

Precision of prick and puncture tests

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Since the recognition of the allergic cause of hay fever, skin tests have represented the primary diagnostic tool in IgE-mediated allergy. They can provide useful confirmatory evidence for a diagnosis of specific allergy that has been made on clinical grounds. Their characteristics—simplicity, rapidity of performance, low cost, and high sensitivity when properly performed—explain the key position that cutaneous testing occupies in allergy.¹⁻³ However, to avoid erroneous results, the tests should be performed by skilled personnel.

Skin tests have many uses other than the strict diagnosis of IgE-mediated allergy. They are becoming an invaluable tool in the characterization of allergy in epidemiologic studies.⁴ Changes in skin sensitivity are used for the standardization of allergen extracts,^{5,6} for the assessment of specific immunotherapy,^{7,8} and for pharmacologic studies.⁹ Skin tests and methods derived from them can also be used to better understand the pathophysiology of the allergic reaction and help to evaluate the mechanisms of action of antiallergic treatments.

Several methods, including scratch, intradermal, prick, and puncture tests have been used for decades without major modification. However, in recent years they have been refined to reduce their variability, and a number of standardized devices have been proposed for puncture testing.^{2,3} The value of skin tests in their different applications depends on the quality of the technique. Among the various parameters that should be considered are the quality of the extracts as well as the reproducibility, sensitivity, and specificity of the skin test technique.

Allergen extracts have been significantly improved within the past 15 years, and batch-to-batch reproducible extracts of known potency and shelf life are now available for many common aeroallergens. These standardized extracts have led to the greater use of prick and puncture tests and to the decreased use of intradermal skin tests for allergy diagnosis and epidemiologic studies.^{2-4, 10} On the other hand, intrader-

mal skin tests remain of importance in allergen standardization or when low-potency extracts are used.⁵

Skin prick tests were proposed in 1924 by Lewis and Grant,¹¹ but they became widely accepted only after their modification by Pepys¹² in 1972 in which a hypodermic needle was used. Prick or puncture tests with various devices such as the smallpox needle, the Wyeth bifurcated needle, the chalazion knife, the Greer DermaPIK (Greer Laboratories, Lenoir, N.C.) or the Greer Pen (Greer Laboratories) have been used alternatively. All of these methods are still widely used, both in the diagnosis of allergy and for research purposes. However, they do not make it possible to quantify the exact amount of injected material, and the skin response depends on the reliability of the device, its dimensions, the depth of the prick or puncture needle, and the force, duration, and angle application of the device as well as the skill of the investigator.^{10, 13}

To introduce a defined amount of allergen and reduce the variability of prick and puncture tests, standardized devices made from plastic or metal have been developed. In these methods the test instrument is inserted perpendicular to the skin, and the device is standardized. They are thought to increase the standardization of the performance of skin tests and should reduce their variability, especially when untrained investigators perform the tests. Among these devices, the Morrow Brown (Aller Guard, Topeka, Kan.) metallic needle and the Østerballe (Dome-Hollister-Stier, Paris, France) standardized needle were the first puncture tests resembling the prick test.^{14, 15} Most of the puncture tests derived from them had a needle pin of 1 mm. Many devices made from metal or plastic, such as the Phazet (Phazet Pharmalgen, Pharmacia Diagnostics, Uppsala, Sweden) and the Stallerpoint (Stallergenes Laboratories, Fresnes, France), were then introduced with the same pin length but different inclusive angles. Opinions concerning these methods vary according to the skill, experience, and preference of the nurse or physician. The reproducibility of these techniques is of importance, and studies previously carried out have shown that with a trained investigator the coefficients of variation for different tests range from 8.4% to 30%¹⁵⁻²¹; however, Basomba et al.²² found a much greater variability. Overall, these studies show that plastic devices with a 1 mm pin length are less reproducible than metallic devices and induce a high rate of false-negative reactions. The pin length

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remained identical for all metal devices studied, since it has been found that they possess a high degree of reproducibility and induce a very low rate of false-positive or false-negative results. On the other hand, to improve the precision of some plastic devices, the pin length was increased and the pin shape modified. This is the case of the Morrow Brown plastic needle, for which the pin length was increased to 1.3 mm and then 1.6 mm or 2 mm, and the point was modified to the current four-sided point.^{23, 24} The results obtained with use of these plastic devices are more reproducible,^{21, 23, 24} but the rate of false-negative or positive skin test results remains unknown.

