Acute, chronic and physical urticaria: A brief guide for healthcare professionals

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Section 1: Urticaria

What is urticaria?

The term urticaria is used to describe a rash that is recognisable as raised itchy, areas with surrounding erythema. Urticaria is often referred to as wheals, hives, bumps or nettle rash.

It is worth noting that most cases of urticaria are not allergy related and there are other mast cell conditions that can cause rashes.

Presentation of the rash

- Variable in size, shape and number. It can range from diffused small, raised bumps to widespread erythematous large patches.
- Can be localised to one area or more generalised, covering large areas of the body with limbs, trunk, neck and face commonly affected.
- Can appear as red, purple/violet or skin coloured depending on the skin tone. Redness will be more visible on lighter skin tones. On darker skin tones there may be no obvious skin colour change.
- Look for other indicators such as intense itch, discomfort or pain to the area, localised heat, swelling to skin or changes to the texture of the skin.
- Urticated patches are usually transient and resolve within 24 hours, although new patches can appear on the skin near to original patch which gives the appearance that the wheals do not disappear.

Erythematous raised

Widespread wheals DFTB

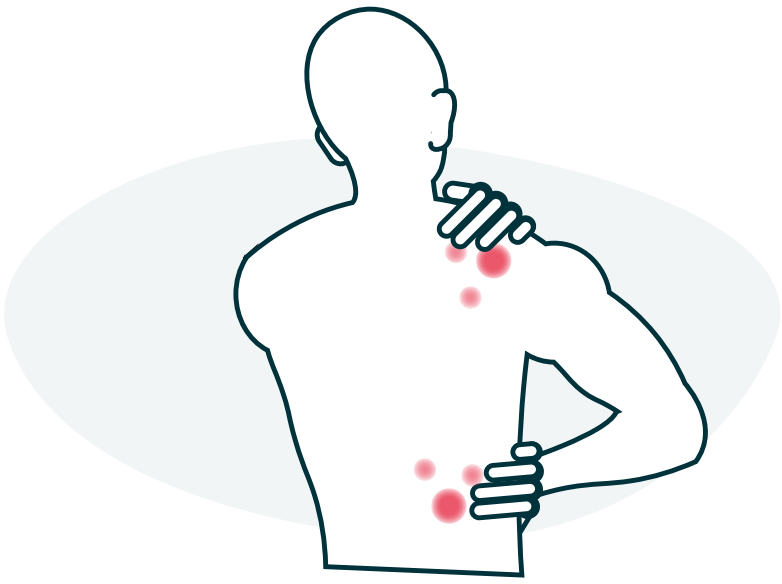
Blotchy macular erythema

Causes of urticaria

Urticaria is commonly mistaken as occurring due to allergy, but most cases of urticaria have no allergic involvement. Although the urticaria will typically occur as a result of a release of histamine caused by mast cell degranulation which causes vasodilation to appear, the mechanism is not IgE related.

Common causes of urticarial rashes include:

- Infection (viral and bacterial)
- Connective tissue disorders
- Hyperthyroidism
- Diabetes
- Pregnancy
- Intestinal parasites
- Cancer
- Lymphomas
- Medication
- Foods
- Insect bites and stings
- Stress



Different forms of urticaria - Physical / inducible

Urticaria less than six weeks

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Acute urticaria

Urticaria more than six weeks

↓

Chronic Urticaria

↓

Chronic Spontaneous Urticaria

Physical/Inducible Urticaria

Dermographism

Pressure

Heat

Cold

Solar

Vibratory

Cholinergic

Aquagenic

Contact

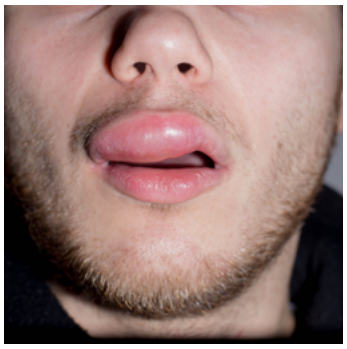
Different forms of urticaria

Acute urticaria – urticaria lasting less than six weeks

- Acute urticaria will typically resolve within hours (however viral induced urticaria can take up to a week or more to resolve).
- Common causes of acute urticaria include viral or bacterial illness, allergy (including food), medication (this can be IgE or pseudo allergy), insect stings and bites as well as skin contact with an allergen e.g. latex.
- Acute urticaria is not always allergy related. When it is triggered by allergy, symptoms will commonly occur **within minutes** or up to an hour after contact or ingestion of the allergen. It will then often resolve quickly once the offending allergen has been removed.

Angioedema

Angioedema is a swelling in the deep layers of the subcutaneous and sub mucosal tissue. This occurs as a result of transient leakage of fluid into the interstitial space due to a release of immune mediators including, histamine, prostaglandins and leukotrienes, causing increased vascular permeability and the familiar swelling associated with angioedema.



- Angioedema is often asymmetrical.
- Often affecting the face, gut and larynx, but can affect any site of the body including extremities and genital area.
- First sign is often an itching, tingling and/or a tight sensation in the skin.
- Swelling is often described as painful rather than itchy.
- Angioedema can take between 48-72 hours to resolve and can be mast cell mediated or bradykinin mediated.
- Angioedema can occur alone without urticaria, but urticaria does occur alongside angioedema in approximately 40% of cases.
- Angioedema can be acute or chronic in nature.

Angioedema Red Flags:

- ACEi induced angioedema – where bradykinin mediated angioedema is suspected stop ACEi and review in three months.
- In individuals with angioedema without urticaria, consider hereditary angioedema, this commonly affects the subcutaneous sites, gut and larynx.
- Angioedema affecting the face and neck, especially the tongue or throat, can restrict or compromise the airway and should be treated as a medical emergency.

Chronic urticaria - urticaria lasting more than six weeks

- Chronic urticaria is urticaria lasting longer than six weeks.
- It can be a persistent urticarial rash or sporadic in nature.
- It often has a severe impact on an individual's quality of life leading to lack of sleep, and impacting mental health, the ability to carry out daily activities (including walking and sitting), the ability to work, attending school, hobbies/ sports and choice of clothing.
- Chronic urticaria may also be accompanied by systemic symptoms of joint pain, headache, fatigue, flushing, gastrointestinal symptoms, sensation of palpations, wheezing and breathlessness.

Chronic Spontaneous Urticaria (CSU)

- Wheals (urticaria) must be present daily for at least six weeks.
- Urticaria is considered spontaneous when no reproducible trigger can be found.
- It is more common in adults between ages of 20-40 years, but can affect children.
- In around 80% of individuals it resolves spontaneously after one to two years. However, in 20% of individuals CSU can continue for longer than 10 years.
- It is an unpredictable and debilitating condition which can affect daily life in many ways including sleep deprivation, anxiety and social isolation.
- CSU is linked with autoimmune disease in about 50% of individuals, especially in individuals not responding to antihistamine therapy.
- Aggravating factors can include medication, stress and infection.
- **TREATMENT**: Following initial diagnosis, commence a daily non-sedating antihistamine, identification and avoidance or reduction of any possible trigger factors e.g. stress, medication etc. For more information, see Section 6: Management and treatment of urticaria.

