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Allergy testing and referral in children

Background

Allergic diseases (asthma, atopic dermatitis, allergic rhinitis and food allergy) are the commonest chronic diseases of childhood. General practitioners commonly encounter children with allergic diseases and need to be aware of when referral to a paediatric allergist should be considered. An understanding of what diagnostic tests the allergist may use in confirming the diagnosis is also necessary.

Objective

This article discusses the criteria for referral to a specialist paediatric allergist and also details the tests that may be used by the allergist as part of the diagnostic work up.

Discussion

Management of allergic diseases requires accurate diagnosis and avoidance of offending allergens where possible. The diagnosis of an IgE mediated allergy requires both a history of symptoms on exposure to the allergen and detection of allergen specific IgE. The most commonly employed diagnostic methods in clinical allergy assessment are skin prick testing, RAST and clinical oral food challenge procedures. The use of alternative or unorthodox tests may provide misleading results and delay correct diagnosis and therefore should not be used.

■ **Allergic diseases – eczema, asthma, rhinoconjunctivitis and food allergy – are the commonest chronic diseases of childhood¹ and Australia has one of the highest prevalence rates of allergic diseases in the world.² Management of these conditions requires correct diagnosis and identification, and avoidance of offending allergens where possible. A number of tests are now commonly employed in assessing both children and adults with allergic diseases. The general practitioner needs to be aware of these tests and when referral to an allergist should be considered.**

Referral to an allergy specialist

History is the mainstay of diagnosis of allergic diseases. The GP should take a detailed history with particular attention to: timing of the onset of symptoms, nature and extent of symptoms (organ systems involved), duration of symptoms, reproducibility of symptoms (if previously exposed) and other factors required to induce symptoms (eg. exercise).

Referral to an allergy specialist should be considered in any child with a history of:

- suspected IgE mediated food allergy – IgE mediated reactions generally occur rapidly upon ingestion of the offending food (within 30 minutes to 1 hour) and can involve the skin (urticaria, angioedema), gastrointestinal system (vomiting, diarrhoea, abdominal pain), respiratory system (cough, wheeze, stridor, chest tightness, change in voice, tongue swelling) or the cardiovascular system (hypotension, collapse)
- suspected non-IgE mediated food allergy – non-IgE mediated reactions are generally delayed in onset with symptoms developing several hours to days after ingestion of the offending food. They present predominately with gastrointestinal symptoms (diarrhoea, vomiting, abdominal pain). However, 10–15% present with food protein induced enterocolitis syndrome (FPIES) (severe vomiting and



associated pallor and collapse). There is no specific diagnostic test to confirm the diagnosis of a non-IgE mediated allergy and diagnosis is made by elimination of the offending food and subsequent rechallenge when appropriate

- asthma that requires preventer therapy – to assess the possible role of environmental allergens and provide advice about implementation of avoidance strategies where possible
- allergic rhinoconjunctivitis that has not responded to maximal medical therapy – to define offending allergens, provision of allergen avoidance strategies and consider indication for specific immunotherapy
- atopic dermatitis where there has been a poor response to topical management or where dietary precipitants are suspected – to assess the possible role of dietary and environmental allergens
- suspected drug or latex allergy
- systemic reaction to an insect sting – for consideration of immunotherapy where available.

Allergist review is not appropriate for:

- a single episode of idiopathic urticaria
- autism and behavioural disease
- migraine headaches
- reactions to respiratory irritants (eg. smoke, perfumes).

The allergy consultation and testing

The allergy specialist may use one of several methods as part of the diagnostic work up. These tests most commonly include: skin prick testing (SPT), radio-allergosorbent test (RAST) and oral food challenge procedures.

Skin prick testing

Indications

Skin prick testing is performed to detect the presence of allergen specific IgE to foods, aeroallergens, some venoms, antibiotics and latex. It is easy to perform, relatively inexpensive and results are immediately available. Skin prick testing should be performed only by medical practitioners trained in both performing the test and interpreting the results. As SPT can trigger allergic reactions, medical practitioners must have experience in identification and management of allergic reactions and access to appropriate resuscitation facilities.

What does it involve?

Skin prick testing is performed on the skin of either the back, or on the volar surface of the forearm in older patients. It involves the introduction of a very small amount of commercially available standardised allergen extract into the epidermis using either a lancet or prick device. The interaction of the allergen and previously formed specific IgE bound to cutaneous mast cells results in the release of histamine and other inflammatory mediators with a resultant wheal and flare reaction (*Figure 1*). This reaction peaks at 15–20 minutes, which is when the result is read. The diameter of

Figure 1. Child having skin prick testing



the resulting wheal is measured in two dimensions and the result recorded as the mean of the two values. Negative and positive controls must always be used to enable interpretation of test results. By convention, a positive skin prick test is taken as being >3 mm than the negative control.