The Multi-Test (Center Laboratories, division of EM Pharmaceuticals, Inc., Port Washington, N.Y.) was initially proposed for delayed type of hypersensitivity and later used for the diagnosis of IgE-mediated allergy.²⁵⁻²⁷ It is injection molded from acrylic and has eight test heads each containing nine fine pins arranged in an area of 4 mm²; the heads were 2.4 mm long in the original device. This first version of the Multi-Test was not strictly a prick test device because its needles were long enough to penetrate through the dermis. The opinions concerning the Multi-Test vary widely. Some investigators state (1) this is a highly reproducible device inducing a very low rate of false-negative reactions, and (2) although pins are placed 2 cm apart, false-positive reactions are not common.^{28, 29} In contrast, other investigators have found that the Multi-Test is less reproducible than other prick or puncture tests, and that a very high rate of false-positive reactions (up to 50%) may be observed.^{20, 26} It was proposed that false-positive reactions may be due to the short distance between pin heads, as has been demonstrated for histamine prick tests performed 2 cm apart and/or to the large amount of allergen introduced by the nine pins.³⁰ However, most investigators were using the older version of the device with pin sizes of 2.4 mm, whereas in the study of Garibaldi and Slavin,²⁸ the pin length was 1.9 mm. In this issue of the JOURNAL Berkowitz et al.³¹ studied the reproducibility and user variability of the newer version of the Multi-Test as well as the effects of positive reactions on adjacent negative sites. These researchers observed that this method was reproducible, especially when elevated histamine concentrations were used (higher than usually recommended), and that there were no false-positive reactions when the instructions in the package insert were followed. The two nurses who performed the tests were highly qualified. No data are available on the use of the Multi-Test by untrained investigators. This study suggests that the newer version of the Multi-Test may be appropriate for the diagnosis of IgE-mediated allergic diseases.

A second report on the sensitivity and precision of skin tests appears in this issue of the JOURNAL. Engler et al.³² have compared the Multi-Test with 1.9 mm pin heads, two standardized puncture tests (the 1.3 mm pin Morrow Brown plastic needle and DermaPIK), and one nonstandardized puncture test (Greer Pen). This is the first study to examine the precision of the DermaPIK. Adequate methodology was used to show that all puncture tests used except the Morrow Brown needle had a similar reproducibility for the wheal, and that as expected the flare is difficult to analyze with the Multi-Test device. The rate of false-negative reactions was found to be higher with the Morrow Brown needle, and the authors estimated (without giving numbers) that the Multi-Test and the DermaPIK induced a higher background response. By use of a higher histamine concentration, the Morrow Brown needle showed a greater reproducibility.

One of the problems raised by false-negative and false-positive skin test results is their interpretation. It is clear that the size of any allergen-induced skin test must be interpreted by comparison with a positive (histamine or a mast cell secretagogue such as codeine) and a negative control solution (glycerosaline solution). However, some tests, such as the Multi-Test or the DermaPIK, may induce a wheal of 5 mm in diameter with the negative control solution, and the test result may be considered by some as negative,^{31, 33} but it may be considered positive by others. It is particularly important to note that in the study of Berkowitz et al.³¹ the mean sizes of histamine skin tests were 6.2 and 7.2 mm depending on the nurse. Thus the difference between a negative skin test result and a positive skin test result may be very small. On the other hand, a reaction of under 3 mm is usually considered as negative. This criterion for negative reactions does not make the interpretation of the Multi-Test easy in practice, although some clinicians have used it for many years in the United States.

Taken altogether, studies suggest that single-pin metal devices and possibly multiple-pin plastic devices show the best reproducibility for research purposes. In clinical practice, other parameters that have been tested by Engler et al.³² should also be examined. They have observed that the Morrow Brown needle was the preferred skin test device by the patients, and that the DermaPIK and Greer Pen allowed allergy skin testing to be performed more quickly. The cost of each device should also be examined, since one of the best standardized needles was withdrawn because of its very high production cost. Thus according to the purpose of the study and the skin test parameters examined (wheal or flare), different methods may be selected. When the flare is examined, the Multi-Test is inappropriate.

It must be pointed out that the pin lengths of the Multi-Test or the Morrow Brown needles were modified without any clear notification from the manufacturers. Thus some clinicians or researchers may use different devices bearing the same name but which are not identical. Care should be taken when the results from different studies are compared.

Moreover, very few studies have been performed, and new data should be provided to better assess the reproducibility of the newer versions of some devices and to characterize the rate of false-negative reactions induced by single-pin plastic devices as well as the rate of false-positive reactions caused by the Multi-Test. Other studies are also needed to appreciate fully the value of each device in clinical practice and research. Finally, more data are needed to characterize the clinical relevance of positive and negative test results with use of all devices.

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