

# ABC OF ALLERGOLOGY

## TESTING FOR IMMEDIATE (IgE) ALLERGIC HYPERSENSITIVITY– THE GOOD, THE BAD AND THE UGLY

**Adrian Morris, MB ChB, DCH, MFPG, Dip Allergy (SA)**  
*Allergy Clinic, Constantiaberg MediClinic, Cape Town*

In this article we review the currently available allergy tests used to determine immediate allergic hypersensitivity. Testing for allergies is never 100% accurate and should always be guided by a good allergy history taking into account the clinical scenario. If the clinical picture is highly suggestive of a specific allergy but the test available reads negative, a high index of suspicion about a specific allergy should still be maintained. Conversely many patients might be sensitised to an allergen on testing, but remain asymptomatic, suggesting a latent allergy with an innate tolerance mechanism and a raised threshold level for disease manifestation.

In each clinical scenario, it is vital to take a thoroughly detailed allergy history and only then perform appropriate confirmatory allergy tests.

We will focus on validated and accurate IgE testing by means of skin-prick testing and blood RAST. We then briefly examine the role of other diagnostic tests including a plethora of 'alternative' intolerance tests which can be explored in depth elsewhere.

### Allergen skin-prick testing (SPT)

Skin-prick testing (SPT) is probably the most common and accurate allergy test performed on a global scale. First performed in Britain by Dr Charles Blackley back in 1854, these tests indicate immediate (IgE) sensitivity to various allergen extracts when applied by pricking the skin. This is very useful for determining the exact cause of inhalant allergies such those that occur in asthma, allergic rhinitis and eczema. Foods can also be tested in this manner by applying fresh extracts onto the skin, which is usually more accurate than commercially available extracts. When using the suspected fresh food, the prick-to-prick method should be employed (pricking the suspected food and then transferring allergen to the skin on the lancet). Up to 25 different allergens can be tested on the skin in this manner in a single consultation.

#### Principle of SPT

A droplet of the specific allergen extract is applied on the skin of the forearm or back at 3 cm intervals. The skin is then pricked through the droplet at 90 degrees using a special 1 mm pointed lancet. Always use a positive (histamine 10 mg/ml) and a negative (saline/glycerol) control to compare reactions. The patient must avoid all antihistamine and tricyclic antidepressant medication for at least 48 hours before testing. After 15 minutes each allergen-induced wheal and flare reaction's diameter is measured in millimetres (Fig. 1). Any wheal 3 mm larger than the negative control is consid-

ered a positive result. The greater the wheal size, the greater the level of specific IgE produced by that person. However, it should be noted that the size of the reaction does not predict the intensity of an allergic reaction. Negative SPT to specific allergens is a useful indicator that no IgE-mediated allergy exists. SPT is very safe to perform even in children from 4 months of age. It is however recommended that injectable adrenaline should always be available for rare adverse events and caution should be exercised when testing individuals with documented anaphylaxis to specific allergens such as nuts and horse dander. SPT kits are marketed in South Africa by Labspec (ALK-Abello) and Stallergenes. For more details contact ALLSA on 021-447-9019.



Fig. 1. Skin-prick testing with wheal and flare reaction.

RAST (**R**adio-**A**llergo-**S**orbent **T**est) testing was first developed in 1974 after the discovery of the IgE antibody by Johansson and Ishikara in 1967. It is now best performed utilising the more refined ImmunoCAP system that employs allergen in a small container (cap) which latches onto the patient's serum-specific IgE. After a fluorescent enzyme 'labelled' anti-IgE is added (radio isotopes are no longer used), the amount of specific IgE can then be accurately quantified. Total serum IgE (a combination of specific and non-specific IgE) can be measured but is not specific to allergy as high levels of non-specific IgE production does occur in certain



Fig. 2. UniCAP multi-channel RAST analyser.

