
Skin prick test in duplicate: is it necessary?

Irene Devenney, MD and Karin Fälth-Magnusson, MD, PhD

Background: Duplicate skin prick testing has previously been recommended because of reports that accidental negative tests are common. However, duplicate tests also mean an extra allergen load, which may increase the risk of inducing a generalized reaction at the test situation, at least in the youngest infants.

Objective: To investigate whether the occurrence of both a positive and negative test result is a common feature when performing duplicate skin prick tests and can therefore justify the duplicate method.

Methods: A retrospective analysis of all skin prick tests performed in duplicate at the pediatric clinic at University Hospital in Linköping, Sweden, in 1997.

Results: Of 1,087 skin prick tests, 14 resulted in one positive and one negative test, or 1.3%. The corresponding figure in the youngest age group, (ie, <2 years of age) was 3 of 340 (0.9%).

Conclusions: Considering the risk of inducing a summation of the reactions, and thereby a generalized allergic reaction, when applying an extra allergen load on the limited surface of the small arm, we conclude that the results of this study justify using single prick test, at least in the youngest age group and probably when testing children of all ages.

Ann Allergy Asthma Immunol 2001;87:386–389.

INTRODUCTION

Allergy is an increasing problem in the pediatric population, and recent studies report allergic manifestations in >40% of Swedish schoolchildren.¹ In early childhood, food allergies dominate, occurring in 3% to 5% of all children.²

When studying IgE-mediated hypersensitivity, skin prick testing is a widely used diagnostic tool. The method is usually considered quick, pedagogic, and relatively inexpensive. However, it takes an experienced tester to produce reliable results. Differences in technique and quality of extracts can influence the results. Further, the interpretation of the test result requires skill and experience, as a positive test is not synonymous with allergic disease. However, the larger the test reaction, the more likely the clinical significance.³

Skin prick testing is considered to be a safe procedure. No anaphylactic re-

actions after skin prick test were observed by Turkeltaub et al,⁴ and adverse reactions were very uncommon. Nevertheless, the skin prick test can induce systemic reactions in highly sensitive patients.^{3,5,6} We have recently reported six cases of generalized reactions, all in children younger than 6 months of age, after skin prick tests when duplicate tests were standard in our clinic.⁷

When interpreting the results of skin prick test, a mean wheal diameter of 3 mm is commonly used as a practical lower limit for positivity.^{6,8,9}

Wheals of 1 to 2 mm in diameter might be induced by pricking the skin, even with a dry needle.¹⁰ However, a clear and significant hyporeactivity to histamine has been observed in infants, especially before the age of 6 months. The same study confirms, however, that skin prick test can be performed and interpreted without difficulties in infants after the age of 3 months, bearing in mind that the prick test wheals might be smaller.¹¹

Because very young children are not likely to be sensitized to as many allergens as older children, fewer prick

tests need to be performed. Sensitization is most apt to reflect exposure to allergens encountered in earliest life, primarily foods, but also dust mites, indoor molds, and animal danders.³

Performing duplicate tests with each solution at the test situation has previously been recommended as it has been reported that accidental negative tests are common. Dreborg et al¹² have demonstrated that even if the cutoff limit of 3 mm is used, many patients react with both positive and negative tests to the same concentration of the test substance. As many as 18 of 20 patients (90%) showed both positive and negative test results when tested for timothy and dog with an allergen concentration of 160 BU/mL. With an allergen concentration of 800 BU/mL, 5 patients of 20 gave both positive and negative responses. Thus duplicate tests have been recommended when screening for sensitization to avoid negative results.¹² Recent reports, however, recommend single skin tests in very young infants to minimize the allergen load at the test situation.^{7,9}

One reason for using duplicate tests is the possibility of difference in skin sensibility between different parts of the forearm. However, several studies have shown that there were no differences in the wheal when the tests were performed on one arm and both arms, or proximally and distally in the test area on one arm.^{13–15}

In this study, covering all duplicate tests performed in 1997 at the pediatric clinic in Linköping, we investigate whether the occurrence of both positive and negative test results is a common feature and can justify the use of duplicate tests in infants where an extra allergen load on the limited surface of the small arm may increase the risk of summation of the reactions and, therefore, the risk of generalized reaction.

