Diagnosis and management of chronic spontaneous urticaria in primary care

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**Symptoms of urticaria**

**Wheals (hives)**
- Skin lesion that is raised or has central oedema
- Almost always surrounded by a reflex erythema
- Lasts <24 hours
- Associated with pruritus and sometimes a burning sensation

**Angioedema**
- Sudden pronounced oedema
- Erythematous or causes discolouration of the skin
- Inflammatory process occurs in the deep dermis and the subcutaneous cell tissue, commonly affecting the submucosal tissues
- Pruritus is less common
- Lasts up to 72 hours

>20% of patients with chronic spontaneous urticaria (CSU) reported ≥1 hour of missed work in the past 7 days due to problems with their CSU

47% of people with CSU reported concomitant anxiety/depression

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Definitions

**Allergy:**
Hypersensitivity reaction caused by specific immunological mechanisms. Hypersensitivity describes the onset of objectively reproducible signs and symptoms after exposure to specific stimuli at doses usually tolerated by the population.\(^3,4\)

**Autoimmunity:**
The system of immune responses that target “self”. Patients with autoimmune CSU typically produce IgE to autoallergens, IgG anti-IgE or IgG anti-Fc\(\varepsilon\)RI (the high-affinity IgE receptor).\(^5\)

**Urticaria:**
Disease characterised by the sudden appearance of wheals, angioedema, or both, that can be caused by allergic, autoimmune or other pathogenic causes.\(^1\)
- Acute urticaria: lasts <6 weeks
- Chronic urticaria: lasts ≥6 weeks

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20% of people will experience acute urticaria at some point in their lives\(^1\)

CSU point prevalence varies between studies, it has been shown to be between 0.02–1% of the population\(^6,7\)

45% of CSU is autoimmune with the other 55% of unknown cause (idiopathic)\(^8\)
### Acute urticaria triggering factors

- Idiopathic (50%)
- Infection (40%)
- Physical stimuli
- Medicinal products (9%) – intolerance or allergy
- Food (1%) – most common in children
## DIAGNOSIS AND MANAGEMENT OF CHRONIC SPONTANEOUS URTICARIA IN PRIMARY CARE

### Spotting urticaria

<table>
<thead>
<tr>
<th><strong>DIFFERENTIAL DIAGNOSIS</strong></th>
<th><strong>SCABIES</strong></th>
<th><strong>TOXICODERMA</strong></th>
<th><strong>ANGIOEDEMA</strong></th>
<th><strong>CELLULITIS</strong></th>
<th><strong>LOCALISED ECZEMA</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ELEMENTARY LESIONS</strong></td>
<td>Sulci, vesicles, papules and excoriations</td>
<td>Maculopapular/urticariform exanthema</td>
<td>Erythematous, oedematous plaque</td>
<td>Painful and hot erythematous plaques</td>
<td>Erythematous, oedematous plaques + vesicles and/or scabs</td>
</tr>
<tr>
<td><strong>KEY DIAGNOSTIC ELEMENTS</strong></td>
<td>Hands and wrists, genitals, armpits and nipples</td>
<td>Generalised and symmetrical, predominantly in skin folds</td>
<td>Eyelids, lips, genitals, around the joints</td>
<td>Sensation of burning/heat &gt; pruritus</td>
<td>Pruritus Exudation Distribution as if it were self-inflicted</td>
</tr>
<tr>
<td><strong>QUESTION</strong></td>
<td>Pruritus in co-habitants</td>
<td>Medicinal products in the last 6 weeks</td>
<td>Association with wheals (urticaria) Other causes: - Medicinal products (ACE inhibitors, ARBs, sitagliptin, etc.) - Cases in family members</td>
<td>Entry point Predisposing factors (diabetes, alcoholism, immuno-suppressive therapy, HIV, etc.)</td>
<td>Contact products (pharmaceutical creams, cosmetics, etc.)</td>
</tr>
</tbody>
</table>

### Chronic urticaria worsening factors

- Aspirin and other NSAIDs
- Infection of the upper respiratory tract and other viral infections
- Physical stimuli (inducible urticaria)
- Premenstrual period
- Stress
- Alcohol
- Food pseudoallergens (for example food additives and salicylates)

ACE: Angiotensin-converting enzyme inhibitors; ARBs: angiotensin receptor blockers; CRP: C-reactive protein; GI: gastrointestinal

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Diagnosing urticaria

The first step to diagnose CSU is a thorough patient history\(^1\)

