Skin testing in asthma and hay fever

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Introduction

Skin sensitivity testing is one of few methods to identify allergens responsible for triggering symptoms in allergic diseases. Through the years it has evolved from a poorly understood and unreliable procedure to become the gold standard in current state-of-the-art allergy investigation.

The skin test

The principle of the test is the application of a minute quantity of an antigen into the dermis where it crosslinks two specific IgE molecules on the surface of mast cells. This leads to the release of biologically potent mediators which act on receptors in nearby capillaries resulting in exudation of fluid and the observable 'wheal and flare' reaction. The size of the wheal and flare corresponds to the amount of the mediators released. This in turn is dependent not only on the amount of antigen and concentration of mast cells with specific IgEs, but also on the reactivity of the capillaries and the tissue receptors. Note that the skin test is normally intended to represent the IgE mediated sensitivities only.

When a person is sensitised against an antigen, mast cells reactive to that antigen can be eventually found throughout the body. The reaction of the skin can therefore represent the type and to some degree the extent of clinical allergy in the respiratory tract.

There are several techniques for allergy skin testing. The most widely accepted method is the skin prick test. A small drop of allergenic solution is placed on the skin and a prick is made through the drop into the dermis with a special lancet. After about two minutes, the allergenic solution can be wiped or dabbed off. Initially a stinging sensation can be felt by most patients sensitive to the allergen, and within a few minutes a wheal with a surrounding red flare can be seen. This reaction is maximal between 15 to 20 minutes and starts to fade by 30 minutes. The wheal is measured in two diameters perpendicular to each other, and the mean is recorded. Sometimes pseudospots appear at the edges of the wheal. This indicates a severe reaction and should be reported. Delayed reactions of swelling and pain can occur several hours after the skin test. This reaction is produced by IgG precipitating antibody and is known as the Arthus reaction. A positive control (using 1/100 histamine) and negative control (using the antigen dilutant) must be performed at the same time. Sometimes a codeine control is also done.

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Commonly used areas for skin testing are the volar surface of the forearm or the back. The skin must be cleaned first before antigen is applied. Most centres now report the actual measurements in millimeters rather than the zero to three plus range. For comparison purposes and follow-up of repeated tests, the skin test can be assessed as the degree of the reaction relative to the positive control. Skin prick test is very safe. Systemic reactions are extremely rare with only peanut and treenut allergy causing systemic reactions in patients with very severe allergies to these allergens. Patients with a clear anaphylactic history to these foods should be tested using the RAST technique. Foods should never be tested with intradermal testing unless the operator and patient fully accept that anti-anaphylactic treatment may be needed and is available.

The RAST test

Another useful test is the radioallergosorbent test (RAST). This directly measures the amount of specific IgEs in the blood. There is good (80% or more) correlation with skin tests for pollen and food, medium (50–60%) correlation for house dust mite and low (40%) correlation for moulds. RAST has the advantage of being not dependent on the availability of good skin space (e.g. generalised eczema), very reactive skin (dermatographia) or recent history of medications (e.g. antihistamines) which may affect mast cell release or tissue reactivity in skin testing. However, it is much more expensive, lacks the immediacy of the

Table 1

History suggests allergy	
NEGATIVE SKIN TEST	**POSITIVE SKIN TEST**
Check medication that may block reactivity Repeat testing during high natural exposure Consider provocation challenge	Strong possibility that antigen is responsible

result for patient information, and is slightly limited by the availability of the large variety of allergens needing to be tested. (The selection of available allergens is expanding with the development of newer reagents.)

Clinical correlation

Sensitivity testing (both skin test and RAST) demonstrates the presence of specific IgE but not necessarily allergic disease to the allergen. The disease state depends on the breakthrough of symptoms as a result of the degree of reaction to an allergen, the threshold of the target organ and the detection of disease by the clinician. Between 30–60 per cent of the population demonstrates detectable specific IgEs but only 15–35% shows evidence of allergic diseases. However, follow-up of positively tested patients shows a tenfold increase of hay fever development compared with subjects with negative results. As sensitisation builds up, mast cells migrate to the skin before responding to skin testing, so time and the age of the patient become a factor in the reliability of the skin test. Skin testing in the recent cetirizine study for severe infant eczema shows that although positive tests can be identified under the age of one, maturation of the skin is achieved after age six for both house dust mite and pollen. The reactivity of the skin reaches a peak in the third decade and falls rapidly after age 50.

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Table 2

History does not suggest allergy
POSITIVE SKIN TEST
Observe patient during season of high exposure Consider provocation test

It is important to understand that the skin test only identifies the presence of specific IgE, and in itself does not identify the presence or degree of allergic disease state in relationship to the allergen. Whether a patient actually has a disease is very dependent on the organ itself as much as the response to treatment already given to a patient. For example, asthmatics adequately treated with inhaled steroids may not react to deliberate exposure to house dust mite despite a strong positive skin test reaction to it, although successful reduction of house dust mite in the environment might allow the patient to require less inhaled steroids for the control of asthma. Also, when a patient completes hypo-sensitisation to an allergen, the skin test may still show significant specific IgE presence, but the patient will have new mechanisms to block the disease expression.