Division of Pediatrics, Department of Health and Environment, University of Linköping, Linköping, Sweden.

Received for publication February 20, 2001.

Accepted for publication in revised form July 10, 2001.

MATERIALS AND METHODS

The present study is a retrospective analysis of all skin prick tests performed in duplicate at the pediatric clinic at University Hospital in Linköping, Sweden in 1997. Tests performed with the single prick method ($n = 33$) were excluded from the study.

All test results are kept in the medical record of each child. In the study, all wheals have been measured, and mean diameter has been registered. We also registered whether the outcome was two positive, two negative, or one positive and one negative test result.

The skin prick test was considered positive when the mean diameter (= half the sum of the largest diameter and its perpendicular) was at least 3 mm for foods, and at least 2 mm for inhalation allergens. If the wheal of the histamine reference solution was <3 mm, a wheal the same size as, or larger than, the positive control would also be accepted as positive.⁸

The skin tests were performed by the same two specially trained and very experienced nurses in a standardized manner. The volar aspect of the arm was used as test area, and the skin was marked with a ballpoint pen for the allergens to be tested.⁹ All tests involving food allergens were performed as prick-puncture tests.³ The tip of the lancet was first dipped in the test solution or the fresh or frozen food specimens. When using inhalant allergens, a drop of test solution (ALK-Abéllö, Hørsholm, Denmark) was placed close to the respective mark on the skin. The tip of the lancet was then pressed at a right angle against the skin surface for 1 second using the volar aspect of the finger tip. The lancet used for pricking the skin was a metallic lancet with a 1-mm tip. As a negative control, a prick with a clean lancet was used. The positive control was histamine HCl 10 mg/mL. The reaction was read 15 minutes after the test was finished. The test results were documented by first outlining the wheal with a pen and then transferring the result to cellotape. The results was stored in the child's record. The mean

diameter (the longest and the midpoint orthogonal) was measured with a transparent plastic ruler by the same investigator for all measurements.⁹

Statistics

Confidence interval 95% for one proportion was calculated according to Altman.¹⁶

RESULTS

At the pediatric clinic in Linköping, a total of 224 children were tested with duplicate skin prick tests in 1997. Of these, 138 (62%) were male and 86 (38%) were female. There were 90 very young infants, ie, <2 years of age, 59 (66%) male and 31 (34%) female.

In total, 1,087 duplicate tests were performed, resulting in 310 (28.5%) with duplicate positive test; 763 (70.2%) with duplicate negative test; and 14 (1.3%, 95% confidence interval 0.6 to 1.9%) with one positive and one negative test. (Fig 1)

Of 340 tests performed on infants younger than 2 years of age, 83 (24.4%) gave two positive results; 254 (74.7%), two negative; and 3 (0.9%, 95% confidence interval 0.2 to 2.6%), one positive and one negative. (Fig. 2)

The skin prick tests comprised both food and inhalation allergens. Of the 1,087 tests, 566 (52%) were food and 521 (48%) were inhalation allergens. For the infants <2 years only, the corresponding figures were 303 of 340 (89%) and 37 of 340 (11%), respectively.

The test results with one positive and one negative included both food allergens ($N = 6$) and inhalation allergens ($N = 8$). It could be noted that of the 14 results, the negative test result in 6 was below the cutoff limit for a positive result (ie, 3 mm for food allergens and 2 mm for inhalation allergens, but was still detectable), whereas 8 displayed a result that was totally negative (0 mm; Table 1).

