Referral to Allergy clinic: ADULTS (and children 16 years and older)

Guidance for Primary Care Teams

Clinical conditions covered by the guidelines:
1. Anaphylaxis
2. Suspected Food Allergy
3. Acute and Chronic Urticaria
4. Angioedema (Including C1 esterase inhibitor deficiency)
5. Rhinitis
6. Insect venom allergy
7. Eczema
8. Asthma
9. Suspected drug allergy

The purpose of Allergy Clinic referral guidance
- There has been an increase in allergy referrals over recent years with waiting times for new patients exceeding 16 weeks.
- The majority of allergic conditions in children and adults can be managed effectively and safely in Primary Care.
- This guidance aims to empower GPs, using the latest evidence, to refer patients to an Allergy service based on clinical need. Application of this guidance will result in more effective use of the Allergy clinic and reduce waiting times for patients who need Specialist investigation or management, or who need urgent assessment.
- Patients do not require referral to the Allergy Clinic primarily for testing. Allergy testing can be undertaken in Primary Care, for the appropriate clinical situation, by sending a serum sample to the Immunology Laboratory requesting specific IgE to the relevant suspected allergens.

Box 1: Non-Allergic (Non-IgE-mediated Conditions).

Unexplained multiple symptoms: weight loss or gain, headache, confusion, depression, lack of concentration, vertigo, tiredness (including chronic fatigue syndrome) hair loss, isolated vague abdominal symptoms such as bloating.

Food intolerance: Symptoms reproducibly induced by exposure (e.g., food ingestion) but are not consistent with immediate hypersensitivity. Examples are lactose intolerance causing diarrhoea or chocolate precipitating classic migraine.

Unrecognised/unknown syndromes: there is no good evidence that ‘systemic candidiasis syndrome’ or ‘multiple chemical sensitivity syndrome’ are discrete physical entities, or that they are due to those agents from which they derive their name. There are no validated diagnostic tests or therapies.

Non-allergic substances: some substances are simply not recognised allergens, e.g. tap water, sugar, caffeine, and dental amalgam. There is no evidence that patients who consider themselves intolerant of various scents or odours (e.g., bleach, “chemical smells”, pot pourri, air freshener, perfume) are suffering from allergy to these substances.
NOTE: Listed medications are suggested options. Please refer to your own Formulary / Prescribing Committee Guidelines.

1. Patients who have experienced Anaphylaxis

Patients with Systemic Anaphylaxis require urgent treatment and transfer to Hospital.

This guidance relates to patients who have experienced Systemic Anaphylaxis and who require outpatient investigation and management.

A. If a patient has had a suspected acute allergic episode, assess whether their symptoms represented Systemic Anaphylaxis.

Symptoms and signs of anaphylaxis are variable but may include:

- cardiovascular collapse (hypotension, shock), chest pain.
- bronchospasm (wheeze), dysphonia, stridor, cough, rhinorrhoea.
- angioedema, flushing, urticaria, pruritus.
- gastro-intestinal symptoms (vomiting, diarrhoea), dysphagia.
- Anxiety / altered mental state, sense of ‘impending doom’, tunnel vision.

If the acute systemic symptoms included those in bold, then conclude that the patient has had Systemic Anaphylaxis.

B. Refer all cases of Systemic Anaphylaxis urgently to the Allergy clinic for further investigation and management.

- Ideally, these patients should have been referred to the Allergy Clinic directly from the Emergency Department. However, many patients attend Emergency Departments not local to where they live and require referral when they return home.
- Include a careful history of exposure to possible causes (food, insect stings, drugs). Advise avoidance of the allergen, if known, and provide 2 adrenaline autoinjectors for emergency use (Epipen, Emerade or Jext depending on local prescribing guidelines and availability). It is recommended that 2 adrenaline auto-injectors are prescribed, which patients should carry at all times rather than keeping 2 in multiple locations. (MHRA guidance Aug 2017)

2. Suspected Food Allergy

The clinical diagnosis of food allergy is determined by the nature and timing of the symptoms / signs after ingestion ie these are consistent with IgE-mediated allergy. The intention of testing is to confirm the clinical diagnosis and to determine cross-reactivities. For non-severe food allergy, the diagnosis can be made by clinical history and specific IgE testing to the relevant suspected allergens (serum sample sent to nearest Laboratory).

