Urticaria

Urticaria refers to a group of disorders affecting adults and children, in which red patches and weals occur in the skin. The release of chemicals such as histamine from mast cells in the skin causes small blood vessels to leak and results in tissue swelling. The weals can be a few millimetres or several centimetres in diameter, coloured white or red, often surrounded by a red flare, and frequently itchy. Each weal may last a few minutes or several hours, and may change shape. Weals may be round, or form rings, a map-like pattern or giant patches. The surface weals may be accompanied by deeper swelling of eyelids, lips, hands and elsewhere. The swelling is called angioedema. Angioedema may occur with or without urticarial weals (10%).

Rarely, urticaria results from an autoinflammatory disease such as systemic lupus erythematosus or Schnitzler syndrome, or an inherited condition such as Muckle-Wells syndrome or cryopyrin-associated periodic syndrome.

Generalised ordinary urticaria

Generalized ordinary urticaria (hives) presents with spontaneous weals anywhere on the body. It is often classified according to how long it has been present.

- Acute urticaria is of recent onset (hours, days or a few weeks).
- Episodic urticaria describes intermittent attacks of urticaria, which may last a few days or a few weeks.
- Chronic urticaria has persisted for several months or years.
Urticaria may not be present all the time. Some find it more noticeable at certain times of day, or when they are warm or emotionally upset.

**Acute urticaria** is sometimes due to allergy. Allergy depends on previous exposure to the material, and the development of an immune reaction to it. An immunoglobulin called IgE is involved, which attaches itself to a receptor on the mast cell and causes it to release its chemical mediators.

The cause of an allergy may be:

- **Medicine**: most often an antibiotic, but many other drugs have been reported.
- **Food allergy**: tiny amounts of fish, eggs, nuts and kiwifruit (many others have been reported less often).
- **Bee or wasp stings**.
- **While most allergies involve ingestion, injection or inhalation of the allergen, sometimes allergic urticaria can result from skin or mucosal contact with an allergen e.g. rubber latex.**

Most allergies are mild, but very allergic individuals may develop serious **anaphylactic shock** within a few minutes of exposure. The most frequent causes are antibiotic injections, bee stings or ingestion of peanuts. Anaphylaxis results in urticaria, a tight chest, wheezing, faintness and collapse. Medical attention must be sought urgently. A subcutaneous adrenaline (epinephrine) injection will usually be given. Those prone to anaphylaxis should carry an emergency supply (e.g. an EpiPen™).

Most cases of urticaria are NOT due to allergy. Histamine and other vasoactive chemicals can be released into the skin for many reasons. In these cases urticaria can occur the first time that a person is exposed to the material.

Non-allergic causes of acute urticaria include:

- **Infection**, including sinusitis, helicobacter (a cause of stomach ulcers), dental abscess, viral hepatitis, infectious mononuclosis and candida (thrush).
- **Serum sickness**, due to blood transfusion, viral infection or medicines (e.g. Ceclor™): urticaria is accompanied by fever, swollen lymph glands, painful joints and nausea. It is thought to result from immune complexes of the allergen and antibodies lodging in small blood vessels.
- **Non-allergic release of mast-cell granules** by medicines, especially morphine, codeine, other opiates, and radiocontrast agents. Urticaria provoked by aspirin and other non-steroidal anti-inflammatory drugs involves leukotriene formation.
- **Non-allergic food reactions**, from salicylates in fruit, azo dye food colouring agents, benzoate preservatives and other food additives, or from histamine due to bacterial decomposition e.g. scombroid fish poisoning.

**Chronic urticaria** is often due to autoimmune disease (allergy to one’s self), and may be associated with other autoimmune conditions such as thyroid disease and coeliac disease. Circulating ‘anti-idiotypic’ antibodies activate IgE bound on mast cells to cause excessive release of chemicals. More commonly there is no evidence for autoantibodies, and the patient is said to have chronic idiopathic urticaria.

**Recurrent angioedema without urticaria** may be due to C1 esterase deficiency (the protein C1 INH is missing or abnormal); there is often a family history of similar problems. It may also be caused by angiotensin converting enzyme (ACE) inhibitors such as captopril, quinapril, enalapril and others, which are used to treat heart failure and hypertension. These drugs inhibit kinin breakdown. Angioedema may also be idiopathic (of unknown cause).