A total of 13 infants displayed one positive and one negative test result, one of them having two tests with discordant results. All but one had a family history of allergic disease. Eight presented with eczema, 7 with asthma, 3 with eye/nose problems, 2 with symptoms from the mouth/throat, 2 with urticaria, and 1 with erythema. In the youngest age group (ie, <2 years

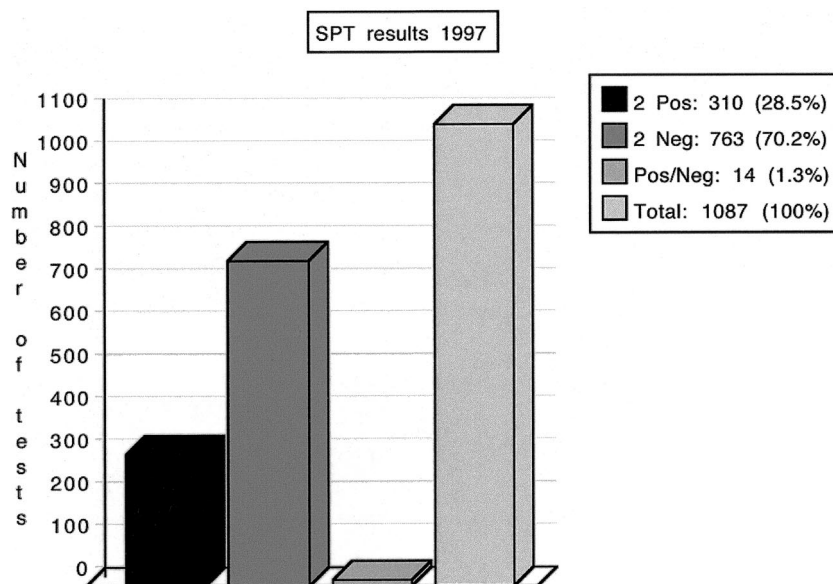


Figure 1. In total, 1,087 duplicate tests were performed in children 0 to 18 years of age in 1997. The figure shows the relationship among the results of duplicate positive, duplicate negative, and diverging results with one positive and one negative wheal. Fourteen of 1,087 tests show diverging results, corresponding to 1.3% (95% confidence interval 0.6 to 1.09%).

of age) all 3 had eczema, and 1 child also had asthma. No other symptoms were expressed in this group.

Four of the older children had presented with more generalized allergic reactions, including: 1) urticaria and itch in the throat when eating peanut. This child was tested for milk, egg and peanut. The result was positive for milk and egg as well as one positive and one negative for peanut. 2) Generalized erythema and itch in the throat when eating peanut. The test was performed for peanut, hazelnut, pollen, and cat, with a positive result for cat, one positive and one negative for peanut, whereas the others were negative. 3) Urticaria of unknown genesis. This child was tested for peanut, hazelnut, horse, and mold. The test was positive for horse, discordant for mold, and negative for the remainder. 4) Urticaria of unknown genesis. The test was performed for pollen, cat, dog, and milk. The result was positive for birch, one positive and one negative for timothy, and negative for cat, dog, and milk.

Of the 14 one negative/one positive results, the negative results in eight cases were totally negative and did not even express erythema.

DISCUSSION

Duplicate skin prick testing has previously been recommended and has been used routinely in our department.¹² However, because of six cases in 1996 to 1998 where infants developed generalized allergic reactions in connection with the test situation, the routine has been altered and, since mid-1998, the infants have been tested with single skin prick tests only.⁷ Since the single test was introduced we have only had one case of generalized allergic reactions when performing skin prick test.

Earlier reports that accidental negative tests are common have been the reason for performing the skin prick test in duplicate. Indeed, some authors still recommend duplicate tests.