Refer to the Allergy Clinic for:

Invalidated diagnostic tests: positive results obtained by unorthodox techniques, such as electrodermal testing (e.g. the Vega test) are irrelevant to the diagnosis of food allergy and are best ignored – they do not justify referral to the allergy service. In addition, IgG antibodies to food allergens, as measured by some private laboratories, have not been shown to be of diagnostic value.
a) Severe food allergy (respiratory / cardiovascular / systemic symptoms) – See notes on Anaphylaxis.

b) Suspected food allergy but where initial tests are negative or there is no clearly identifiable allergen

c) Multiple Food allergies where avoidance may lead to effects on nutrition.

Common food allergies: egg white, cows’ milk, peanut, tree nuts (hazel, almond, brazil, walnut, cashew, pistachio), sesame, soya, fish, shellfish.

A note on Oral Allergy Syndrome:

This is the commonest form of food allergy in adults. Allergies to some raw fruits (eg apples, stoned fruits), vegetables (eg carrots, potatoes) and nuts (eg hazel) occur as a complication of tree pollen allergy (IgE cross-reactions). Patients usually tolerate the cooked versions of the foods and anaphylaxis is uncommon. Testing is not always needed, especially if symptoms are mild. Rapid acting anti-histamines (acrivastine) may be useful but symptoms are often of short duration. Refer for investigation if patients have had systemic reactions to these foods, or are symptomatic when eating cooked versions of the foods.

3. Acute and Chronic Urticaria (with or without Angioedema)

Urticaria (hives) and angioedema (swelling) are symptoms and not diagnoses. They may occur in combination or alone. These may be manifestations of an IgE-mediated process (immediate hypersensitivity or allergy) but may be non-IgE-mediated / non-allergic. The symptoms may follow a number of patterns.

Episodic: Discrete single episodes but asymptomatic between episodes.

Take a history for possible triggers, e.g. foods, medicines (NSAIDs), or physical factors such as exercise. Test for suspected food allergies based on history.

Acute: Frequent, often daily episodes, lasting < 6 weeks. Usually are non-allergic. May be preceded by acute infection / illness.

Chronic: Frequent, often daily episodes, lasting > 6 weeks. Usually non-allergic, called Chronic Spontaneous Urticaria or Chronic Inducible Urticaria.

Management:

Episodic: Rapid acting non-sedating anti-histamine, as necessary eg Acrivastine.

Persistent: Consider stopping NSAIDs unless the patient has been on long-term maintenance NSAIDs. Review other recently started medications, particularly ACE inhibitors, which can sometimes exacerbate both urticaria and angioedema.

Treat with regular oral non-sedating antihistamines, once to twice per day. (eg cetirizine, loratadine, levocetirizine, desloratadine, fexofenadine). These may be increased up to a maximum of 4x the normal licensed dose / 24 hours$^2$.

If symptoms are poorly controlled, add in montelukast 10 mg at night or an H2-blocker (eg ranitidine, twice per day off label)$^1$ and refer to the Allergy Clinic for assessment for specialist treatment (omalizumab, immunomodulators).

Oral prednisolone (30 – 40 mg / day) for 5-7 days may be used for short-term control of severe symptoms.
4. Angioedema (without Urticaria)

Consider sending to ED for emergency treatment if there is evidence of angioedema involving the upper airways.

- Is the patient on an ACE inhibitor? If so change to an angiotensin-II receptor antagonist and reassess.
- Consider other drug-induced causes of angioedema e.g. NSAIDs.
- Refer to the Allergy clinic if angioedema reoccurs after 3 months of stopping the ACE inhibitor/other relevant medication. Or, swelling involving the tongue or throat/upper respiratory tract and the patient was not on an ACE inhibitor/other relevant medication.
- If angioedema but no urticaria and the patient was not on an ACE inhibitor consider C1 esterase inhibitor deficiency. Check C4 complement level. Values >0.20 g/L excludes C1 inhibitor deficiency.
- Note that angioedema that is followed by dryness or peeling of the skin in the affected area likely represents acute dermatitis. Consider a diagnosis of contact allergic dermatitis eg cosmetics, hair dye, wet wipes. (see section 7 on eczema).

