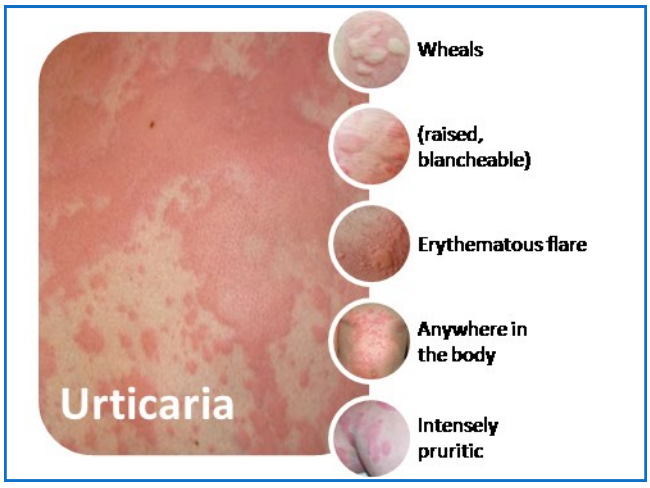
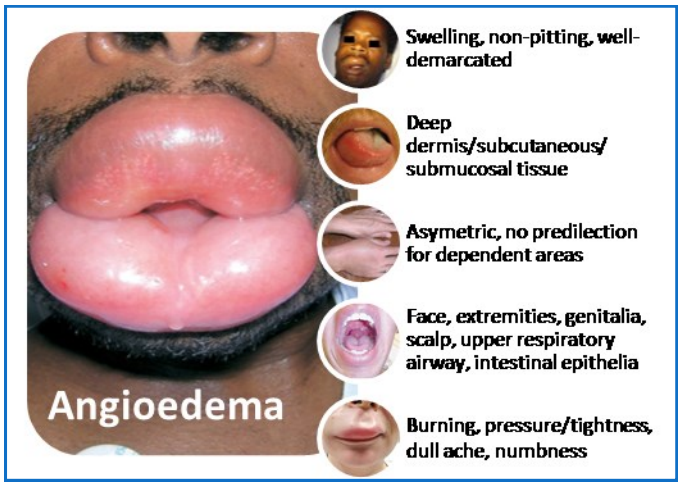
URTICARIA
Referral and Management Pathway for Primary Care





Is urticaria present (with or without angioedema)?
(confirmed on examination/photographs)

N.B. If individual lesions last >24h and leave bruising or scarring → **refer to Dermatology** as this could be urticarial vasculitis

yes

Do any of these apply?
- Reasonable suspicion of specific allergic triggers[1]
- Additional features suggestive of anaphylaxis[2]

Caution: do not over-interpret minor symptoms readily attributable to anxiety

no

Do any of these apply?
- At least some urticaria is present most days (with/without major flare-ups)
- There are clear physical triggers[3]

yes

Chronic spontaneous or inducible urticaria
- Treat following a stepwise management plan[5,6]

no

Acute/intermittent urticaria
- Treat symptomatically with a non-sedating antihistamine[4]
- Patient diary → episode characteristics, frequency, duration, suspected triggers

Not resolved?

Refer to Specialist Urticaria Service
(Dermatology, Allergy, Immunology, as per local provision)

Resolved?

Continue management as above[4/5,6]

no

Is there angioedema only?

yes

Is the patient on ACEi?

yes

Stop ACEi and wait 3 months[7]

Not resolved?

Refer to Allergy/ Immunology

Resolved?

