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Opinion

Allergy Testing in Primary Care

Introduction

Allergic diseases are a common and increasing problem in Western societies, the commonest manifestations of which are respiratory and dermatological in nature - eczema, allergic rhinitis and asthma - and which are usually of mild or moderate severity. Less common problems include food, drug and insect venom allergy, which can be associated with severe or life threatening symptoms. Allergy testing can be helpful on two counts: firstly, to identify a specific allergen trigger when there is potential to avoid it; and secondly, to diagnose atopy, that is, to provide evidence of IgE sensitisation to common airborne allergens in order to assess the likelihood of sensitivity to other, less common allergens.

Confirmation of non-atopic status can be helpful to exclude IgE-mediated food and drug allergy (but not venom), as both conditions are rare in non-atopic individuals.

Symptom presentation

The basis of allergy diagnosis is the taking of a complete and careful history aiming to link allergen exposure with the acute onset of suggestive symptoms. Allergic symptoms are caused by release of mediators (particularly histamine and leukotrienes) from mast cells and basophils sensitised by binding to allergen-specific IgE which is then cross-linked by allergen. Allergic symptoms therefore reflect histamine release and include itching, sneezing, rhinorrhoea, bronchospasm, laryngeal oedema with subsequent hoarse voice and upper airway obstruction, urticaria with or without angioedema, and hypotension. Symptoms are characterised by their immediacy following allergen exposure and their reproducibility within individuals, although the spectrum of symptoms depends to an extent on the amount and route of exposure.

Is allergy testing necessary?

There is good evidence that the majority of patients presenting in primary care with suspected allergic disorders can be managed without formal identification of the specific allergen trigger. This is a function of three factors: first, the pre-test likelihood of correctly diagnosing or excluding an allergic disorder is high if appropriate clinical questions are asked; second, existing common therapeutic options for managing allergic problems are relatively safe; and third, there is insufficient evidence from randomised controlled trials to support current approaches which attempt to avoid aero-allergen exposure. The probability of rhinitis symptoms, for example, being allergic in nature is significantly increased if symptoms are triggered by animals or pollen, or if the patient has a personal history or a family history of allergy.[1] The need for a diagnostic test should therefore depend on whether or not the identification of an allergen trigger will influence the treatment decision.

The role of empirical treatment

Given the challenges in avoiding exposure to allergen triggers, in most individuals there is little merit in identifying the underlying allergenic trigger. Empirical treatment is therefore justified as an initial step for rhinitis or asthma patients with a convincing history of allergy; that is, patients with a personal or family history of asthma, eczema or hay fever who have symptoms which occur within minutes of exposure and fit the pattern of histamine release in one or more target organs (i.e. redness, itching or swelling).

The role of allergy testing

If, however, allergen avoidance is both effective and possible (as is the case with food or drug allergy), or an allergen-specific treatment such as immunotherapy is being considered, then identification of the specific allergen trigger is essential – although again, accurate history taking is of primary importance in establishing the role of allergy and interpreting test results. The medical history, related to the nature and timing of the symptoms, trigger factors, and evidence of personal and family history of allergic disease, should guide the need for, and choice of, diagnostic test.[1]

Types of allergy testing and the procedures involved

In community settings, both skin prick tests and blood tests are available to identify IgE-mediated disease, although neither is commonly used. Skin prick tests are simple (although relatively time-consuming) and results are visible and available immediately. Testing involves applying drops of allergen extracts to the volar aspect of the forearm which are then pricked at 90° with individual sterile lancets. Drops are blotted with a tissue. Tests for 'quality control' are also included (allergen diluent (negative control) and histamine dihydrochloride (positive control). The tests are read at 15 minutes, and are considered positive when a skin wheal of >2mm bigger than the negative control is observed. A positive response to the negative control identifies patients who have dermatographism, a traumatically-induced urticaria in response to the prick of the lancet which may result in false positive results. Histamine, the end mediator released by mast cells in the skin, should produce a positive result in all patients. If the histamine test is negative the test should be repeated. Reasons for false negative responses to histamine include: the patient having taken anti-histamine tablets in the previous 48 hours; the extensive use of topical steroids on the skin being tested (which drives local mast cells out of the skin); and the deterioration of allergens on storage. Allergen solutions have an expiry date and should therefore be stored carefully in a refrigerator when not being used.