Physical or inducible urticarias

Inducible/physical urticarias (Zuberbier et al. Allergy 2014 Jul;69(7):868-87)

- Physical urticarias are urticarias that can be induced by a physical trigger or stimulus. These can include heat, cold, water, pressure, vibration and ultraviolet light. The wheal and flare reaction usually appears within minutes and should disappear within an hour after removal of the physical trigger or stimulus. There are exceptions to this rule, one of which is delayed pressure urticaria.
- **TREATMENT**: Inducible urticarias may require a higher dose antihistamine therapy than other forms, and some forms, such as delayed pressure urticaria, can often remain refractory to treatment. (BSACI 2015)

Types of physical or inducible urticarias

Dermographism

- Dermographism (meaning to write on the skin) is the most common inducible urticaria occurring in 2-5% of the population.
- It is an exaggerated wheal and flare response. When the skin is stroked or scratched a reproducible raised area will appear.
- There are various forms of dermographism.
- **TREATMENT**: Often no treatment is required if mild, but where dermographism is accompanied by pruritus, antihistamine therapy is often used effectively.

Pressure urticaria

- Occurs when pressure is applied to an area e.g. shoulder, and a wheal and flare response appears.
- Presents as a swollen, red or discoloured area.
- Areas affected include the extremities (hands and feet) as well as the face, trunk, buttocks legs and arms.
- Common stimuli that induce pressure urticaria include tight clothing, sitting on a hard surface, carrying a bag or weight on the shoulder, standing and walking.

- **TREATMENT**: Avoidance of the trigger stimuli, where practicable, should be advised. Many patients with pressure urticaria require high doses of antihistamines and can remain refractory to treatment, so referral to a specialist is advised.

Delayed pressure urticaria: The wheal and flare response can occur up to four to six hours after pressure has been applied to the area and the reaction may last for hours or days.

Cold urticaria

- Is relatively uncommon.
- Causes a wheal and flare in response to the rewarming of the skin to cold exposure (e.g. water and objects). The symptoms occur within minutes of exposure, usually lasting one to two hours.
- Diagnosis is usually confirmed via provocation test (ice cube test or TempTest).
- **TREATMENT**: Patients refractory to antihistamine therapy or at risk of severe reactions should be referred for specialist review.

It is important to advise individuals with cold urticaria:

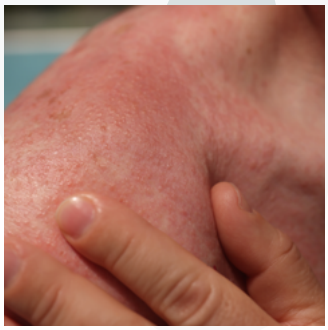
- To take care when participating in outdoor activities and any activities that can expose them to the cold or a rapid drop in body temperature, including swimming, surfing and canoeing etc.
- Advise on diagnosis when referring for medical procedures, as individuals can suffer severe reactions during procedures that lower their body temperature e.g. anesthesia during surgery.

Red Flag: One of the most serious complications that occur with cold urticarias is anaphylaxis. This can occur when exposed to cold temperatures or there is a rapid drop in body temperature. If severe reactions to cold are suspected, then the individual should be prescribed and advised to carry adrenaline auto-injectors, and this should be noted in any referrals for medical procedures.

Heat urticaria

- Rare.
- Swelling, erythema, wheal and flare occurs within minutes of contact with the heat source and resolves within one to two hours.
- Heat urticaria can be localised to the area of contact, generalised, or trigger a delayed reaction some hours later.
- Occurs as a result of direct contact with a warm stimulus on the skin, including steam, sun exposure (not to be confused with solar urticaria), heat sources e.g. hair dryer, hair straighteners, heater, hot water bottle or warm water.
- Diagnosis is usually by provocation test and the wheal will usually occur once the heat stimulus has been removed.
- **TREATMENT**: Non-sedating daily antihistamines are generally effective for around 60% of patients – if refractory to treatment, consider referral to a specialist.

Solar urticaria



- Rare.
- A reaction to sunlight causing an intensely itchy rash to appear on body parts exposed to sunlight.
- Rash occurs within minutes to sun exposure.
- Any skin type can be affected by solar urticaria.
- This reaction may be more obvious in areas that are only exposed to sunlight occasionally e.g. back and arms. Areas such as the face, hands and neck may be less affected as they may have become acclimatised or desensitised over time to sunlight.
- Differential diagnosis: Polymorphic Light Eruption (PLE) is a delayed hypersensitivity reaction to sunlight and can occur two to three days after exposure to sunlight. Other considerations include drug-induced photosensitivity, lupus, photo contact dermatitis.
- Diagnosis: Referral to photodermatology department for phototesting (ultraviolet (UV) light testing).
- **TREATMENT**: Individuals should protect their skin with high factor sunscreen e.g. factor 50 and protective clothing. Antihistamines may help to reduce itch, but often moderate to potent application of steroid creams are required for a short burst to reduce symptoms.

Vibratory urticaria

- Vibratory urticaria occurs within minutes of exposure to a vibrating stimulus and most often occurs in areas of direct contact e.g. the hands and trunk.
- **TREATMENT**: Avoid contact with vibrator equipment due to the risk of severe systemic reactions when exposed for long periods of time. A trial with non-sedating antihistamines can be effective for some, but often vibratory urticaria requires higher doses of antihistamine to control the symptoms. Patients refractory to higher doses of antihistamine, should be referred for specialist care.

Red Flag: Although most cases will only affect the skin, systemic reactions can occur, including widespread erythema, headaches, hypotension and dizziness.

Cholinergic

- Also referred to as cholinergic angioedema urticaria or heat bumps.
- Small (pinpoint) itchy raised areas with erythema (flushing) to the affected area.
- Settles very quickly once the stimuli is removed.
- More common in people between the ages of 10-30 years.
- Triggers include exercise, sweating, increased body temperature, eating spicy foods and emotional stress.
- **TREATMENT**: Identification of the trigger and avoidance where practicable, along with a daily non-sedating antihistamine. Patients refractory to treatment should be referred for specialist care.

Red Flag: Although most cases of cholinergic urticaria only affect the skin, in some cases more severe reactions can be induced, including bronchoconstriction and systemic reactions including anaphylaxis.

Aquagenic (PCDS)

- Very rare.
- Triggered by contact with any water source; still or running, fresh or sea water or water in sweat and tears.
- The temperature of the water does not affect the reaction.
- Wheals occur less than an hour after contact with the water source.
- Wheals can occur on the body, mainly the trunk and upper arms, with the palms and soles usually spared.
- Unlike cold urticaria, aquagenic is rarely life threatening.
- **TREATMENT**: Includes use of non-sedating daily antihistamines as a first line treatment to minimise symptoms.

Contact urticaria

- Occurs as a result of contact with an allergen or irritant trigger. These can include chemicals, foods, plants, animals and animal products.
- Causes wheals within minutes at the site of contact.
- **TREATMENT**: Detection, removal and avoidance of the contact allergen is often enough to prevent repeat occurrence. In some cases, where avoidance of the substance is not practicable, the use of gloves can be used as a barrier to prevent contact – however for latex allergy avoid using latex gloves.

Red Flag: Reactions can occasionally be severe, for example in people allergic to rubber/latex.

