

Allergy and Urticaria

Graham Ogg

MRC Senior Clinical Fellow, Nuffield Department Clinical Medicine
Hon Consultant Dermatologist, Churchill Hospital

Allergy and Oxford

- Dermatology (Graham Ogg and locum John Reed) and clinical immunology (Siraj Misbah) joint clinic
 - adult allergy, drugs (SM)
- Clare Robertson
 - paediatric allergy
- David Warrell
 - bee and wasp venom allergy
- ENT
 - hayfever

CASE 1

27 year old male

- 2 years intermittent rash
- Itchy, raised. Not scaly
- Transient, lasting less than 24 hours
- Occurs any time
- Occurs at any site
- Possibly worse at sites of pressure
- Possibly worse after NSAIDs
- Now approx 3 days per week



CASE 2

39 year old female

- 6 months history intermittent itchy swellings
- Occurs any site
- Occurs any time
- Transient, lasting less than 24 hours
- 1 month ago attended A&E with tongue swelling. No problems breathing

PMH

- hypertension

DH

- ACE inhibitor started 2 years ago



Case 3

- 35 year old nurse
- 6 months history of immediate erythema and pruritus affecting hands with latex gloves
- Non-latex gloves fine
- Possible worsening of her existing asthma when wearing gloves for prolonged periods

Case 4

- 18 year old male
- Several years of slight lip swelling with various fruits (apple, peaches, pears).
- Hayfever. No asthma
- 1 episode of throat swelling, difficulty breathing and collapse after eating hazelnuts

Urticaria definition and classification

- Urticaria is a transient eruption of erythematous or oedematous swellings of the dermis which is usually pruritic.
- Angio-oedema consists of transient swellings of deep dermal, subcutaneous and submucosal tissues.
- Anaphylaxis is a life-threatening allergic reaction consisting of erythema, urticaria, angio-oedema, hypotension and/or respiratory compromise.

Urticaria classification

Recent classification based on aetiology:

1. **Physical**
2. Hypersensitivity (IgE) – oral or contact
3. Pharmacological (non-IgE)
4. Systemic disease
5. Inherited
6. Idiopathic

Physical urticaria

Physical stimuli can induce mast cell degranulation:

Dermographism

Delayed pressure

Cholinergic urticaria (heat)

Cold urticaria

Solar urticaria

Aquagenic urticaria

Urticaria classification

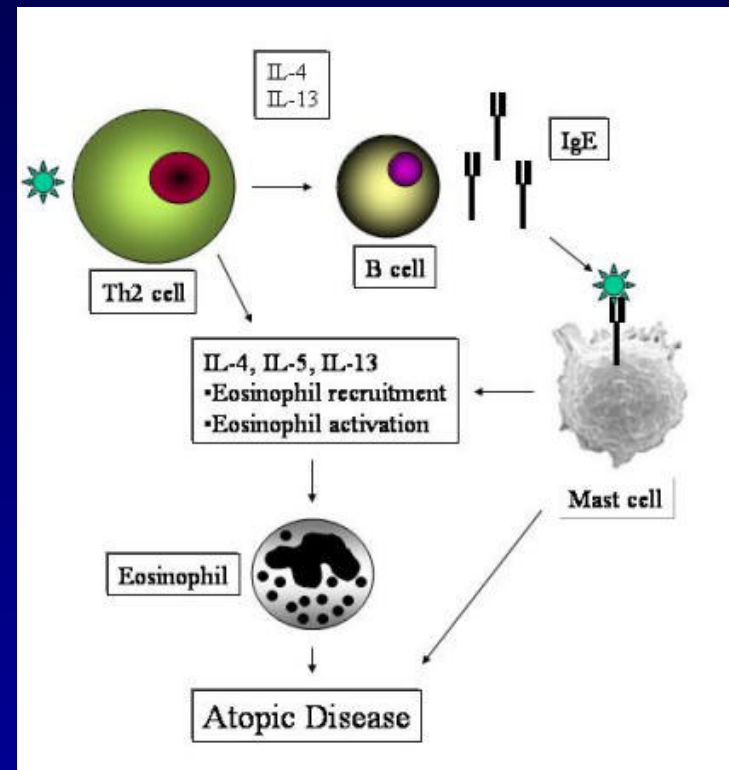
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Hypersensitivity urticaria (IgE-mediated)

