Guidelines for referral of patients to the Immunology Allergy clinic

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CLINICAL SITUATIONS UNRELATED TO ALLERGY

Patients frequently attribute a wide variety of symptoms to allergy. This perception has often been reinforced by "information" in the press and other popular media, and by the results of privately available "diagnostic tests" which are not only inherently implausible but have no established validity. In many cases, the patients' belief that their symptoms are due to allergy are deeply entrenched and not amenable to rational debate.

The following should be borne in mind when considering whether such patients should be referred:

- weight loss, weight gain, headache (including migraine), confusion, depression, lack of concentration, vertigo, tiredness (including chronic fatigue syndrome) and hair loss can never be explained in terms of allergy. The same is almost always true of isolated vague abdominal symptoms such as bloating (these can, however, be due to irritable bowel syndrome, undiagnosed coeliac disease or other organic pathologies). Even if "food intolerance" (e.g. to wheat) does exist as a diagnostic entity, there are no validated diagnostic tests or therapies (other than avoidance).
- there is no good evidence that "systemic candidiasis syndrome" or "multiple chemical sensitivity syndrome" or amalgam sensitivity are discrete physical entities, or that they are actually due to those agents from which they derive their name. There are no validated diagnostic tests or therapies.
- some substances are simply not recognized allergens, e.g. tap water, sugar, caffeine, 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, perfumes) are suffering from allergy to these substances.
- 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.

Patients in these categories hardly ever benefit from being seen in an orthodox allergy setting, unless they can countenance the possibility that their problem may not be allergic in aetiology.

Immunodeficiency- When to refer

- Eight or more new ear infections within 1year,(Children)
- Two or more serious sinus infection in one year
- Two or more pneumonia's within 1 year
- Recurrent deep skin or organ abscess
- Unusual infective organism
- Two or more deep seated infections, such as meningitis, osteomyelitis, cellulitis or sepsis
- Surgical intervention for chronic infection, such as lobectomy for bronchiectasis, recurrent insertion of grommets or recurrent incision of boils
- Two or month of appropriate antibiotic therapy with little effect
- Persistent thrush in mouth or elsewhere
- Failure of an infant to gain weight or grow normally
- A family history of immunodeficiency

ANAPHYLAXIS

Any patient with a history of anaphylaxis[1] should be referred to the clinic.

*1: This implies that the patient has suffered from an **acute collapse with bronchospasm, pharyngeal oedema and/or hypotension.** This is usually, but not always, accompanied by other visible features such as flushing, urticaria, or angioedema.*

URTICARIA AND ANGIOEDEMA

Urticaria (hives, wheals or "nettle rash") and angioedema (soft tissue swelling) can occur alone or together. They can be allergic or non-allergic in aetiology. Contrary to popular perception, these symptoms are much more commonly non-allergic — most patients have idiopathic urticaria/angioedema, for which extended antihistamine treatment is often necessary.

Many patients with urticaria and/or angioedema are referred as cases of possible food allergy — *"to find out what they are allergic to"*. In the majority of cases, food allergy is not the cause and can be excluded on the basis of the clinical history alone, without the need for any investigation.

The presence of any of the following features suggests symptoms are *not* due to food allergy:

- **Symptoms occur more than 2 hours from ingestion**

- there is no consistent relationship to a particular food trigger, either by ingestion,[2] or contact (in the case of localised contact urticaria)
- symptoms are spontaneous, without any apparent triggering factor, or come on overnight or first thing in the morning, before or soon after rising
- symptoms have physical triggers, such as minor trauma, temperature change, sweating or exposure to water
- symptoms persist for several days at a time, with or without variation in intensity over that period
- the patient develops angioedema while on treatment with an ACE inhibitor or other drugs r[3]

2: patients frequently examine what foods they have eaten the previous day in the search for a connection with their symptoms. There is no rational basis for this as, ***in genuine food allergy, symptoms usually occur within 30 minutes of exposure to a single food, or well-defined group of foods, and a delay of more than 2 hours is virtually unknown***.

3: angioedema is a well documented adverse side-effect of ACE inhibitors particularly, but also NSAID's, and can occur for the first time even after prolonged treatment.