Anaphylaxis

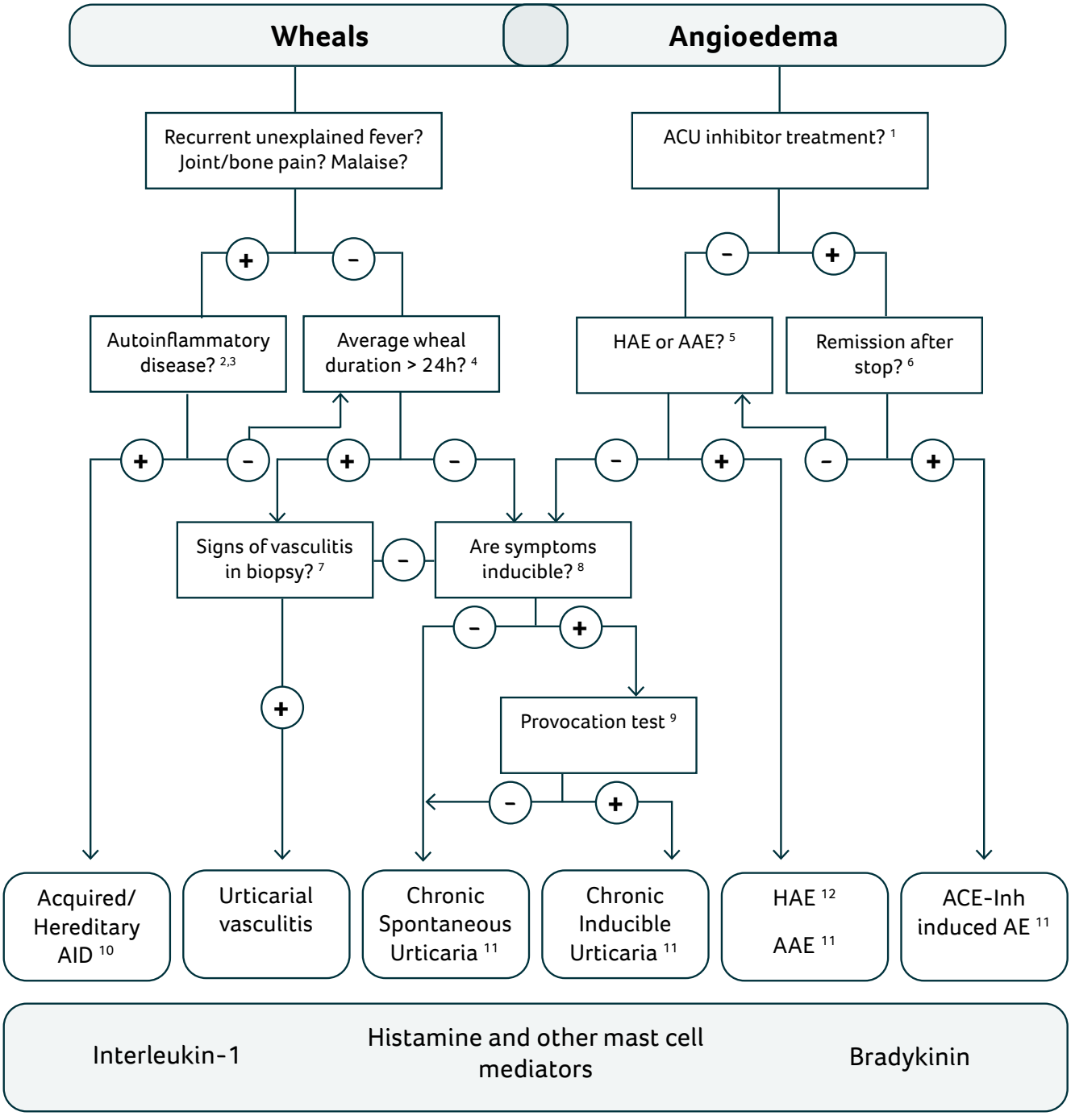
(Anaphylaxis Symptoms and Action Sheet)

Urticaria, without any other associated symptoms, can have a considerable impact on a person's quality of life, but is not life threatening.

However, in rare cases urticaria can also be a manifestation of a more serious allergic reaction called anaphylaxis. This is where the individual may experience breathing difficulties, abdominal pain, rapid irregular heartbeat, hypotension, shock or collapse in addition to their skin symptoms.

Section 2: Diagnosing urticaria and angioedema

Diagnostic algorithm for patients presenting with wheals and/or angioedema lasting longer than six weeks.



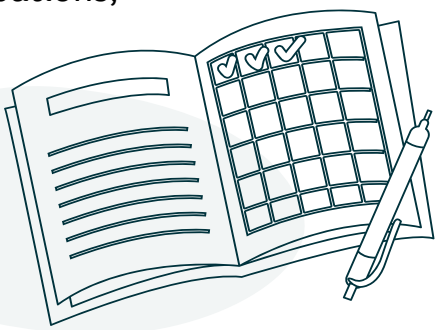
Reference: Zubier et al 2022, The international EAACI/GA²LEN/EuroGuiDerm/APAACI guideline for the definition, classification, diagnosis, and management of urticaria.

Section 3: Taking a clinical history

When taking a clinical history, it is important to use the five **Cs: Confirm, Cause, Cofactors Comorbidities and Consequence.**

Confirm the diagnosis

- Time/age of onset – when did symptoms start?
- Frequency, duration, pattern, recurrence of wheals
- Is this acute, chronic or physical urticaria/ angioedema? Do symptoms last more or less than six weeks or is it episodic?
- The shape, size and distribution. The nature of the wheals, are they itchy or painful?
- Severity of symptoms - consider using a validated tool such as the Urticaria Activity Score (UAS7) dermatology life quality index or the urticaria control test.
- For patients with other underlying medical conditions, the systemic symptoms of chronic urticaria may also be accompanied by joint pain, headache, fatigue, flushing, gastrointestinal symptoms, sensation of palpations, wheezing and breathlessness.
- Treatments tried and what response they had to the treatment. How long where they on the treatment for? What dose? Etc.



Cause and cofactors

- Are symptoms inducible, is there a differential diagnosis e.g. drug allergy?
- Look for potential symptom triggers, that can act as the cause or as potential co-factors for the symptoms e.g. stress, exercise, infections, ACEi inhibiters, NSAIDS, contraceptive pill, food or insects. Asking to keep a symptoms diary can help identify triggers.
- **Note**: IgE mediated allergy is rarely a trigger for CSU. IgE mediated food allergy symptoms typically occur within one hour of exposure to the allergen.

Comorbidities

- Family history of atopy or urticaria/ angioedema.
- Co-existing medical conditions – previous or current allergies, autoimmune disorders, infections, psychosomatic or psychiatric disease.
- Individuals with chronic urticarias may be more susceptible to autoimmune diseases including, thyroid disease, rheumatoid arthritis, systemic lupus erythematosus, type I diabetes mellitus and coeliac disease.

Consequence

- The effect of CSU on health-related quality of life, including sleep impairment, diminished physical and emotional wellbeing and poor performance at school or work, is well documented. In some cases, symptoms can affect the ability to carry out simple daily tasks such as walking, sitting or sleeping. The impact on relationships and sexual function can be a risk factor for mental health issues, including anxiety and depression.
- **Note**: Individuals may present with more than one form of urticaria, for instance CSU and pressure or cold urticaria, which can further impact their quality of life.

Physical examination

- Urticaria will typically present as wheals (raised rash or patches), surrounded by erythema (red, raised inflamed skin).
- Wheals can vary in size, from small pinpoint raised bumps to hand sized erythematous patches. They can be restricted to one area or generalised, and can affect any part of the body.
- Urticaria can affect any skin type or tone, and any age.
- In lighter skin tones - Urticaria is usually seen as white, red or pinkish in colour, with erythema to surrounding skin.
- In darker skin tones – Urticaria is usually seen as raised patches, often matching the surrounding skin tone, or can be slightly lighter or darker, often no visible red flaring of the skin, making the diagnosis of urticaria difficult.

- Wheals often change shape before resolving within 24 hours, but as one wheal resolves others can develop and the rash can present for long periods.
- It can be referred to as intensely itchy, but can also be described as painful or have a burning sensation.
- The rash does not cause any lasting damage to the skin, but in darker skin tones post inflammatory hyperpigmentation (darkening of the skin to the area that has been affected) can occur and may take months to settle.
- Dark inner thigh on brown skin, hyperpigmentation and darkening of inner thigh on brown skin
- Urticaria is accompanied by angioedema in approximately 40% of patients. Commonly on the face, neck, hands or feet, but can also occur in the genitalia.

