

The relationship between latex skin prick test responses and clinical allergic responses

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Background: Allergic responses to latex have been reported more frequently in the past 5 years. Although commercial skin prick test solutions are available and can be used in the diagnosis of latex allergy in some countries, the characteristics of patients sensitized to latex relative to their skin test responses have not been reported.

Objective: The purpose of this study is to relate the clinical characteristics of patients with latex sensitivity to the size of their latex skin prick test response.

Methods: A retrospective review of patients who were attending a hospital-based allergy and asthma clinic and who had positive skin test responses to a commercial latex skin test solution was undertaken.

Results: Of 47 patients who had skin test responses to latex, 36 had a mean wheal diameter at least 3 mm greater than the negative control (diluent). Sixty-eight percent were health care workers. There was a positive association between the size of skin test response and severity of latex-induced symptoms ($p < 0.001$). A history of banana sensitivity was also associated with larger skin test responses ($p < 0.05$).

Conclusion: The size of the skin prick test response to latex solution that is commercially available in Canada reflects the severity of latex-induced clinical allergic responses.
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Key words: Latex, allergy, skin tests

Use of natural rubber latex products in health care has increased dramatically in the last decade, primarily to prevent the spread of viral infection.¹ With the rise in latex use came the first reports of latex sensitivity.² The number of reports continues to increase.³ There is a wide range of clinical sensitivity: contact urticaria, allergic rhinitis and conjunctivitis, asthma, and generalized anaphylactic reactions.⁴⁻¹⁰ With the increasing use of latex, there has been an increase in systemic and serious reactions.¹¹ Populations at greatest risk of developing latex allergy include: (1) health care workers,¹²⁻¹⁴ (2) workers at plants manufacturing latex products,¹⁵ and (3) children with spina bifida and children or adults who have undergone multiple

Abbreviations used

NU: Noon units

SPT: Skin prick test

surgical procedures.¹⁶⁻²⁰ The presence of atopy appears to add to this risk.

Investigators have attempted to find an accurate, safe, consistent, and easy way to identify latex allergy.²¹ History, of course, is an integral part of the diagnosis. Different tests have been used to objectively supplement the history. These include RAST^{20, 22, 23} or fluorescent enzyme immunoassay for latex-specific IgE²⁴ and skin prick tests (SPTs) with extracts of specific latex products²⁵⁻²⁸ or commercially prepared latex skin prick solutions.²⁹ The RAST and the other IgE-specific serologic methods are very specific, but not as sensitive as skin tests, and they are expensive and time-consuming.²⁰ SPTs with eluates from specific latex products are specific but not necessarily sensitive for the different latex products.²⁶ The commercially prepared SPT solutions of low ammoniated raw

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latex preparations (Bencard Laboratories, Mississauga, Ontario, Canada and Laboratoires Stallergènes, Paris, France) are safe, very specific, sensitive (up to 92%) and easy to use.²⁹ However, they are not yet standardized for allergen content.

In this report we relate the clinical features of patients with a range of positive SPT responses to a commercial latex skin test solution to the severity of symptoms on exposure to latex.

METHODS

A retrospective review of the medical charts of 47 patients with an SPT response to latex in an outpatient allergy and asthma clinic population in the Toronto Hospital between 1990 and 1994 was performed. All patients had been evaluated in a standardized manner by one physician. Twenty-six patients (55%) were specifically referred to the clinic for possible latex allergy investigation. The remaining 21 were identified as having a response to latex on routine skin testing.³⁰

Occupational history, exposure to latex products, and previous operations were recorded. Symptoms after exposure to latex products including pruritis, eczema, urticaria, conjunctivitis, rhinitis, dyspnea, wheezing, or generalized anaphylactic reactions were recorded. A history of atopy (childhood eczema, allergic rhinitis, or asthma) and food-related symptoms were also noted.

