
DEVICES FOR EPICUTANEOUS SKIN TESTING

John J. Oppenheimer, MD

Credit for the first skin testing device goes to Charles H. Blackley, who in 1865 abraded a quarter-inch area of skin with a lancet, producing a dermatographic reaction. He then applied pollen grains that had been placed on a piece of wet lint and covered the scarified area with an occlusive bandage. This resulted in intense itching and a very large response with swelling that was maximal at 2.5 by 1.5 inches by the end of 6 hours.²⁶ Further historical aspects of skin testing are reviewed by Cohen elsewhere in this issue.

Early clinicians used the von Pirquet borer for epicutaneous testing as well as other devices. In 1924, Lewis and Grant first described the prick skin test method,¹⁴ but scarification methods and intradermal testing were advocated emphatically by most clinicians in the United States. In a 1931 report, Rappaport described a multiple scarifier—the Mueller device.²⁴ He noted that a significant problem with the scarification technique was a lack of uniformity in the abrasion. The Mueller device was designed to make six uniform abrasions 1.5 mm long and 15 mm apart. This level of uniformity was thought to be a great innovation in the attainment of reproducible skin testing. Also, this device seemed to reduce the pain associated with the skin testing procedure.

In 1950, Squire reported use of a straight Hagerdorn-type surgical cutting needle (about 5 cm long) for prick skin testing.²⁵ He described a technique in which the noncutting portion of the needle was held between the forefinger and thumb, allowing friction to give fine control in the degree of penetration when the needle was plunged through the drop of test material into the skin while attempting to avoid bleeding.

From the University of Medicine and Dentistry of New Jersey; and the Pulmonary and Allergy Associates, Morristown, New Jersey

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Pepys' description of the modified prick skin test method in 1968 renewed interest in this technique.²² He used a hypodermic needle (40 mm long $\times$ 0.8 mm diameter) that was directed through a drop of extract at an angle of 60° to 70° to the skin. With the needle point only catching the skin and lifting it, a canal is made through which the extract can enter the skin. The needle is then pulled out carefully in the inverse direction, and the drop of extract is wiped.

In the 1970s the scarification method continued to be used with such devices as the Cross scarifier (Hollister-Stier Laboratories of Canada). Studies comparing scarification with prick skin testing demonstrated increased false-negative and false-positive results in scarification.^{11, 12} As a result of such studies, use of the scarification technique diminished.

MODERN OPTIMIZATION OF SKIN TESTING DEVICES

Although current epicutaneous skin testing methods seem safer, easier to use, and more consistent with clinical disease than intradermal testing, the major limitation of prick or puncture methods has been their higher degree of variability. Potential causes of this variability include depth of penetration into the skin, amount of antigen entering the cutis vera, angle of penetration, duration, and skill of the investigator.³ It is for this reason that Brown and Thantrey examined optimal needle length in their 1981 report.⁵ The authors developed an adjustable needle that was jabbed into the skin at a right angle through an extract of 1 mg/mL histamine hydrochloride. They found that a length of 1 mm resulted in the largest wheal response. With longer needle lengths, no greater wheal size was seen; however, bleeding did occur. When this device was compared with the Pepys and Squire methods in testing with grass pollen extracts, it demonstrated superior reproducibility. They also demonstrated that with this standardized level of skin trauma, using a fixed optimal length needle, concentrated extracts resulted in large irregular wheal size with significant variability in size. This problem, however, could be resolved with use of diluted extract. In an earlier report, Østerballe described significantly greater variability in wheal size when examining a disposable lancet with a similar 1-mm length cutting surface.²⁰ Brown and Thantrey state that this disparity in result may be caused by the chisel point of the disposable lancet resulting in a cut of the skin versus the prick seen in their needle device.⁵

Several similar devices have been brought to market throughout the world, many of which have not been available in North America. They were developed to improve reproducibility of the prick skin test method, even in the hands of unskilled medical staff. Several of the devices used are similar to the Morrow Brown needle (Aller Guard, Topeka, KS) and include the Stallerpointe (Stallergènes Laboratories, Fresnes, France), Østerballe precision needle (Dome-Hollister-Stier, Paris, France), and the Phazet (Pharmacia Diagnostics, Uppsala, Sweden). The Stallerpointe was

also similar to the Morrow Brown needle but had a different needle inclusion angle.¹⁰ The Phazet was similar to the Morrow Brown needle but contained a standardized quantity of dried extract to simplify the procedure.² Other metallic devices for epicutaneous testing include the bifurcated smallpox needle and the Greer Pen (Greer Laboratories, Lenoir, NC), which is a 54-mm-long, solid stainless-steel needle with an angled tip. A pen with similar design to a mechanical pencil holds the needle. One needle is used per patient and wiped between each extract tested.