Consultation point

Chronic urticaria is often unpredictable and will come and go. You may find patients can attend appointments with no obvious symptoms or skin involvement at that moment, so it is a good idea to advise the patient to;

- **Take pictures of the rash / swelling** – suggest pictures are taken by a friend or partner where possible so that the images are clear and in focus.
- **Draw around a wheal** – this will help to document that the wheals are transient and not staying in the same place (vasculitis).
- **Keep a diary / account of their symptoms** - keeping a symptom diary for approximately two to four weeks can be useful if patients report symptoms to triggers. Encourage them to record when they first begin experiencing them, how long they last, and possible triggers or cofactors such as; food, medication, stress, infection, or hormonal changes. This will show any patterns to their symptoms. The CRUSE app can be useful.
- **Discuss medications** - including current and occasional medication use e.g. over the counter medications (OTC), NSAIDS (Non-steroidal anti-inflammatory) and ACEi inhibitors, as medication can exacerbate or trigger urticarial reactions.
- **Document disease severity** - use a validated scoring tool to assess quality of life and symptoms severity and review regularly.

Section 4: Practical support tips

Self-help tips to reduce symptoms can include:

Soothe the skin

Applying an ice pack, taking a cool bath or placing cream-based emollients in the fridge (not advised for those with cold or aquagenic urticaria).

Emollients

Applying cream-based emollients can help reduce itch and soothe the skin. Emollients containing antipruritic (anti-itch) ingredients can be very soothing.

Reassure

Educate your patients about the condition and reassure that only in rare circumstances can this condition lead to severe symptoms (anaphylaxis).

Educate your patients in techniques to avoid scratching

Scratching releases more itch chemicals (histamine) from the skin and perpetuates the itch-scratch-cycle e.g. pinching or patting, but not rubbing or scratching, when the skin feels an itch sensation can help prevent scratching.

Practicing deep breathing or other relaxing techniques can also be useful to reduce any built-up stress and help distract from scratching.

Clothing

Wearing loose light breathable clothing can help reduce itch and increase comfort.

Avoiding aggravating factors

Advise on the importance of avoiding/ reducing lifestyle factors that may aggravate or trigger symptoms e.g. stress, alcohol, caffeine, extremes of temperature.

Medications

Review current and occasional medication use, including over the counter medications (OTC). Medications such as aspirin, NSAIDS (Non-steroidal anti-inflammatory), opiates e.g. codeine and ACEi inhibitors can exacerbate or trigger urticarial reactions.

Section 5: Useful investigations

(NICE 24 / BMJ)

For the majority, urticarial rash investigations are not usually required, especially for acute urticaria. A good clinical history and examination of the skin should help to confirm the diagnosis (if the skin is clear at the point of examination you could request to see photos of the skin to confirm diagnosis).

There is no special test to reliably identify urticaria. However, where the urticaria is refractory to treatment (or symptoms do not fit with the norm) investigations may be useful to rule out a differential diagnosis.

Basic tests

(BSACI 2015 NICE CKS 2024 EAACI 2021)

Testing required	Used to exclude differential diagnosis	To confirm
Full blood count (FBC)	Raised eosinophils Raised neutrophils Leukopenia / leucocytosis	Parasitic infection/ drug Vasculitis Viral / bacterial chronic
Thyroid function (TFTs)	Check for autoimmune urticaria	Chronic
Auto-antibodies ESR CRP	Check for underlying autoinflammatory conditions	Chronic infection, Vasculitis, Paraproteinaemia
Total IgE and IgG anti-thyroid antibodies	Check for auto allergic or autoimmune disorders	Chronic Vasculitis
Allergy testing Not routinely - only if indicted in the clinical history taking	Skin patch test Skin prick test or specific Ige blood test	Contact urticaria Immediate / IgE mediated allergic urticaria

Complement studies C3 and C4	Especially if patient is taking ACEi inhibiters Screen for HAE	Bradykinin mediated disorders – angioedema (without urticaria)
Urinalysis	Check for urinary tract infection / vasculitis	Vasculitis
Coeliac screen	Check for coeliac disease	Coeliac disease
Physical urticarias	Induction of symptoms can be useful to confirm diagnosis but advisable only under specialist assessment due to risk of systemic reactions	Physical urticaria

Further testing should be performed only as indicated by the results of the history, physical examination and basic testing.

Further information on basic testing

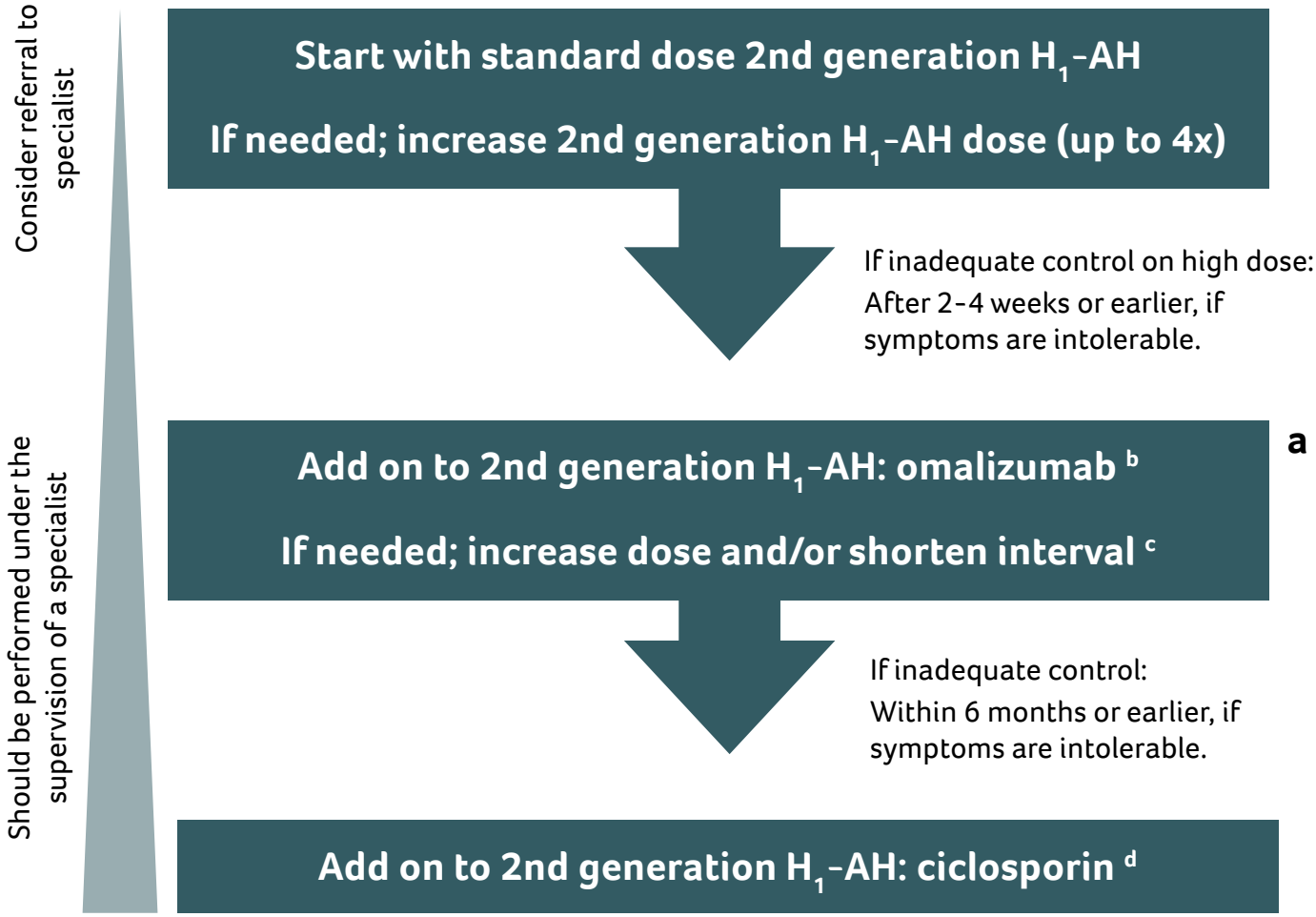
Full blood count (FBC)	The eosinophil count may be elevated in parasitic infections and in some drug induced reactions. An elevated neutrophil count can be associated with urticarial vasculitis.
Thyroid function (TFTs) and auto-antibodies	The presence of thyroid auto-antibodies is associated with chronic urticaria in both children and adults and suggests a diagnosis of autoimmune urticaria. Approximately 20% of patients with chronic urticaria have antithyroid antibodies compared to 6% in the general population.
Erythrocyte Sedimentation Rate (ESR) or C-Reactive Protein (CRP)	An elevated ESR and/or CRP suggests an underlying systemic condition such as chronic infection, vasculitis and a high ESR with normal CRP may indicate paraproteinaemia.
Total IgE and IgG anti-thyroid antibodies	Understanding these can be useful when screening for CSU to indicate presence of auto allergic or autoimmune mediated reaction.

