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Urticaria

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Urticaria

The term urticaria refers to a vascular reaction of the upper dermis marked by the transient appearance of slightly elevated patches (weals), that are redder or paler than the surrounding skin and often accompanied by severe itching. It is commonly referred to as hives, or nettle rash (the word urticarial comes from the Latin, *urticus*, meaning nettle). This article explores the causes of urticaria and its management in general practice.

The GP Curriculum and urticaria

GP curriculum example 3.21: Care of people with skin problems requires GPs to be able to:

- Demonstrate appropriate history-taking for patients with skin problems
- Recognise the importance of skin-specific symptoms, e.g. itching and rash distribution
- Understand how to recognise common skin conditions in primary care and instigate appropriate treatment
- Recognise rarer but potentially important conditions and know when to refer to secondary care, e.g. vasculitis
- Recognise emergency skin conditions, e.g. anaphylaxis, and act appropriately
- Empower patients to adopt self-treatment and coping strategies, where possible
- Understand and implement the key national guidelines that influence healthcare provision for skin problems

Features of urticaria

Roughly 1 in 10 people will have an episode of urticaria in their lifetime (Zuberbier, Blake, Worm, Edenharter, & Maurer, 2010). People suffering from urticaria usually present with a characteristic rash that is easily recognisable in a GP's surgery (Fig. 1). Skin lesions arise suddenly; they consist of raised areas of skin (weals) of 1–2 cm diameter. Weals can be red or white, and are itchy and surrounded by an area of redness (flare). Weals may coalesce with others, making the rash look extensive and map-like ('geographic rash').

In most cases weals last less than 24 hours and then fade before the surrounding flare, giving the skin a blotchy appearance. As weals disappear others may appear elsewhere, or the rash may disappear completely only to reappear within hours or days. Apart from itching, the person usually remains well other than the rash.

Classification of urticaria

Several clinical classifications of urticaria are in common usage and terminology can be confusing. The simplest classifications are based on duration of symptoms and cause.

Classification by duration

Classification of urticaria by duration is summarised in Box 1. Although most acute urticarial rashes last 24–48 hours and then disappear spontaneously, acute urticaria is defined as an urticarial rash and/or angio-oedema lasting for less than 6 weeks. Acute urticaria is much more common than chronic urticaria. It is more common in children, in women aged 30–60 years and in people with atopy.

Box 1. Classification of urticaria by duration of symptoms.

- Acute – up to 6 weeks of continuous activity
- Chronic – 6 weeks or more of continuous activity
- Episodic – acute intermittent or recurrent activity

Chronic urticaria is urticaria on a daily or almost daily basis lasting for longer than 6 weeks. Chronic urticaria is usually classified together with episodic acute intermittent urticaria in which symptoms last for hours or days but recur over months or years. Lifetime prevalence for chronic urticaria is 1.8% and 0.8% of the population will have experienced chronic urticaria in the past year (Zuberbier et al., 2010). Chronic urticaria may remit and relapse with relapses triggered by illness, stress, drugs



Figure 1. Skin lesions of urticaria.
 Reproduced with permission from DermNet NZ, website of New Zealand Dermatological Society Incorporated.

or alcohol and hormonal changes such as menstruation. Duration of symptoms is very variable. Half of all cases resolve in 3–5 years, but one in five cases persists for more than 10 years. People with physical urticaria and those with severe episodes tend to have a longer duration of urticaria.

Chronic urticaria has a severe impact on the quality of life of the patient. The itching and rash causes distress, poor self-image and social isolation. Poor sleep may affect work or school performance and impact on personal relationships. It is thought that up to 14% of patients with chronic urticaria develop depression as a result of their illness (Sheehan-Dare, Henderson, and Cotterill, 1990).

Classification by cause

Urticaria may be caused by a variety of immune and non-immune mechanisms. Classification by cause is summarised in Box 2. The duration that individual weals last can be helpful in distinguishing between clinical patterns (Box 3).

