DORSET MEDICINES ADVISORY GROUP

Urticaria - Primary Care Treatment Pathway

Urticaria – also known as hives or nettle rash – is a raised, itchy rash that can occur on just one part of the body or be spread across large areas. The weals of urticaria last less than 24 hours although patients may develop new weals on a daily basis. If urticaria clears completely within six weeks, it is known as acute urticaria. Urticaria occurring for more than six weeks is referred to as chronic urticaria. Most cases of chronic disease occur without an obvious trigger (chronic spontaneous urticaria). Some urticaria has a physical trigger such as pressure (symptomatic dermographism or delayed pressure urticaria), cold or exercise (cholinergic urticaria), or may be drug induced (e.g. by NSAIDS, ACE inhibitors and opioids). All forms of urticaria can be treated with antihistamine although physical urticaria is less likely to respond to treatment than spontaneous urticaria. Most cases of urticaria settle spontaneously within two years but the condition can last for decades in some patients.

Referral criteria

Refer routinely to dermatology if patients are not responding to standard treatment (see primary care treatment below, up to step 4), they can then be considered for immunomodulation treatment such as ciclosporin (can be very useful for patients thought to have an autoimmune basis for their urticaria), methotrexate or omalizumab.

The diagnosis of urticaria is primarily clinical therefore do not routinely refer for allergy testing. The British Association of Dermatologists (BAD) has produced a patient information leaflet which covers this in detail for patients.

PRIOR TO SPECIALIST REFERRAL -conduct a full blood count (FBC), erythrocyte sedimentation rate (ESR), thyroid function tests (TFTs), liver function tests (LFTs), and Helicobacter pylori screening (if gastrointestinal symptoms are present).

Primary Care Treatment

If patient does not meet referral criteria, treat in primary care :

- Step 1: **non-sedating oral antihistamines**

1) Start with a standard dose of one tablet a day regularly.
2) If the response is inadequate increase the dose up to a maximum of four tablets per day. This unlicensed dose is evidence-based and recommended in the European guidelines on urticaria. Give the lowest dose that controls the symptoms; continuous dosing is more effective than on demand treatment. Dosing can be given OD or BD – BD dosing may reduce the risk of sedation and give better all-day symptomatic relief. If the patient is getting little response try a different antihistamine - not all antihistamines are the same for every patient. Long term systemic steroids are not recommended but short courses of prednisolone (at a dose up to 40mg) can be given for up to 5-7 days for acute urticaria and acute flares of chronic urticaria.
3) At higher doses it is important to exercise caution in patients with kidney, liver and cardiac disease. Fexofenadine and cetirizine are excreted by the kidneys, and loratadine and desloratadine are metabolised by the liver.
4) Note that antihistamines as a medicine class have been associated with the adverse reactions, tachycardia and palpitations in patients with a history of or ongoing cardiovascular disease.
5) Reassure the patient that it is safe to take antihistamines for as long as is needed and the dose can be reduced intermittently to check that the condition is still active and requiring treatment.

- Step 2: **sedating antihistamines**

1) Can be added in at any point in step 2 for patients who have symptoms interfering with sleep
2) An example is hydroxyzine tablets, in adults the dose is 25-50 mg nocte(can be increased to 100mg at night although this dose is off-label, and note MHRA advice on risk of QT interval prolongation and Torsade de Pointes especially in the elderly)
3) Warn the patient that it could make them feel drowsy in the morning
4) Sedative antihistamines should only be used intermittently

- Step 3: **2nd line agent , anti-leukotriene**

1) Add in a leukotriene receptor antagonist e.g. montelukast 10mg OD
2) They should be added in to the antihistamines
3) If there is no response after six weeks stop.