The following management plan is suggested for patients presenting with urticaria/angioedema:

When the history suggests non-allergic symptoms:

A. PATIENTS WITH URTICARIA ONLY —

- check that symptomatic episodes have not followed ingestion of a non-steroidal anti-inflammatory drug, such as aspirin[4]
- **<u>give an oral long acting non sedating antihistamine</u>**, such as fexofenadine 180 mg, cetirizine 10 mg or desloratidine 5mg once daily (*prn*, if symptoms are infrequent)[5]
- if necessary, double the dose of antihistamine

- **<u>Refer only to Immunology or Dermatology if</u>**

1. **Symptoms do not respond to these measures**

2. **History suggests underlying allergy (Immediate hypersensitivity to Immunology, delayed to Dermatology)**

Notes

4: some patients may have pharmacological hypersensitivity to NSAIDs and sporadically be taking one or more proprietary medications containing aspirin. (NB: there is no need to stop treatment in patients who have been stabilized on long term maintenance NSAID therapy.)

5: in pregnancy, only chlorpheniramine *(Piriton)* is recommended.

B. PATIENTS WITH ANGIOEDEMA (WITH OR WITHOUT URTICARIA) —

- in general, follow paragraph **'A'** above, but with the following additional considerations:
- **if the patient is taking an ACE inhibitor, this should be stopped[5] (no patient should be referred until they have been shown not to respond to this intervention)**
- even if the patient is not taking an ACE inhibitor, these should be avoided in the future
- refer if there has been involvement of the tongue or throat/upper respiratory tract (unless this only happened while on an ACE inhibitor)
- in patients with angioedema but not urticaria, exclude C1-inhibitor deficiency (check complement component C4 — values above 0.15 g/l virtually exclude this condition)

Notes

5: our current policy is to change patients to an angiotensin II receptor antagonist. Although angioedema has also been reported with these, the risk appears to be much less.

When the history suggests that symptoms ***are*** due to food allergy:

- advise avoidance of the likely allergen
- supply the patient with an oral antihistamine
- the prescription of an *Epipen* adrenaline injector can be considered if the perceived risk of anaphylaxis merits this
- Ensure that asthma is well controlled
- This should be enough for simple, single food allergens with few episodes of anaphylaxis
- If complex refer for diagnostic testing and further advice on management

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RHINITIS

Rhinitis can be allergic or non-allergic, although both forms can coexist.

Allergic rhinitis is likely if symptoms are seasonal or episodic, and obviously coincide with exposure to known aero-allergens, such as pollens and animal dander's. Allergic rhinitis due to house dust mite antigen (which is relatively ubiquitous and tends to cause perennial symptoms) is least easy to distinguish clinically from non-allergic rhinitis. To a variable degree, patients with allergic rhinitis can also have ocular symptoms; sometimes, these are the main feature.

Nasal polyps are not an allergic phenomenon (although these patients sometimes have pharmacological hypersensitivity to NSAIDs), but it is often useful to know whether there is an *additional* allergic component to the rhinitis.

Referral of patients with rhinitis to the ENT or Immunology clinic is justified if it is:

- to confirm the agent(s) responsible for allergic rhinitis so that advice can be given on avoidance (if the allergen is already obvious clinically, e.g. pollen or cats, this may not be necessary)

- NB 5mls of clotted blood for Rast to HDM, Tree, Grass pollen and Cat or Dog if appropriated may save a clinic visit.
- to advise on treatment[7]
- to offer allergen desensitization therapy[8]

7: it is reasonable to optimize medical treatment as much as possible in the GP setting:

- if nasal polyps do not respond adequately to topical steroid — e.g. Betnesol drops for 2–3 weeks (given in the "lying down, head back position"), followed by maintenance with a steroid spray — referral to ENT for polypectomy is usually indicated
- in allergic rhinitis, ***combined*** treatment with a topical steroid spray *plus* one or more of: topical and/or oral antihistamine, topical cromoglycate/nedocromil sodium and topical ipratropium bromide (particularly effective if rhinorrhoea is a major symptom) is often necessary. Topical antihistamine and cromoglycate preparations are also available for eye symptoms.

8: **Allergen desensitization**

Can be considered for patients whose symptoms of allergic rhinitis are not adequately controlled by the measures suggested in '7' above, and for those who genuinely cannot tolerate the treatment. Before referral for possible desensitization, patients should to be aware that:

- the treatment involves a 3-year course of subcutaneous injections (weekly for the first 9 to 15 weeks depending on allergen, monthly thereafter)
- it can only be given in the hospital clinic, and at a set time during the week
- there is a mandatory period of at least one hour after each injection, during which the patient must wait behind in the clinic for observation
- fatal anaphylaxis is one possible outcome of the treatment, even though the risk of this is extremely small.