In 40–50% of patients with urticaria the cause is unclear. In these cases, the urticaria is classified as 'ordinary' or 'idiopathic'. Patients may present with spontaneous weals anywhere on the body, with or without angio-oedema. Triggers may include viral infections (particularly in children), stress or alcohol.

'Physical' urticarias are triggered reproducibly by one or more physical stimuli. Identifying the stimulus allows the patient to minimise or prevent urticaria through avoidance.

'Contact' urticaria occurs repeatably and reliably, but only when the eliciting substance is absorbed into the body. This may be IgE-mediated allergic urticaria resulting from exposure to or ingestion of an allergen (for example, latex allergy, food allergy or allergy to an insect sting), or non-IgE mediated resulting from ingestion of certain other chemicals such as drugs or food additives. Implicated drugs include the opioids, aspirin, non-

Box 2. Classification of urticaria by cause.

- Ordinary or idiopathic – unknown cause; may be triggered by stress or viral infections
- Physical – reproducibly induced by the same physical stimulus
- Mechanical – delayed pressure; symptomatic dermatographism; vibratory
- Thermal – cold contact; localized heat
- Other – aquagenic (caused by water); solar (caused by sunlight); exercise-induced; cholinergic (caused by sweat)
- Contact – caused by contact with allergens (e.g. nuts, shellfish, milk, eggs, penicillin, insect stings, latex) or chemicals
- Urticarial vasculitis
- Inflammatory or autoimmune syndromes – hereditary or acquired

Box 3. Duration of weals according to the cause of urticaria.

- Physical urticaria – weals last less than an hour (except weals in delayed pressure urticaria, which take 2–6 hours to develop and up to 48 hours to fade)
- Contact urticaria – weals last up to 2 hours
- Ordinary urticaria – weals typically last 2–24 hours
- Vasculitic urticaria – weals last days

steroidal anti-inflammatories (NSAIDs), and radio-contrast media. Common food additives that cause urticaria include azo dyes, naturally occurring salicylates and food preservatives.

Urticarial vasculitis presents clinically with urticaria, but histologically there is small vessel vasculitis. The clinical picture may be indistinguishable from chronic ordinary urticaria, but suspect urticarial vasculitis if:

- Urticaria is relentless rather than transient and self-limiting
- Individual lesions last for longer than 24 hours
- Lesions are burning or painful rather than itchy, and have a darker appearance than other urticarial lesions
- Lesions leave scaling, bruising, purpura or petechial haemorrhages

The individual may also have systemic symptoms, such as fever, malaise and arthralgia. Diagnosis is confirmed on skin biopsy.

Urticaria can be also caused by underlying inflammatory or autoimmune illness. This may be hereditary (for example, cryopyrin-associated periodic syndromes associated with CIAS1 gene mutations) or acquired (for example, patients with systemic lupus erythematosus). Patients are usually unwell and develop weals in addition to other symptoms specific to their disease.

Associations

Thyroid autoimmunity is roughly twice as prevalent among patients with chronic ordinary urticaria (COU) compared with population controls (14% as opposed to 6%) (Leznoff & Sussman, 1989). There is also a significantly higher prevalence of coeliac disease in children and adolescents with severe chronic urticaria than case-matched controls (Caminiti et al., 2005).

Anaphylaxis

Most patients with urticaria do not have systemic reactions, but allergic urticaria and some physical urticarias may occasionally progress to anaphylaxis. However, urticaria is often a feature of anaphylactic reactions.

Anaphylaxis is likely when all of the following three criteria are met:

- Sudden onset and rapid progression of symptoms, usually over a period of minutes
- Life-threatening **A**irway and/or **B**reathing and/or **C**irculation problems
- Skin and/or mucosal changes: flushing, erythema, urticaria and/or angio-oedema, rhinitis and/or conjunctivitis

Other symptoms include abdominal symptoms such as abdominal pain, vomiting or incontinence. Often patients are also anxious and have a sense of impending doom.