C1 inhibitor deficiency: hereditary and acquired angioedema

C1 inhibitor deficiency causes oedema of the skin and mucosal surfaces due to dysregulation of the complement and contact systems. It can be fatal if the airway is compromised. Hereditary angioedema is an autosomal dominant condition, with symptoms typically starting in childhood. However, the degree an individual is affected varies considerably and so there may not be a clear family history of the disorder. Acquired angioedema is less common and typically presents in older patients where it may be associated with lymphoproliferative or autoimmune conditions.

If the patient has:

- Unexplained episodic angioedema (which is non pruritic) +/- abdominal pain / nausea / vomiting / breathing difficulties, without urticaria

AND

- Complement component C4 ≤ 0.14g/L
- Refer to the Immunology clinic urgently to exclude C1 inhibitor deficiency
- Take a history for triggers e.g. stress, and advise avoidance if possible.
- Treat infection promptly.
- There is no need to measure C1-inhibitor levels in general practice and no need to refer if angioedema only occurred while on an ACE inhibitor.

5. Rhinitis

May be Allergic (typically symptoms include nasal or ocular itching) or Non-Allergic (eg chronic blocked nose without other symptoms, or rhinorrhoea alone).

Seasonal: Usually allergic due to pollens (tree pollen in spring, grass pollen in summer) or outdoor mould spores (autumn)
Perennial: May be allergic (house dust mite, indoor moulds, animals) or non-allergic.

Investigations: These are only needed for severe persistent symptoms. Send serum sample and request ‘specific IgE to aeroallergens’ (includes grass pollen mix, tree pollen mix, house dust mite, cat, dog and mould mix) and any other suspected allergens eg other animals.

- In mild allergic rhinitis advise or prescribe non-sedating antihistamines.
- In moderate/severe/persistent rhinitis affecting the quality of life advise or prescribe regular topical nasal steroids (eg fluticasone, beclomethasone, mometasone). For seasonal symptoms these are best commenced pre-emptively early in the pollen season.
- If there is a poor response to either category then combine treatments.
- If rhinorrhoea is a prominent feature prescribe topical nasal ipratropium bromide.
- For severe persistent symptoms consider prescription of AVAMYS (fluticasone furoate) or DYMISTA (fluticasone with azelastine – 3rd line for seasonal allergic rhinitis but check local formulary).
- For eye symptoms, advise or prescribe topical antihistamines or sodium cromoglycate.

Refer to Allergy Clinic if
- Poorly controlled symptoms despite good compliance with treatment
- OR
- Allergen remains unknown and symptoms are difficult to control
- Considered for Desensitisation (see below).

Allergen-specific immunotherapy (desensitisation)

Indicated for:

1. Severe seasonal Allergic rhinitis (pollens) with poor response to conventional treatment (anti-histamines and topical nasal steroids) and impacting on sleep, work, schooling or social life.
2. Severe perennial Allergic rhinitis (house dust mite) with poor response to conventional treatment (anti-histamines and topical nasal steroids) and impacting on sleep, work, schooling or social life AND failure to respond to dust mite control measures.
3. Severe perennial or episodic Allergic rhinitis due to occupational exposure to animals, with poor response to conventional treatment (anti-histamines and topical nasal steroids) and impacting on ability to work.

Non-allergic rhinitis / rhinosinusitis

- If infective rhinitis/rhino sinusitis with orbital cellulitis refer to ENT urgently.
- Otherwise treat with nasal douching +/- antibiotics, if severe pain or fever.
- If chronic / recurrent consider an immune deficiency. Check serum immunoglobulins and specific IgE to aeroallergens (see above).
- If there is nasal crusting, bleeding or nasal deformity then refer to ENT.
• If there are nasal polyps treat with steroid drops (betamethasone or fluticasone) for 2-3 weeks + maintenance with a topical nasal steroid spray.
• If obstructive symptoms persist refer to ENT.
• If unilateral symptoms / signs persist after medical treatment refer to ENT to exclude nasal or sinus tumours, or mechanical obstruction e.g. septal deviation.
• If there is no obvious cause of the rhinitis then consider autonomic / hormone / drug-induced, e.g. topical decongestant over-use, ACE inhibitors. Treat underlying cause. Consider topical nasal steroids.

If non-allergic and there is no improvement with symptoms troublesome then refer to ENT clinic.

6. Insect Venom Allergy (wasp and bee stings)
Wasps sting more often than bees. Wasp stings are more common in certain occupations (eg gardeners, roofers, plumbers). Beekeepers, their family members and neighbours are at greatest risk of bee stings.