Interpretation of results

A positive skin prick test only indicates sensitisation (ie. the presence of allergen specific IgE) and does not always equate to clinically relevant allergy.³ A positive skin prick test result must be interpreted in the context of clinical history, clinical signs and allergen exposure. The overall positive predictive accuracy is <50% with suspected food allergy.⁴ If the history is clear, a positive skin test can confirm the diagnosis of IgE mediated allergy. However, if the history is uncertain, the significance of a positive skin test may need to be confirmed by formal oral food challenge.

A negative skin prick test is very helpful as it almost eliminates the diagnosis (negative predictive accuracy of >95%) of IgE mediated food allergy.⁴

The size of the skin prick test result measurement does not correlate with severity of the potential allergic reaction; however the larger the size of the test result, the greater the likelihood that it is clinically significant. Diagnostic skin prick test decision points have been defined for several food allergens – these are cut off values for skin prick test wheal diameters that predict a positive food challenge result with greater than 95% accuracy.⁵ These diagnostic decision points vary according to the age of the child and the allergen being tested. If the skin prick test result is equivocal or discordant with the clinical history then the test should be repeated with the fresh food if possible, or with a RAST.

Requirements for skin prick testing

There are no specific age requirements for performing SPT, however skin reactivity may be reduced in very young children and the elderly.



Table 1. Drugs that interfere with skin prick testing

Class of drug	Time required to withhold before skin prick testing
Antihistamines	72–96 hours
Tricyclic antidepressants	7–14 days
H2 antagonists	24 hours
Neuroleptics	Withholding period not established, may be up to 2 weeks or more

Young children may also develop larger flares and have smaller wheals. There is an increased risk of triggering anaphylaxis in children, therefore SPT in children less than 2 years of age should be performed by specialist paediatric allergists.

Skin prick testing requires an adequate area of normal skin – it cannot be performed if there is widespread skin disease (eg. active atopic dermatitis) or in patients with significant dermatographism. Skin prick testing must be delayed until 4–6 weeks after an anaphylactic reaction due to risk of false negative results in this period. A number of medications may also interfere with skin prick test results and must therefore be ceased before testing (Table 1).

Risks of testing

Skin prick testing is generally a safe procedure. However, it is not without potential risks. Minor discomfort and itch are common, and, rarely, patients may experience marked swelling and discomfort at the site of the test. Marked swelling can be treated with an antihistamine medication, topical corticosteroid cream or ice pack. Systemic reactions can also occur, with the risk of triggering an anaphylactic reaction reported as being 0.02%.⁶ The risk of anaphylaxis is increased when SPT is performed with food allergens (particularly fresh foods), latex and drugs, therefore it is recommended that testing to these allergens is performed only by allergy specialists.

The radio-allergosorbent test

The RAST detects free antigen specific IgE in the serum. It can be used to diagnose all types of allergy but is generally less sensitive and specific than SPT. The RAST can be reported semi-quantitatively as a score or preferably using newer CAP RAST technology as a quantitative measurement. The RAST is particularly useful where SPT is contraindicated and has the advantage that it may be ordered by the primary physician while waiting for specialist allergy review. The results of RAST are not affected by prior antihistamine use or other drug use and can be performed in patients with widespread skin disease. The results may however be difficult to interpret in patients with very high levels of total IgE (>1000 kU/L), which is not uncommon in patients with severe eczema. Testing is available for a wide range of food and environmental allergens. However, in clinical practice in Australia, the Medicare rebate restricts the number of allergens that can be tested at any one time to four. The use of allergen mixtures (eg. food mix) for RAST is not recommended.

There is published data for a restricted range of foods (egg, milk, soy and peanut) correlating the level of serum specific IgE to the probability of the child reacting to that food.⁷ As with SPT, a positive RAST does not always equate to clinically significant allergy and must always be interpreted in the context of clinical history. The GP may use RAST results to guide allergen avoidance while the patient waits for specialist allergy review.

A comparison of the main features of SPT and RAST is shown in Table 2.