In our study, however, we found 14 duplicate results with one positive and one negative wheal of the 1,087 tests performed. This corresponds to only 1.3% of the tests. In the young-

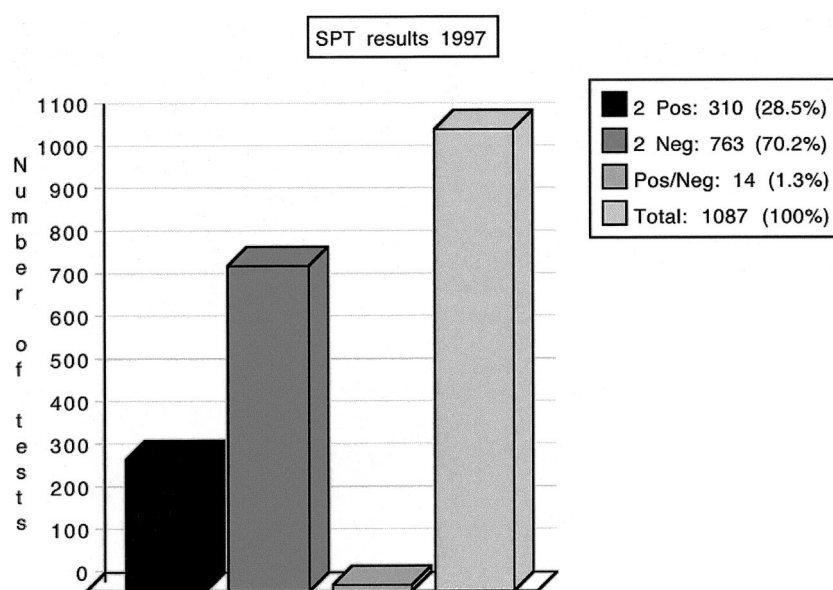


Figure 2. In infants younger than 2 years of age, 340 duplicate tests were performed in 1997. The figure shows the relationship among results of duplicate positive, duplicate negative, and diverging results with one positive and one negative wheal. Three of 340 tests show diverging results, corresponding to 0.9% (95% confidence interval 0.2 to 2.6%).

Table 1. Summary of 14 Patients where Skin Prick Testing with Food and Inhalation Allergens Using the Duplicate Method Showed Diverging Results

	1 pos and 1 neg wheal (0 mm)	1 pos and 1 neg wheal (<3 and 2 mm, resp.)
<2 years	Peas (6.0/0)	Wheat (3.0/2.5) Hazelnut (3.5/2.5)
2-18 years	Peanut (4.5/0) Rabbit (3.0/0) Horse (5.5/0) Horse (4.0/0) Dog (3.5/0) Timothy grass (2.5/0) Timothy grass (4.0/0)	Peanut (4.0/2.5) Egg (3.0/2.0) Timothy grass (3.5/1.5) <i>Mucor racemosus</i> (2.5/1.0)

The first column shows totally diverging results where the negative wheal was 0 mm. The second column shows diverging results with one positive and one negative wheal, using a cutoff limit of 3 and 2 mm, respectively, for food and inhalation allergens. Numbers in brackets are the mean diameter of the wheals.

est age group (<2 years), even fewer, 3 of 340 (0.9%), had an outcome of one positive/one negative test result. In the younger age group, significant hyporeactivity has been previously reported and, therefore, smaller prick test wheals. This suggests that a lower cutoff limit might have to be allowed in this age group for positive skin prick test results. If 2 mm is used as the limit for food allergens in the youngest age group, the outcome

of the present study would be only 1 of 340 (0.3%) with one positive/one negative test result.

In children under 2 years of age, tests for food allergens predominate, ie, 89% of all tests performed. Because few standardized food-allergen extracts are available on the market, and those that are available are titrated in weight/volume, which is a very unsatisfactory method of titration, fresh or frozen food specimens are recom-

mended.^{9,17,18} The allergen concentration is likely to vary in nonstandardized extracts. For that reason, they are known to be a risk factor for inducing generalized reaction.¹⁸ However, the use of nonstandardized extracts does not seem to increase the test outcomes with diverging results between the wheals, which amounted to only 0.9% in this age group. This finding supports the use of the single prick test.

