Clinical Immunology & Allergy Unit	LEEDS TEACHING HOSPITALS NHS TRUST

REFERRAL GUIDELINES - SUMMARY

THESE GUIDELINES ARE DESIGNED TO ENSURE THAT PATIENTS REQUIRING SECONDARY CARE ARE SEEN EFFICIENTLY AND APPROPRIATELY.
THIS SUMMARY SHOULD BE READ IN CONJUNCTION WITH THE FULL GUIDELINES DOCUMENT.
Referrals without the requested information or confirmation of initial management will be returned to the requesting GP

1. URTICARIA AND ANGIOEDEMA

Refer if any of the following:

1. Patient is experiencing life-threatening symptoms, severe anaphylactoid-type reactions or atypical urticarial lesions e.g. urticarial vasculitis.
2. Failure to respond to two regular different antihistamine combinations each tried for a period of six to eight weeks.
3. No benefit from avoidance of NSAID or ACE inhibitor therapy after six weeks

Refer patients with angioedema alone if any of the following:

1. They experience life-threatening laryngeal episodes.
2. The oedema presents at a young age – under 40 years.
3. Withdrawal of potentially implicated medication fails to control the episodes.
4. The condition fails to respond to antihistamine therapy.
5. There is a suspicion of hereditary or acquired angioedema.

2. ADVERSE FOOD REACTIONS (including urticaria and angioedema)

Refer if:

1. History suggests **true food allergy**, (nearly always includes urticaria and angioedema, often with gastrointestinal disturbance, upper and lower respiratory tract symptoms and occurring within two hours of ingestion of the potential allergen).
2. Total & specific IgE (previously termed RAST) for common food mix, nut mix (and shellfish mix if specifically implicated) have been undertaken - Referrals will only be accepted where specific IgE have been undertaken.

3. RHINITIS

Refer if:

1. There is severe disease (poor quality of life, decreased function) AND an inhaled allergen mix specific IgE (available for testing in the laboratory) has been undertaken - referrals will not be accepted without this information being available.
2. Patients in whom conventional management has failed and who are compliant with therapy should be referred for consideration of desensitisation.

The Clinical Immunology and Allergy Consultant and Specialist Registrar staff are always available to discuss patients by telephone:

Dr. P. Wood	0113 206 7256	OR via hospital switchboard
Dr. H.C. Gooi	0113 206 5567	OR via hospital switchboard
Specialist Registrar	via above numbers	OR via hospital switchboard

REFERRAL GUIDELINES

Introduction

The Clinical Immunology and Allergy Service based at Leeds Teaching Hospitals NHS Trust provides a service to Primary Care from across the West Yorkshire region. We are committed to delivering high quality, timely and appropriate care for patients with immunological and allergic disorders. The introduction of targets for out patient referrals has placed additional demands on our service and requires us to ensure that patients are appropriately seen in the service.

There has been an increase both in the incidence of true allergic disorders and in the public perception that allergies can explain a variety of symptoms. In reality, true allergies are manifest in a relatively narrowly defined spectrum of clinical signs and symptoms.

The Clinical Immunology and Allergy Consultant and Specialist Registrar staff are always available to discuss patients by telephone and these referral guidelines aim to assist GPs in the diagnosis and management of allergic disorders and highlight those situations in which referral or a specialist opinion is recommended.

1. URTICARIA AND ANGIOEDEMA

Urticaria (also known as nettle rash or hives) is an itchy, erythematous, elevated, well-defined and irregularly shaped rash that can occur anywhere on the body and may last from only a few minutes up to twenty-four hours.
Rashes with features of blistering, desquamation of the skin or with individual lesions lasting longer than 24 hours are not urticarial and an alternative diagnosis needs to be considered. A dermatology referral may be considered in these circumstances.

Angioedema occurs secondary to the same pathophysiological process occurring deeper in the skin. Both lesions result from degranulation of mast cells in the skin with release of histamine and other vaso-active mediators, resulting in vasodilatation, pruritis and tissue oedema.

Urticaria and angioedema can occur in two forms; **acute and chronic.**

Acute Urticaria

- Single episodes of urticaria may be the manifestation of a food allergy if there is a clear history of ingestion of an implicated food. **Appropriate initial testing for food allergy can be carried out in primary care (see below).**
- More commonly it results from intercurrent viral infection or drug ingestion, particularly with non-steroidal anti-inflammatory drugs.
- Non-recurring episodes of urticaria are highly unlikely to be due to any type of allergy and the patient should be reassured about this.

Chronic Urticaria
Urticaria which last longer than six weeks is termed **chronic**.

- A cause is not usually identified – some cases appear to be autoimmune in nature.
- Patients should be advised that testing for multiple allergies is not going to be of diagnostic benefit. If patients request referral for allergy testing, the following tests should be undertaken BEFORE REFERRAL:
    - Total IgE
    - Baseline specific IgE (previously termed RAST) for nut mix and food mix.
- If the results are negative, it should be emphasised to the patient that further allergy testing is unlikely to be undertaken at the clinic.