Several plastic devices are available, including the MultiTest (Lincoln Diagnostics, Decatur, IL) and DermaPik (Greer Laboratories). The Multitest has gone through several revisions. The present version (MultiTest II) is an eight-headed device in which nine tines of 1.9 mm length are grouped in two rows of four (Fig. 1A) Each head is separated by 2 cm, and the two rows are separated by 3 cm. In an earlier version, the tines were 2.4 mm long. After the tines are loaded with extracts, the device is pressed against an area of skin large enough to allow all eight heads to have contact with skin with sufficient pressure to puncture the

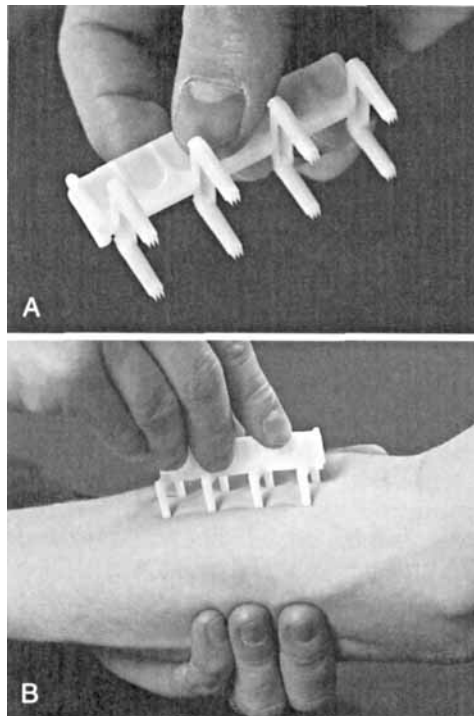


Figure 1. A, The Multitest device has eight heads that are grouped in two rows of four. Each head has nine points for puncturing the skin. B, It is important to press all eight heads of the device into the skin with sufficient pressure to puncture the skin and allow adequate penetration of its points.

skin and allow adequate penetration of its points (Fig. 1B). The DermaPik is a single headed device that is 41 mm long with six 0.81-mm points arranged in a 2-mm circle. This device is intended for puncture or a puncture-and-twist technique. When using the twist technique, the device is pressed gently into the skin and rotated approximately a quarter turn. To speed the process of skin testing, the MultiTest and DermaPik tips may be placed in wells that allow extract to be drawn by capillary action.

STUDIES OF SKIN TESTING DEVICES

Many reports have examined individual epicutaneous skin test devices.^{2, 5, 7, 10, 13, 15, 16, 20, 21, 23} Bousquet and Michel observed that with trained investigators, the coefficient of variation (CV) of wheal size ranges between 8.4% and 30%.⁴ Five published studies have examined multiple devices simultaneously.^{1, 6, 8, 17, 18} The first of these studies, by Adinoff and colleagues,¹ involved 15 subjects who underwent epicutaneous skin testing on the back with histamine phosphate (10 mg/mL) and 50% glycerosaline with six different devices to determine the devices' precision and patient preference as a reflection of lack of pain or discomfort in test performance. The devices included the smallpox needle (Hollister-Stier Laboratories, Spokane, WA), bifurcated needle (Allergy Laboratories of Ohio, Columbus, OH), Greer Pen, blood lancet by prick method (Becton Dickinson, Rutherford, NJ), Morrow Brown needle, and MultiTest. This study used the earlier version of the MultiTest with 2.4-mm tines. Each of the devices was tested in quintuplicate to histamine and once to glycerosaline, except for the MultiTest which had five heads filled with histamine and three heads filled with glycerosaline. Testing was performed by one of two highly trained technicians. The resultant reaction was outlined by felt tip pen and transferred to a permanent record using transparent tape at 10 minutes following test application. These records were then magnified 10 times, and wheal areas were calculated using computerized planimetry. Reproducibility was determined by calculation of the coefficient of variation. When examined individually, the precision of MultiTest was significantly less than the smallpox needle, bifurcated needle, Morrow Brown needle, and Greer Pen ($P < 0.05$) but not statistically different from the lancet. As a group, the smallpox needle, bifurcated needle, Morrow Brown needle, Greer Pen, and lancet demonstrated a CV of 26.9 ± 9.3 , and the MultiTest demonstrated a CV of 39.5 ± 26.6 ($P < 0.001$). False-negative reactions to histamine were not seen with use of the smallpox needle, bifurcated needle, or Greer Pen and only rarely were seen with the MultiTest, lancet, and Morrow Brown needle (1%–3%). This finding did not represent a significant difference between the devices. False-positive reactions to glycerosaline were observed more frequently with MultiTest compared with any other device: MultiTest (49%), bifurcated needle (6%), Greer Pen (6%), smallpox needle (3%), Morrow Brown needle (0%). With

regard to patient-assessed pain or discomfort, the bifurcated needle was most accepted and the MultiTest was least accepted.

