
Skin prick tests may give generalized allergic reactions in infants

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Background: Skin prick testing, a widely used method of studying sensitization, is usually considered quick, pedagogic, and relatively inexpensive. Previous studies have shown very few negative reactions and no fatalities. In contrast, both anaphylaxis and death have been reported as a result of intracutaneous tests.

Objective: To examine detailed case studies of generalized allergic reactions in connection with skin prick testing in order to identify possible risk factors and thereby increase the safety of the test procedure.

Method: A retrospective study of medical records of six cases with generalized allergic reaction occurring during the study period 1996–1998 at the Pediatric Clinic, University Hospital of Linköping, Sweden. Data about the total number of children tested during the period were collected from the clinic's database.

Results: All six cases with generalized reactions were infants <6 months who showed positive skin prick tests to fresh food specimen. Other common features were active eczema and a family history of allergic disease. All infants received prompt treatment and recovered well. The overall rate of generalized reactions was 521 per 100,000 tested children. In the age group <6 months, the corresponding figure was 6522 per 100,000.

Conclusion: The risk of generalized reactions after skin prick test with fresh food specimens in young children ought to be acknowledged and should lead to increased precautions when performing the test.

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INTRODUCTION

Skin prick testing is a widely used diagnostic tool when studying IgE-mediated hypersensitivity. The method, used extensively in children, has several advantages. Reactions can be read in 15 minutes, making it quick. Parents can see the reaction of the positive test result on the skin. Finally, it is relatively inexpensive compared with serologic methods for allergy investigation.

The method, however, also has disadvantages. It takes an experienced tester to give reliable results. Even with a very experienced user, the result

will vary considerably because of differences in technique and quality of extracts, with standardized extracts giving the highest efficiency.^{1,2} Further, the interpretation of the positive test requires skill and experience because a positive test is not synonymous with allergic disease.

Two different methods of allergy skin tests have been widely used. One is the intracutaneous method, which applies the allergen more deeply. The other is the skin prick test, which gives a more superficial application of the allergen in the skin.

The skin test methods have been extensively studied with regard to adverse reactions. Lin et al reported two cases of generalized allergic reaction when performing intracutaneous tests, whereas in the same study 10,400 skin prick tests showed no negative reactions.³ In another study of lethal reactions to skin testing or hyposensitization, Lockey et al showed two

cases of deaths in connection with skin testing. In all cases, intracutaneous techniques were used. No lethal reaction has been reported after skin prick tests.⁴

Skin prick testing is therefore considered to be a safe procedure. Turkeltaub et al reported minor adverse reactions occurring in a maximum of 0.49% of the tested patients.⁵ Nevertheless, the skin prick test can induce systemic reactions in highly sensitive patients, even if such reactions are rare. Two cases of anaphylactic reactions in adults were reported in 1995 by Novembre et al after skin prick test using fresh food as the test substance.⁶ Furthermore, Valyasevi et al, in their recent study of over 18,000 patients, reported six systemic reactions when skin testing was performed. No systemic reaction was severe. Five of the cases reacted after skin prick tests. The remaining reaction followed an intradermal skin test. None of the reacting patients were tested for food allergens.⁷

The interest in safety precautions for the skin prick test has been further increased by the fact that investigators have lost their former respect for skin testing as skin prick tests have largely replaced intradermal testing. For instance, nowadays the test is sometimes also used in settings other than hospitals, eg, primary health care centers.

In the present study, covering 1,152 skin prick tests performed during 1996–1998 in children 0 to 19 years of age, we report six cases of generalized reactions, all of which occurred in infants less than 6 months of age. We studied in detail the history of the cases observed to see whether the children shared any common features that could be regarded as risk factors. Identifying

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such factors could help to make the procedure safer.

METHODS AND MATERIALS

The present study is a retrospective analysis of medical records of six infants, all of whom developed generalized allergic reaction in connection with skin prick tests 1996–1998. Tests were performed on the babies at the Pediatric Clinic at the University Hospital in Linköping, Sweden. Information about the total number of tests were performed during the period and the distribution according to age was collected from a computerized database at the clinic.

Procedure for Skin Prick Testing

Skin prick tests were performed by two trained and experienced nurses. The volar aspect of the arm was used as the test area. The skin was marked with a ballpoint pen for the allergens to be tested. All tests involving food allergens were performed as prick-prick tests, ie, the tip of the lancet was first dipped in the fresh or frozen food specimens. For milk, fresh low-fat milk was used and for egg, frozen egg white. The tip of the lancet was then pressed at right angles against the skin surface for one second using the volar aspect of the finger tip. A metallic lancet with a 1-mm tip (ALK) was used to prick the skin. As a negative control, the skin was pricked with a clean lancet. The positive control was histamine

HCL 10 mg/mL. The reaction was read 15 minutes after the test was finished.

