# ABC OF ALLERGOLOGY

## DEALING WITH CHRONIC URTICARIA

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Of all the conditions presenting to the allergist, chronic urticaria or hives is the most difficult to control. Patients with chronic urticaria usually feel abandoned by their doctor and can become extremely depressed with constant itching and the unsightly rash which may persist or recur for many years.

Urticaria predominantly affects adult females and up to 20% of the population suffer from it at some time in their life. It presents as a diffusely raised itchy wheal and flare reaction which migrates over the skin surface (Fig. 1). All forms of urticaria may occur in association with deeper skin swelling or angioedema and equally, angioedema may occur in isolation with no apparent urticaria (when hereditary angioedema (HAE) due to a deficiency of the C1 esterase inhibitor enzyme should be suspected).

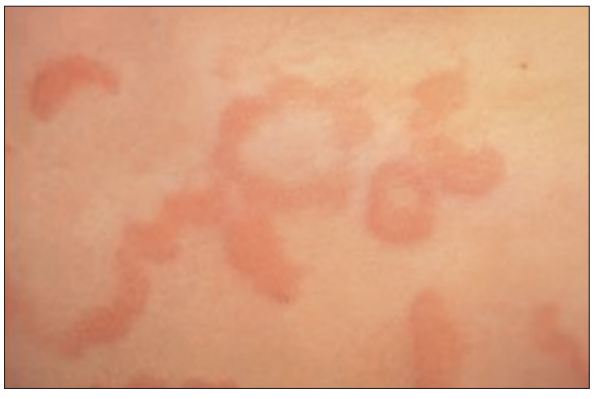

*Fig. 1. Ordinary urticaria lesions migrate.*

We classify ordinary urticaria as acute urticaria when the rash duration is under 6 weeks and chronic urticaria when it persists for over 6 weeks. Physical urticaria is due to an external physical trigger such as heat, cold, pressure or exercise. Urticarial vasculitis is a rare condition associated with underlying auto-immune connective tissue diseases which requires specialist referral.

The actual cause of **acute ordinary urticaria** is relatively easy to identify as the trigger seems immediately apparent and the reaction is reproducible. Examples include: shellfish, penicillin, bee or latex allergy and the rash associated with a streptococcal or viral hepatitis infection.

In **chronic ordinary urticaria** it is far more difficult to identify a specific trigger and the cause of over 50% of cases remains unknown; we then label this chronic 'idiopathic' urticaria (CIU). Chronic ordinary urticaria may be triggered by systemic illnesses such as autoimmune thyroid disease, collagen vascular disease, chronic parasitic infections, chronic sinusitis, *Helicobacter* pylori and chronic dental infections. One third of cases are due to auto-antibodies directed against IgE or the mast cell IgE receptor. Occasionally food additives (benzoate, sulphites and azo dyes) can trigger chronic urticaria, but true food allergy is unlikely to cause chronic ordinary urticaria.

**Physical urticaria** in its most benign form usually presents as dermatographism. Physical urticaria is triggered by reproducible physical stimuli such as heat, cold, sun exposure, vibration, exercise, deep pressure and even occasionally from water exposure. The lesions occur within minutes of the stimulus and disappear rapidly within an hour or two. Just to complicate matters, physical urticaria often occurs in conjunction with chronic ordinary urticaria, while **contact urticaria**, an immediate IgE-mediated allergy, occurs after skin contact with fresh food, pet saliva or latex and settles within a few hours.

**Urticarial vasculitis** although rare, presents with painful non-migratory lesions which persist for over 24 hours, often together with fever, purpura and arthralgia. The association with underlying auto-immune diseases such as serum sickness, systemic lupus erythematosus (SLE) and Sjogren's syndrome should not be overlooked. **Urticaria pigmentosa** is a diffuse, dark, freckle-like rash that urticates on rubbing the skin and is due to excess mast cells in the skin (cutaneous mastocytosis). Children frequently develop discrete itchy **papular urticaria** from insect bites.

*If a specific urticarial trigger can be identified then avoiding that trigger is obviously the most desirable course of action, but very often no underlying cause is ever identified. The main thrust of management is then to try to alleviate symptoms while the urticaria slowly 'burns' itself out and eventually resolves - a process that can take many months or even years.*

### *Pharmaceutical management of urticaria*

**Antihistamines:** The second-generation non-sedating antihistamines are the mainstay of current urticaria treatment and trebling the normal recommended dose is often necessary to obtain symptom control (for example **cetirizine** 10-30 mg, **loratadine** 10-30 mg or **fexofenadine** 180-540 mg). Once the urticaria is controlled, the dose can slowly be reduced. Older sedating antihistamines such as chlorpheniramine, diphenhidramine or hydroxyzine may help at night with sleep disturbance caused by itching. Tolerance to antihistamines can develop and it may help to periodically rotate through different antihistamines. **Ketotifen** may be effective in children with its antihistamine and mast-cell-stabilising properties. If it is necessary to use antihistamines in pregnancy, **chlorpheniramine** although sedating, is safest. Gastric histamine H2-blockers such as **ranitidine** or **cimetidine** offer additive antihistamine, and are effective if used with conventional antihistamine medication.

