedema, and cholinergic urticaria can be a cause of exercise-induced anaphylaxis. Very occasionally there is a food-dependant exercise-induced urticaria and angio-oedema. Here exercise within a few hours of eating either a particular food or any food induces urticaria, when neither the food(s) alone or exercise alone can induce the lesions.

Figure 3. Weals occurring within 5 minutes of writing firmly on the back.

Cholinergic urticaria is more common in young atopic adults. It can be mild, but often it significantly disrupts physical activities. Although there is a tendency towards improvement it can last for many years.

Heat contact urticaria: This is an extremely rare form of urticaria where local application of heat induces wealing within minutes at the site only, in contrast to cholinergic urticaria (Higgins and Friedman, 1991).

Figure 4. Small itching weals occurring within minutes of exercise, lasting less than 1 hour.

Cold urticaria: The vast majority are idiopathic cold contact urticarias (Wanderer, 1990). Here exposure to cold (*Figure 5*) induces itching and wealing at the exposed sites lasting up to 1 hour. Handling cold objects and drinking cold liquids can induce symptoms. Widespread wealing with systemic symptoms, anaphylaxis and drowning have occurred after bathing in cold water, which must be avoided. In a rarer form generalized cooling of the body, rather than local skin cooling, is necessary to induce generalized wealing. Here local application of an ice cube does not induce wealing.

Solar urticaria: This is a rare condition when exposure to natural or artificial sunlight and visible radiation induces itching and wealing in exposed areas (Leenutaphong et al, 1989). The condition is usually idiopathic, and can be severe and difficult to treat.

Aquagenic urticaria: This is also rare. Contact of the skin with water of any temperature induces itching weals within minutes lasting up to 1 hour (Sibbald et al, 1981). There are no symptoms from drinking water. Other factors related to the temperature (cold and cholinergic urticaria) and force (dermographism) of the water must be excluded. Aquagenic urticaria is not associated with any systemic disease.

It must not be confused with aquagenic pruritus where there is severe itching in contact with water of any temperature without any skin signs. Patients with aquagenic pruritus need long-term follow up as some may develop haematological abnormalities (Steinman and Greaves, 1985).

Figure 5. A weal occurring after application of an ice cube.

Urticarial vasculitis

This accounts for approximately 5% of urticarias, but is important to recognize so that appropriate investigations and treatment can be undertaken. It is thought to be an immune complex disease which can affect other organs. The weals of urticarial vasculitis are similar in appearance to those of ordinary urticaria. However, vasculitic weals persist for longer than 48 hours, may be tender and sometimes bruise (Kobza Black, 1999) (*Figure 6*).

Angio-oedema occurs in 40% of cases, and arthralgia and abdominal pain is more common than in ordinary urticaria. Occasionally there is pulmonary, renal and rarely other organ involvement. The condition does not respond well to antihistamine therapy. Diagnosis is made on histological examination of a weal. This shows features of venulitis, characteristically with a dermal perivascular neutrophil rich infiltrate, with leucocytoclasis (nuclear fragmentation), fibrinoid deposits and red cell extravasation.

Contact urticaria

Here there is an itching erythema and wealing within 1 hour of skin contact with an irritant or allergen (Warner et al, 1997). There is a wide

Figure 6. These weals had persisted for over 48 hours. On biopsy there was evidence of vasculitis.

spectrum of severity from itching erythema, through weals, to widespread urticaria and anaphylaxis. Non-immunological urticaria where a causative agent can cause itching and urticaria in normal individuals on first exposure is common and is usually mild with localization of weals to the contact site. Immunological contact urticaria is more common in atopic individuals who have had previous exposure to the allergen, e.g. some foods or latex. These reactions can be severe and lead to anaphylaxis.

Angio-oedema

Angio-oedema can be associated with all forms of urticaria, most commonly with ordinary urticaria (Greaves and Lawlor, 1991). However, in 10% of patients with the ordinary form, angio-oedema is the sole manifestation. Angio-oedema alone may also be caused by medication such as non-steroidal anti-inflammatory drugs and angiotensin-converting enzyme inhibitors. In sole or predominant angio-oedema, it is most important to exclude the rare C1 esterase inhibitor deficiency angio-oedema (Agostoni and Cicardi, 1992), whether inherited or acquired. In this condition, trauma to the skin such as surgical and dental procedures and stress can induce swellings. These often do not itch, but are painful and last for days. Abdominal pain, vomiting or diarrhoea may occur at the same time or independently. Significant mortality has occurred from laryngeal oedema, particularly during surgery.

DIFFERENTIAL DIAGNOSIS

Urticaria and angio-oedema are distinguished by the evanescent nature of individual swellings, which resolve to leave normal appearing skin. Papular urticaria (from insect bites, lasting weeks), erythema multiforme (often on acral sites with target lesions or blisters), prebullous eruptions of pemphigoid (red itchy plaques persisting for many days) and acute contact dermatitis must be distinguished from urticaria. Facial swellings occur with lymphoedema and some collagen vascular disease such as lupus erythematosus and dermatomyositis, but these are persistent. HM

Figures 1–6 *are courtesy of the Medical Illustration Department, St John's Institute of Dermatology, St Thomas Hospital, London.*
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KEY POINTS

- A detailed focused history is crucial in establishing the diagnosis of urticaria and angio-oedema.
- When weals subside the skin should be normal in appearance, and presence of excoriations, scaling and pigmentary changes may suggest another diagnosis.
- Physical urticarias should be distinguished by history and challenge, to prevent inappropriate investigation and to enable suitable advice and treatment to be given
- It is important to consider and confirm a diagnosis of urticarial vasculitis and look for systemic involvement
- For predominant or sole angio-oedema it is essential to exclude C1 esterase inhibitor deficiency angio-oedema.