Skin and mucosal changes can be subtle or absent in up to 20% of anaphylactic reactions. It is also important to remember that skin or mucosal changes on their own are not a sign of an anaphylactic reaction, although they may develop into one. If anaphylaxis is suspected, start treatment immediately with intramuscular adrenaline in accordance with the Resuscitation Council's anaphylaxis guideline (Fig. 2) and admit to hospital as a blue-light emergency.

Differential diagnosis

The differential diagnosis of urticaria is summarised in Box 4. However, if the rash is not witnessed, for example, if symptoms only occur at night, urticaria can be confused with any cause of pruritus.

Box 4. Differential diagnosis of urticaria.

- Any cause of pruritus (scratching may cause skin lesions that look similar to urticaria)
- Insect stings/bites
- Scabies
- Atopic dermatitis
- Contact dermatitis
- Erythema multiforme
- Early lesions of bullous pemphigoid
- Early lesions of dermatitis herpetiformis
- Pruritic urticarial papules and plaques of pregnancy (pregnant women)
- Erythema toxicum (infants)
- Cutaneous mastocytosis (infants)

Skin lesions of urticaria can be confused with erythema multiforme, however, the lesions of erythema multiforme are usually fixed and have a 'target' appearance and they may be associated with a prodromal illness. The early lesions of bullous pemphigoid and dermatitis herpetiformis also have a similar appearance to an urticarial rash.

In pregnancy, consider pruritic urticarial papules and plaques of pregnancy (PUPPP). This condition is associated with first and/or multiple pregnancies or excessive weight gain in pregnancy. It develops after 35 weeks gestation and appears as a rash usually confined to the lower abdomen and/or buttocks. It may appear in stretch marks. PUPPP usually clears spontaneously within 6 weeks, and often just a few days after delivery. It does not usually recur in subsequent pregnancies.

In small babies, erythema toxicum may have a similar appearance to urticaria. Skin lesions resolve spontaneously within the first few weeks of life. Urticaria pigmentosa, or cutaneous mastocytosis, appears in infancy, and usually within the first 2 weeks of life. Dark, freckle-like lesions on the face, limbs or trunk become urticarial when the skin is rubbed (Derier's sign). No treatment is needed and the condition clears spontaneously in childhood.

Investigation of urticaria

Investigations are not usually indicated for patients presenting with acute urticaria in primary care. However, for patients with chronic urticaria, consider checking a full blood count, erythrocyte sedimentation rate or C-reactive protein, and thyroid function tests.

