

Improvements in skin-testing technique

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ABSTRACT

Allergy skin testing is the primary modality used in the diagnosis of allergic diseases and guides development of treatment and avoidance plans. The goal of the Allergist is to skin test the appropriate population with a device and technique that minimizes pain while maximizing sensitivity and specificity. The debate involving the use of intradermal versus skin-prick testing in the diagnosis of aeroallergy has been long lasting. Past and present medical literature will be reviewed, establishing the lack of diagnostic use of intradermal testing in the setting of aeroallergy. New skin devices continue to be developed with a trend toward production of multidevices. Performance characteristics of various skin test devices will be reviewed with an emphasis on sensitivity, specificity, and variability of skin-prick testing devices. Significant statistical differences exist between all devices tested and reported in the literature. Whether these statistical differences equate to clinical differences is not known. With this review the practicing allergist should carefully evaluate multiple different devices and choose a device that suits their practice needs. In addition, allergists must ensure that technicians are sufficiently trained on the correct use of their device and should conduct continuing education to ensure that proper skin testing techniques are being used in their practice. Finally, the use of skin testing in pediatrics will be reviewed with a focus on safety. Care should be taken when skin testing infants ≤ 6 months of age, especially in the setting of eczema and a family history of atopy. (Allergy Asthma Proc 27:100–103, 2006)

The goal for the allergist is to perform allergy skin testing in an appropriate patient population using a device that minimizes both false negative and false positive findings. In addition, it is desirable to use a device that results in minimal patient discomfort. The U.S. Joint Council of Allergy, Asthma, and Immunology¹ and the European Academy of Allergology and Clinical Immunology² recommend percutaneous testing as the primary test for diagnosis of immunoglobulin E-mediated allergic disease. Skin testing is also the preferred method for selecting allergens to be included in immunotherapy.³ Given this, the findings on the initial skin test panel are very important clinical data. If a particular test is too sensitive (resulting in false positives), the patient may receive an antigen that is not required to achieve clinical benefit. On the other hand, a high false negative rate for a particular test will result in a patient not receiving a needed antigen while undergoing immunotherapy.

There has been a recent trend in the production of disposable skin test devices that can apply multiple skin tests simultaneously, the so-called multidevices. The presumed benefit of these devices is that one can apply multiple tests at one time and thus be able to

perform more skin tests over a shorter time, and in a busy allergy practice this may improve productivity. However, this theory of increased productivity still has to be proved. In addition, it is common practice to have a set panel of allergens to test patients with. It also is presumed that a multidevice can help standardize this practice. Finally, there is an underlying thought that the use of multidevices will make it easier to test pediatric and more difficult patients with a standard panel of allergens over a shorter amount of time and with less complexity. All of these presumptions may be valid in a given practice; however, they are yet to be proven. In this review I will discuss recent literature that has compared the use of multidevices with the use of single devices with a focus on various performance characteristics to include sensitivity, specificity, variability, and pain. In addition, I will review the value of intradermal (ID) skin testing in the diagnosis of aeroallergy and skin testing in special populations.

SKIN-PRICK TESTING VERSUS ID

Allergy skin testing in comparison to *in vitro* testing generally offers the advantage of being more sensitive and less costly. Skin testing also may be more time efficient by providing information about the patient's allergen sensitivities during the office visit rather than at some later point in time as is the case with *in vitro* testing. When discussing skin testing, generally, there are three approaches used in the diagnosis of allergy: skin-prick testing (SPT), ID testing, and patch testing. Patch testing is used primarily for the diagnosis of type IV hypersensitivity and is outside of this discussion. I will focus primarily on the two modalities used for the diagnosis of type I hypersensitivity.

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SPT involves either pricking the skin through a drop of antigen or pricking the skin with a device that has 'preloaded' antigen. The latter method generally is one of the most common methods used in current clinical practice. ID skin testing involves injecting a small amount of antigen into the skin.