ACEi-induced angioedema[7]

no

Other skin problem (with/without systemic features)

Refer to Dermatology (urgently if with systemic features)

NOTES

Note 1
Reasonable suspicion of specific allergic triggers for urticaria

- Usually single (or multiple cross-reactive) suspected culprit(s); e.g. nuts; penicillins, etc.
- Onset of urticaria/angioedema within 2 hours of exposure (usually less)
- Consistent association between exposure to suspected culprit(s) and onset of episodes (*i.e.* urticaria/angioedema occur *only* when exposed and upon *every* exposure)

Note 2
Additional features suggestive of anaphylaxis

- Significant mucosal angioedema (visible tongue swelling, upper airway obstruction)
- Bronchospasm
- Syncope

Note 3
Inducible urticarias - physical and other triggers

- Pressure/trauma → **dermatographism, delayed pressure urticaria**
- Cold → **cold urticaria**
- Heat → **heat urticaria**
- Vibration → **vibratory urticaria/angioedema**
- Sunlight → **solar urticaria** (consider more common differential diagnosis of polymorphic light eruption)
- Increased body temperature/exercise/sweating → **cholinergic urticaria**
- Contact with allergens (e.g. animal dander, grass pollen, latex, etc.) → **contact urticaria**

Note 4
Treatment of acute/intermitent urticaria and angioedema

- Treat symptomatically - when required until full resolution of urticaria and angioedema
- Use a **non-sedating antihistamine**, 2 tablets at the first sign of symptoms and continue with 1 or 2 tablets once or twice daily until resolution:
    - **cetirizine 10mg** - cost-effective 1st line: available OTC
    - **loratadine 10mg** - cost-effective alternative; available OTC
    - **fexofenadine 180mg** - suitable alternative if the above do not lead to symptom resolution
- Review patient diary and:
    - implement allergen avoidance measures (e.g. foods/drugs), if appropriate
- Consider referral/discussion with Allergy/Immunology if allergy strongly suspected

NOTES Continued

Note 5

Information on chronic spontaneous urticaria and angioedema (CSU) and chronic inducible urticarias (CIndU)

- Chronic urticaria and angioedema is defined by the presence of swellings and/or wheals, usually on most days of the week, for a duration of longer than 6 weeks
- In most cases, the pathogenesis is incompletely understood
  - An exogenous aetiology can be identified in only about 10% of patients.
  - In the majority of patients, **this is not an allergic condition**; rather, it is *spontaneous* and thought to be due to a mast cell activation disorder
  - Although not thought to be causative, there may be factors that exacerbate the condition, such as physical stimuli, stress, infection or ingestion of aspirin and other non-steroidal anti-inflammatory drugs (NSAIDs); as an example, patients may notice worsening of their symptoms following a hot shower, although in general, their symptoms wax and wane independent of any triggers
  - In most cases of chronic spontaneous urticaria and angioedema, without clinical signs or symptoms of an underlying disease, routine laboratory tests are normal
- Chronic spontaneous urticaria and angioedema is a self-limiting condition: ~50% of patients will have complete resolution after 6 months; ~70% after 3 years; ~90% after 5 years; ~92% after 25 years
- Management is symptomatic: antihistamines are effective in the vast majority of patients; other drugs may be considered if required
- See also the **BSACI Primary Care Guideline on Management of Chronic Urticaria and Angioedema** at: http://www.guidelines.co.uk/bsaci/urticaria

Note 6

Stepwise management plan for chronic spontaneous urticaria and angioedema (CSU), and chronic inducible urticarias (CIndU) - as per European and British guidelines[Refs 1-3]

- Provide information on CSU and /or CIndU (can co-exist), including natural history and managemnet plan → detailed below + patient information leaflet from British Association of Dermatologists available at http://www.bad.org.uk/for-the-public/patient-information-leaflets/urticaria-and-angioedema
- Management is symptomatic: antihistamines are effective in the vast majority of patients; other drugs may be considered if required
- Provide advice on control of inducible urticaria, if applicable and practicable; e.g. exposure to cold, heat, trauma (loose-fitting clothes), etc.
- Treatment is based on the frequency and severity of symptoms following a **stepwise plan**, below:
  - If episodes are relatively mild/infrequent (as per patient perception), consider taking a **non-sedating antihistamine (e.g. cetirizine/loratadine/fexofenadine)** on an as-needed basis as per Note 4
  - If episodes are more severe/frequent, consider regular treatment; start with 1 tablet a day, which can be incrementally increased up to 4 tablets per day (e.g. 2 tablets twice daily); leave periods of 1-4 weeks between each incremental step
  - If symptoms remain inadequately controlled despite the above, addition of **montelukast** 10mg daily may provide additional benefit; similarly, addition of **ranitidine** 150 mg twice daily may be tried
  - Once complete control is achieved, remain on corresponding step for ~3-6 months before considering stepping down in a similar stepwise fashion, starting with ranitidine (if used), followed by montelukast (if used), and then by gradual reduction of the non-sedating antihistamine; attempt medication changes every 4-6 weeks
  - If at any stage urticaria/angioedema recur, go back to the previous step that provided complete control and re-attempt stepping down ~3-6 months later. Recurrence of symptoms with decreasing treatment is not, in itself, a reason for referral
- Advise patient to seek immediate medical assistance if there is angioedema associated with breathing compromise
- Occasional and brief courses of oral **prednisolone** (e.g. 20 - 40 mg daily for 3 days) may be used to control *severe* episodes. If there is apparent steroid dependency consider referral
- Please refer if patient remains uncontrolled despite maximum treatment as per the plan above, when we will consider other strategies