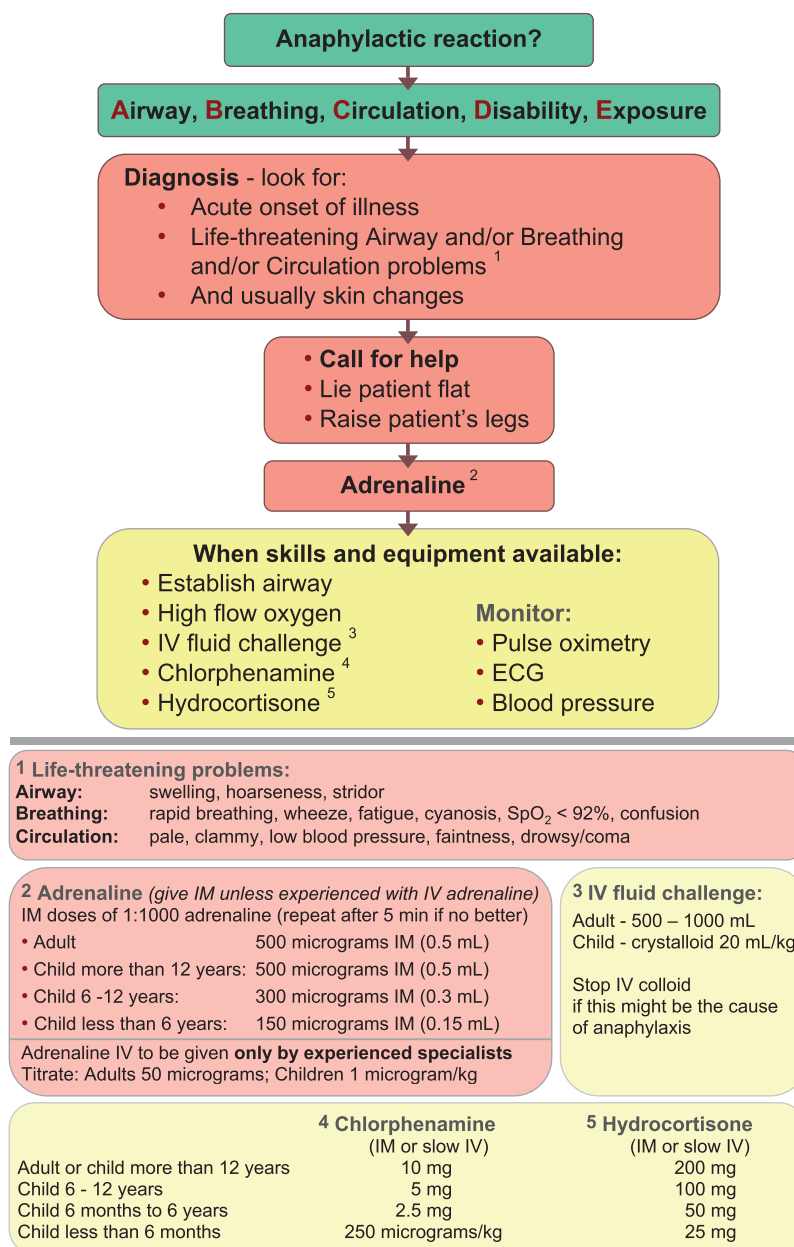


Figure 2. Resuscitation Council UK anaphylaxis treatment algorithm.
 Reproduced with the kind permission of the Resuscitation Council (UK).

Management of acute urticaria

For most patients, acute urticaria is not life-threatening and attacks are self-limiting. Treatment is not needed if the episode is mild. Self-help measures include:

- Trying not to scratch: advise patients to rub their skin with the palms of their hands if they must itch, and to keep nails short and clean
- Choosing clothing that does not irritate the skin (such as cotton)

- Using lubricating, alcohol-free, hypoallergenic products on their skin
- Trying calamine lotion or cool baths to soothe the itch

If symptomatic treatment is needed, offer a non-sedating antihistamine to control daytime symptoms. Suitable choices include cetirizine, loratadine (both available to purchase over the counter) or fexofenadine. Response and tolerance to antihistamines varies considerably between individuals, so if one antihistamine is not effective, try another. Consider adding a sedative antihistamine, such as chlorphenamine or hydroxyzine, at night if the itching interferes with sleep. Loratadine or chlorphenamine are safe antihistamines to use in pregnancy or

for breast-feeding mothers. A moisturiser (such as Dermol or Diprobase) chilled in the fridge or topical Dermacool can be used as an alternative to, or in addition to, an oral antihistamine.

For patients with severe symptoms, consider a short course of oral corticosteroids (such as prednisolone 40 mg daily for 3–5 days) in addition to the oral antihistamine. If rebound symptoms occur after a short course of corticosteroids, seek specialist advice.

Management of chronic urticaria

For all patients with chronic urticaria, assess the severity of symptoms and their impact on the day-to-day life of the individual. Specifically ask about problems with sleep and the psychological effects of the urticaria on the patient. Although it is not always possible to identify a cause for chronic urticaria, take a detailed history to exclude possible triggers. If a trigger is identified, advise avoidance wherever possible.