The following exclusion criteria apply:

- asthma which is severe enough to require long-term maintenance treatment with a steroid
- patients on Beta-blocker or ACE-inhibitor therapy.

It should be noted that desensitization, with its attendant risks, cannot be offered as a "lifestyle" treatment in cases where the allergen could *reasonably* be avoided without this having a devastating effect on the patient's daily activities or employment.

ASTHMA

Testing of asthmatics for allergy can be a useful guide to advice on allergen avoidance. Try 5mls of clotted blood for Rast to suspected allergens

Unfortunately, desensitization therapy is currently not recommended as a treatment for asthma *per se,* because of concerns over safety in this clinical context.

ECZEMA

Patients with troublesome eczema are often keen to discover some avoidable dietary cause of their symptoms. Unfortunately, although trials of exclusion diets are sometimes of clinical benefit in cases of eczema, prior allergy testing does not reliably predict the response to this intervention. Indeed, many patients with eczema will demonstrate apparent sensitisation (positive skin *prick* test and/or circulating IgE) to dietary antigens which they know they can tolerate — this can lead to unnecessary food avoidance.

If the history suggests *contact* eczema, skin *patch* testing may be worthwhile — this investigation is performed in the dermatology clinic.

In the absence of symptoms of actual food allergy, there is little to be gained by referring patients with eczema beyond the dermatology clinic.

SUSPECTED DRUG ALLERGY

Antibiotics are the commonest cause of suspected drug allergy. When considering whether to refer a patient for investigation of possible drug allergy, please note the following:

- diagnostic tests are only available/recommended for those cases where the symptoms (urticaria, angioedema, bronchospasm, acute collapse) suggest the possibility of an IgE-mediated reaction (i.e. type I or immediate-type hypersensitivity)
- even in these cases, although positive tests are informative, negative tests do not guarantee that a drug can be administered safely in the future
- the absolute standard for diagnosis is direct drug challenge — many patients will prefer simply to avoid future exposure than to undergo this
- when the symptoms are other than those described above (e.g. vasculitic or purpuric rashes, etc.), the diagnosis is purely clinical and avoidance is advised if the history suggests a drug reaction — there is unlikely to be any additional benefit from referral to the allergy clinic

Although **NSAIDs** can cause symptoms indistinguishable from those of IgE-mediated allergy (up to and including anaphylaxis), the "hypersensitivity" is pharmacological rather than immunological. The diagnosis is clinical, there is no diagnostic test, and these drugs should be avoided if there is a strong index of suspicion. Most of these patients can take paracetamol without any difficulty.

ACE-inhibitors are well known to cause or exacerbate angioedema (please see section on urticaria and angioedema). Again, this reaction is not immunologically mediated and there is no diagnostic test.

Anaesthetic allergy: We provide a regional service for investigation. Usually instigated by the Consultant aneathetist or Dental practioner for latex allergy.

ALLERGY TO BEE OR WASP VENOM

Any patient with a history of respiratory symptoms or a systemic allergic reaction (generalized urticaria, angioedema, bronchospasm or anaphylaxis) following a bee or wasp sting *should* be referred for assessment. Many of these patients will need their own supply of adrenaline for emergency use; allergen desensitization will be appropriate for some.

It is *not* necessary to refer patients:

- for "screening", because they have other allergies
- who have only had local reactions to stings (even though these can be quite intense)[9]
- because another family member is allergic to bee or wasp venom[9]

9: if there is anxiety because of these situations, send blood for circulating specific IgE ("RAST") against bee and wasp venom. If these are undetectable, the patient is at very low risk.

C1-INHIBITOR DEFICIENCY

This rare problem, which can be hereditary or acquired, is likely to present as angioedema and be considered under the criteria given above (see **URTICARIA AND ANGIOEDEMA**). However, it deserves special mention as the presentation may be atypical and, in some cases, a patient with a known family history of hereditary angioedema may not yet have experienced symptoms.

Any patient with:

- unexplained episodic angioedema and/or abdominal pain
- a family history of the above (or of known hereditary angioedema)

AND

- complement component C4 measured at less than 0.15g/l, a normal C4 unless on treatment excludes the diagnosis.

should be referred to exclude C1-inhibitor deficiency. (It is not necessary to measure C1-inhibitor in general practice as there are subtle problems associated with this.)