NOTES Continued

Note 7
ACE inhibitor-induced angioedema

- ACE inhibitors (ACEi) are a common cause of drug-induced angioedema → ~1% of recipients
- It can occur with any ACEi and is not related to dose
- In >50% of cases, angioedema occurs during the first week of exposure, although it may occur any time during the course of therapy, from hours after starting to years of stable therapy
- Patients commonly present with swelling of the lips, tongue, upper airway (pharynx, larynx, and subglottic area) or face; another (less common) presentation is episodic abdominal pain and diarrhoea due to intestinal angioedema
    - Urticaria and itching are notably absent
    - Early signs of laryngeal oedema may include hoarseness of the throat and inspiratory stridor, which may progress to airway obstruction in up to 10% of cases. Rare cases of fatalities due to massive tongue swelling and asphyxiation have been reported.
- The diagnosis of ACEi-induced angioedema is clinical, based upon the presence of angioedema in a characteristic anatomic site, without itching or urticaria, in a patient taking ACEi; there are no definitive tests to identify those at risk or diagnose this condition
- The management of ACEi-induced angioedema is **discontinuation of the culprit drug and strict avoidance of all ACEi**
- Episodes of angioedema may persist for 3-6 months or more after this (though usually reduction of frequency and severity is observed shortly after); if episodes persist after this period, other causes must be investigated
- Angioedema associated with angiotensin receptor blockers (ARBs) has been occasionally reported and hence their use in individuals with ACEi-induced angioedema has been questioned but is not contra-indicated
- Antihistamines, glucocorticoids, and adrenaline are usually considered ineffective or minimally effective in treating ACEi-induced angioedema
- Angioedema episodes tend to resolve spontaneously, but urgent in-hospital attention is required if the airway is threatened

Specialist Services provided by:

- **Greater Manchester**
    - Salford Royal NHS Foundation Trust
    - Allergy Centre, Wythenshawe Hospital, Manchester University NHS Foundation Trust
    - Immunology and Allergy Service, Manchester Royal Infirmary, Manchester University NHS Foundation Trust
- **Liverpool**
    - Royal Liverpool and Broadgreen University Hospitals NHS Trust
- **Lancashire**
    - Lancashire Teaching Hospitals NHS Foundation Trust

Based on:

- Zuberbier T, Aberer W, Asero R et al. The EAACI/GA2LEN/EDF/WAO Guideline for the definition, classification, diagnosis, and management of urticaria: the 2013 revision and update. Allergy 2014;69(7):e1-29; EAACI—European Academy of Allergy and Clinical Immunology
- BSACI Primary Care Guideline—Management of chronic urticaria and angioedema: http://www.guidelines.co.uk/bsaci/urticaria
- Powell R, Leech S, Till S et al. BSACI Guideline for the management of chronic urticaria and angioedema. Clin Exp Allergy 2015;45:547-65
- Patient information leaflet from British Association of Dermatologists (BAD) available at http://www.bad.org.uk/for-the-public/patient-information-leaflets/urticaria-and-angioedema; multiple languages available