Examples:

- Foods eg nuts, shellfish, fish, milk, eggs
- Drugs eg penicillins, cephalosporins, insulin, latex
- Insect stings eg bee and wasp



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Pharmacological

Examples of precipitants of non-immunological urticarial reactions:

- Aspirin
- Non-steroidal anti-inflammatory drugs
- Radiocontrast media
- Plasma expanders
- Local and general anaesthetics
- ACE inhibitors
- Opiates
- Antibiotics eg rifampicin, ciprofloxacin, vancomycin

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Systemic disease and urticaria

- Thyroid disease 11-20% of CIU (vs 3-5% controls) have positive anti-thyroid peroxidase, but clinical thyroid disease rare (0-50% of thyroid antibody positive). Some reports of improvement in urticaria in thyroid antibody positive individuals with thyroxine treatment. Controversial.
- Paraproteins eg Schnitzler's syndrome
- Vasculitis eg lupus erythematosus, Sjogren's syndrome.
- Infection eg hepatitis (controversial), H pylori (controversial), intestinal parasites, intercurrent viral infections.
- ?Solid cancer (controversial, but no convincing association)
- Others: eg Familial Mediterranean fever.

NB Urticarial lesions lasting longer than 24 hours may have a vasculitic aetiology.

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Hereditary angio-oedema

- Rare
- 5% of all angio-oedema
- AD, chromosome 11
- Usually onset in childhood

- Recurrent swellings of skin and mucous membranes throughout life, often with nausea vomiting, abdo pain, urinary symptoms. Lesions may be painful and usually don't itch. Appear spontaneously or after trauma eg dentist. Between attacks patient is well.

- Relative deficiency of C1 esterase inhibitor. C2, C4 are low during attacks and in most C4 is low between attacks. No clear correlation between lab and severity of clinical disease.

- Poor response to antihistamines
- Treatment is with danazol or stanazol which stimulate production of inhibitor. Can be given longterm (risk of androgenic problems) or for prophylaxis before procedures. FFP can be used as prophylaxis. Purified C1 esterase inhibitor is also available and can be used to treat acute severe attacks.

- Prognosis dominated by laryngeal involvement

- Nb there is also an acquired form associated with B cell lymphoma, SLE.

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Chronic idiopathic urticaria and angio-oedema

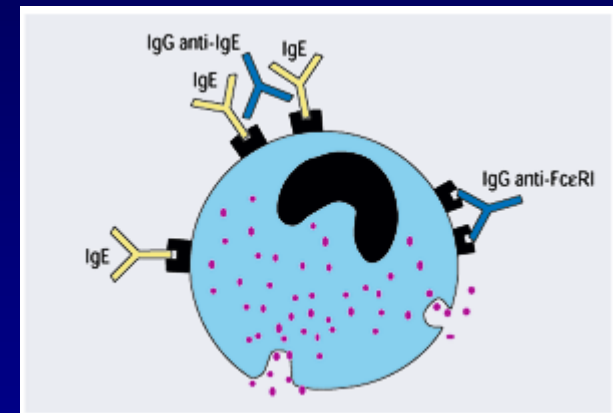
- urticaria on most days for longer than 6 weeks.

- cause is rarely identified

Possible aggravating factors:

- 40% have an associated physical urticaria
- 30-60% aggravated by aspirin and NSAIDs
- ACE inhibitors can provoke angio-oedema
- intercurrent infections can aggravate
- airborne allergens can aggravate if highly sensitised
- Exercise can aggravate
- Alcohol may aggravate
- Popular held belief that food additives play a role, but rarely sustained in double blind challenges. Possibly relevant in a small percentage eg tartrazine, sodium glutamate.

