

The Role of Intradermal Skin Testing in the Evaluation of Allergic Disorders

MICHAEL A. SPRINGER, M.D.

ABSTRACT

Intradermal (ID) skin tests are used commonly by allergists in the evaluation of allergic diseases. This article reviews the literature concerning ID skin testing, especially as it relates to its specificity and its ability to both predict future allergic symptomatology or to confirm the lack of allergy. It appears that ID testing is still a very worthwhile procedure. However, more studies are needed to evaluate the correlation between ID skin tests and the response to immunotherapy.

INTRODUCTION

SKIN TESTING, both epicutaneous and intradermal (ID), has been used for more than 80 years in the diagnosis of atopic diseases. It is well accepted that skin testing with allergenic extracts is effective in the diagnosis of IgE-mediated diseases, such as hay fever, asthma, urticaria, and eczema.⁽¹⁾ Most practicing allergists use epicutaneous testing followed by ID testing for questionable antigens. In fact, in a 1989 survey by the Joint Council of Allergy and Immunology, 89% of board-certified allergists reported using epicutaneous testing and 87% reported using ID testing. The purpose of this article is to look more closely at the role of ID testing in the evaluation of atopic diseases by examining the sensitivity (how likely is the test to detect all patients who are truly positive) and the specificity (how likely is the test to detect only patients who are truly positive) of ID testing as well as its ability to predict the occurrence of allergies in an asymptomatic population.

LITERATURE REVIEW

The proven efficacy of ID testing in the diagnosis of asthma and hay fever has been known since the work of Efron and Boatner in 1941.⁽²⁾ These investigators, using relatively weak concentrations (1:5000 w/v through 1:100,000,000 w/v) of pollen extract for ID testing, were able to show a diagnostic efficiency (ability to detect true positives and true negatives) of greater than 90% for all concentrations of extract used. Since that time, there has been much controversy concerning the optimal concentrations that should be used for ID testing. Ideally, the concentration for ID testing should range from the weakest dose able to detect sensitivity or predict the occurrence of future allergy to the strongest dose failing to produce nonspecific reactions. These

Knoxville, Tennessee.

parameters would render excellent sensitivity and specificity. The efficacy and sensitivity of ID testing have never been in question. However, the specificity of ID testing has come under critical attack.

The issue concerning specificity of ID testing has been covered by several authors.^(3,4) Linblad and Farr examined the incidence of positive intradermal reactions with various concentrations of extract in an asymptomatic population.⁽⁵⁾ They then looked for the presence of skin-sensitizing antibodies to help differentiate irritant reactions from specific IgE-mediated responses not yet producing clinical symptoms. They used glycerinated extracts and found that at concentrations of 1:100 w/v, false positive reactions were secondary to irritant reactions with negative Prausnitz-Kuestner (PK) reactions. However, at concentrations of 1:1000 w/v, positive ID reactions in asymptomatic subjects frequently were associated with positive PK reactions, indicating the presence of specific IgE antibody. Intradermal testing at 1:1000 w/v has been shown clearly to be helpful in testing young children, probably because of the decreased skin reactivity in infants and young children, in whom higher concentrations of antigen are sometimes required to elicit a response. Hannaway and Hyde compared results of skin testing by scratch and intradermal methods in 250 atopic children and concluded that intradermal testing is a worthwhile and necessary procedure in this population.⁽⁶⁾ This conclusion was based on their finding that 12.4% (31 of 250) of the atopic children had completely negative epicutaneous tests but positive ID tests. They also found that 80% of the children (202 of 250) had one or more ID tests that were 10 mm or greater than the corresponding scratch test. However, no attempt was made to correlate these skin tests with bronchial or nasal provocative challenges. Businco et al. found that ID skin tests with *Dermatophagoides pteronyssinus* in asthmatic children had a 92% (33 of 36) correlation with bronchial provocation tests.⁽⁷⁾ They also concluded that ID tests are a reliable method for allergic diagnosis in asthmatic children.