Double-prick test, ie, two tests of each allergen at the same session, was standard, although a single prick test was performed if the skin was highly affected by erythema or eczema. Milk and egg were always tested at the same session. This is because it is common to find positive results to egg several months before milk, even though the child reacts clinically to both foods. The skin prick test was regarded as positive when the mean diameter (= half of the sum of the largest diameter and its perpendicular) of the wheal was at least 3 mm.

Children with extensive eczema or other manifestations of allergy, (eg, asthma) or with an ongoing respiratory infection were examined and evaluated by a doctor before the test was performed.

In the event of an immediate systemic reaction to the skin test, the nurse who performed the skin test was responsible for administering appropriate treatment until the doctor arrived.

The six infants received immediate treatment with antihistamine and/or epinephrine. They were examined without delay by a pediatrician, who added steroids to the treatment in three cases. The pediatrician made the clinical decision as to when the child could be dismissed from the ward after recovery.

RESULTS

Six cases of generalized reactions to skin prick tests were reported between 1996 and 1998. Information about the children is summarized in Table 1. The outcomes of the skin prick tests appear in Table 2. Total number of tested children, distribution according to age, and the rate of cases with generalized allergic reactions are summarized in Table 3.

All six generalized reactions affected babies less than 6 months of age. All had eczema, although the severity varied. Four of the children were breastfed only, one was given formula, and one was both breastfed and given formula. There was a family history of atopic disease in all cases. None of the children had previously had any wheezing episodes. Two children had an ongoing cold at the time of the skin prick test. The onset time of the generalized reaction was between a few to 20 minutes.

In five of the cases, a positive test result for food allergy could be read. In one case the test result was impossible to read due to extensive skin reaction. Six cases of generalized reaction out of 1,152 tested children give an overall rate of 521 generalized reactions per 100,000 skin prick tests performed. In the age group <6 months, the corresponding figure was 6522 per 100,000.

Table 1. Summarized Information About the Six Children who Developed a Generalized Reaction at Skin Prick Tests

Child	Sex	Age at Test	Heredity	Food	Eczema†	Infection‡	Year
1	F	5 months	2 sibs	Breastmilk	Mild to moderate	No	1996
2	M	2.5 months	m. f.	Breastmilk	Extensive, severe	Yes	1997
3	M	3 months	m.	Formula	Extensive	No	1998
4	M	3.5 months	m. f. s.	Breastmilk	Mild to moderate	No	1998
5	M	5 months	s.	Breastmilk	Mild to moderate	Yes	1998
6	F	5 months	f.	Breastmilk + Formula	Extensive, severe	No	1998

Abbreviations: F = female, M = male, m = mother, f = father, s = sister, and sibs = siblings.

† Eczema means active eczema when the test was performed.

‡ Infection means signs of upper respiratory tract infection.

Table 2. Summarized Information About Allergens Applied at Skin Prick Tests, Positive Test Results, the Acute Symptoms Noted and Treatments Given Against the Systemic Reaction

Child	SPT Applied	Histamine Wheal	Positive results of SPT	Symptoms	Treatments
1	Egg, milk, fish, c. hyd.	6.0	Egg 1 10.0, Egg 2 9.5, Milk 1 7.0, Milk 2 7.0, Fish 1 4.5, Fish 2 4.5.	Urticaria, rhonchi	0.3 mg epinephrine SC 2.5 mg cetirizini dihydrochloride PO 5 mg betamethasone PO 0.15 mg epinephrine SC
2	Egg, milk	Not readable due to the reaction.	Not readable due to the reaction.	Generalized erythema	0.125 mg clemastine PO 0.15 mg clemastine PO
3	Egg, milk	20.0	Egg 1 4.5, Egg 2 5.5, Milk 1 4.0, Milk 2 3.0.	Generalized erythema, crepitations	0.175 mg clemastine PO
4	Egg, milk, fish, c.hyd.	7.0	Milk 9.5.	Generalized erythema	0.1 mg epinephrine SC 0.2 mg clemastine PO 5 mg betamethasone PO 0.35 mg clemastine PO
5	Egg, milk.	5.0	Egg 1 8.0, Egg 2 7.5, Milk 1 7.5, Milk 2 5.0.	Urticaria, hoarseness, cough	4 mg betamethasone PO
6	Egg, milk, c.hyd., w.hyd.	7.0	Egg 11.5, Milk 8.0.	Generalized erythema	

Abbreviations: SPT = skin prick tests, C.hyd. = casein hydrolysate, and W.hyd. = whey hydrolysate.