Urticaria should be distinguished from urticarial vasculitis, in which weals persist for longer than 24 hours and vasculitis is found on skin biopsy. It results from immune complex deposition.
Physical urticaria

Physical urticaria refers to urticaria induced by external physical influences. The weals take about 5 minutes to develop, and last 15 to 30 minutes. Some people suffer from a mixture of different types of physical urticaria and generalized urticaria. The cause is unknown. Dermographism means ‘skin writing’. Stroking the skin causes it to weal in the line of the stroke. This is very itchy, but scratching causes more wealing. Dermographism usually starts quite suddenly. Weals come up where clothes or furniture touch, especially when the affected person is hot or upset. A warm shower followed by rubbing with a towel can result in itchy weals all over. Cholinergic urticaria results from sweating. In severe cases, hundreds of tiny red itchy spots develop after running, when warm, or when concentrating. Cold urticaria affects skin warming up after a reduction in temperature, especially in winter. Weals can be widespread and may cause fainting attacks. Affected individuals should not expose large areas of the skin to the cold or wind. They should be advised never to swim alone. Contact urticaria results from absorption of an eliciting substance through the skin or through a mucous membrane. It may be allergic or non-allergic in origin. It may result in wealing confined to the site of contact or spreading more widely. IgE antibodies on mast cells react to chemicals in white flour, cosmetics, and textiles, or to proteins in latex rubber, saliva, meat, fish and vegetables may cause contact urticaria. Non-allergic examples include the stinging reaction of certain plants (e.g. nettles), animals (hairy caterpillar) and medicines. Localised heat urticaria, aquagenic urticaria (water contact), solar urticaria (sunlight), vibratory angioedema and delayed pressure urticaria are less common.

Investigations

In most cases of urticaria, there is no need for specific investigations. However, the following tests may be helpful in some cases.

- Full blood count to identify eosinophilia caused by allergy or parasitic infestation, and low white blood count from systemic lupus erythematosus.
- Thyroid antibodies and function in chronic urticaria if autoimmune origin is considered likely.
- Skin prick testing and blood tests for specific allergy (RAST, or radiolallergosorbent tests, or CAP fluoroimmunoassay).
- Autologous serum skin prick test (if available) in chronic urticaria.
- Complement tests in case of angioedema without urticaria or urticarial vasculitis.
- Skin biopsy if weals are prolonged, to identify vasculitis.

Treatment of urticaria

Treatment depends on the type of urticaria, its severity and how long it has been present. Oral antihistamines control wealing and itching for the majority of patients with urticaria. They do not affect the underlying cause of the rash. Antihistamines may need to be taken intermittently or continuously until the underlying tendency to urticaria disappears. Luckily, most people eventually recover. Non-sedating antihistamines include:

- loratidine
- desloratidine
- fexofenadine
- levocetirizine
- cetirizine.
Cetirizine is the quickest acting of these medications, and desloratidine is the most long-lasting. Conventional antihistamines such as chlorpheniramine or promethazine may be preferred at night as they tend to have a sedative effect. Hydroxyzine or diphenhydramine may be taken during the day and in some people they appear more effective than newer, non-sedating antihistamines. Response and tolerance varies, so if the first antihistamine is not effective, consult your doctor. You may need to increase the dose, or use a different drug. Usually any sedative effect wears off in a week or so. Sometimes a combination of antihistamines works better than a single type alone. Other treatments may be tried for urticaria that fails to clear with antihistamines.

- Off-license addition of H2 blockers, such as cimetidine or ranitidine, can also reduce urticaria but these medications are more often prescribed to reduce stomach acidity.
- Oral steroids (prednisone) in moderate dose for a few days are useful for severe acute urticaria. They are rarely recommended long term because of serious adverse effects. In rare cases, alternate day steroids may be warranted.
- Tricyclic medications such as amitriptyline, nortriptyline and doxepin are thought to help because of antihistaminic and neuropathic properties.
- Antileukotriene agents, such as montelukast, occasionally help; they are usually prescribed for asthma.
- Ultraviolet radiation treatment (narrowband UVB and PUVA) reduces the severity of wealing in some patients.
- Antibiotics, dapsone, sulfasalazine and antifungal agents are used to clear an assumed underlying infection or for their presumed anti-inflammatory action.
- Immunosuppressive medications. The most effective of these appears to be ciclosporin. Methotrexate, plasmapheresis and intravenous immunoglobulins) are reported to help but may have serious side effects.
- Antifibrinolytic agents (tranexamic acid, androgenetic steroids such as danazol) are mainly used for treatment-resistant angioedema or angioedema due to C1 esterase inhibitor deficiency. In emergency situations, C1 esterase inhibitor concentrate or fresh frozen plasma may be transfused.

Intramuscular injection of adrenaline (epinephrine) is reserved for life-threatening anaphylaxis or swelling of the throat.

**General measures**

- Do not take the medications your doctor has told you to avoid. Minimise use of aspirin and codeine. It is usually safe to take paracetamol to relieve pain. Nonsteroidal anti-inflammatory agents should be avoided in those that react adversely to aspirin. ACE inhibitors should be avoided in those with angioedema.
- Dietary changes may help. Some urticaria is aggravated by salicylates in certain fruits, or additives including amines, tartrazine (102), benzoates (210-220) and other food chemicals. Whether or not these need to be avoided can be determined by appropriate food challenge tests.
- Avoid alcohol (it causes the surface blood vessels to dilate). Try not to overheat. Cool the affected area with a fan, cold flannel, ice pack or soothing moisturising lotion.