- Role of autoimmunity eg IgG to high affinity FcR for IgE, or IgG to IgE.



Current UK standards management of urticaria and angio-oedema

Acute urticaria

No investigations are required except where suggested by the history. IgE-mediated reactions to environmental allergens (such as latex, nuts or fish) as a cause of acute urticaria and contact urticaria can be confirmed by skin-prick testing (where there are resus facilities) and specific IgE in blood. Results of both have to be interpreted in the clinical context. With all IgE antibody tests for food allergy (skin prick tests or blood), positive results do not always indicate clinical reactivity (poor sensitivity and specificity), whereas negative results have a relative high negative predictive value.

Chronic urticaria

Mild disease responding to antihistamines needs no investigation. Moderate or severe disease then FBC, ESR. Consider thyroid autoantibodies and TFTs. Consider immunoglobulins.

Angio-oedema

C4. If low then C1 esterase inhibitor levels and function.

Prolonged urticarial lesions

Biopsy and vasculitis work up.

Management

Avoidance of trigger

Non-sedating antihistamines.

eg cetirizine.

Sedating antihistamines.

eg hydroxyzine

H2 antagonist

eg cimetidine 400mg bd

Leukotriene receptor antagonist

eg montelukast

Children

Chlorpheniramine now licensed from 1 month

Trimeprazine (Vallergan) licensed from 6 months

Pregnancy

If possible, it is best to avoid all antihistamines in pregnancy, especially during the first trimester, although none have been shown to be teratogenic in humans. Chlorpheniramine is often chosen because of its long safety record.

Oral steroids

Oral corticosteroids may shorten the duration of acute urticaria (e.g. prednisolone 50 mg/day for 3 days in adults) but risk of side-effects. Intravenous hydrocortisone is a useful adjunct for severe laryngeal oedema and anaphylaxis when given as a stat dose although its action is delayed. Short tapering courses of oral steroids over 3-4 weeks may be necessary for urticarial vasculitis and severe delayed pressure urticaria but longterm oral corticosteroids should not be used in chronic urticaria except in very selected cases.

Immunosuppressants

Cyclosporin

Plasmapheresis

Immunoglobulin

Desensitisation

Bee and wasp sting allergy

Seasonal allergic rhinitis

Epipen

300mcg (or 150mcg children 15-30kg) adrenaline by IM injection.

DTB suggests following indications in children: severe previous reaction (laryngeal oedema, hypotension), any respiratory symptoms, occurred with trace allergen exposure, or occurred in someone who has asthma requiring regular inhaled corticosteroids.

MedicAlert bracelet

Prognosis idiopathic urticaria, angio-oedema

- 50% of chronic urticaria will resolve in 6 months
- 50% of chronic angio-oedema will resolve in 12 months
- 50% of chronic urticaria and angio-oedema will resolve in 10 years

However severity is often greatest initially with subsequent waning.

Prognosis of food allergy

- For egg, milk most children grow out by age 5-10 years
- For nut most children persist (upto 25% do outgrow)
- If allergy is present at 10 years then usually life long

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Case 1

Investigations

FBC, ESR, thyroid peroxidase antibody negative, Igs normal

Diagnosis

Chronic idiopathic urticaria with NSAID and physical exacerbation

Management

Avoid aggravating factors eg NSAIDs

Non-sedating antihistamine gave satisfactory control

Treatment break every few months

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Case 2

Diagnosis

Probable ACE inhibitor associated angio-oedema

Management

Avoid ACE inhibitors

Problem resolved

Should probably also avoid angiotensin II receptor antagonists (debated)

Nb If still persistent then: FBC, ESR, thyroid peroxidase antibody, C4.

Work up management strategy as described above.