**Oral steroids:** Although **prednisone** (>30 mg) is most effective in the short term for rapid symptom relief, with long-term use it will lead to undesirable side-effects and problematic rebound urticaria on withdrawal. Occasionally long-term alternate-day regimens may be necessary to control chronic recalcitrant urticaria.

**Steroid-sparing options:** The tricyclic antidepressant **doxepin** (10-50 mg daily) has histamine-blocking properties and is useful as an adjunct especially if there is co-existent depression with the urticaria. **Montelukast** (10 mg at night) has been used with variable success, and is most effective when used in combination with non-sedating anti-histamines. Montelukast is particularly useful in aspirin-sensitive individuals (who are prone to urticaria, nasal polyps and asthma).

Other drugs such as **colchicine, warfarin, nifedipine, danazol, dapsone, methotrexate and sulfasalazine** have been used with varying success in chronic urticaria. Auto-immune thyroid disease with associated urticaria may respond to oral **thyroxine** supplementation even if the patient is biochemically euthyroid. Immune suppressive therapy such as **cyclosporin** is effective but can cause serious side-effects such as renal impairment and uncontrolled hypertension. Oral **sodium cromoglycate** may benefit food-related exercise-induced[w1] urticaria. Stress (public speaking, examinations, exercise and arguments) may trigger cholinergic urticaria and **propranolol** will reduce symptoms. Other possible treatments include intravenous Immunoglobulin and serum plasmaphoresis.

**Non-pharmacological interventions/advice:**

- Resist the temptation to rub the itchy and painful lesions.
- Try to keep cool at all times and wear loose-fitting clothing.
- Avoid all alcoholic drinks, which non-specifically trigger urticaria.
- Try to reduce stress by doing relaxation exercises and yoga.
- Keep the skin well moisturised with bland emollients.
- Avoid topical antihistamine creams (mepyramine, antazoline, diphenhydramine) which are potent skin-contact sensitisers.
- Topical steroid creams are of no value in ordinary urticaria.
- Avoid non-specific physical triggers such as excess heat, cold, exercise and rapid temperature changes.
- Avoid food colourings (tartrazine), additives (sodi um benzoate), and natural salicylate (berry fruit, spices and Ceylon tea)
- Avoid all aspirin-containing flu remedies and other non-steroidal anti-inflammatory (NSAI) medication such as ibuprofen, mefenamic acid and diclofenac as well as codeine (opiate analgesics) and coloured multivitamin tablets which may also act as triggers. Paracetamol is the only painkiller or flu treatment that can safely be used in urticaria.
- Apply calamine, aqueous cream with menthol 1% or 10% crotamiton (Eurax) lotions to soothe the skin. Doxepin cream (Xepin), if available, has anti-pruritic properties.

**Iatrogenic causes: If aspirin and salicylate intolerance** is suspected then all forms of salicylate including toothpaste, muscle rubs and peppermints should also be avoided. Aspirin-sensitive individuals tolerate the newer cyclo-oxygenase-2 (COX-2) selective inhibitors or NSAI medications such as meloxicam. [w2]

Angiotensin-converting enzyme inhibitor **(ACE inhibitor)** antihypertensives are a common trigger for angioedema and urticaria, especially lisinopril and enalapril. ACE inhibitors may trigger angioedema after many years of use. The angiotensin-II receptor anatagonists (ACE 2) such as valsartan and candesartan are less likely to induce angioedema and urticaria.

Many patients with chronic urticaria derive benefit from a low vaso-active **amine diet**. Histamine contained in foods such as dark fish, fermented cheese and cured meats may act non-specifically by perpetuating the urticaria. Avoidance of these foods will help reduce itch and flushing (Table I).

**Table I.**
**Foods with high vaso-active amine (histamine) content**

| | |
|---|---|
| Fish | *Mackerel, tuna, smoked salmon, sardines, pickled herring* |
| Cheese | *Emmenthal, Parmesan, Camembert, Cheddar, Roquefort* |
| Cured meat | *Salami, dried ham, vienna sausage, chicken liver, biltong* |
| Fruit & Vegetables | *Eggplant, spinach, red beans,avocado, bananas, dates* |
| Alcohol | *Red wine, cider, homebrewed beer* |
| Others | *Marmite, soy sauce, tomato ketchup* |

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## RECOMMENDED READING


- Greaves M, Kaplan A, eds. **Urticaria and Angioedema.** Marcel Dekker Inc: 2004 (Available from www.amazon.com)
- Motala C. Chronic urticaria in childhood. *SA Paediatric Review* 2004; 1(4): 4-13.