- Step 4 : **referral to dermatologist for :**

1) Consideration of an immunomodulant – ciclosporin, omalizumab.
2) Urticarial vasculitis (presents as an urticarial rash that leaves bruising or purpura after the weals). Consider adding in dapsone (in Secondary Care as further clinical assessment and blood monitoring required)
3) Delayed pressure urticaria - consider adding in daspone or sulfasalazine (in Secondary Care as blood monitoring required)
4) If hereditary angioedema is present (without weals) consider tranexamic acid

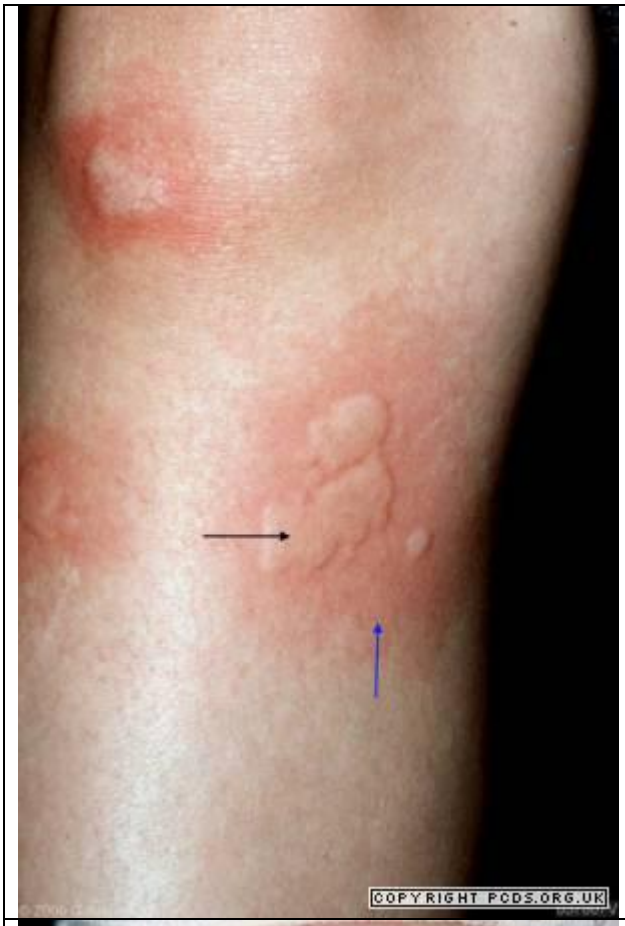
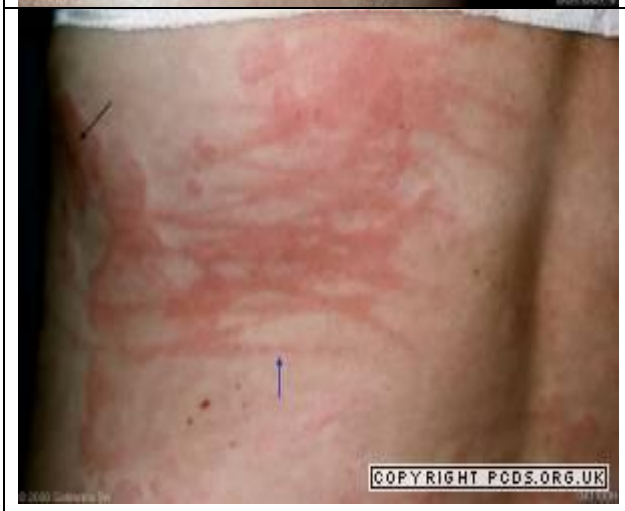
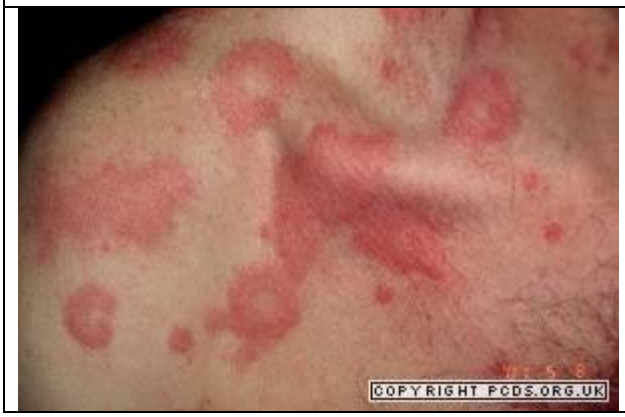
Illustrated Table of Treatment Steps