Positive results = mean wheal size in millimeter.

Urticaria means urticaria over the whole body, not only locally.

Generalized erythema means an erythema over the whole body surface with severe itching but no definite urticariae.

Table 3. Summarized Information About Total Number of Children Tested 1996–1998, Distribution According to Age and Generalized Reaction Rates

Age Group	Children Tested	Children with G.R.	Rates per 100,000	CI (95%)
<6 months	92	6	6522	1476–11567
6–12 months	144	0		
1–19 years	926	0		
Total	1152	6	521	105–937

G.R. = generalized reaction and CI = confidence intervals.

DISCUSSION

Skin prick testing is a relatively easy way to test children for allergy. It is most often carried out without problems. In the present study, however, we report six cases demonstrating a generalized reaction. During the study period, 6.5% had a generalized reaction in the age group <6 months. The figure for all tested children during the period was 0.52%. This indicates a higher risk of adverse reactions in very young infants than previous studies have shown. There are, however, limitations when comparing different studies. In some studies standardized extracts have been used. In others, including ours, non-commercial products have been chosen.⁶ We used fresh

foods as test substances. This is because very few standardized food-allergen extracts are available and many commercial food-allergen extracts are titrated in weight/volume, which is a very unsatisfactory method of titration.^{6,8} Despite the limitations adherent to a retrospective study, the following common features were observed among all the six cases: active eczema, age below 6 months, positive reactions to food items, and a family history of allergic disease. The first three are naturally interrelated. Eczema is a dominant reason for investigating allergic disease in this age group, and foods are the main suspects of sensitization. The test was applied in duplicate to four of the cases, which caused an extra aller-

gen load on the limited surface of the small arm. Duplicate tests, like multiple skin tests, increase the risk of summation of the reactions and therefore also the risk of generalized reaction. All six cases were infants < 6 months of age. No adverse reaction in connection with skin prick test has been observed at our clinic in children >6 months of age. Young age should therefore be considered a risk factor for developing generalized allergic reactions when undergoing skin prick tests.

Dreborg has previously suggested a number of precautions. If possible, avoid skin prick tests when there are ongoing allergic reactions. Perform skin prick tests only in the presence of

both a nurse and a doctor who have epinephrine at hand. Finally, skin prick tests using nonstandardized extracts should only be performed under the supervision of a specialist with knowledge of the risks and precautions involved in such testing.⁹

We suggest increased precautions when testing infants of very young age, especially if the child is affected by an extensive eczema. If testing is necessary, it should only take place in a setting where the safety precautions are optimal. To avoid a summation of reactions, we suggest the application of only one allergen at each visit, and no application in duplicate.

Despite the risk of adverse reactions, delaying the investigation is not recommended since early diagnosis will spare the child unnecessary suffering from the symptoms of allergy. The aim, however, should be to perform the test under optimal conditions.

A larger, prospective study on the safety of skin prick testing is currently

in progress in southeastern Sweden. We hope that this will show that skin prick tests are a safe and valuable method if used with care.

REFERENCES

1. Dreborg S, Backman A, Basomba A, et al. Skin tests used in type I allergy testing. Position paper. EAACI Subcommittee on skin tests. Dreborg S, ed. *Allergy* 1989;44(Suppl 10):1–59.
2. Dreborg S. Skin testing. The safety of skin tests and the information obtained from using different methods and concentrations of allergen. *Allergy* 1993;48:473–475.
3. Lin MS, Tanner E, Lynn J, Friday GA. Nonfatal systemic reactions induced by skin testing and immunotherapy. *Ann Allergy* 1993;71:557–562.
4. Lockey RF, Benedict LM, Turkeltaub PC, Bukantz SC. Fatalities from immunotherapy(IT) and skin testing(ST). *J Allergy Clin Immunol* 1987;79:660–677.
5. 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;84:886–896.
6. Novembre E, Bernardini R, Bertini G, et al. Skin prick test induced anaphylaxis. *Allergy* 1995;50:511–513.
7. Valyasevi MA, Maddox DE, Li JTC. Systemic reactions to allergy skin tests. *Ann Allergy Asthma Immunol* 1999;83:132–136.
8. Lemanske RF, Taylor SL. Standardized extracts, foods. *Clin Rev Allergy* 1987;5:23–36.
9. Dreborg S. The risk of general reactions to skin prick testing (SPT) [Letter]. *Allergy* 1996;51:60–61.

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