In the European study by Demoly and colleagues⁶, eight nonatopic volunteers underwent testing with histamine hydrochloride 10 mg/mL using the Pepys modified prick method (with both a 25-gauge and 22-gauge needle), uncoated Phazet, Stallerpointe, Østerballe standardized needle Pricker, Wyeth bifurcated needle, Stallerkit (Stallergènes Laboratories), Allerprick (Hall Allergen Laboratories, Haarlem, The Netherlands), and Morrow Brown standardized needle. Histamine tests were performed on the volar aspect of the arm and separated by 3 cm. The Allerprick and Pricker are similar to the Morrow Brown needle, except the Allerprick has a slightly longer point length of 2 mm, and the Pricker is a metallic device with a slightly wider needle width of 5 mm versus the 3 mm width of the Morrow Brown needle. The wheals were read at 10 minutes and recorded using the transparent tape technique. All tests were performed in octuplicate with reproducibility determined by calculating the coefficient of variation. Overall the Phazet, Pricker, and bifurcated needles induced the largest wheals and were most likely to induce bleeding. The Stallerpointe, Morrow Brown needle, and modified prick methods (using both size needles) induced the smallest wheals. The CV differed greatly, from 8.4% to 21.7%. Greatest variation was seen with the Morrow Brown, and the Phazet had the least variation. The investigators found no significant difference in CV when comparing the two sizes of hypodermic needles using the modified Pepys technique.

In 1992, Engler and coworkers compared four devices available in North America: the Greer Pen, DermaPik, MultiTest (newer device with 1.9-mm-long tines), and Morrow Brown needle.⁸ In this study, the Morrow Brown needle used was a different version than in the previous study with a slightly longer point length of 1.25 mm. The study evaluated 20 subjects who underwent testing with each device. Eight half-log serial dilutions of histamine phosphate (0.005 to 5 mg/mL) were placed on the back. Each test (except the MultiTest) was separated by 5 cm. Sensitivity, time required for placement, patient preference, and the CV of each device were investigated. The Greer Pen and DermaPik were found to be the most sensitive. The DermaPik required the least time for placement, and the Greer Pen required the most time. The Morrow Brown resulted in the least discomfort to the subjects, although the MultiTest was preferred by many subjects as it allowed placement of multiple tests to be done all at one time. A similar level of precision was noted for wheals with the DermaPik, Greer Pen, and MultiTest (CV, 21.2%, 23.1%, and 24.5%, respectively), and the Morrow Brown needle was less precise with a CV of 59.9%. Unlike the Adinoff study,¹ the MultiTest device had a similar level of precision compared with the other devices. The authors postulate that this improvement may have been a result of the shorter length of tines in the new MultiTest device. As noted by Garibaldi and Slavin, these shorter tines allow less entrance into the dermis, causing a reduction in the irritant response.⁹ On the other hand, the authors note that in interpreting flares one must be

cautious with using the MultiTest as there may be overlapping reactions secondary to the close placement of the points. It also was found that negative Morrow Brown results must be interpreted with caution. Precision of the Morrow Brown needle was increased with use of more concentrated histamine (10 mg/mL), resulting in a CV of 16.5%. Higher background noise, which may result in a false-positive response, was seen with use of the MultiTest and DermaPik devices. Thus, it is particularly important to examine negative controls with these two devices.