The specificity of ID testing in adult atopic individuals is more controversial. Reddy et al. determined the clinical relevance of positive ID tests when epicutaneous tests were negative in 34 adult patients with perennial rhinitis.⁽⁸⁾ They found that none of these patients had positive RAST or leukocyte histamine release (LHR) assays. In addition, only 1 of the 34 patients had a positive nasal provocation test. They concluded that when epicutaneous tests are negative in adult patients with perennial rhinitis, positive ID tests are not likely to indicate the presence of allergy. The results of the RAST and LHR assays are not surprising, since RAST is no more sensitive than epicutaneous testing, and LHR is less sensitive than RAST. However, the discordance between nasal provocation and ID testing is more difficult to explain and presents strong evidence for a lack of specificity of ID tests in adults with perennial rhinitis. Other studies have found contrasting results.⁽⁹⁻¹²⁾ For example, when evaluating all inhalant allergens, Bronsky and Ellis found that a positive ID test in patients with negative epicutaneous tests was corroborated by positive bronchial challenges 23% of the time.⁽¹³⁾ When examining only pollen under similar conditions, the correlation fell to 9%.

Another test of the sensitivity and specificity of skin testing is the ability of these tests to predict the onset of allergy in an asymptomatic person. Hagy and Settignano found that positive epicutaneous tests in college students were associated with a tenfold increase in the development of hay fever over the next 3 years.⁽¹⁴⁾ Their data suggested that the positive pollen epicutaneous test reaction precedes the onset of clinical symptoms of hay fever. Chambers and Glaser studied the incidence of subsequent ragweed pollinosis in symptom-free persons having positive epicutaneous or ID skin tests to ragweed extract.⁽¹⁵⁾ They found that 53% of such patients developed ragweed pollinosis, of which 88% did so within 10 years of the skin tests. There was a greater tendency to develop ragweed pollinosis in patients under 16 years of age, and there was no relationship between development or failure of development of pollinosis and the type of skin test performed. This indicates that ID testing was as efficacious as epicutaneous testing in predicting the development of ragweed pollinosis. Biederman found that of 154 patients with pollinosis who had positive skin tests to pollens not involved in their current seasonal symptoms, 5.5% developed such pollen symptoms the following year.⁽¹⁶⁾ These findings raised the interesting question of whether immunotherapy for those allergens would decrease the likelihood of these asymptomatic, skin test-positive patients developing symptoms. Biederman addressed this issue when he found that the development of pollen symptoms in his asymptomatic patients could be prevented by the injection of these pollens along with the pollens to which the patients were clinically sensitive at that time.

DISCUSSION

When reviewing the literature, it becomes apparent that studies examining ID testing are very difficult to compare because of various reasons: lack of standardization among extracts, different concentrations of extract and different methods of interpretation for ID testing, different methods used for provocative challenge, and different allergic diseases studied. However, several important points can be made. Concerning specificity, an allergist needs to individually discern the importance of finding the small population of patients who have negative epicutaneous tests but clinically relevant positive ID tests. Considering Bronsky's study, this may range from 9% to 23% of patients, depending on the allergens studied. Some allergists may believe that it is not worthwhile to perform ID testing in an effort to discover this small population. Others believe that if no ID tests are performed, a significant number of allergic patients are not diagnosed and, therefore, are left untreated. It is important to realize that there are no studies of the effects of immunotherapy on patients who are negative on epicutaneous testing but positive on ID testing. However, since positive inhalational challenges have been present in these patients, one might assume that the same principles of immunotherapy would apply to this group. At the least, environmental control measures would still be advantageous.

An additional role for ID testing is to serve as a conclusive indicator for the lack of allergy (true negative). In patients with negative epicutaneous skin tests, ID testing can be extremely useful in ruling out a particular antigen as an allergen. Because of the exquisite sensitivity of ID testing, many allergists used ID testing as a conclusive test in evaluating patients who have negative epicutaneous tests but have a clinical history consistent with symptoms produced by a particular allergen. Not only is ID testing an excellent method of verifying a lack of allergy, but it may also hold some promise in predicting future allergy.

In conclusion, most studies tend to support the continued use of ID testing. More data are present to support the use of ID testing in young children than in adults, probably secondary to decreased skin reactivity in infants and young children. As long as the concentration for ID testing does not exceed reasonable limits, the specificity of ID testing is good. Since some investigators believe that an epicutaneous test needs to be 1000 times more potent than an ID test to produce similar skin test reactions,⁽¹⁷⁾ most allergists use ID testing at a dose of one log concentration stronger than the equivalent epicutaneous dose. Therefore, a maximum reasonable concentration for ID testing seems to be 1:1000 w/v in adults. Further studies are needed to determine the possible benefit of stronger concentrations for ID testing and to examine the response to immunotherapy in these patients.

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Address reprint requests to:
Michael A. Springer, M.D.
801 Weisgarber Road, Suite 200
Knoxville, TN 37909

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