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Skin prick tests for foods are less reliable than those for aero-allergens, resulting in a high rate of false positives.

Skin prick testing is remarkably safe, particularly with aeroallergens, but the safety of skin prick testing is still viewed with concern. However, the procedure is well tolerated by patients and by nurses performing the tests in primary care, and anaphylaxis following skin prick tests to common aero-allergens has not been reported. Skin prick tests for foods, drugs and insect venom carry a small risk of systemic reactions and should only be performed by staff who are trained to recognise symptoms of anaphylaxis and have the facilities to treat them promptly and efficiently. Adrenaline at an adult dose of 0.3-0.5ml (0.15-0.3 ml in children depending on weight) of 1/1000 for intra-muscular injection should always be immediately available.

Measurement of allergen-specific IgE (sIgE) antibodies in the serum is an alternative and comparably reliable way of diagnosing atopy when skin prick tests are not available. They are a particularly useful test for allergens which carry the risk of adverse reactions if used as a skin prick test (e.g. food allergens, venom, penicillin). Specific serum IgE testing can usually be arranged via the local biochemistry/pathology laboratory.

Requesting a total IgE level is not a reliable indicator of atopic status and cannot be used diagnostically. In terms of cost, skin prick tests appear to be the cheaper option, although the comparative costs of skin prick test solutions/sterile lancets and specific IgE blood tests should take into account a number of factors including the number of allergens needed, the longevity and stability of the test solutions, the cost per test, (including nurse time for skin prick testing), and the cost and availability of phlebotomy services. Specific IgE blood tests become more cost-effective compared to skin prick tests when testing for allergens such as foods, venoms or drugs which are used less frequently and which substantially increase the skin prick testing cost per test.

Interpreting tests

When interpreting allergy tests, it is essential to appreciate that many patients who produce IgE specific for particular allergens never have any corresponding clinical disease. For example, fewer than 50% of patients who produce IgE to grass pollen, as indicated by a positive skin prick test or blood test, ever develop allergic rhinitis. This has important consequences for the interpretation of allergy tests. It means that, while these tests have a very good negative predictive value (i.e. allergic reactions are extremely unlikely in the absence of detectable allergen-specific IgE), they also have a very poor positive predictive value (i.e. many patients with positive tests to particular allergens will never have symptoms on exposure).

As a rough guide skin test responses greater than 6mm in diameter, and specific IgE levels of approximately 11kU/l to airborne allergens, are more likely to be associated with clinical symptoms on exposure to the relevant allergen.[2] With food allergy, diagnostic cut-off levels for skin prick tests and specific IgE tests have been developed.[2,3] These cut-offs can be used to predict the likelihood of developing symptoms on exposure and may obviate the need for costly and time-consuming food challenges. There is a relatively good correlation between skin prick tests and blood tests, and so the choice of test is likely to be based on the nature of the symptoms, safety, availability of extracts, costs, and operator expertise in the performance of the test and the interpretation of results.

Ideally, identification of specific IgE should precede referral for a specialist allergy opinion in patients in whom there is diagnostic uncertainty or those for whom allergen-specific therapy is being considered, as well as those patients who have potentially life-threatening symptoms, or - particularly in children - concomitant food allergy and asthma.

Further training and information

Accredited allergy training for health professionals results in significant improvements in disease-specific quality of life in patients with rhinitis.[4] Post registration allergy education can be divided into a number of levels[5] based on the extent of experience and competency required. One day short courses, as well as diploma and degree level allergy modules are available from Education for Health (http://www.educationforhealth.org.uk). Allergy UK runs Masterclasses in Allergy (http://www.allergyuk.org/edu_masterclasses.aspx), and Southampton University runs a Masters course in allergy (http://www.soton.ac.uk/postgraduate/pgstudy/programmes/2007/medicine/msc_allergy.html) . Membership of the British Society for Allergy & Clinical Immunology (http://www.bsaci.org) provides information and support for health professionals and has a committee dedicated to improvement the management of allergy in primary care.

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Further reading

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