Correspondence: Dr A Morris, 112 Constantiaberg MediClinic, Plumstead 7800. Tel 021-797-7980, fax 021-683-5335, e-mail adrian-morris@absamail.co.za

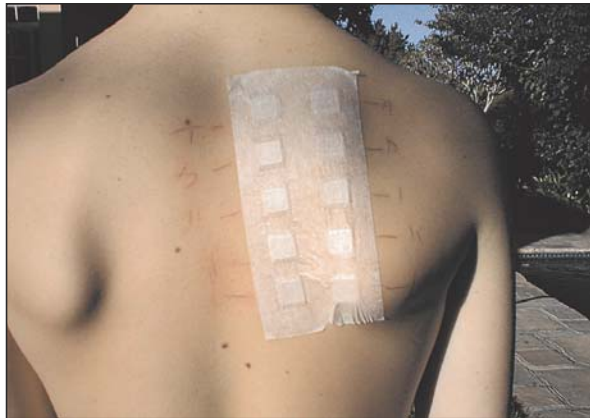


Fig. 3. Allergy patch test.

non-allergic conditions, such as with extensive eczema and parasitic infestation with worms. It is however accepted that raised total serum IgE is frequently associated with atopy and thus increases the likelihood of an individual having a specific allergy. The practice of measuring umbilical cord blood IgE in newborns as a predictor of allergy has not been shown to be a reliable allergy measure.

### Allergy screening panels

ImmunoCAP (Pharmacia Diagnostics) provide allergy screening panels for testing IgE in blood for common groups of allergens. The Phadiatop inhalant allergy panel includes house-dust mite, cat, dog, grass, weed & tree pollen mixes and mould spores, while the paediatric food allergy panel (also called fx5) includes cow's milk, hen's egg, wheat, soy, codfish and peanut. These panels are useful for screening if no one particular allergen is suspected. Raised IgE titres (>3.5 kU/l) for both Phadiatop and fx5 have strong predictive values (97.4%) for the presence or development of allergic diseases such as asthma, allergic rhinitis and eczema. Remember that not all children sensitised to allergens will develop allergies and many may remain relatively symptom-free. However, once sensitised, they have a greater likelihood of developing clinical allergies, but this may only occur in adulthood. Quantification and monitoring of specific IgE levels over time may be useful in predicting whether allergy will manifest or whether it will resolve. Children who experience food anaphylaxis but have low food-allergen specific IgE tend to outgrow their disease and this can be seen in about 20% of peanut-allergic children. When the sum of allergen-specific IgE levels is greater than 34 kU/l or alternatively when there is raised specific IgE to more than 4 of the 14 common inhalant and food allergens, it raises the risk of an allergic disease occurring in that individual to over 75%.

Testing a certain profile of airborne and food allergens and utilising the sum of the IgE antibody levels in combination with the number of allergens that elicit positive test results may be a more efficient diagnostic tool, rather than using single positive IgE results only.

Other food allergy panels include the fx1 nut allergen panel (peanut, brazil nut, almond, hazelnut, coconut), fx2 seafood panel (cod, tuna, shrimp, blue mussel, salmon) and fx3 cereal panel (wheat, oat, maize, sesame, buckwheat).

Over 450 allergens can be tested using individual

UniCAPs, including environmental inhalant allergens, food allergens, insect venom, antibiotics and occupational allergens. These tests are best suited to a situation when a large number of allergens need to be tested. They are also particularly useful when SPT is not available, when the patient is on antihistamine medication or for those with extensive eczema which makes skin testing difficult.

The ImmunoCAP results are graded from negative 0 (<0.35 kU/l) to positive grade 1 (>0.35 kU/l) up to grade 6 (>100 kU/l). If an anaphylactic reaction is suspected but there remains uncertainty (especially under anaesthesia) – serum tryptase levels can be measured up to 6 hours after the event and anaphylaxis then confirmed. It should be borne in mind that serum tryptase is curiously not highly elevated in food-related anaphylaxis.

The negative predictive value of skin and RAST testing is very useful in excluding an immediate IgE-mediated allergy, but the positive predictive value is less sensitive, as less than 80% of individuals who test positive will have an allergic disease caused by that allergen. This further endorses the importance of a clear and detailed allergy history and compounds the fact that allergy testing alone may not be in the patient's best interest.

### Other useful tests to determine allergic hypersensitivity

#### Atopy patch testing (APT) (Fig. 3)

Atopy patch testing (APT), originally used to detect contact allergen sensitisation in allergic contact dermatitis, may be employed to detect delayed hypersensitivity reactions. This is particularly useful if used together with SPT, and improves the predictive value in food-induced eczema and where a delayed hypersensitivity to a food or other allergen is suspected.

#### Intradermal skin tests

Dilute allergen extract (0.05 ml of 1:100) is injected intradermally and a positive reaction is a 5 mm or greater wheal developing over 15 minutes. It is about 100 times more sensitive than SPT but more likely to induce an adverse systemic reaction. Positive (histamine) and negative (saline) controls should also be performed. Intradermal testing may be used following negative SPT, when diagnosing drug allergy to antibiotics, anaesthetic agents and in insect-venom allergy.