The discussion of whether to use ID skin testing in addition to (or instead of) SPT has been the source of significant debate. There are potential advantages and disadvantages of each testing modality. Generally, it is agreed that ID skin testing is the preferred testing technique in the diagnosis of insect and drug allergy. However, in the following discussion I will review why the use of ID testing in the diagnosis of allergy to specific aeroallergens may have limited use.

In the Tucson epidemiologic study, for patients who had negative SPT, there was no difference in the prevalence of ID test in patients with rhinitis and/or asthma and those without.⁴ In this review the relationship between SPT and ID testing and serum levels of immunoglobulin E (total and specific) was evaluated in 311 subjects. These results were reviewed in relationship to the allergic state of each subject. There was a significant relationship between the presence of allergy and the presence of any positive prick test. However, this relationship did not hold true when looking at ID testing, such that 49.2% of the nonallergic patients with negative SPT tests had a positive ID test. Thus, in patients with a negative SPT the result of ID testing had no correlation to respiratory allergy.

Furthermore, in patients who had a history of seasonal allergic rhinitis but had negative SPT to timothy extract there was no difference in nasal challenge or correlations of symptoms with pollen counts during the grass season in those with positive or those with a negative ID to grass.⁵ In this study, four different groups were examined to determine if ID testing should be done routinely when the SPT results are negative. The first group examined those patients with a history of seasonal allergic rhinitis, negative SPT, and positive ID testing. Group 2 had positive SPT in the setting of respiratory allergy and group 3 had negative SPT and ID in the setting of a history of respiratory allergy. Finally, group 4 had no respiratory allergy and had negative skin tests. In this population, diagnosis of respiratory allergy was confirmed by nasal challenge and symptom scores during pollen season. The conclusions of the authors were that in the setting of a negative SPT, positive results on ID testing did not indicate the presence of clinically significant allergy to timothy grass. Finally, Wood *et al.* examined the use of SPT, ID, and radioallergosorbent testing in the setting of cat allergy and showed that the a positive SPT and radioallergosorbent testing had favorable likelihood ratios for the diagnosis of clinical allergy, but ID results were essentially clinically insignificant.⁶ Therefore, in

the setting of aeroallergen skin testing there is limited value of ID testing, but a clear value exists in the diagnosis of venom and drug allergy. In the setting of strong clinical suspicion for respiratory allergy and a negative SPT, the physician should consider repeating the SPT rather than performing ID testing.

WHAT DEVICE SHOULD I USE?

Several studies have shown variability between SPT devices.⁷⁻¹⁰ Some of the earlier studies have indicated variability between anatomic location such as arm and back results as well as differences between sun-damaged and normal skin. To contribute to this body of evidence, a head-to-head prospective comparative study of eight different common SPT devices was conducted.⁷ This study specifically examined four single devices and four multidevices. Single devices included Greer pick (Greer Labs, Lenoir, NC), Accuset (ALK Abello, Inc., Round Rock, TX), Sharptest (Panatrex, Inc., Placentia, CA), and the Quintip (Hollister-Stier, Spokane, WA). Multidevices tested were Quintest (Hollister-Stier), Quantitest (Panatrex, Inc.), Greer Track (Greer Labs), and the Multi-Test II (Lincoln Diagnostics, Inc., Decatur, IL).

In this study the devices were testing in all anatomic locations that are commonly used in clinical practice to control the effects of anatomic location. Areas of the body tested were the upper arm, lower arm, upper back, and lower back. This study attempted to control for technician variability by using one technician to place all of the skin tests and another blinded technician to read all of the reactions. At the conclusion of the study, there were nearly 7000 individual skin test sites available for evaluation.