Consider EpiPen

Case 3

- 35 year old nurse
- 6 months history of immediate erythema and pruritus affecting hands with latex gloves
- Non-latex gloves fine
- Possible worsening of her existing asthma when wearing gloves for prolonged periods

Case 3

Investigations

IgE latex negative (can occur in approx 15% of latex sensitives)

Skin prick test to:

1/100 latex negative

1/10 latex negative

1/1 latex positive

Done with resus facilities available



(nb can also skin prick test through problematic glove or do finger or whole glove challenges, but higher risk of systemic reactions esp if asthmatic)

Anti-histamines can block responses

Diagnosis

Latex allergy

Latex sensitivity

Main risk factors: atopy and exposure (particularly high protein, powdered gloves)

- Approx 1-6% of UK population
- Up to 17% of UK health care workers (1994)
- Up to 50-60% of spina bifida patients (1993)
- Up to 6% non-atopics France (1993)
- Up to 36% of atopics exposed France (1993)

- Up to half of those with latex-specific IgE will have clinical symptoms

- Can be cross-reaction with certain foods and other allergens eg banana, avocado, kiwi fruit, chestnut, pollens.

Medical and Household Latex containing articles

Latex gloves

Bite blocks

Blood pressure cuffs

Bulb syringes

Catheters^{*}

Dental coffer dams^{*}

Elastic bandages

Electrode pads

Endotracheal tubes and airways

Enema syringes^{*}

Ventriculo-peritoneal shunts

Finger cots

IV access injection ports

Manual resuscitators

Penrose surgical drains

Pulse oximeters

Stethoscope tubing

Stretcher mattresses

Tourniquets

Vascular stockings

Adhesives

Balloons^{*}

Carpet backing

Condoms^{*}

Contraceptive diaphragms

Elasticated fabrics^{*}

Feeding nipples

Household gloves^{*}

Diapers and incontinence pads

Infant pacifiers

Rubber bands

Shoes

^{*}Reported as sources of allergenic sensitivity.

Management

- Routine use of low protein (<50µg/g), powder-free latex gloves in those who are not sensitised. This carries a very low risk of inducing sensitisation even in atopics (Jones KP et al 2004)
- Non-latex gloves for those that are sensitised
- Latex-free environments for those rare individuals with severe sensitivity

- Portable self-injectable adrenaline (if severe reactions or active asthma)
- Antihistamines
- Bronchodilators if wheeze

- In hospital then also oxygen, fluids if necessary.

- ?anti-IgE antibody

- Medicalert

Case 4

- 18 year old male
- Several years of slight lip swelling with various fruits (apple, peaches, pears).
- Hayfever, no asthma
- 1 episode of throat swelling, difficulty breathing and collapse after eating hazelnuts

Case 4

Investigations

- Positive skin prick test to hazelnuts
- NB fruit skin testing hard to interpret

Diagnosis

- Oral allergy syndrome which can include nut allergy

Management

- Avoid all nuts. Avoid fruits giving rise to symptoms.
- Medical alert.
- Antihistamines, EpiPen

Oral allergy syndrome

Common foods which may cause oral allergy syndrome

- Apple
- Peach
- Pear
- Nectarine
- Strawberries
- Melon
- Camomile tea
- Carrot
- Potato
- Fennel
- Spinach
- Brazil nut
- Watermelon
- Spices e.g. cumin, coriander, parsley
- Walnut
- Peanuts
- Wheat
- Hazelnuts
- Celery
- Cucumber
- Cherries
- Plum
- Honey
- Almonds
- Apricots
- Tomato

NB: Only the foods identified by the patient and clinic are to be avoided and not all the foods on the list.

Can progress with age

Common questions:

What about the patient with multiple variable symptoms that they ascribe to “allergy”?

Does desensitisation work?

High Street “allergy” services?

Contact details

Graham Ogg
Department of Dermatology
Churchill Hospital
Oxford

Graham.ogg@ndm.ox.ac.uk