**PATIENT WITH PRURITUS**

**SYSTEMIC SYMPTOMS?**

**RULE OUT ANAPHYLAXIS AND URTICARIAL VASCULITIS**

**ANGIOEDEMA ONLY**

**CLINICAL HISTORY OF WHEALS?**

**DO INDIVIDUAL WHEALS LAST <24 HOURS?**

**RULE OUT TOXICODERMA, BITES, CONTACT ECZEMA, SCABIES**

**WHEALS +/- ANGIOEDEMA**

**SYMPTOMS FOR ≥6 WEEKS**

**ACUTE URTICARIA**

**SYMPTOMS PERSIST FOR ≥6 WEEKS**

**CHRONIC URTICARIA**

**BRADYKININ-INDUCED ANGIOEDEMA**

**RECEIVING TREATMENT* THAT MAY CAUSE BRADYKININ-INDUCED ANGIOEDEMA?**

**SEE MANAGING URTICARIA PROTOCOL**

**SCRE NC**

**CRP: C-reactive protein; ESR: Erythrocyte sedimentation rate; *Angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs)**

Use of diagnostic tests for urticaria:

**ACUTE URTICARIA:** None

**CHRONIC URTICARIA:**

Basic blood test with ESR or CRP.
Further examinations completed by specialist if suspected through clinical history

Most cases of urticaria ARE NOT CAUSED BY ALLERGIES. Therefore, routine allergy tests are not necessary\(^1\)

The spontaneous appearance of wheals, angioedema or both:\(^1\)

**Acute urticaria:** a few days up to <6 weeks
**Chronic spontaneous urticaria:** ≥6 weeks

**DIAGNOSIS AND MANAGEMENT OF CHRONIC SPONTANEOUS URTICARIA IN PRIMARY CARE**

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Managing urticaria

**PRIMARY CARE**

SYMPTOMS AT PRESENTATION

- **<6 WEEKS**
  - **ACUTE URTICARIA**
  - **AVOID TRIGGERING FACTORS (IF IDENTIFIED)**

- **≥6 WEEKS**
  - **CHRONIC URTICARIA**
  - **AVOID WORSENING FACTORS**

SECOND-GENERATION H1-ANTIHISTAMINE (SGAH)

If symptoms persist
>6 weeks despite
2–4 weeks' treatment

If symptoms persist
≥6 weeks

REMISSION

A short course of glucocorticosteroids may be considered in cases of severe exacerbation, but should be avoided where possible due to the risk of adverse events. Other treatment options are also available.

**SPECIALIST CARE**

REFER TO SPECIALIST

- **ADD OMALIZUMAB TO SGAH**
  - **SYMPTOM CONTROL**

- **ADD CICLOSPORIN TO SGAH**

*Referral may be possible sooner depending on patient symptom and medication history prior to presentation.*
Managing urticaria

Second-generation, non-drowsy H1-antihistamines form the basis of first- and second-line therapy in CSU\textsuperscript{14–22}.

<table>
<thead>
<tr>
<th>Name</th>
<th>First-line dose in adults</th>
<th>Licensed age in CSU patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bilastine</td>
<td>20 mg/day</td>
<td>≥12 years of age</td>
</tr>
<tr>
<td>Cetirizine</td>
<td>10 mg/day</td>
<td>≥6 years of age</td>
</tr>
</tbody>
</table>
| Desloratadine | 5 mg/day          | ≥1 years of age (oral solution)  
                            ≥12 years of age (tablet) |
| Ebastine  | 10 mg/day                 | ≥18 years of age            |
| Fexofenadine | 180 mg/day             | ≥12 years of age            |
| Levocetirizine | 5 mg/day          | ≥2 years of age (oral solution)  
                                ≥6 years of age (tablet) |
| Loratadine| 10 mg/day                 | ≥2 years of age and bodyweight >30 kg |
| Mizolastine| 10 mg/day                | ≥12 years of age            |
| Rupatadine| 10 mg/day                 | ≥2 years of age (oral solution)  
                                ≥12 years of age (tablet) |

The use of first-generation, sedating antihistamines is not recommended\textsuperscript{1}

*Antihistamine availability may differ between countries
Paediatric patients
• Cetirizine, desloratadine, levocetirizine, loratadine and rupatadine are indicated in paediatric populations (N.B. at differing licensed ages)
• Bilastine, fexofenadine, mizolastine as well as the above agents are licensed for adolescent (≥12 years of age) patients

Liver insufficiency (LI)
• Bilastine, desloratadine, fexofenadine, levocetirizine: no dose adjustment
• Ebastine: in severe LI, do not administer more than 10 mg
• Rupatadine: not recommended at present due to current lack of evidence but no specific warnings or pharmacological alerts

Renal insufficiency
• Fexofenadine, bilastine*, ebastine: no dose adjustment
• Cetirizine, loratadine, desloratadine, levocetirizine: precaution and dose adjustment
• Rupatadine: not recommended at present due to current lack of evidence but no specific warnings or pharmacological alerts

Cardiovascular issues
• Ebastine: precaution in patients with known CV risk
• Rupatadine: no causal link to cardiac effects with studies showing no clinically relevant effects on QTc

*Avoid concomitant use with P-glycoprotein inhibitors in moderate to severe renal insufficiency
References

2. Maurer M et al. *Allergy* 2017; [Epub ahead of print].
17. Ebastine Summary of Product Characteristics.