CONCLUSION

Considering the risk of inducing a summation of the reactions, and thereby a generalized allergic reaction, when applying an extra allergen load on the limited surface of the small arm, we conclude that the results of the present study justify using single prick test, at least in the youngest age group and likely when testing children of all ages.

ACKNOWLEDGMENTS

The study was financially supported by the Health Research Council in the Southeast of Sweden and the Swedish Asthma and Allergy Association's Research Foundation. Sincere thanks also to Professor N. I. Max Kjellman for valuable and useful advice.

REFERENCES

1. Åberg N, Hesselmar B, Åberg B, Eriksson B. Increase of asthma, allergic rhinitis and eczema in Swedish schoolchildren between 1979 and 1991. *Clin Exp Allergy* 1995;25: 815–819.
2. Halvorsen R. The Importance of Food Allergies in Atopic Dermatitis in Children and Adults. Workshop for Treatment of Atopic Dermatitis 1999. Medical Products Agency: Uppsala, Sweden.
3. Bernstein LI, Storms WW. Practice parameters for allergy diagnostic testing. *Ann Allergy Asthma Immunol* 1995;75:543–625.
4. Turkeltaub PC, Gergen PJ. The risk of adverse reactions from percutaneous prick-puncture allergen skin testing, venipuncture, and body measurements: data from the second National Health and Nutrition Examination Survey 1976–1980 (NHANES II). *J Allergy Clin Immunol* 1989;84:886–890.
5. Novembre E, Bernardini R, Bertini G, et al. Skin prick test induced anaphylaxis. *Allergy* 1995;50:511–513.
6. Valyasevi MA, Maddox DE, Li JT. Systemic reactions to allergy skin tests. *Ann Allergy Asthma Immunol* 1999;83:132–136.
7. Devenney I, Fälth-Magnusson K. Skin prick test may give generalized allergic reactions in children. *Ann Allergy Asthma Immunol* 2000;85:457–460.
8. Fälth-Magnusson K, Kjellman NI. Development of atopic disease in babies whose mothers were receiving exclusion diet during pregnancy—a randomized study. *J Allergy Clin Immunol* 1987;80:868–875.
9. Dreborg S. Method for Skin Prick Test, in *Vitro IgE Tests (Specific IgE), and Food Challenges*. Workshop for Treatment of Atopic Dermatitis. 1999. Medical Products Agency Uppsala, Sweden.
10. Dreborg S. The skin prick test. Methodological studies and clinical applications. [doctoral dissertation]. Linköping, Sweden: Linköping University; 1987.
11. Ménardo JL, Bousquet J, Rodière M, et al. Skin test reactivity in infancy. *J Allergy Clin Immunol* 1985;75: 646–651.
12. Dreborg H, Holgersson M, Nilsson G, Zetterström O. Dose response relationship of allergen, histamine, and histamine releasers in skin prick test and precision of the skin prick test method. *Allergy* 1987;42:117–125.
13. Østerballe O, Weeke B. A new lancet for skin prick testing. *Allergy* 1979;34: 209–212.
14. Malling HJ, Andersen CE, Boas MB, et al. The allergy pricker. Qualitative aspects of skin prick testing using a precision needle. *Allergy* 1982;37: 563–567.
15. Menardo JL, Bousquet J, Bataille A, et al. Effects of diluents on skin tests. *Ann Allergy* 1983;51:535–538.
16. Altman DG. *Practical Statistics for Medical Research*. London: Chapman & Hall, 1991.
17. Lemanske RF Jr, Taylor SL. Standardized extracts, foods. *Clin Rev Allergy* 1987;5:23–36.
18. Dreborg S. The risk of general reactions to skin prick testing (SPT). *Allergy* 1996;51:60–61.

Requests for reprints should be addressed to:
Karin Fälth-Magnusson
Division of Pediatrics
Department of Health and Environment
University of Linköping
S-581 85 Linköping, Sweden
E-mail: karin.falth-magnusson@lio.se