A profile of the various forms of urticaria and how to treat them

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There are various types of urticaria and, while generally easy to diagnose, it can be confusing. It is also important to recognise when to refer to secondary care.

<table>
<thead>
<tr>
<th>Physical urticaria</th>
<th>Trigger</th>
<th>Clinical characteristics</th>
<th>Diagnostic and other tests</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dermographism</td>
<td>Friction</td>
<td>Patient itchy, then scratches, after which linear weals appear. Worse if warm</td>
<td>Graded gentle friction against the skin (see Figure 1)</td>
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<tr>
<td>Cholinergic urticaria</td>
<td>A rise in core temperature, usually with sweating, eg with heat, emotion or exercise</td>
<td>Tiny weals, about 2mm in diameter, with big surrounding flare, sometimes confluent. Often on trunk and proximal limbs</td>
<td>Hot bath test (10 minutes at 42°C) or exercise test, with monitoring</td>
</tr>
<tr>
<td>Delayed pressure urticaria</td>
<td>Pressure, such as tight clothing, carrying heavy items, or standing on a ladder</td>
<td>Weals occurring at sites of pressure</td>
<td>Weights on the skin for 20 minutes, assess at 6 hours</td>
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<tr>
<td>Cold urticaria</td>
<td>Cold object, wind or water, or cold food/drink. In a minority a drop in core temperature is needed</td>
<td>Weals usually localised to areas of cold skin/mouth. Weals may only appear on rewarming</td>
<td>Ice cube test. Also check cryoglobulins and cold agglutinins</td>
</tr>
<tr>
<td>Aquagenic urticaria</td>
<td>Water of any temperature</td>
<td>Similar appearance to cholinergic urticaria. Aquagenic pruritus (no weals) may be associated with myeloproliferative disease.</td>
<td>Tepid bath tests (10 minutes at 37°C). Check FBC annually in aquagenic pruritus</td>
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<tr>
<td>Solar urticaria</td>
<td>Sun</td>
<td>Weals at sites of sun exposure, with sparing of covered sites</td>
<td>Photo-testing. Must be differentiated from other photosensitive rashes. ANA and porphyrins</td>
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*Antihistamines must be withdrawn for three days before testing

Urticaria is a common condition, affecting up to 20 per cent of the population at some time in their lives. It is more common in women. It is characterised by itchy red weals, which usually resolve within 24 hours, leaving no mark. About 40 per cent of patients with urticaria also have angioedema. Systemic symptoms such as wheezing, breathlessness, gastrointestinal upset, dizziness, joint pain and malaise may accompany severe disease.

Urticaria can be divided into acute and chronic forms, with chronic urticaria persisting for six weeks or more. Chronic urticaria is further subdivided into spontaneous and physical (or inducible) urticarias. Less common forms of urticaria include urticarial vasculitis and urticaria associated with autoimmune or rarely auto-inflammatory diseases such as Schnitzler’s syndrome or Muckle-Wells syndrome.

**Acute urticaria**
Acute urticaria is the most common type of urticaria, and may occur at any age. The cause is unknown in more than half of cases. However, triggers include infections, particularly viral upper respiratory tract infections, and multiple different drugs, most often NSAIDs and antibiotics. Less frequent causes include type I hypersensitivity reactions to food, latex or insect stings. Acute urticaria may be one of the presenting symptoms of anaphylaxis.

**Physical (or inducible) urticarias**
Physical urticarias can occur at any age, but are probably most common in young adults. Weals appear reproducibly within a few minutes of being triggered by a specific physical stimulus (see Table 1), and settle often within 10–20 minutes but at most within two hours.
The exception is delayed pressure urticaria (DPU) where weals appear 30 minutes to 12 hours after pressure against the skin, and last for two to three days. The prolonged weal duration may make it difficult to distinguish DPU from urticarial vasculitis.  

Physical urticarias may occur together and/or with chronic spontaneous urticaria. Some of the physical urticarias, such as cholinergic, cold or solar urticaria, can produce a spectrum of symptoms from pruritus, urticaria, angioedema, to, in rare and severe cases, anaphylaxis. Physical urticarias may result in a significant reduction in quality of life. Indeed, it may be impossible to do heavy physical work with severe delayed pressure urticaria, or to work in a cold environment with significant cold urticaria.  

Chronic spontaneous urticaria  
Chronic spontaneous urticaria (see Figure 2) affects approximately 0.1 per cent of the population. The disease is not life threatening, but can be very disabling and again may have a significant affect on quality of life. By definition no cause can be identified, but about one-third of patients have auto-antibodies against the high affinity immunoglobulin E (IgE) receptor, or against IgE.  

Urticarial vasculitis  
This should be suspected if weals last for more than 24 hours, leave residual bruising, are associated with severe systemic symptoms or respond poorly to treatment. It can be difficult to distinguish urticarial vasculitis from DPU, since in both weals are prolonged and may occur at pressure sites. It is important to identify urticarial vasculitis, as it is more likely than other forms of urticaria to be associated with other underlying diseases, such as systemic lupus erythematosus.  