Reactions of note:

Large local swelling: Often delayed with peak of symptoms > 12 hours after sting. Treat with oral non-sedating anti-histamines and consider oral prednisolone (30 – 40 mg 1-2 doses 24 hours apart). Allergy clinic referral is generally not required.

Moderate Systemic reaction or Systemic Anaphylaxis: Often rapid onset. May include urticaria and / or angioedema distant from the site of sting, dyspnoea, wheeze, airways obstruction or cardiovascular collapse. Treat as emergency (see above). Refer to Allergy Clinic urgently for further investigation and management. Prescribe adrenaline auto injector. (According to local guidelines and availability)

Desensitisation ( Immunotherapy) for insect venom allergy is indicated for:
• Systemic anaphylaxis
• Moderate systemic symptoms AND if
  - high risk of re-sting OR
  - severe anxiety regarding re-sting / risk OR
  - raised baseline serum tryptase.

7. Eczema
Atopic Eczema is primarily a defect of skin barrier function. People with eczema have an increased risk of other atopic diseases (asthma, rhinitis, food allergy) but eczema is not primarily caused by food allergy. An exception is food-induced contact eczema, but this is mostly occupational.

Patients with or without underlying atopic eczema may develop contact allergic dermatitis. This may be due to a variety of substances including metals (eg nickel), fragrances, hair dye or chemicals within wet wipes, rubber or cosmetics.

In patients with severe eczema, poorly responsive to topical emollients and steroids, or when contact allergic dermatitis is suspected, Refer to Dermatology.
8. Asthma

- See British Thoracic Society guidelines on management of Asthma.
- If an allergic component is suspected – send serum sample for specific IgE to aeroallergens (see section 5: Rhinitis).
- Refer to Respiratory / Airways clinic if asthma remains sub-optimally controlled despite stepwise management as per guidelines.

9. Suspected drug allergy

For reactions involving anaphylaxis, urticaria or angioedema, refer to the previous sections.

Take a careful drug history. Adverse reactions can occur after taking a drug for many years and may also continue to occur for a few days after discontinuation of the causal drug. Many adverse reactions are not immunological i.e. are due to pharmacological side effects, dose effects, drug interactions or idiosyncratic drug effects.

Immunological adverse reactions may be IgE or non-IgE-mediated and often manifest with cutaneous symptoms.

Common causes are:

- Antibiotics e.g. penicillins, cotrimoxazole
- Aspirin or NSAIDs
- ACE inhibitors (see section on angioedema)
- General Anaesthetics.

While there are tests to investigate some IgE and T cell mediated drug reactions, routine or validated tests are not available for the majority of drugs, and patients may not be prepared to risk a direct drug challenge at the Allergy clinic. It is usually safer for patients to simply avoid the drug.

If a firm clinical diagnosis can be made from the history then there is unlikely to be any additional benefit from referring to the allergy clinic.

Consider referral to the Allergy clinic if:

- The symptoms suggest IgE-mediated or delayed drug exanthem AND
- The suspected drug is unclear i.e. multiple drugs were being taken at the time of the symptoms OR
- The reaction was systemic anaphylaxis OR
- The drug is essential for treatment and thus Desensitisation is needed e.g. cancer chemotherapy drugs, penicillin for infective endocarditis, OR
- For antibiotic reactions AND the patient has a need for repeated antibiotics (immunodeficiency, cystic fibrosis, COPD, asplenia).

- **NOTE**: Referrals for the investigation of General Anaesthetic Allergy must be made by the Anaesthetist involved in the case, using a standard pro-forma.
For further information and guidance on referring to our services, please go to: https://www.epsom-sthelier.nhs.uk/referring-to-our-services.

If you are uncertain about the merit of a referral please use “Advice & Guidance” on the Electronic Referral System (ERS). Referrals will be rejected if they do not meet these guidelines.

**Do not refer:**

1. Patients with symptoms that are not consistent with Allergy. See Box 1.
2. Patients who need patch tests. Refer to Dermatology.
3. Patients with mild chronic urticaria / angioedema, particularly if anti-histamines have not been stepped up as stated in the guidelines.
4. Patients with simple Oral Allergy Syndrome without severe symptoms.
5. Patients with mild rhinitis who are not candidates for desensitisation.

**References:**

1. NICE TA339: Omalizumab for previously treated chronic spontaneous urticaria.