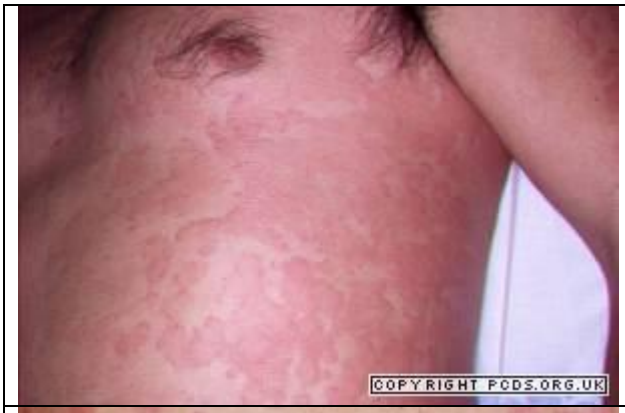
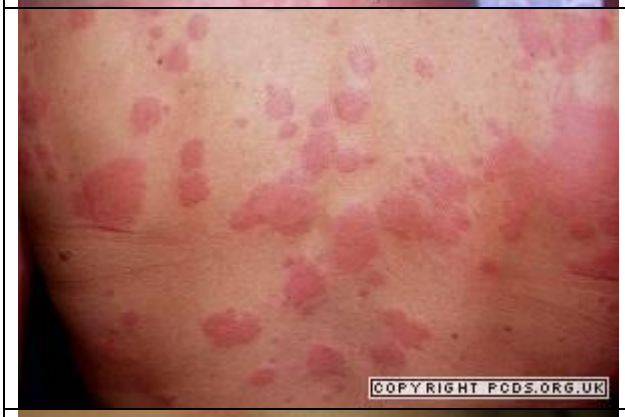
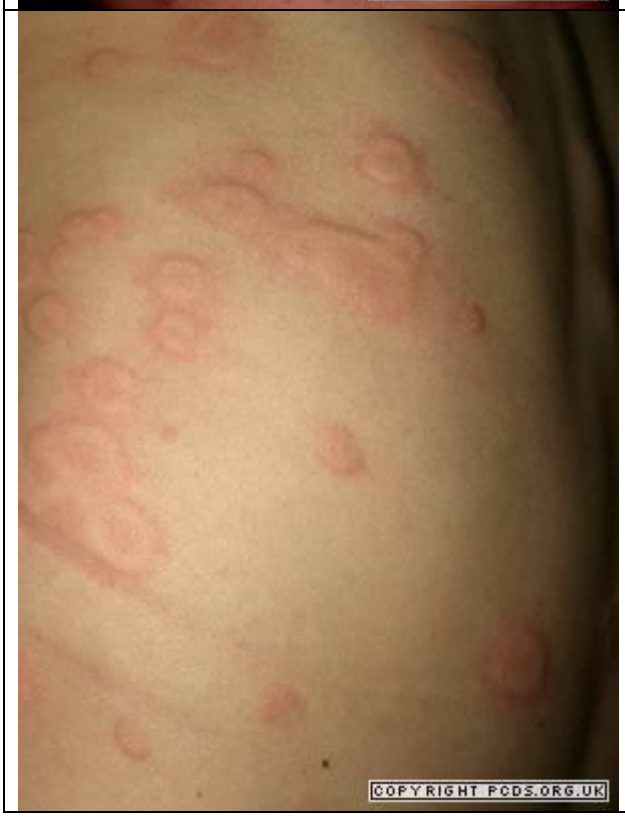
Identification of Triggers			
Education and avoidance of triggers			
1) Standard dose non-sedating H1 antihistamine	**2) Up-dosed H1 antihistamine (up to four-fold standard dose)**	**3) Consider adding monteleukast or ,if angioedema is present, use tranexamic acid**	**4) Consider an immunomodulant (e.g. omalizumab , ciclosporin) or alternative agent in secondary care.**

Self-care advice – General Measures

- Lifestyle - keep the skin cool, reduce stress
- Avoid any obvious physical / other triggers
- Medications - drugs such as aspirin and other NSAIDs, and opioid analgesics may aggravate or cause symptoms. ACEI can cause angioedema without urticaria. It is important to check for both prescribed and over the counter medications
- Provide a patient information leaflet from BAD on urticaria and angioedema.
- Diet - although chronic spontaneous urticaria is not an allergic condition, in some patients pseudoallergens (such as salicylates, azo dyes and food preservatives) may play a role. If a patient has a strong belief that diet is playing a role the patient information leaflet above provides some information on keeping a food diary.