The drawback of the skin prick test is that relatively concentrated antigens are needed for testing, and that a small percentage of patients show false negative reactions. False negative reactions can be caused by weak or denatured allergen (especially in warm climates), poor puncture technique, diseases attenuating the skin response, extremes of age, or drugs modulating the skin response. The test is blunted by the patient having taken antihistamine, decongestant, antitussive or tricyclic medication. Patients on betablockers such as propanolol will enhance the skin reaction. Oral corticosteroids and sodium cromoglycates do not alter the skin prick test.

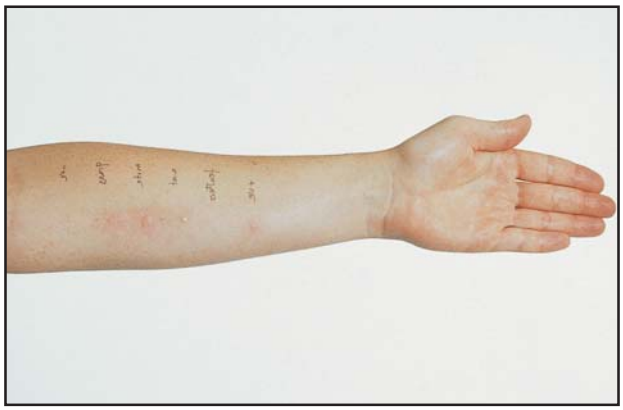
Sometimes a negative skin prick test may contribute to the correct diagnosis in suspected asthma, and may constitute a simple, fast, safe, inexpensive and reliable method to predict the absence of asthma in young adults.

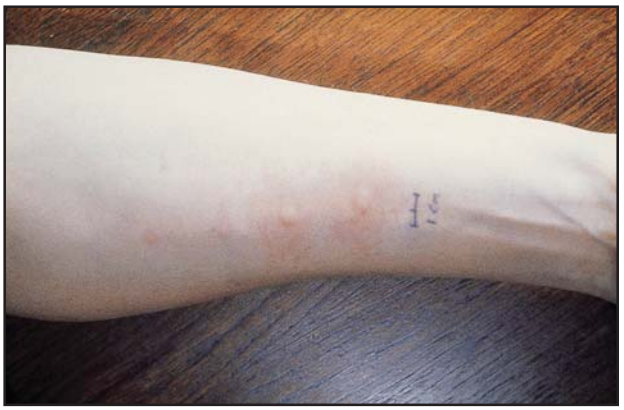
The proper clinical relevance of the skin test requires a thorough knowledge of the history and physical findings. One may not cover all the allergens responsible, or the clinical syndrome may be related to non-IgE mediated responses or even to non-specific irritants or adjuvants.

The choice of allergens must be considered dependent on the likeli-

Key Points

- Although positive tests can be identified under the age of one, maturation of the skin is achieved after age 6 for both house dust mite and pollen. The reactivity of the skin reaches a peak in the third decade and falls rapidly after age 50.
- Cockroach is an important allergen second only to house dust mite in certain areas, especially those with warmer climates and or in multi-storey housing units.
- Correct identification of allergens and specific avoidance measures do indeed reduce the disease load and results in a reduction of broncho-hyperreactivity and reduction of medication.





hood of exposure. Storage mites and the citrus red mite may be more important than the house dust mite in rural areas and in orchards, for example. Cockroach is an important allergen second only to house dust mite in certain areas, especially those with warmer climates and or in multi-storey housing units. The skin prick test is now also increasingly used in deciphering which specific antigens are responsible for occupational and environmental asthma, e.g. mould related asthma.

Seasonal variation of IgE synthesis has been demonstrated for allergens such as grass and tree pollen, with progressive reduction in the specific IgE synthesis after the season, and build up again during the pollen season.

As skin testing is only related to IgE mediated reactions, food reactions in adults have less relevance for this means of assessment as most food reactions are related to intolerance or to the effect of food metabolites. In children, while positive skin prick test correctly indicate the presence of specific IgE to the food, consumption of small quantities of the food does not necessarily cause a clinical problem as the gastrointestinal barrier may prevent the antigen being absorbed in sufficient quantity to cause an effect, and the continuing digestion of the food progressively reduces any reaction. Milk protein allergy is a good example of this process. Clinically, children appear to develop tolerance to milk (which can and also does occur) as the child grows. On the other hand, allergens such as peanut can be absorbed through intact skin, and a reaction can occur even with the barrier of a more mature gastrointestinal tract.

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The availability of potent general anti-allergy agents such as non-sedative long-acting anti-histamines and potent anti-inflammatories such as inhaled steroids may appear to make skin testing redundant. However, more and more research reveals that correct identification of allergens and specific avoidance measures do indeed reduce the disease load and result in the reduction of broncho-hyperreactivity and reduction of medication. Indeed, for occupational asthma in workers who were previously non-asthmatic, successful avoidance of the offending allergen within the first year of clinically-related exposure can result in total reversal of asthma related to the occupational agent, whereas continuing exposure progresses to irreversible airway remodelling. A similar situation may occur in home environmental aero-allergen related asthma. We therefore need new tools to identify offending triggers early in life before permanence sets in.

In summary, skin prick test for allergic diseases remains a high yield, low risk and inexpensive means of investigation.

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