Clearly written information sheets (for example, those available from the British Association of Dermatologists, or Patient.co.uk) can be very helpful to patients. Explain the likely course and prognosis of the condition. Advise patients to avoid non-specific aggravating factors, such as overheating, stress, alcohol, and drugs with the potential to worsen urticaria such as aspirin and codeine. NSAIDs should be avoided in aspirin-sensitive patients with urticaria.

In all cases, recommend a topical antipruritic treatment (such as calamine lotion or Dermacool) to relieve itch, however, the mainstay of medical management in primary care is with regular antihistamines. As for acute urticaria, use a non-sedating antihistamine to control day-time symptoms and consider adding a sedating antihistamine if sleep is disturbed. It may be necessary to try several antihistamines before one is found that suits the patient and works. If this does not control symptoms, in adults not known to have QT syndrome or impaired renal or liver function, consider doubling the standard dose of the antihistamine being used. Although unlicensed at this dose, this approach is widely used and is not known to be harmful (National Institute for Health and Care Excellence (NICE), 2011).

If treatment in primary care fails, consider specialist referral. Specialist treatments include higher doses of antihistamines or a combination of non-sedative antihistamines. Other treatments frequently tried in addition to a regular antihistamine are H₂ receptor antagonists, such as cimetidine or ranitidine (unlicensed indication), or antileukotrienes such as montelukast (unlicensed indication). Response to these agents is highly variable.

Specialist treatment for urticarial vasculitis is with steroids and/or other immunosuppressive agents.

Specialist referral

There are a number of circumstances when specialist referral is appropriate for patients with urticaria (Box 5).

Box 5. Specialist referral of patients with urticaria or angio-oedema.

Emergency referral to the Accident and Emergency Department:

- Anaphylaxis
- Airway compromise as a result of angio-oedema

Referral to dermatology or the allergy clinic (dependent on local protocols) – speed of referral is dependent on the nature of the individual's symptoms:

- Urticaria with angio-oedema not involving the airway
- Acute urticaria which is severe and thought to be due to a food or latex allergy
- Chronic persistent urticaria which is troublesome despite the use of antihistamines and avoidance of known trigger factors.
- Rebound urticaria following a course of steroids
- Vasculitic urticaria: suspect if lesions are painful and persistent

Referral to rheumatology or other appropriate specialism:

- Suspected underlying autoimmune disease resulting in urticaria (e.g. systemic lupus erythematosus)

Angio-oedema

Angio-oedema is a swelling in the dermis, subcutaneous and submucosal tissues (Fig. 3). Angio-oedema may be considered part of the continuum of anaphylaxis but, in isolation, without respiratory difficulty or hypotension, it is not anaphylaxis. Women are more frequently affected than men and angio-oedema is commonly associated with urticaria (only 20% present with angio-oedema alone). Conversely, roughly half of those with COU have episodes of angio-oedema too.

Skin swelling is less well defined than in urticaria. Swellings can occur anywhere on the body, but most often involve the eyes, lips, genitalia, and hands or feet. The surface of the skin may appear normal. The swellings are often more painful than itchy, and last



Figure 3. Angio-oedema affecting the lips.
Reproduced with permission from DermNet NZ, website of New Zealand Dermatological Society Incorporated.

longer than urticarial weals. Without treatment, angio-oedema may last up to 3 days.

Systemic involvement can occur, affecting the bowel and the airway. Bowel involvement may cause abdominal pain with or without nausea, vomiting or diarrhoea. Airway involvement may cause tongue swelling, shortness of breath and/or wheeze. If there is airway compromise, always consider the possibility of anaphylaxis.

Causes

Any cause of urticaria may also cause angio-oedema (see Box 2). If angio-oedema occurs alone without urticarial weals, consider hereditary angio-oedema (HAE) or a drug cause. The most common drug causes of angio-oedema are angiotensin converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs) or NSAIDs.