Angioedema without wheals - complement studies	Complement investigations in patients with angioedema without wheals should include C4 and C1 inhibitor. The C4 level will be low in most cases of Types I and II HAE (hereditary angioedema) even between attacks. C1 inhibitor deficiency is not associated with urticaria, and hence, if urticaria is present, measurement of C1 inhibitor is not required.
Check blood pressure and urinalysis	A screen for haematuria and proteinuria will help to detect the presence of urinary tract infection and renal involvement in vasculitis.
Skin biopsy	Useful if there is an unusual pattern of presentation or in cases of suspected urticarial vasculitis.
Allergy testing	Testing for allergy is only useful if there is evidence of a reaction to a specific trigger allergen identified in the clinical history, testing this may involve: • Patch testing for contact allergens. • Skin prick or IgE blood testing for specific allergens. In certain circumstances complement testing may be performed. Food allergy can usually be excluded if there is no temporal relationship (usually symptoms within one to two hours of ingestion or contact).
Medication	Certain drugs e.g. NSAIDs, ACEi inhibiters can cause or aggravate urticaria.

Section 6: Management and treatment of urticaria

Treatment

Recommended treatment algorithm for urticaria – ref Zerbier etal 2021



a) Second line and third line treatment apply only for CU
b) 300mg every 4 weeks
c) Up to 600mg every 2 weeks
d) Up to 5mg/kg body weight

Red flags indicating need for referral:

- Urticaria that is painful and persistent (suspect vasculitis urticaria).
- Symptoms not well controlled or worsening on antihistamine treatment.
- Angioedema with no wheals that does not respond to first line treatment.
- Acute severe urticaria thought to be due to food, latex or drug allergy.
- Chronic inducible urticaria that may be difficult to manage in primary care e.g. solar, cold urticaria.
- Any urticaria that presents with severe systemic symptoms such as difficulty breathing or anaphylaxis.
- Where symptoms are having an adverse effect on quality of life or mental health.

When referring a patient, it is useful to include images of the patient's rash.

Step 1

A. Diagnosis of urticaria - commence a non-sedating antihistamine. Non-sedating antihistamines work by selectively blocking peripheral receptors, thereby having reduced risk of causing sedation and better safety profile than first generation antihistamines.

B. If symptoms don't improve, increase the dose. The antihistamine can be increased up to four times the recommended dose to achieve symptoms relief, depending on individual circumstances and co factor risks. It is recommended, to avoid polypharmacy, to increase the dose with the antihistamine of choice.

C. Consider a referral to a specialist, especially where treatment is refractory to the maximum antihistamine dose (four times), where there is doubt over the diagnosis, the condition is intolerable or has a huge negative impact on quality of life or mental health.

A one-off short course of corticosteroids may be offered in severe flare ups, but should not be used repeatedly due to the risk of serious side effects.

Step 2 - Secondary care

Biologic therapies are designed to target a certain part of the immune system and modify or suppress the immune response, to gain control of symptoms and provide relief from the condition. These treatments should only be started under supervision from specialist departments (e.g. dermatology, allergy or immunology).

Monoclonal Antibody Therapies (MABs) work by blocking specific interleukins and therefore reducing the inflammatory process. There is currently only one treatment licensed by NICE in the UK, and available within the NHS for patients from 12 years of age with chronic urticaria. It has been approved for use in other conditions such as asthma, chronic rhinosinusitis with nasal polyps, and IgE-mediated food allergy. Treatment is given by regular injection. Some monoclonal antibody therapies have also been shown to have a therapeutic impact on other co morbidities, including atopic asthma and atopic eczema.

Other potential treatments that are in the pipeline include:

- Tumor Necrosis Factor Alpha (TNFa) inhibitor - is currently being researched as a potential treatment. Individuals with CSU can often express high levels of TNFa as a result of mast cell activation.
- Bruton Tyrosine Kinase (BTK) inhibitor - is currently in phase three trials and is an oral treatment designed to block the BTK cascade and prevent the release of histamine that causes itchy hives (wheals) and swelling.

Monitoring on biologic therapies

The use of biologic therapies will be closely monitored by the specialist department and will usually be continued if the treatment is well tolerated and there is an improvement in symptom severity or quality of life. However, if there is no significant improvement after 16 weeks, as per NICE guidelines, then the biologic therapy will stop and different therapy will be sought. It is important to note that any patient starting on biologic therapy will need long term monitoring. Clinicians must be vigilant and record and report any changes in the individuals health status while they are taking the medication.

Step 3

Where biologic therapies do not provide adequate control of symptoms, third-line therapy can be introduced, this includes systemic immunosuppressive treatments, such as ciclosporin. These treatments are designed to suppress the immune system and reduce the inflammatory process. The action of these medications means that they are not selective i.e. they have a suppressive effect on the whole immune system. However, ciclosporin has a higher rate of success and lower risk of side effects than long term corticosteroid therapy. Immunosuppressive treatments are usually started by specialists and require regular monitoring, including blood testing, to reduce the risk of unwanted side effects.

Special considerations

Urticaria in children

Acute urticaria triggered by allergens or infections are more common than chronic urticarias in children. Within the induced urticarias, cold and pressure urticaria are the most common. The majority of children will respond to antihistamine therapy and avoidance of trigger factors. The diagnostic workup for children is similar to adults, however, be aware of Mastocytosis and Cryopyrin-Associated Periodic Syndrome (CAPS), a rare disease with an urticaria-like rash that manifests in childhood.

Urticaria in pregnancy and breastfeeding

Urticaria can persist, worsen or improve during pregnancy and may also be caused by a rise in hormone levels in late pregnancy. Although no medication can be advised to be risk free during pregnancy or breastfeeding, non-sedating second generation antihistamines, such as cetirizine or loratadine, have been shown to have a higher safety profile. First generation H1 antihistamines should be avoided. It is advised that during pregnancy and breastfeeding, if medication is required, then it is to be taken at the lowest possible dose that offers symptom control.

Breastfeeding – loratadine and cetirizine appear safer, with only low levels found in breastmilk, and therefore, these drugs could be considered if required (BSACI 2015). However, seek guidance from local prescribing formularies.