The fourth of the comparative device studies was performed by Nelson and colleagues,¹⁸ in which they examined the reproducibility, patient acceptance, and occurrence of false-negative and false-positive results with the Hollister-Stier lancet, bifurcated needle by both prick and puncture technique, ALK lancet (ALK Laboratories, Milford, CT), MultiTest, and DermaPik. This study consisted of two parts. In the first part, which examined reproducibility of the devices, 12 subjects underwent repeated testing with histamine placed on the back. In the second part of the study, 21 subjects who previously had demonstrated a significant reaction to at least one allergen extract underwent testing with each of the devices to assess the size of reactions at 50% glycerosaline negative control sites and to determine the occurrence of false-negative skin tests at sites with histamine or allergen. Data were pooled from both parts of the study to assess patient acceptance of the devices. One skilled technician performed all skin testing, and a second technician outlined the reactions and transferred the results to a permanent record with transparent tape. From this record, the longest and orthogonal diameters were measured and the mean diameter was determined for analysis. With regard to reproducibility, although wheal size and standard deviation (SD) were disparate (smallest wheal size and SD seen with the Hollister-Stier lancet and largest wheal size seen with the DermaPik), the CV values were similar, varying from 15% for the Hollister-Stier lancet to 19% for the bifurcated needle by prick-and-puncture technique. When subjects were asked to rate the acceptability of the devices, most favorable scoring was seen with use of the Hollister-Stier lancet, and least favorable scores were seen with use of the DermaPik. False-negative results essentially were nonexistent. On the other hand, devices differed significantly in the occurrence of false-positive response at negative control sites. The most frequent and largest reactions occurred with the DermaPik and MultiTest, intermediate responses were seen with the bifurcated needle, and least and smallest responses occurred with the lancets. In the discussion section of this article, it again is stressed that the underlying difference in these devices is the degree of skin trauma. With greater trauma, a larger reaction to histamine and allergen is seen while the likelihood of a false-negative reaction is lessened significantly. On the other hand, with greater trauma comes greater likelihood of a false-positive response and a greater level of discomfort to the patient.

In the most recent of these comparative studies, Nelson and colleagues examined two newer devices—the Duotip Test (Lincoln Diagnos-

tics, Decatur, IL) (Fig. 2) and Quintest (Bayer Allergen Products, Spokane, WA) (Fig. 3)—and re-examined the smallpox needle, MultiTest II, and DermaPik.¹⁷ Beyond attempting to attain better reproducibility and speed of application (both devices rely on preloaded wells for fast application), much of the impetus to develop newer devices was spurred by Occupational Safety and Health Administration (OSHA) recommendations in 1995 that warned against using one device per patient with wiping between extracts. It was believed that this practice potentially could increase the chance of health care needle sticks.¹⁹ In this 1998 study, standard techniques were used for the smallpox needle, Quintest, and MultiTest, and the Duotip and DermaPik were examined using the prick technique and prick-and-twist technique. The Duotip is a plastic device that is 41 mm long with a bifurcated needle tip measuring 2-1/2 mm. Penetration into the skin using this device is less than 1 mm (G. Hein, personal communication, 2001). The Quintest is a metal-tipped device in which five heads measuring 1.2 mm in length are each separated by 30 mm, allowing five allergens to be placed at a time. Both devices rely on capillary action to speed skin testing by allowing transfer of allergenic extracts from preloaded wells to the skin for testing. Testing to glycerosaline and histamine base 10 mg/mL was performed on the back by an experienced technician for five to eight times with each device. Skin test results were read at 15 minutes for saline and 8 minutes following application for histamine. Results were transferred to a permanent record using a felt tip pen outline of reaction and transparent tape technique. The reproducibility of histamine reactions was expressed using the evaluation of the SD.

Variability was the least for the MultiTest, followed by the Quintest, smallpox needle, DermaPik by prick, Duotip Test by twist, Duotip Test by prick, and Derma by twist. Pseudo-false-negative responses were noted when the wheal was less than 3 mm or flare was less than 10 mm to histamine. Although somewhat rare, there was significant variation



Figure 2. The Duotip Test device (Lincoln Diagnostics, Decatur, IL), primarily intended for puncture testing, is made of plastic and has a bifurcated tip.

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Figure 3. A and B, The Quintest device (Bayer Allergen Products, Spokane, WA), intended for puncture testing, has five metal-tipped heads separated by 30 mm.

in the result with MultiTest the most common pseudo false-positives followed by Duotip by prick, Quintest, smallpox needle, Duotip by twist, and no such errors seen with the DermaPik. With regard to the specificity of a 3-mm wheal, if one is attempting a 99% specificity, only the Quintest, smallpox needle, and Duotip by prick would achieve this threshold. If the threshold of specificity is reduced to 95% with a 3-mm wheal, all devices/methods would achieve these criteria, except for the Duotip by twist method.

SUMMARY

In nearly 100 years of clinical use, skin testing has undergone significant innovations. Like our allergy forefathers, investigators con-

tinue to strive to attain reproducible results that ideally can be performed reliably by technicians with varying skill levels using methods and devices that permit quick testing without inflicting significant pain to the patient. There are several options available when choosing an epicutaneous test device. It is imperative that the allergist understands the characteristics of the device chosen.

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Address reprint address to
John J. Oppenheimer, MD
12 North Ridge Road
Denville, NJ 07834

e-mail: nalllopp@pol.net