Images of Urticaria

	**Spontaneous urticaria - wheal and flare** Wheal (black arrow) and flare (blue arrow)
	**Spontaneous urticaria with dermographism** Urticarial plaque (black arrow) with dermographism (blue arrow
	**Spontaneous urticaria** Copied with kind permission from Dermatoweb

	**Spontaneous urticaria** Copied with kind permission from Dermatoweb
	**Spontaneous urticaria** Copied with kind permission from Dermatoweb
	**Spontaneous urticaria** Copied with kind permission from Dermatoweb

Treatment of Urticaria

1st line treatment choices (green traffic light categorised)	**Non –Sedating antihistamine** • **Cetirizine** • **Loratidine** • **Fexofenadine (use the antihistamines above first unless contra-indicated, 3rd choice only)** **Sedating antihistamine** • **Hydroxyzine**
2nd line treatment choices (where 1st line ineffective, contra-indicated or not tolerated)	• **Leukotriene Receptor Antagonist, Montelukast - (green traffic light categorised)** • **Tranexamic acid - (green traffic light categorised)** • **Ciclosporin- (amber traffic light categorised)** • **Dapsone (red traffic light categorised)** • **Omalizumab-(red traffic light categorised)** • **Methotrexate (pending DMAG submission)**
Notes	• Starting points and rate of progression between steps depends on clinical severity and response. Short course of corticosteroids (up to a maximum 40mg total daily dose for 5-7 days) for severe exacerbations. • Menthol creams can be used (with / without antihistamines) to relieve itching.

Prices and prescribing information

Product name	Dose	Price
Cetirizine	10mg once daily	10mg 30 tablets £0.86 10mg 7 capsules £2.91 1mg / 1ml Solution S/F 200ml £1.45

Loratidine	10mg once daily	10mg 30 tablets £0.86 5mg / 5ml Solution 100ml £1.88
Fexofenadine	180mg once daily	180mg 30 tablets £3.13
Hydroxyzine	25mg to 50mg at night(can be increased to 100mg at night although this dose is off-label)	25mg tablets 28 tablets £0.62
Montelukast	10mg once daily (in the evening)	10mg 28 tablets £1.81 5mg chewable 28 tablets £1.69
Tranexamic acid	15–25 mg/kg (maximum 1.5 g) 2–3 times per day (1)	500mg 60 tablets £4.43
Ciclosporin	Not stated - suggested low dose	25mg 30 capsules £13.05* 50mg 30 capsules £25.50* 100mg 30 capsules £48.89* (*capimune) 100mg / ml solution 50ml £93.51
Omalizumab		£256.15 for a 150 mg prefilled syringe (excluding VAT; 'British national formulary' [BNF] online October 2014). A single dose of 300 mg costs £512.30 and the cost for a 24 week course of treatment is £3073.80 (excluding VAT). Based on Omalizumab commissioning statement.

(Ref: Prices from Electronic Drug traffic http://www.nhsbsa.nhs.uk/PrescriptionServices/4940.aspx Accessed August 2016 unless otherwise stated)

Based on

Primary Care Dermatology Website Clinical Guidance on Spontaneous Urticaria accessed December 2015 via: http://www.pcds.org.uk/clinical-guidance/urticaria-spontaneous-syn.-chronic-ordinary-urticaria

National Institute for Health and Care Excellence. Clinical Knowledge Summaries. Urticaria. Last revised in December 2011 Accessed via http://cks.nice.org.uk/urticaria#!scenario in January 2016

British Society for Allergy and Clinical Immunology. Guideline for the management of chronic urticaria and angioedema accessed December 2015 via: http://www.bsaci.org/Default.aspx?PageID=8611258&A=SearchResult&SearchID=2188326&ObjectID=8611258&ObjectType=1

References

1. Powell R.J , BSACI guideline for the management of chronic urticaria and angioedema , Clinical and experimental allergy journal. 2015;45: 547-565

First Edition, approved by DMAG July 2016

For review July 2018, unless new guidance dictates a review sooner