Section 7: Differential diagnosis

(NICE CKS PCDS dermnet nZ)

When is it not urticaria?

Where diagnosis is unsure or for any individual rash that lasts longer than 24 hours, refer onwards for assessment and possible biopsy.

Urticarial vasculitis

- The lesions usually last longer than 24 hours and generally stay in a fixed location.
- Look for bruising, petechial haemorrhage, purpura.
- May also be accompanied by malaise, fever and arthralgia.

Urticaria pigmentosa

(maculo-papular cutaneous mastocytosis)

- Typically look like moles or hyperpigmented papules (red or brownish appearance)
- When stroked (Dariers Sign) can become inflamed, itchy and swollen giving the appearance of hives.
- Occasionally can develop systemic symptoms, including racing heartbeat, diarrhoea, wheezing, headache, fainting and anaphylaxis.

Erythema annulare

- Small raised pink papules that slowly enlarge over a few days to form a ring shape, the centre flattens with a lighter appearance than the outside ring.
- Lesions don't often cause any symptoms and usually appear on the legs, but can appear on the arms, trunk and face.

Erythema multiforme minor

- Lesions are usually fixed with a target like appearance, dark centre, lighter middle area and erythematous margin.
- Triggered by infection in 90% of cases e.g. herpes simplex virus. Other triggers include medications and vaccinations.

Some conditions can initially develop lesions that are pruritic and can have a similar appearance to an urticarial rash. These include:

Atopic eczema

Itchy lesions can appear urticarial initially (Atopic Eczema for Healthcare Professionals).

Pemphigoid (bullous)

Itchy lesions often affect the skin around the skin folds and usually develop blisters after a few weeks.

Dermatitis herpetiformis

Causes intensely itchy rash with red raised patches commonly appearing on the knees, elbows and buttocks.

Contact dermatitis

Rash usually occurs at the site of contact, very itchy with widespread erythema and raised rash and itch lasting longer than 24 hours.

Polymorphic eruption of pregnancy

Urticarial itchy papules mainly occurring in the third trimester of pregnancy, often starting on the abdomen.

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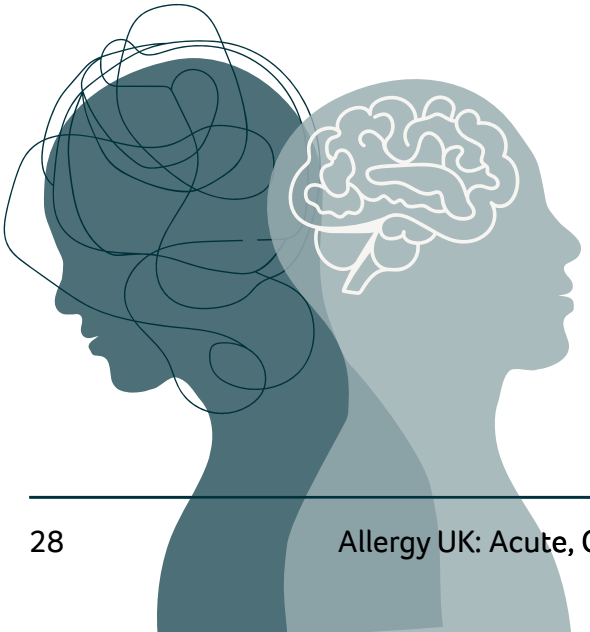
Section 8: Psychosocial impact of chronic spontaneous urticaria

Written by Professor Christina Jones, Director of Research for the School of Psychology, Professor in Clinical Health Psychology.

Chronic Spontaneous Urticaria (CSU), also known as chronic idiopathic urticaria, is a common dermatological condition characterised by the recurrent appearance of wheals (hives), angioedema, or both lasting more than six weeks[1]. While CSU is primarily recognised as a dermatological disorder, its impact extends beyond the physical symptoms affecting both objective functioning and subjective wellbeing[1]. The psychosocial implications of CSU are often underestimated but can be profound, affecting an individual's quality of life, mental health, and social wellbeing. This article explores the psychosocial impact of CSU, highlighting its far-reaching consequences and discusses the importance of a comprehensive approach to its management.



The burden of chronic spontaneous urticaria

CSU is a complex condition with a prevalence of approximately 0.5-1%[2]. It primarily affects adults, with a female predominance, and often lasts for months or even years[2]. The hallmark symptom is the unpredictable appearance of itchy, red wheals on the skin, which can be distressing and debilitating. Although the physical symptoms can be challenging to manage, it is the psychosocial aspects of CSU that can be particularly burdensome for individuals.

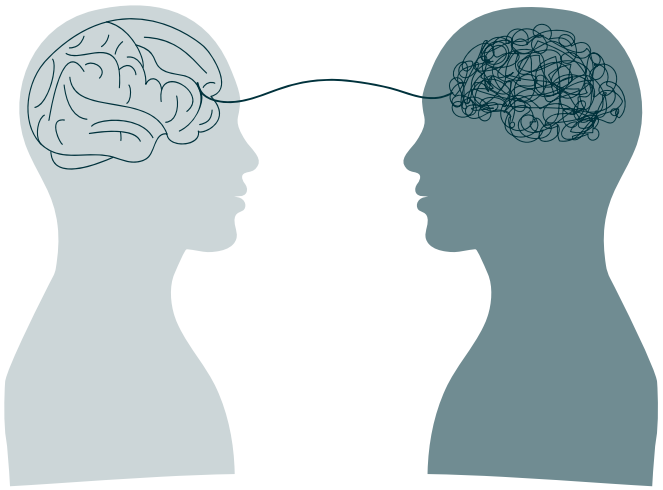
Quality of life

It is not often easy to provide care to individuals with CSU. This is due to the frequent difficulty of identifying an underlying cause, the unpredictable nature and course of symptoms, lack of quality sleep, coupled with lack of efficacy of approved standard therapies which lead to frustration amongst individuals and treating physicians and high disease burden[2]. The chronic and unpredictable nature of CSU

can have a profound impact on an individual's quality of life. Individuals with CSU often live in constant fear of when the next urticarial outbreak will occur. The discomfort, itching, and unsightly wheals can make it difficult for them to engage in daily activities and enjoy their lives to the fullest. Studies have reported that individuals with CSU experienced a significantly impaired quality of life, equivalent to individuals with severe coronary artery disease waiting for bypass surgery[3]. Furthermore, individuals with CSU demonstrated significantly poorer physical, emotional, pain and general functioning compared to those with respiratory allergy and healthy individuals[4]. The impact on quality of life extends beyond physical discomfort. Patients may avoid social gatherings, public places, and physical activities due to the embarrassment and distress caused by the visible hives.

Psychological wellbeing

The psychological impact of CSU should not be underestimated as quality-of-life impairments and social isolation can add to feelings of frustration, sadness, anxiety and depression linked with the recurring nature of the condition[5]. Psychiatric comorbidities presenting as anxiety, depression and somatoform disorders have been found in individuals with CSU[6-7]. Anxiety may manifest in avoidance of potential triggers making often unfounded changes to their diet, exercise and lifestyle more generally[8]. It has also been reported that individuals with CSU are more likely to have a diagnosis of Post-Traumatic Stress Disorder (PTSD) compared with health controls[9]. This is important as prolonged stress can increase inflammation, leading to impaired immune function, and increased sensitivity of mast cells[10]. Whilst stress may be indicated as a trigger, the symptoms associated with CSU outbreaks are also likely to lead to heightened levels of distress[5] and the associated discomfort can lead to a sense of powerlessness and frustration causing a vicious cycle. Moreover, the constant itching and discomfort can interfere with sleep, leading to sleep disturbances and exacerbating feelings of fatigue, irritability, and mood swings. These factors collectively contribute to the overall psychological burden of CSU.