The low ammoniated raw latex SPT solution was obtained from Bencard Laboratories. This laboratory also supplied the SPT extracts of common allergens: *Alternaria spp.* (1:20 wt/vol), *Cladosporium spp.* (1:20 wt/vol), *Aspergillus spp.* (1:20 wt/vol), cat (50% wt/vol), dog (75% wt/vol), *Dermatophagoides farinae* (1% wt/vol), tree pollen mix (25,000 Noon units [NU]/ml), grass pollen mix (25,000 NU/ml), ragweed (25,000 NU/ml). A negative control solution (carbol saline) and a positive control solution (0.1% histamine) were applied to all patients. Before SPT application, patients were asked if they had experienced symptoms after exposure to latex products. When appropriate, the latex solution was diluted in sterile water (up to 1:1000) for the first skin test. If the result of the test with the dilute solution was negative, then the SPT was reapplied by increasing the concentration 10-fold sequentially up to the undiluted solution. SPTs were performed with 25-gauge disposable needles. Patients had discontinued short-acting antihistamines for at least 4 days before testing and astemizole for at least 6 weeks, and all exhibited a positive histamine SPT response.

SPT responses were interpreted 10 minutes after application. The mean wheal diameter was taken as the mean of the longest wheal diameter and the midpoint orthogonal wheal diameter. The difference between the mean wheal diameter for latex and the negative control was graded as 1+ (1 to 2 mm), 2+ (3 to 5 mm), 3+ (6 to 9 mm), and 4+ (10 mm or greater). A skin test response

of 2+ or greater was considered positive. Responses to latex of 1+ were considered of questionable significance and were analyzed as a group separate from the positive responses. Atopy was defined as the presence of one or more positive (2+ or greater) responses to the common allergens. Statistical analyses were done with chi square and Fisher's exact tests.

RESULTS

There were no adverse reactions to the latex SPTs. The mean age of the entire group of 47 patients was 39.4 ± 10.9 years (range, 23.3 to 63.3 years). The group included 38 women (mean age, 39.3 ± 9.9 years) and nine men (mean age, 40.2 ± 14.6 years). Of the 47 patients with latex skin test responses, 11 (23%) had a 1+ response, a reaction of questionable clinical significance; seven (15%) had a 2+ reaction; seven (15%) had a 3+ reaction; and 22 (47%) had a 4+ reaction (Table I). Of the 22 patients with a 4+ SPT response, 11 had this response with undiluted latex solution, eight with a 1:10 dilution of latex solution, and three with 1:100 dilution. Of the 36 patients whose SPT response to latex was 2+ or greater, the mean age was 38.7 ± 10.4 ; 30 were women, and six were men.

Among patients with 3+ or 4+ skin test responses, all except one were women; conversely, five of the seven patients with 2+ responses were men. Atopy was common, present in 55% of the whole group and 47% of those with 2+ or greater SPT responses to latex. Excluding those with borderline (1+) responses, a significantly larger latex SPT response was recorded in patients referred to the clinic for investigation of latex-attributed symptoms than in those referred for other complaints ($p < 0.005$). Patients who described respiratory or anaphylactic responses to latex had significantly larger SPT responses to latex than those with contact symptoms alone ($p < 0.001$). If patients with 1+ reactions were not included, these results were still significant ($p < 0.01$).

There were 32 (68%) health care workers (nurses, physicians, pharmacists, laboratory technicians, housekeeping staff, and dental assistants). They were significantly more likely than non-health care workers to have large (3+ or 4+) responses to latex on SPT, and they accounted for 86% of these large SPT responses ($p = 0.05$). Fifty-three percent of the non-health care workers had only borderline (1+) responses to latex SPTs. Of those with larger responses, two of the seven non-health care workers described frequent use of latex products; four were not using latex products regularly but had undergone more than two operations; only one was

TABLE I. Relationship of skin test response size to patient characteristics

	Latex SPT response				Total
	1+	2+	3+	4+	
No.	11	7	7	22	47
Age (yr)	42.0 $\pm$ 12.7	35.2 $\pm$ 12.6	40.9 $\pm$ 12.4	39.0 $\pm$ 9.5	39.4 $\pm$ 10.9
Male	3	5	1	0*	9
Atopy	9	7	3	14	33
Health care workers	3	4	5	20*	32
Food-attributed symptoms					
Excluding banana	6	4	2	3	15
Caused by banana	0	0	1	3	4
Latex-attributed symptoms					
None	8	2	0	0†	10
Contact symptoms only	1	4	2	2†	9
Respiratory symptoms	2	1	5	20†	28
Anaphylaxis	0	0	0	3	3
Referred for latex allergy investigations	0	1	5	20‡	26

Statistical analyses exclude the 1+ group.

