ALLSA POSITION STATEMENT: ALLERGEN SKIN-PRICK TESTING

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ABSTRACT

Allergen skin-prick testing is described as the 'cornerstone' of allergy diagnosis and has become highly standardised over the years. This position statement addresses important issues such as standardised allergens and test materials, testing procedure, technique, interpretation, reproducibility and safety of allergen skin-prick testing as recommended in clinical allergy practice in South Africa.

INTRODUCTION

Allergen skin testing was first used by Dr Charles Blackley to diagnose pollen as the cause of his hay fever in 1873. In 1924 the current skin-prick test (SPT) method was introduced and in 1975 Prof. Jack Pepys proposed the modified skin-prick testing method.[1] Today the allergen extracts and lancet are standardised and this technique for diagnosing immediate IgE-mediated allergy is used universally.

Allergen skin testing is an extremely safe procedure and only one death as a result of skin-prick testing has ever been recorded.[2, 3] Therefore there is a theoretical possibility of this test inducing an anaphylactic reaction in highly allergic individuals. Mild systemic reactions with itching and generalised rashes have also been recorded but are unusual and occur in 1:3000 patients tested by SPT.[3]

AGE OF PATIENTS

There is no lower limit for allergen skin-prick testing, and consensus indicates that the tests are of value from 4 months of age.[4] However, infants and the elderly tend to have a less reactive skin with fewer mast cells than older children and adults.[5] In the past, the lowest age limit was incorrectly set at 3 years.

TEST SITE

The usual site for testing is the inner (volar) aspect of the forearm between the wrist and elbow. This sensitive area of skin reacts well if the allergens are placed 2-3 cm apart. They should not be placed closer than 5 cm to the wrist or less than 3 cm from the elbow crease as skin sensitivity to skin testing varies two-fold between the elbow and wrist.[6] The skin of the upper back can also be used if there is dermatitis on the forearms, or in children with small forearms. The individual allergen test sites should be marked in two columns about 3 cm apart, with a felt tipped or ballpoint pen at 2-3 cm intervals. Any number from 1 to 40 allergens may be tested in a single session[4] (the average being 6-12).

THE LANCET

A special standardised lancet should be used with a 1 mm pointed tip and blunt shoulder to prevent excessive trauma to the skin. The lancet is pressed through the drop of allergen at 90 degrees to the skin allowing puncturing of the skin. Lancets should be replaced after each allergen pricked, or thoroughly wiped with alcohol to prevent cross-contamination of allergens. The lancet should always be discarded after performing the histamine control prick. A conventional hypodermic needle should not be used instead of the standardised lancet as this will cause varying skin penetration and the puncture depth will be difficult to control.[6]

Intradermal (ID) skin testing employing the injection of allergen into the subcutaneous tissue should not be confused with standardised skin-prick testing. This ID method used to test venom and drug allergy usually injects a far higher amount of allergen. It has a much greater risk of inducing anaphylaxis, and has been reported to have induced a number of anaphylactic deaths over the last century.[7]

ALLERGEN SOLUTIONS

Purified standardised allergens which are commercially prepared should be used for inhalant allergen testing and these usually include house-dust mite, cat dander, dog dander, tree pollens, grass pollens and mould spores. In order to stabilise the allergen extract, glycerol is added in a strength of 50% of volume. Additional inhalants may be added to the panel of allergens used and will depend on the age of the child, the allergy case history and the geographic region.

Common standardised food allergens include cow's milk, hen's egg, wheat flour, soy, codfish and peanut. Other standardised food allergens include various nut and shellfish allergens. Fruit or vegetable allergens are best tested using the fresh fruit employing the prick-prick method of puncturing the fruit with the lancet, or dipping the lancet into the food and then pricking the skin with the fresh fruit residue.[8] Because these fresh allergens are not standardised and the extract used has unknown allergen content, the prick-prick method carries a higher theoretical risk of inducing a systemic reaction.[9] For safety reasons, some investigators suggest first applying the wet food/fruit to the intact skin for some minutes before performing the prick-prick test.[10,11]

All SPTs should include a positive and negative control test to assess normal skin reactivity for the person being tested. The negative SPT is performed using buffered saline in the glycerol base used to preserve the other allergen substances. No wheal reaction should be recorded with the negative control unless the person suffers from dermatographia. The positive control employs a drop of histamine 10 mg/ml or occasionally codeine. This test should induce a wheal and flare reaction and the wheal should be at least 3 mm in diameter. A smaller wheal or no wheal at all at the positive control site should alert the tester to the possibility of concomitant medication. Drugs such as antihistamines, antidepressants or topical steroids will suppress the control test and the rest of the allergens tested cannot be interpreted because of this overall suppression.[6,12]

Standardised allergen extracts for skin-prick testing are widely available and distributed in South Africa by companies such as ALK-Abello (Denmark), Stallergenes

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(France), Allergopharma (Germany) and Leti (Spain) or their local agents.