Oral food challenge

Oral food challenges are regarded as the 'gold standard' for diagnosis of food allergy.⁸ They may be performed to confirm the diagnosis of food allergy where it is not clear cut, or more commonly, to determine if resolution of a previously documented food allergy has occurred. Food challenges should only be performed by specialist

Table 2. Comparison of skin prick testing and RAST

Skin prick testing	RAST
Requires adequate training to perform reliably	Widely available – can be ordered by the GP
Requires adequate area of normal skin	Can be performed where there is extensive skin disease or in patients with dermatographism
Certain drugs (eg. antihistamines, tricyclic antidepressants) interfere with results	Can be performed if the patient is unable to cease taking medications
Must be delayed for 4–6 weeks after an anaphylactic reaction (results may not be interpretable if there has been massive mast cell degranulation)	Can be performed in the setting of recent anaphylaxis
Minor discomfort – itch	Venesection may be painful or anxiety provoking
Wide range of allergens can be tested (including fresh foods)	Some food allergens, drugs and rarer pollens may not be available
Large number of allergens can be tested at any one time	Number of allergens tested is limited by Medicare rebate (maximum of four allergens can be tested at any one time)
Results available immediately	Results may not be available for several weeks
Elevated IgE levels do not affect results	False positives may occur in patients with high total IgE levels



units trained in early identification of allergic reactions and equipped for management and resuscitation. Oral food challenges generally involve a half day hospital admission and are usually open, but can be single or double blinded or placebo controlled. Oral food challenges involve giving small incremental doses of the food and carefully monitoring for any reaction. The challenge is stopped once any objective reaction has occurred. A range of vehicles (solid and liquids) can be used to disguise foods. Tolerance of a serving size portion of a food is generally considered evidence of lack of reactivity. Challenge testing may also be performed with drugs and latex.

Management

If the allergist believes that the results are indicative of clinically relevant food allergy, avoidance measures will be indicated; however if there is uncertainty an oral food challenge may be considered. Where multiple foods are to be avoided, dietician referral is recommended. Appropriate allergy management plans must also be provided to guide patients and their carers on management in the event of an episode of inadvertent exposure to a food allergen with a resultant allergic reaction. This may include provision of an adrenaline autoinjector (eg. EpiPen®) (see *Patient education*).

If aeroallergens are thought to exacerbate asthma, atopic dermatitis or allergic rhinitis then avoidance measures will be advised where practical. If symptoms of allergic rhinitis cannot be controlled with maximal medical therapy, desensitisation therapy to the allergen may be considered.

It is important that children are regularly reviewed by their allergist, particularly those with a diagnosis of food allergy. Most children develop tolerance to most common food allergens (ie. egg, milk, wheat and soy) by the time they are 5–6 years of age. Therefore periodic re-evaluation is important to identify foods that no longer need to be avoided. It is recommended that SPT be repeated every 1–2 years for food allergens and that supervised oral food challenge be considered when appropriate.

In contrast, peanut and tree nut allergy tends to be ongoing into adult life in up to 80% of children. However, periodic re-evaluation of these children is also important to ensure appropriate allergy management plans are in place and any allergic comorbidities are adequately managed.

Unorthodox allergy tests

A number of unorthodox tests for diagnosing allergy are now widely used in Australia. These tests provide misleading results and may delay correct diagnosis and lead to inappropriate dietary restriction. Unorthodox tests include: vega testing, kinesiology, radionics, pulse testing, iridology, hair analysis and voice bio. Tests such as measurement of food specific IgG4 are also increasingly being used inappropriately in the diagnosis of food allergy. IgG4 antibodies are found commonly in healthy children and adults with no history of allergic disease. The presence of IgG4 antibodies reflects exposure to

the allergen not the presence of allergic disease and should not be used in the diagnosis of allergic disease.

The future

There is no test currently available that can accurately predict the severity of a reaction that a patient is likely to have. Research is currently underway to improve diagnostic methods. Possible future tests include analysis of IgE binding to specific epitopes that may indicate an increased risk for clinical reaction, and studies of in vitro T cell responses.

Summary of important points

- Diagnosis of IgE mediated allergy requires both a history of symptoms on exposure to the allergen and the detection of allergen specific IgE.
- A positive skin test only indicates sensitisation and does not always equate to clinically relevant allergy.
- Skin prick testing, RAST and oral food challenge testing (in selected cases) are the only validated and useful investigations for suspected allergy.
- Unorthodox tests may provide misleading results and may lead to a delay in correct diagnosis and inappropriate management.
- Referral to a specialist allergist should be made in the case of suspected food allergy, asthma requiring the use of preventer therapy, allergic rhinitis that has failed to respond to medical therapy, suspected latex and drug allergy, and systemic reactions following insect stings.

Resource

Australasian Society of Clinical Immunology and Allergy
www.allergy.org.au.

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