HAE is caused by C1 esterase inhibitor deficiency and this is usually inherited as an autosomal dominant condition. Rarely C1 esterase deficiency can be acquired in association with lymphoma or connective tissue disorders such as systemic lupus erythematosus. HAE is characterised by acute recurrent attacks of angio-oedema with more gradual onset than allergic angio-oedema. These attacks usually start after puberty. Attacks may be precipitated by stress, trauma, minor operations and dental surgery. Swellings most commonly affect the hands and the feet and are painless. However, up to one in four sufferers have airway involvement and gastrointestinal symptoms are common. Rarely abdominal symptoms may mimic an acute abdomen.

Differential diagnosis

Skin infections such as cellulitis and erysipelas can present with localised skin swellings, although usually these are associated with fever, erythema and tenderness. Local skin reactions, such as contact dermatitis, can also be confused with angio-oedema, but in these conditions there are usually changes to the overlying skin

and the skin is intensely itchy. Lymphoedema may present with localised skin swelling too, but the swelling is usually chronic and the skin is often thickened and firm. Other rare differential diagnoses include idiopathic scrotal oedema in children, in which the swelling is limited to the scrotum, and Rosenthal–Melkersson syndrome, which causes recurrent non-resolving facial oedema, peripheral facial nerve palsy and fissuring of the tongue.

Management of the acute attack

If the patient has angio-oedema and any airway compromise, even if anaphylaxis is not suspected, refer the patient immediately to hospital. If anaphylaxis is suspected, give adrenaline immediately and follow the Resuscitation Council algorithm for management of anaphylaxis (Fig. 2). In hospital, C1 esterase inhibitor concentrate can be given for emergency treatment of serious angio-oedema attacks. Fresh frozen plasma may be used as a substitute in an emergency if C1 esterase inhibitor concentrate is not available.

If a decision is made not to admit the patient, try to identify the underlying cause of the angio-oedema. Give an oral non-sedating antihistamine (such as cetirizine, loratadine or fexofenadine) combined with an oral corticosteroid (e.g. prednisolone 40mg once a day for 3–5 days). Monitor the patient closely and at least daily until symptoms have resolved. Monitor patients more frequently if they have poor social circumstances or are vulnerable due to their age or level of understanding, and have a lower threshold for admission to hospital. Give patients verbal and written instructions about circumstances, such as worsening of symptoms or airway compromise, in which they should seek further help or go directly to the emergency department. Consider admission if there is no improvement after treatment in primary care, or any worsening of symptoms during treatment.

Investigations in primary care

Investigations are not usually necessary in primary care, but consider checking a C4 level if HAE is suspected. C4 is one of the proteins in the complement cascade that is affected if there is insufficient C1 esterase inhibitor; a reduced C4 level (less than 30% of expected levels) is strongly suggestive of a diagnosis of HAE and should prompt referral to a specialist allergy or immunology clinic for assays of C1 esterase inhibitor.

Referral

Refer all patients who have had an attack of angio-oedema to an immunologist or allergy clinic, except patients taking ACE inhibitors or ARBs. For patients taking ACE inhibitors or ARBs, stop the drug prior to referral. Only refer if the angio-oedema persists for longer than 3 months after stopping the ACE inhibitor or ARB, or if the patient has recurrent episodes of angio-oedema after stopping the drug.

Long-term management

In most cases, long-term management is the same as for patients with chronic urticaria. For people with HAE, maintenance therapy is only necessary for patients with symptomatic recurring angio-oedema or related abdominal pain.

Danazol is the current treatment of choice for most adults with HAE. It acts by increasing hepatic production of endogenous C1 inhibitor. However, virilising side-effects may occur even at low doses and it should be avoided in children. Regular monitoring for hepatic inflammation and hepatocellular adenomas is essential.