Differential diagnosis  
The transient nature of urticarial weals usually makes diagnosis easy. However, confusion may arise. For example, acute eczema may present with redness and swelling, but there is likely to be weeping or vesicle formation, then dryness and scaling, and the rash will be more persistent. Urticarial lesions may be annular, but true target lesions will not occur (at least three concentric rings are needed for a target lesion) thus excluding erythema multiforme. Bullous pemphigoid may present with urticarial lesions as a prodromal phase, but blisters follow in a few days or weeks.  

Investigations  
It is important to avoid over investigation, and a thorough history may be all that is needed. In acute urticaria, prick tests or specific IgE tests may be helpful to identify an allergen, but only if type 1 hypersensitivity is suspected. Tests for the physical urticarias are listed in Table 1. In chronic spontaneous urticaria, only a FBC, ESR and TSH are required, but abnormalities should be pursued. If urticarial vasculitis is suspected, a skin biopsy and full vasculitis screen are indicated.  

Treatment  
Known triggers should be avoided. A cool ambient temperature may reduce itching, as may 1–2 per cent menthol in aqueous cream. In mild disease this may be sufficient.
Orally, H<sub>1</sub> antihistamines remain first-line treatment. The newer low sedating antihistamines are recommended, for example loratadine, cetirizine or fexofenadine. If one does not work, another may.5–7

The older sedating H<sub>1</sub> antihistamines should be avoided unless the patient has had prolonged disease-related periods without sleep, having tried low sedating drugs. If used, the patient should be warned about cognitive impairment the next day, particularly when driving. Unlike newer antihistamines, sedating ones may be dangerous in overdose. Hydroxyzine, given before bed, is usually the drug of choice.5,6

The European Guidelines recommend up-dosing low sedating H<sub>1</sub> antihistamines to up to quadruple dosages for one to four weeks, if licensed dosages fail.5 There is some evidence that more patients will respond. However, all antihistamines lower seizure threshold, some antihistamines are excreted predominantly by the kidneys, while others are metabolised by the liver, some may become sedating at higher dosages, and some interact with other medications. Thus caution is required in patients with co-morbidities including renal or hepatic impairment or epilepsy, in the elderly and in patients on other drugs or at risk of sedation.

In severe acute urticaria, or for a severe exacerbation of chronic spontaneous urticaria, a short course of prednisolone may help. It is best to limit the duration of treatment to one to two weeks, because of the risk of significant adverse effects with prolonged use. Additionally, tachyphylaxis may occur, in which ever increasing dosages are needed to maintain disease control.

Beyond this, H<sub>2</sub> antihistamines, leukotriene inhibitors, the mast cell stabiliser ketotifen, low dose doxepin, and then immunosuppressive drugs such as ciclosporin, methotrexate or mycophenolate mofetil can be used for chronic disease, although none are licenced for urticaria.5–7 Additionally, although expensive, the anti-IgE antibody omalizumab, appears safe and effective, and thus represents a very promising new treatment.6,11 Drugs other than antihistamines and a brief course of prednisolone may be best initiated in secondary care.

Acute urticaria can be one of the presenting symptoms of anaphylaxis, in which case emergency treatment should be given, including intramuscular adrenaline if appropriate.16

Pregnancy
None of the oral preparations available for urticaria have been proven totally safe in pregnancy. The US Food and Drug Administration put chlorpheniramine, loratadine and cetirizine in category B, and so these antihistamines should be used in preference to hydroxyzine and fexofenadine, which are in category C.

Prognosis
By definition acute urticaria resolves within six weeks, but usually settles within three weeks. The chronic urticarias may persist for years.15,20

The GP’s role
Many patients with urticaria can be managed in primary care, particularly when disease is mild and readily controlled. Suggested reasons for referral are listed in Table 2.

Conclusion
Urticaria is a common condition, but can be very disabling when severe. It is useful to distinguish the different subtypes, and important not to over investigate. The disease can often be treated in primary care, with the avoidance of triggers, and use of low sedating antihistamines.

Referral into secondary care should be considered when disease control is poor, symptoms are severe, if there is diagnostic uncertainty, or if more unusual forms such as urticarial vasculitis are suspected.

Table 2. When to consider referral in to secondary care

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<tr>
<th>Suggested reasons for referral</th>
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<tr>
<td>Severe urticaria</td>
<td>Any treatment not controlled with symptomatic treatment and/or licensed dosages of H&lt;sub&gt;1&lt;/sub&gt; antihistamines</td>
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<tr>
<td>Urticaria not controlled with</td>
<td>For testing for physical urticarias</td>
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<tr>
<td>symptomatic treatment and/or</td>
<td>Where urticarial vasculitis is suspected, or needs to be differentiated from DPU</td>
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<td>licensed dosages of H&lt;sub&gt;1&lt;/sub&gt; antihistamines</td>
<td>If there is an associated fever, or there are high inflammatory markers</td>
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<td>Other atypical features, such as familial or life long disease</td>
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<td></td>
<td>Urticaria in pregnancy</td>
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<td></td>
<td>Diagnostic uncertainty</td>
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References
2. Schafer T, Ring J. Monogr Allergy 1993;31:49–60.

Declaration of interests
None to declare.

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