#### The CAST test

The cellular allergen stimulation test (CAST) and Flow CAST, which measure sulphido-leukotriene release, have been utilised in suspected non-IgE-mediated hypersensitivity reactions to food additives, medication and insect venom. However, the tests are not highly sensitive and can be expensive.

#### Nasal eosinophil smear

Eosinophils counts on nasal mucus smears are a good indicator of allergic rhinitis if more than 10% of the stained cells are eosinophils. The nasal mucus specimen should be collected on a glass rod and assessed under microscopy after application of Hansel's stain.

#### And more...

Estimation of mast cell tryptase. Eosinophil cationic protein (ECP), urinary histamine and basophil histamine release are useful adjuncts used mainly in academic allergy research, and are beyond the scope of this article.



Fig. 4. The VEGA test has never been scientifically validated.

### Provocation tests

Direct conjunctival challenge with allergen, plus direct allergen or histamine and methacholine nasal or bronchial challenges can be utilised in allergen diagnosis. The 'gold standard' in food-allergy testing, the double-blind placebo-controlled food challenge (DBPCFC) test is discussed elsewhere.

### Other less specific tests

Testing for IgG1 and IgG4 antibodies to various foods is best avoided according to international allergy opinion leaders, as IgG response to food is a normal phenomenon and raised food-specific IgG has no predictive role in food allergies. Another dubious testing modality, blood leuco-cytotoxic testing (Nutron and ALCAT test) has been available since 1956 but has no diagnostic value in allergy. There are a number of tests used by chiropractors and homeopaths to diagnose allergy and 'intolerances'. These include the VEGA test (Fig. 4) of electromagnetic fields in acupuncture meridians (called BEST, Listen & Dermatron), applied kinesiology (muscle testing) and iridology which have been shown to be of no diagnostic value in allergology.

The author would like to thank Prof Eugene Weinberg for his invaluable input in reviewing this article.

### RECOMMENDED READING

Holgate S, Church M, eds. *Allergy*. Aldershot:: Gower, 1992.  
 Durham S. *ABC of Allergies*. London: BMJ, 1998.

## Allergy & Immunology Secrets, 2/e

with STUDENT CONSULT Access

M. Eric Gershwin

December 2004, ISBN 1560536195, Hanley & Belfus, R310

As the number of asthma and immunodeficiency cases continues to rise, thorough knowledge of immunologic processes is becoming increasingly important. Despite the seemingly small number of chapters, each chapter provides comprehensive coverage of all the topics necessary to pass the allergy-clinical immunology boards in the easy-to-use Secrets format. Chapters include epidemiology, pathophysiology, asthma, sinusitis, urticaria/angioedema, atopic dermatitis, anaphylaxis, food allergy/intolerance, insect allergy, drug hypersensitivity, immunodeficiency, and systemic mast cell disease.

### Features

- Includes a chapter on alternative medicine treatments for allergy.
- All the most important "need-to-know" questions-and-answers in the proven format of the highly acclaimed Secrets Series®
- Concise answers that include the author's pearls, tips, memory aids, and "secrets"
- Bulleted lists, algorithms, and illustrations for quick review
- Thorough, highly detailed index
- Thought-provoking questions that provide succinct answers
- Presentation of a vast amount of information, but not overly simplistic



Your purchase of this book entitles you to access [www.studentconsult.com](http://www.studentconsult.com) at no extra charge. This innovative web site offers you...

- Access to the complete text and illustrations of this book.
- Content clipping for your handheld.
- An interactive community center with a wealth of additional resources.

## Pulmonary & Respiratory Therapy Secrets 2/e

Polly E. Parsons and John E. Heffner

Aug 2001, ISBN 1560534273, pbk, 450 pp, 50 illus., R475

The new edition of this popular pulmonary/respiratory therapy text in question-and-answer format is completely updated and expanded. The book contains 83 chapters organized in 18 sections, covering all aspects of pulmonary evaluation, disease, and therapy. All chapters are thoroughly revised and updated. The new edition features a new chapter on Interventional Bronchoscopy and expanded coverage of endoscopy. Thorough, highly detailed index.



Orders: Medical Book Seller, PO Box 3784, Tygervalley 7536.

E-mail: [jackie@medbookseller.co.za](mailto:jackie@medbookseller.co.za) Tel: 083 303 8500, Fax (021) 975-1970