Common triggers for chronic urticaria include:

- viral infections,
- non-steroidal anti-inflammatory drugs, including over the counter medication
- physical stimuli such as pressure on the skin or changes in temperature,
- stress
- additives, preservatives and colourants.

It is important to explain the nature of the condition to the patient and emphasise the need for avoidance of the above factors as far as is possible.

The management of chronic urticaria:

- avoidance of the above factors as appropriate
- changing patients who are on regular non-steroidal anti-inflammatory drugs to another class of analgesic.
- Patients who are on Aspirin should be switched to Clopidogrel unless cardiological advice indicates otherwise.

- regular therapy with rapid acting, non-sedating antihistamines such as Cetirizine, Fexofenadine, Loratadine.
- Higher doses e.g. Cetirizine 30mg daily or Fexofenadine 120mg twice daily, may be necessary to achieve control of the condition.
- Adding in a sedating antihistamine such as Chlorpheniramine or Hydroxyzine may provide additional control.
- Although short term steroid therapy is usually of therapeutic benefit, patients should not be maintained on steroid therapy for disease control.

Many cases of chronic urticaria will disappear over time although this may take eighteen months to two years before full resolution and recurrence is common.

With the above measures, the vast majority of patients with chronic urticaria can be managed in primary care.

Criteria for referral to the Clinical Immunology and Allergy Service:

(1) Failure to respond to two different antihistamine combinations each tried for a period of six to eight weeks.
(2) Severe anaphylactoid-type reactions.
(3) Atypical urticarial lesions e.g. urticarial vasculitis.

Referrals without this information will be returned to the requesting GP

Angioedema without Urticaria

- Some patients can experience idiopathic angioedema without urticaria, particularly as a result of non-steroidal anti-inflammatory drug ingestion.
- Another common drug cause for intermittent angioedema are ACE inhibitors. By preventing the breakdown of bradykinin these drugs can cause angioedema that can be life-threatening. It is important that this drug is changed to another class of anti-hypertensive. Although Angiotensin II Receptor Antagonists have occasionally been reported to cause angioedema, the risk appears to be very small.
- The effects of ACE inhibitors can last several weeks after the drug has been stopped. Recurrence of symptoms greater than six weeks following drug withdrawal suggests another cause and referral should be considered.
- Even if the angioedema recurs after the ACE inhibitor is stopped, it is preferable that the drug is not re-started.

Angioedema can also result as a consequence of low functional activity of C1 inhibitor. Hereditary angioedema, caused by mutations in the gene encoding C1 inhibitor results in episodic and potentially life-threatening episodes of angioedema.

- Patients with suspected hereditary angioedema e.g. young age of onset, positive family history or no other identifiable triggering factors listed above, should be referred for assessment.
- Acquired angioedema occurs when autoantibodies generated against the inhibitor block its action and result in both unchecked complement activation and uncontrolled kinin activity resulting in angioedema that can again be life-threatening. This occurs in two main situations; lymphoid malignancy and connective tissue disease.
- Prior to referral, baseline screening for the above conditions should be undertaken. This should include immunoglobulins and serum electrophoresis, urine for free light chain analysis (Bence-Jones Protein) and complement C4 level.

Patients with angioedema alone should be referred for immunology specialist assessment if:-

(1) The oedema presents at a young age – under 40 years.
(2) They experience life-threatening laryngeal episodes.
(3) Withdrawal of potentially implicated medication fails to control the episodes.
(4) The condition fails to respond to antihistamine therapy.
(5) There is a suspicion of hereditary angioedema.
(6) There is concern over acquired angioedema.

The Clinical Immunology and Allergy Consultant and Specialist Registrar staff are always available to discuss patients by telephone and these referral guidelines aim to assist GPs in the diagnosis and management of allergic disorders and highlight those situations in which referral or a specialist opinion is recommended.

2. ADVERSE FOOD REACTIONS

Introduction

Adverse food reactions can result from ingestion of toxins, gastrointestinal infection, reactions to allergens (e.g. peanut allergy), hypersensitivity to food allergens (e.g. coeliac disease) and possible adverse reactions to additives, preservatives or colorants. The field of food intolerance is poorly understood and there is a significant overlap with irritable bowel syndrome. This guideline attempts to help General Practitioners in identifying those patients who may be suffering from allergic adverse food reactions.

Food Allergy

- IgE mediated food allergy occurs most commonly in children and adult onset of food allergy is unusual.
- Most studies implicate a small number of foods as causative in the vast majority of reactions. These are eggs, milk, peanuts, other nuts, soya, fish and seafood.
- Food allergy is manifest by a small range of symptoms, nearly always including urticaria and angioedema, often with gastrointestinal disturbance e.g. vomiting and pain, both upper and lower respiratory tract symptoms and occurring within two hours of ingestion of the potential allergen.
- The initial investigation of IgE mediated food reactions involves the measurement of specific IgE to the potential allergen. This can be done by skin testing or by specific IgE testing.
- It is important to appreciate that specific IgE testing for the above common foods has a high negative predictive value, and therefore a negative result provides strong evidence that a food allergy is **not** the cause of the patient's symptoms.
- The nature of "allergy" to candida species remains unclear, but there is NO evidence that it is IgE mediated.