Alternatively, tranexamic acid may be used for maintenance treatment. This acts by exertion of a C1-inhibitor sparing effect, but is contraindicated in patients with a history of thrombosis. Regular eye examinations and liver function tests are recommended. Prophylaxis before planned surgery or dental procedures includes taking tranexamic acid 2 days before and afterwards, or increasing the dose of established maintenance therapies with tranexamic acid or anabolic steroids.

Several new drugs for maintenance therapy have recently been released including bradykinin receptor antagonists, kallikrein inhibitors and C1-inhibitor replacement therapies. Their place in routine management is still under evaluation. C1 esterase inhibitor concentrate may be used as prophylaxis before surgery in patients with HAE, especially when intubation or dental extractions are necessary.

Key points

- Urticaria (hives) consists of superficial, itchy swellings of the skin known as weals; it is common, affecting one in ten at some point in their lifetime
- Most patients with urticaria do not have systemic reactions but rarely urticaria may progress to anaphylaxis; conversely, urticaria is often a feature of anaphylactic reactions
- Deeper swellings of the skin and alimentary tract are called angio-oedema; weals and angio-oedema often coexist but either may occur alone
- The cause for most cases of urticaria and angio-oedema is unknown; identifiable causes include physical, chemical or allergic, and hereditary causes
- Once anaphylaxis and airway compromise has been excluded, acute flare ups are managed with anti-histamines together with short course

steroids for those with angio-oedema or severe urticaria

- Treatment of chronic angio-oedema or urticaria is with oral antihistamines; refer for specialist management if the patient has angio-oedema, severe symptoms of urticaria despite treatment, or suspected urticarial vasculitis

References and further information

- British Association of Dermatologists. (2012). Urticaria and angio-oedema. Retrieved from www.bad.org.uk/site/740/default.aspx
- Caminiti, L., Passalacqua, G., Magazzu, G., Cornisi, F., Vita, D., Barberio, G., . . . , Pajno, G. B. (2005). Chronic urticaria and associated coeliac disease in children: A case-control study. *Pediatric Allergy and Immunology*, 16, 428–432. doi: 10.1111/j.1399-3038.2005.00309.x
- Grattan, C. E. H., & Humphreys, F. (2007). Guidelines for evaluation and management of urticaria in adults and children. *British Journal of Dermatology*, 157, 1116–1123. doi: 10.1111/j.1365-2133.2007.08283.x
- Leznoff, A., & Sussman, G. L. (1989). Syndrome of idiopathic chronic urticaria and angioedema with thyroid autoimmunity: A study in 90 patients. *Journal of Allergy and Clinical Immunology*, 84, 66–71. doi: 10.1016/0091-6749(89)90180-2
- NICE. (2011). Clinical knowledge summary: Urticaria. Retrieved from <http://cks.nice.org.uk/urticaria#topicsummary>
- Powell, R. J., Du Toit, G. L., Siddique, N., Leech, S. C., Dixon, T. A., Clark, A. T., . . . , Nasser, S. M. (2007). BSACI guidelines for the management of chronic urticaria and angio-oedema. *Clinical and Experimental Allergy*, 37, 631–650. doi: 10.1111/j.1365-2222.2007.02678.x
- RCGP Clinical example 3.21: Care of people with skin problems. Retrieved from www.rcgp.org.uk/GP-training-and-exams/~media/Files/GP-training-and-exams/Curriculum-2012/RCGP-Curriculum-3-21-Skin-Problems.ashx
- Sheehan-Dare, R. A., Henderson, M. J., & Cotterill, J. A. (1990). Anxiety and depression in patients with chronic urticaria and generalized pruritus. *British Journal of Dermatology*, 123(6), 769–774. doi: 10.1111/j.1365-2133.1990.tb04195.x
- Zuberbier, T., Balke, M., Worm, M., Edenharter, G., & Maurer, M. (2010). Epidemiology of urticaria: A representative cross-sectional population survey. *Clinical and Experimental Dermatology*, 35(8), 869–873. doi: 10.1111/j.1365-2230.2010.03840.x

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