Addressing the psychosocial impact

Whilst studies have repeatedly demonstrated the importance of investigating psychosocial factors both as a cause and a result of CSU[5], there is limited evidence of psychosocial interventions to improve outcomes. Two pilot studies have been evaluated, the first of which utilised a Whole-Person Treatment Approach that actively addresses the impact on the body of all kinds of life events and relational dynamics and how CSU emerges in relation to these factors[11]. The second utilised an Acceptance-Based Training Programme consisting of mantra meditation to help disengage from thoughts, memories, emotions and symptoms, in addition to acceptance and self-compassion practices[12]. Both interventions showed promising results in reduction in CSU symptomology though definitive trials are required to show efficacy.

In the absence of peer-reviewed empirical evidence for psychosocial interventions and in order to provide comprehensive care for patients with CSU, it is essential to address not only the physical symptoms but also the psychosocial impact of the condition. This involves a multi-faceted approach, including:

Patient education

Educating patients about the nature of CSU, its chronicity, and the fact that they are not alone in their struggle can help alleviate some of the psychosocial burden. Understanding the condition and its triggers can empower patients to better manage their symptoms. Validation as a therapeutic approach is also known to regulate individual's distress[13], fosters learning, and strengthens self-identity and therapeutic alliance[14].

Psychosocial support

Mental health support is crucial for patients with CSU, especially those experiencing anxiety or depression. Referral to a psychologist or psychiatrist, or integration of psychological support or lifestyle modifications (see 'Lifestyle modification') into their care plan, may make a significant difference.

Support groups

Support groups can offer a safe space for patients to share their experiences and receive emotional support from those who understand their condition. These groups can be in-person or online, providing a sense of community and understanding. Individuals who have attended group sessions have been found to benefit from the normalisation of their illness and symptoms through the shared encounter, and through seeing how others are affected and cope[15].

Lifestyle modification

Patients can benefit from lifestyle changes to reduce triggers and minimise the impact of CSU. Stress management in the form of

mindfulness, relaxed breathing and muscle relaxation (Simple stress management breathing techniques) may also be encouraged in addition to dietary modifications if indicated, and identification of potential allergens can help patients regain control over their condition.

Dermatological treatment

Effective treatment of CSU can alleviate both physical and psychosocial symptoms. Antihistamines, corticosteroids, and newer therapies such as omalizumab have shown promise in managing CSU[16]. Reducing the frequency and severity of outbreaks can contribute to improved quality of life and mental wellbeing.

Regular follow-up

CSU is a chronic condition, and regular follow-up appointments with healthcare providers are essential. This offers an opportunity to assess the effectiveness of treatment, make necessary adjustments, and address psychosocial concerns.

Conclusion

In summary, CSU is not merely a skin condition; it is a complex disorder with significant psychosocial implications. The unpredictable nature of CSU can lead to a reduced quality of life, heightened psychological distress, and difficulties in maintaining healthy social relationships. Recognising and addressing the psychosocial impact of CSU is crucial for comprehensive patient care. Healthcare providers, including dermatologists and mental health professionals, play a vital role in managing CSU. Patients should be educated, supported, and provided with the resources they need to navigate the challenges of living with this condition. By adopting a holistic approach that addresses both the physical and psychosocial aspects of CSU, we can help patients regain their quality of life and wellbeing. Given the role of stress in both precipitating and exacerbating CSU, ways to reduce stress and promote balance in individuals is essential for effective disease management.

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Healthcare professional resources

Useful organisations

- Allergy UK
- British Association of Dermatologists
- British Dermatological Nursing Group
- British Society for Allergy & Clinical Immunology (BSACI)
- Dermnet NZ
- Primary Care Dermatology Society (PCDS)
- Psychodermatology UK
- University of Nottingham – centre of evidence based dermatology
- RCPCH
- Ga2len Network U CARE

Guidelines

- NICE Clinical Knowledge Summary 2024
- The international EAACI/GA²LEN/EuroGuiDerm/APAACI guideline for the definition, classification, diagnosis, and management of urticaria 2022
- BSACI guideline for the management of chronic urticaria and angioedema 2015 https://www.bsaci.org/wp-content/uploads/2020/01/Urticaria_Angioedema2015-1.pdf

Pathways

- North west allergy and clinical immunology network

Tools to assess quality of life and symptoms severity

- Dermatology Life Quality Index (DLQI)
- Urticaria Assessment Score over seven days (UAS7)
- Chronic urticaria quality of life survey (CU-Q2 oL)
- Angioedema Assessment Score (AAS)

Patient resources

- Allergy UK - Urticaria hives other skin allergy
- British Skin Foundation - Urticaria and angioedema
- British Association of Dermatologists (BAD) Patient information leaflets - Urticaria and Angioedema
- NHS Hives
- NHS Inform - Hives
- Patient Inform - Hives/Urticaria

Apps and online resources

- Chronic Uticaria Self Evaluation (CRUSE) app
- My Hives Diary
- My Symptoms Control Online Survey

Appendix

Patients should be assessed for disease activity, impact, and control at the first and every follow-up visit.

Quality of life measures

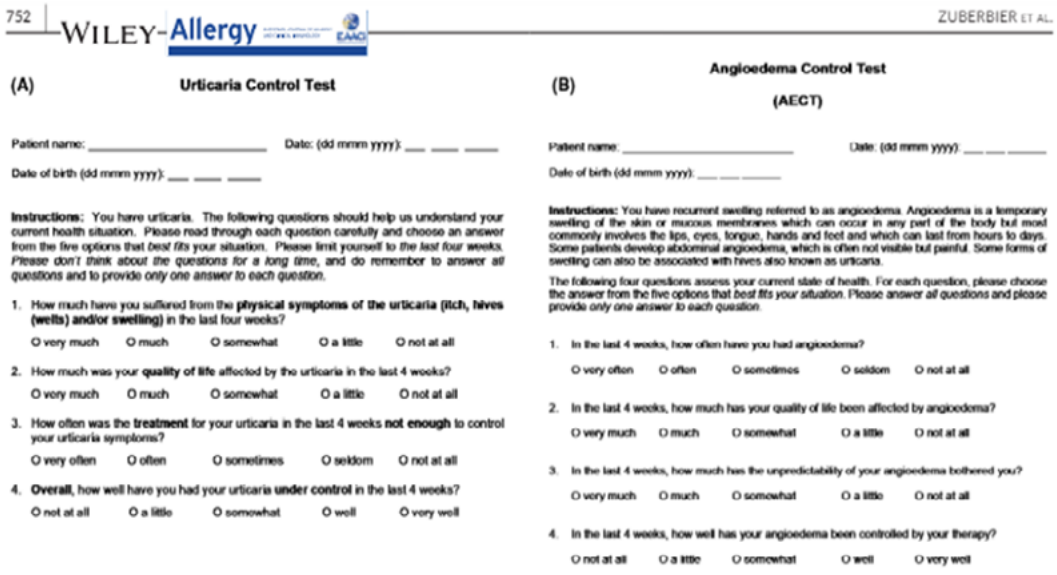
- The chronic urticaria quality of life questionnaire (CU-Q2oL)
- The angioedema quality of life questionnaire (AE-QoL)
- Dermatology life quality index questionnaire

Disease activity measures

- USA7
- Angioedema Activity Score (AAS)

Control measures

- The Urticaria Control Test (UCT),
- The Angioedema Control Test (AECT)



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(A) **Urticaria Control Test**

Patient name: _____ Date: (dd mmm yyyy): __ ___ ____

Date of birth (dd mmm yyyy): __ ___ ____

Instructions: You have urticaria. The following questions should help us understand your current health situation. Please read through each question carefully and choose an answer from the five options that *best fits* your situation. Please limit yourself to *the last four weeks*. *Please don't think about the questions for a long time*, and do remember to answer *all questions* and to provide *only one answer to each question*.