The study confirmed once again that there are statistically significant differences between essentially every device tested. A unique aspect of this study was the comparison of single devices to multidevices. The single devices had larger reactions on the arms whereas the multidevices had larger reactions on the back. Overall, the single devices had very good sensitivities ranging from 92 to 97% and produced minimal pain. More variability was observed when examining the multidevices with sensitivities ranging from 56 to 93%. One device that stood out with the lowest performance in all areas was the Greer Track. This device was the most painful, had the smallest mean histamine wheals and flares, was the least sensitive, and had the greatest degree of intradevice variability.

The variability within a given multidevice during one test was examined also. Each device showed statistical differences between each head during a given single test. It was noted that the corners of each multidevice yielded the largest reactions. The authors felt these differences were caused by the technique of rock-

ing such that greater pressure was exerted at the corners thus yielding larger reactions. Overall, multidevices were more painful than single devices. However, all of the devices in general resulted in minimal pain.

Regarding the Greer Track, the statistically significant findings of performance may well equate to clinically significant differences in performance. However, when examining all of the other devices, it is unknown if the statistical differences noted will equate to clinically significant differences in performance. All of the remaining seven devices had mean histamine wheals >3 mm and mean histamine flares >10 mm, with sensitivities from 86 to 97%. In addition, all of the remaining seven devices had specificities of $\geq 98\%$. The authors concluded that each individual provider should determine which device is best for their practice. It should be noted that this study involved only histamine and saline controls and not allergen extract. It is possible that control solutions may interact differently with the heads of the devices, which may result in different performance characteristics. This possibility is unlikely; however, there is no data to prove or disprove it. In addition, generally, the population studied was healthy young adults with just under one-half of the participants having a stated history of atopy.

In conclusion, multiple studies have shown variability between various skin test devices. In addition, it is well known there are differences between technicians performing the skin testing. Given all of this, a provider should use a device that he/she is well acquainted with and has established proficiency in using. Finally, continuing education and quality assurance in skin testing is recommended in all areas of clinical practice.

SPECIAL POPULATIONS

The value of skin testing in the pediatric population has been questioned in the past because it is generally accepted that the sensitivity and specificity varies when compared with adults. Safety is a great concern in the very young because they are not able to communicate the early signs of anaphylaxis and reliability in infants less than 1 year of age is questionable. The practice parameters state that, generally, fewer prick tests need to be performed in infants and very young children because these age groups are not likely to be sensitized to as many allergens as older children and adults. In younger patients, sensitization is more apt to reflect intense, prolonged exposure to allergens encountered earliest in life rather than pollen.¹¹ Recent reviews of available data report that SPT results in children >1 year old have a high negative predictive value and a positive predictive value of $\sim 50\%$.¹² In children <1 year, the negative predictive value fell to

$\sim 80\%$ while the positive predictive value is not clearly defined.

Devenny and colleagues described a review of 1152 SPTs performed during the years 1996–1998 in children 0–19 years of age.¹³ They reported six cases of generalized reactions, all of which occurred in infants <6 months of age. In this subgroup of pediatric patients all of the tests involved food allergens and testing was done using the prick-prick method. An important note is that all of the patients that reacted had eczema and a positive family history for atopy. In this review there were no deaths. This data yielded an overall rate of 6522 generalized reactions per 100,000 SPTs (6.5%) in the <6-months-of-age group. The overall rate of generalized reactions was 521 per 100,000 SPTs (0.52%). Care should be taken when performing SPTs in infants and given the reaction rate the use of ID testing in this population should be done with great care.

CONCLUSIONS

SPT is the primary recommended modality used for the diagnosis of aeroallergy. The value of ID testing in the setting of a negative SPT is limited at best. With a strong clinical history and a negative SPT, it is recommended repeating the SPT rather than performing ID testing. Regarding which SPT device to use, the practicing allergist should recognize that there is significant variability between available devices. The choice should be tailored to an individual's practice setting and all of the technicians should have shown proficiency with the device. Ongoing education and training is encouraged to maintain limited variability in device performance and reproducibility. Finally, care should be taken when testing the very young for the presence of allergic disease because the results of testing do not correlate as well as the adult population and safety is a great concern in this age group.

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