THE PROCEDURE

The patient should have the skin test procedure carefully explained before skin testing commences and any concerns or questions need to be addressed. The procedure is unlikely to be painful or induce vasovagal syncope if empathetically discussed. Children under 16 years should be accompanied by a parent or guardian. Verbal consent should be obtained from all patients including children old enough to understand the procedure; otherwise their parents should give consent.

A droplet of each purified allergenic extract is placed on the cleansed volar aspect of the forearm at 2-3 cm intervals (Fig. 1). The lancet is pressed through the droplet perpendicular to the skin for one second to puncture the skin at 90 degrees and no blood should be drawn. The 'modified' skin-prick method (as described by Pepys and Mygind) whereby the skin is pricked at 55 degrees and then lifted with the lancet tip, leads to variable skin penetration and is not recommended.[1,6]

Fig. 1. Procedure of skin-prick testing.

One normally starts with the negative control and finishes with the positive control. After all the droplets have been penetrated at 90 degrees by the lancet and the skin gently punctured, the excess allergen droplets are carefully blotted (not wiped) away using a clean absorbent paper towel (cotton wool should not be used).[6] The test results are then interpreted 15-20 minutes after puncturing the skin.[11]

The practice of performing the double skin-prick testing method using two duplicate tests of each allergen at the same session is not widely practised as this increases the allergen load and may cause unnecessary discomfort.[13]

INTERPRETING THE RESULTS

Interpreting the results of SPTs should be done by a doctor or nurse with experience of the procedure to ensure reproducibility and accuracy. The same amount of pressure should be applied with each skin puncture, and the wheal and flare reaction is then measured, with special attention to the diameter of the wheal measured in millimetres. The mean of the longitudinal and vertical wheal diameter is used if the wheal is not concentric. This helps to clarify the size of elongated wheals; however 'pseudopodia' extensions should not be measured. The older assessment using 0 to ++++ is no longer recommended and wheals are now universally measured in millimetres.[13]

The SPT results are measured using a ruler or calibrated see-through gauge and recorded in the patient's notes in millimetres of wheal diameter. Sometimes a transparent adhesive tape is placed over the wheal and the wheal size traced and then stuck into the patient's clinical notes. Irritant delayed reactions which are not indicative of immediate hypersensitivity may occur on the skin 3-5 hours after skin-prick testing.

A positive result to a specific allergen or mix is indicated by a mean wheal diameter measuring 3 mm or more greater than the negative control (Fig. 2). A diameter of 3 mm is equivalent to a surface area of 7 mm^2 (some practitioners use area of wheal instead of wheal diameter). To clarify this, if the negative control is 0 mm then 3 mm or greater wheal for the test allergen represents a positive test but if the negative control measures 2 mm then a positive test would be a wheal of 5 mm or more.

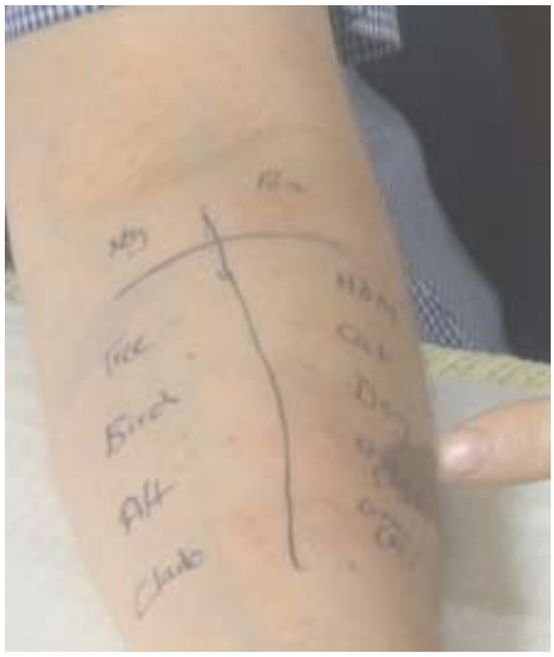

Fig. 2. Results of skin-prick testing.

The presence of the wheal indicates that the person has been sensitised to that specific allergen while the associated flare or erythema is not used as a gauge of allergic sensitisation. Sensitivity to testing increases with the potency of the extract and the pressure applied with the lancet. However, with experience and, after taking an exhaustive allergy history, most well-trained allergists will be able to give a good predictive diagnosis after assessing the skin test results in conjunction with the clinical history.[11,12,14]

While Sporik's studies[15] of children with food allergens such as egg, milk and peanut have suggested that a wheal greater than a certain size may indicate the presence of food allergy, the severity of an allergic reaction cannot be accurately predicted by the size of the wheal alone. For example, some patients with anaphylactic sensitivity to insect venom, latex, antibiotics and local anaesthetics may have wheal size as small as 3 mm while others may conversely have wheals of 10 mm or greater to inhalant and other food allergens but manifest little or no allergic signs if they are exposed to these allergens.

For IgE-mediated food allergy in children, in conjunction with Sporik's work (Table I), Eigermann and Sampson[16] and Hill *et al.*[17] have introduced cut-off points for positive SPTs above which food allergy has a 95% probability. These probabilities have been reproduced by Roberts and Lack[18] using 'likelihood ratios'.