1. How much have you suffered from the **physical symptoms of the urticaria (itch, hives (welts) and/or swelling)** in the last four weeks?
   O very much O much O somewhat O a little O not at all
2. How much was your **quality of life** affected by the urticaria in the last 4 weeks?
   O very much O much O somewhat O a little O not at all
3. How often was the **treatment** for your urticaria in the last 4 weeks **not enough** to control your urticaria symptoms?
   O very often O often O sometimes O seldom O not at all
4. **Overall**, how well have you had your urticaria **under control** in the last 4 weeks?
   O not at all O a little O somewhat O well O very well

(B) **Angioedema Control Test (AECT)**

Patient name: _____ Date: (dd mmm yyyy): __ ___ ____

Date of birth (dd mmm yyyy): __ ___ ____

Instructions: You have recurrent swelling referred to as angioedema. Angioedema is a temporary swelling of the skin or mucous membranes which can occur in any part of the body but most commonly involves the lips, eyes, tongue, hands and feet and which can last from hours to days. Some patients develop abdominal angioedema, which is often not visible but painful. Some forms of swelling can also be associated with hives also known as urticaria.

The following four questions assess your current state of health. For each question, please choose the answer from the five options that *best fits your situation*. Please answer *all questions* and please provide *only one answer to each question*.

1. In the last 4 weeks, how often have you had angioedema?
   O very often O often O sometimes O seldom O not at all
2. In the last 4 weeks, how much has your quality of life been affected by angioedema?
   O very much O much O somewhat O a little O not at all
3. In the last 4 weeks, how much has the unpredictability of your angioedema bothered you?
   O very much O much O somewhat O a little O not at all
4. In the last 4 weeks, how **well** has your angioedema been controlled by your therapy?
   O not at all O a little O somewhat O well O very well

FIGURE 2 A: The urticaria control test (UCT) and B: the angioedema control test (AECT). Copyright for both tools: MOXIE GmbH, Berlin, Germany (www.moxie-gmbh.dc)

Simple stress management breathing techniques

Balloon breathing

Close your eyes and sit comfortably. Imagine that you have a balloon in your stomach and every time you breathe in, the balloon gets bigger. When you breathe out, the balloon gets smaller. Notice what happens as you breathe in and out. Notice what thoughts come to mind, then gently bring your attention back to the breath. If your attention has drifted, gently bring your attention back to your breathing.

Square breathing

- Breathe in as you count 1, 2, 3, 4
- Hold as you count 1, 2, 3, 4
- Breathe out as you count 1, 2, 3, 4
- Hold as you count 1, 2, 3, 4
- Keep your counting even and trace your finger along the 4 edges of a box of tissues or a dice if that helps you to keep focus

Progressive muscle relaxation

Progressive muscle relaxation is an exercise that relaxes your mind and body by tensing and relaxation muscle groups one after the other throughout your entire body. Throughout this exercise you may visualise the muscles tensing and a wave of relaxation flowing over them as you release that tension.

1. Find a quiet place where you can sit comfortably
2. Start by practicing your relaxed breathing
3. Begin by tensing your feet. Curl your toes and flex your feet so that they are as tense as you can make them. Hold this for 5 seconds then release the tension. For the next 10 seconds, feel how relaxed your feet feel. Notice the difference from when they were tense.
4. Do this again with the muscles in your legs by gently raising them and stretching them out in front of you…
    - Your stomach by pushing out the muscles or squeezing them in…
    - Your hands by clenching your fists…
    - Your arms by flexing your arm muscles…
    - Your shoulders by scrunching them up near your ears…
    - Your face by squeezing your eyes tight and pushing your lips together…

You can also search for audio guides on YouTube.

Appendix section 2

BSACI 2015 Algorithm for diagnosing chronic urticaria and or angioedema.

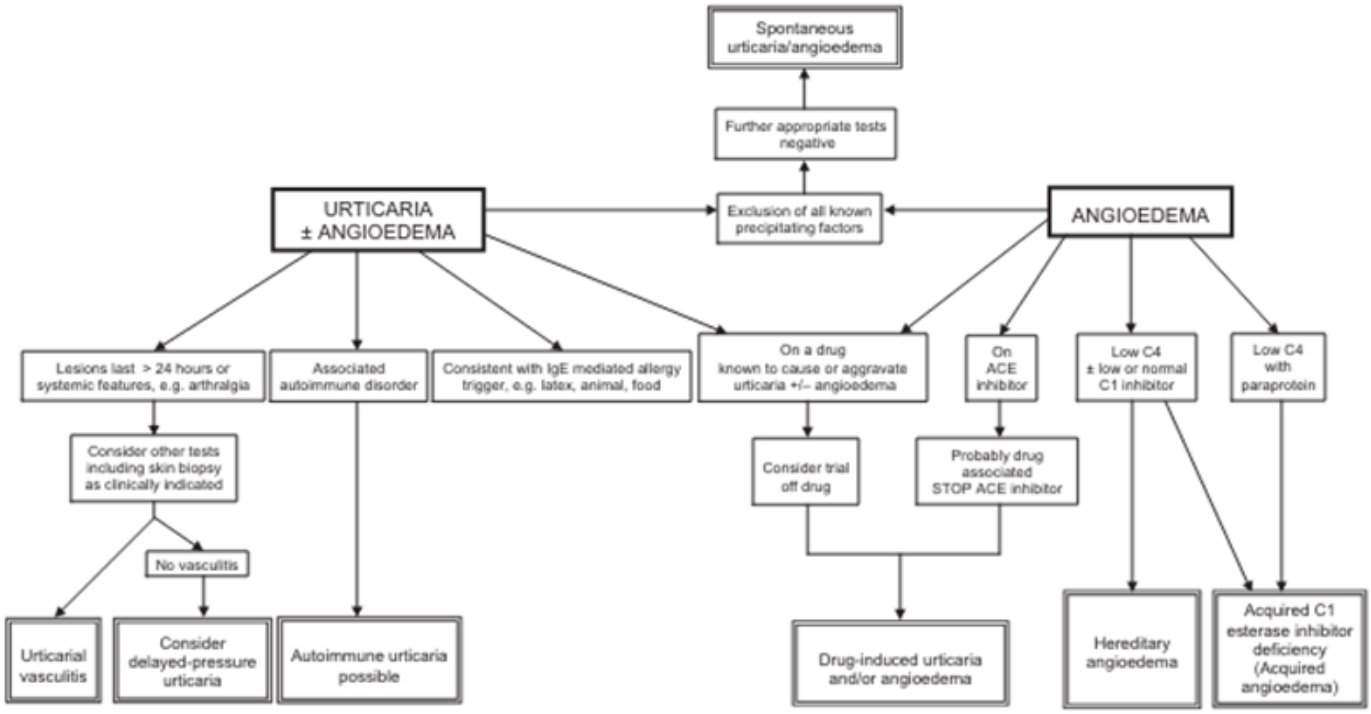

Fig. 1. Algorithm for diagnosis of chronic urticaria and/or angioedema.

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Contact our Helpline
Monday - Friday, 9am-5pm:

Call: 01322 619898
Webchat: allergyuk.org
Email: info@allergyuk.org

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Skin deep is working to improve the diversity of skin images online

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