Food intolerance

- This remains poorly understood.
- It is clear that it is not mediated by IgE related mechanisms.
- There are no scientifically validated tests available in the National Health Service to assess for food intolerance and as outlined above, IgE mediated food allergy can be excluded in the vast majority of cases.
- It should be explained to patients that symptoms involving bloating, alternate constipation, diarrhoea and abdominal discomfort are **not** manifestations of food allergy and referral to an allergist for further assessment is unlikely to identify any obvious triggers.
- Such patients should be given general dietary advice as for IBS with consideration to the use of anti-spasmodics for symptom control.
- Patients in whom the above measures are unsuccessful and where inflammatory bowel disease has been excluded can be referred for further assessment, although it is unlikely that food allergy will be identified in the majority of cases.

REFERRALS FOR ASSESSMENT OF POTENTIAL FOOD ALLERGY WILL ONLY BE ACCEPTED WHERE SPECIFIC IgE TO THE IMPLICATED FOODS HAS BEEN UNDERTAKEN AND SUGGESTS AN ALLERGIC CAUSE.

3. RHINITIS

Introduction

Rhinitis can result from both allergic and non-allergic causes. Both forms result in similar symptoms, namely, sneezing, congestion, nasal discharge and often associated eye symptoms. It is important to establish whether the rhinitis is allergic in origin as therapy differs and, in most cases, this can be done in primary care. The Allergy Service is particularly keen to see those patients for whom desensitisation therapy is appropriate.

ALLERGIC RHINITIS

This can be divided into:

- seasonal allergic rhinitis (also known as intermittent rhinitis)
- perennial rhinitis (also known as persistent rhinitis).

Seasonal Allergic Rhinitis

- This is most commonly due to grass pollen allergy (hayfever) and presents in late spring to early summer with typical symptoms as outlined above.
- Patients can also be allergic to a number of tree pollens, particularly birch, alder and hazel and these can pollinate as early as February. Some patients therefore experience spring onset seasonal allergic rhinitis.
- A smaller group has an isolated allergy to moulds which sporulate in the in the autumn.

- Management of the majority of these patients can be undertaken in primary care.
    - Measures to limit exposure to pollens should be undertaken.
    - Regular antihistamines should be used throughout the pollen season.
    - In addition, a steroid nasal spray should be used and it should be emphasised to patients that they need to use this on a regular basis starting pre-seasonally for maximal efficacy.
    - For many patients eye drops may be necessary for full symptom control.

    - As is well accepted, the use of intra-muscular steroid injections is not advisable.

- **Patients in whom conventional management has failed and who are compliant with therapy, should be referred for consideration of desensitisation (See below).**

Persistent or Perennial Rhinitis

- Allergic rhinitis which is persistent is nearly always in the United Kingdom secondary to house dust mite allergy.
- Patients with allergic rhinitis of this type often have, or are at risk of developing, asthma.
- Management strategies for persistent rhinitis are similar to those outlined for seasonal rhinitis.
- House dust mite reduction measures are probably effective but ONLY if combined with conventional therapy to which the patient is compliant.
- **Patients in whom conventional management has failed should be referred for consideration of desensitisation therapy.**

Desensitisation therapy (Immunotherapy)
Desensitisation for allergic rhinitis has been demonstrated to be successful for both grass pollen and house dust mite, in addition to a number of other animal danders. Contra-indications to desensitisation therapy include:-

1) Uncontrolled asthma
2) Immunosuppression or immunodeficiency
3) Beta-blocker therapy (except for venom allergy)
4) Pregnancy
5) Inability to understand or comply with therapy

- **An initial assessment for allergic rhinitis can be undertaken in primary care with the use of specific IgE to a panel of aero allergens.**
- **An inhaled allergen mix is available for testing in the laboratory and referrals for assessment of rhinitis will not be accepted without this information being available.**

NON-ALLERGIC RHINITIS

- Rhinitis occurring for the first time in adult life in an individual without other atopic disease is more likely to be non-allergic in origin.
- There are many other causes for rhinitis, including
  - inflammatory causes such as vasculitis,
  - local causes e.g. nasal polyps or foreign body's in children)
  - manifestations of systemic disease e.g. thyroid disease.

  - It is essential that these causes are considered and constitutional symptoms such as fever, weight loss or blood stained discharge should raise the possibility of a more sinister cause.
- **An initial assessment for allergic rhinitis can be undertaken in primary care with the use of specific IgE to a panel of aero allergens.**

- With the above blood testing undertaken and specific IgE negative, allergic rhinitis can be effectively excluded
- It is unlikely, in the absence of a clear history that an unidentified allergen will be found as a trigger for the disease.
- It is worth considering whether referral to the Allergy Clinic for patients in whom allergic rhinitis has been excluded, is likely to be of benefit to the patient.

- Non-allergic rhinitis can be managed with antihistamines and steroid nasal sprays as required.
- Intranasal ipratropium is recommended for watery Rhinorrhoea
- Patients should be advised to avoid spicy foods and other foods rich in preservative and additives as these can be chemically irritant and cause symptoms

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