Table I. Skin prick testing: 100% positive predictive value (PPV) for food allergy

Food allergen	100% PPV < 2 yrs (Wheal diameter)	100% PPV > 2 yrs (Wheal diameter)
Cow's milk	6 mm	>8 mm
Hen's egg	5 mm	>7 mm
Peanut	4 mm	>8mm

Source: Sporik *et al.*[15]

CONTRAINDICATIONS TO SKIN-PRICK TESTING

Do *not* apply skin-prick tests to patients when there is a convincing history of anaphylaxis to the test allergens. This is particularly important in nut, latex, horse, drug or severe food allergy. Patients with ongoing food allergic symptoms should not be skin tested until their symptoms are stable.[10] In these cases it is far safer to perform a RAST (ImmunoCAP, Pharmacia) on a venous blood sample to confirm the allergy.

Bear in mind that patients *may* test negative to an allergen that caused their anaphylaxis for up to 6 weeks after the reaction as a result of a relative depletion of specific IgE during this 6-week refractory period (this refractory period also applies to RAST results).[11]

FACTORS THAT INFLUENCE RESULTS

Stop all antihistamine medication for at least 3 days prior to the SPT. Also, stop other medication such as tricyclic antidepressants, mast cell stabilisers, ranitidine, anti-emetics or beta-blockers as well as topical antihistamines, immunomodulatory creams and topical steroids for one week before the test. Oral steroids and asthma inhalers should not be stopped.

If the person has extensive dermatitis, and no clear skin is available for testing then RAST testing should be performed instead. Dermatographism will make skin testing difficult to interpret as all the test sites are likely to react non-specifically with a wheal and flare reaction. Skin responses are lower in the morning than in the afternoon because of circadian rhythm. Wheal size diminishes in ageing skin, which is more easily traumatised as a result of atrophy with bleeding and tends to form marked postpuncture vesicles. The menstrual cycle may influence results and increased wheal response on day 12-16 of the menstrual cycle may be evident.[6]

SAFETY OF SKIN-PRICK TESTING

Skin-prick testing is an extremely safe procedure according to the Royal College of Pathologists (UK) and the American Academy of Asthma, Allergy and Immunology.[4,14] According to the medical literature, only one fatal reaction has ever been confirmed following skin-prick testing and this occurred after testing with 90 commercial allergens![19]

However, studies indicate ID skin testing carries a greater risk of inducing a generalised systemic reaction.[14,20] Mild systemic reactions with itching have occasionally been reported with allergen skin-prick testing but this responded promptly to removal of the allergen from the skin and simple antihistamine medication. Mild reactions are more likely to occur in infants under 6 months of age, children with extensive eczema and in those with severe food allergies when non-standardised fresh food extracts are used for testing.[13] The duplication of skin tests at the same session increases allergen load and potential for enhanced generalised reactions.

Lin *et al.*[21] investigated 10 400 standardised allergen SPTs and found that no adverse reactions were reported. In the largest study of skin-prick testing reactions ever recorded (over 18 000 patients on whom 497 656 individual skin tests to various allergens were performed), only 5 mild systemic reactions were recorded.[3] These all responded promptly to antihistamine medication within 1 hour. However skin-prick testing should not be confused with ID testing and injection desensitisation immunotherapy which both carry a greater risk of inducing systemic allergic reactions.[11,14,20] Lockey *et al.*[22,23] retrospectively reported 6 deaths associated with skin tests between 1964 and 1993, but all occurred in patients using the ID injection method and not standardised skin-prick testing.

Even though skin-prick testing is safe, the theoretical risk of a reaction necessitates that antihistamine medication and adrenaline should be readily available when performing allergen skin-prick testing on adults and children. Children should be weighed prior to testing and the appropriate dose of adrenaline (10 µg/kg intramuscular) noted in case a generalised reaction occurs.

Unlike injection immunotherapy, the patient does not need to wait for an extended period after the testing. The wheal and flare reaction is initially assessed at 15-20 minutes and again at 30 minutes, after which the skin is cleaned with alcohol or soap and the patient may then safely leave the clinic.[23,24]

Despite the greater risk of adverse reactions in the under-6-month age group, delaying the allergy investigation is not recommended since early diagnosis will spare children unnecessary suffering from their symptoms of allergy.[13]

REPRODUCIBILITY AND ACCURACY

The competence of the person performing the test is paramount and the technique employed should be consistent across all test sites.[10] Although the technique appears quite simple, its interpretation requires a thorough clinical allergy history and an experienced practitioner.[10,25]

Standardised allergens should be used wherever possible except for testing with fresh fruit and vegetable extracts using the prick-prick method. The standardised allergens used should be checked for expiry date (all should be clearly labelled) and stored between testing at 2-8°C in a refrigerator. If fresh food extracts are used, these should be prepared freshly every day and discarded after use.[6]

Provided all the above precautions are followed, these tests are very accurate, give immediate results, and there should be no risk of any adverse reaction occurring.[10]

Declaration of conflict of interest

The author has no conflict of interest.

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