Patients with symptoms attributed to banana had larger responses to SPT of latex compared patients with other food-attributed symptoms.

* $p < 0.05$.

† $p < 0.001$.

‡ $p < 0.005$.

not a regular user of latex products and had undergone two or fewer surgical procedures.

All of the patients with symptoms of latex allergy described contact urticaria associated with latex products. Of the 36 patients with 2+ or greater SPT responses, three (8%) also had anaphylactic reactions during operations or on exposure to latex products, whereas 26 (72%) had upper and lower respiratory tract symptoms (rhinitis, conjunctivitis, dyspnea, wheezing), likely related to airborne latex exposure from powdered latex gloves. Eight patients (22%) had contact symptoms without other manifestations, and two patients (6%) had no recognized symptoms on exposure to latex. Twenty-four of these patients (67%) were atopic on the basis of one or more positive SPT responses to common allergens, but this was not associated with larger versus smaller SPT responses to latex within this group.

Food-attributed symptoms were described by 13 of the patients (36%) with 2+ or greater SPT reactions to latex. Twelve of these patients described symptoms suggestive of IgE-mediated responses: four to banana, one to kiwi, one to avocado, four to other raw fruits and/or vegetables (e.g., apples, oranges, celery, potatoes), two to nuts, one to barley, one to chocolate, and one to shellfish. The symptoms reported were urticaria,

angioedema, asthma, rhinitis, or anaphylactic reactions in all but one of the 12 with likely IgE-mediated responses; the exception was a patient who reported only diarrhea after eating bananas. The incidence of symptoms attributed to banana was higher in patients who had a larger reaction to latex SPT, and both patients with symptoms associated with kiwi and avocado had 4+ skin responses to latex. In contrast, other food-attributed symptoms were more common in the 1+ and 2+ groups ($p < 0.05$) (Table I). Three patients described adverse responses to wine, beer, and foods likely containing sulfites (one had a 2+ response to latex and two had a 1+ response). Of the other four patients with borderline (1+) skin test responses to latex, three described symptoms that may have been IgE-mediated—urticaria with buckwheat and shellfish and an itchy mouth with fresh fruits. One described caffeine-related symptoms, which were probably non-IgE-mediated.

DISCUSSION

This study suggests that the larger the SPT response to the latex skin test solution, the more likely patients are to report severe symptoms on exposure to latex. Results of latex SPT may therefore predict the severity of the clinical response to latex exposure. This is useful in advising the pa-

tient as to the extent of precautions that must be taken to avoid such exposure and in determining the likely need for the patient to carry a syringe preloaded with epinephrine or other medications. When a reliable history cannot be obtained (e.g., in cases of cerebrovascular accident or language barrier), the skin test response provides important health information and may allow health care providers to minimize patient risk by avoiding use of latex-containing products.

Although 1+ SPT responses are of borderline clinical significance and may represent normal variability of the prick test technique, they may represent a true low level of sensitization in some patients, as suggested by a history of latex-related symptoms in 27% of patients with this response. Conversely, 70% of patients with 2+ SPT responses and all patients with larger SPT responses to latex described symptoms on latex contact, indicating more clear-cut clinical relevance of such responses.

Knowledge of the clinical severity of symptoms can help in determining a safe starting dilution of latex for prick testing and prevent the occasional case of anaphylaxis reported with such skin tests.^{31, 32} During this study the latex skin test was applied to more than 300 patients with no adverse reactions. This test can be safely performed. We suggest dilution of the current commercial preparation for patients with symptoms of latex allergy. A reasonable starting dilution for patients with mild contact urticaria alone would be 1:10; for those with severe contact urticaria, angioedema, or mild respiratory symptoms 1:100; and for those with a history of latex-related asthma or anaphylaxis, at least 1:1000.

An increased prevalence of atopy among the latex-sensitive group has been documented in other studies,^{8, 20, 33} as has the increased prevalence of health care workers^{12-14, 34} in latex-sensitive adult populations. The larger SPT reaction to latex observed in women may related to the relative lack of men providing health care in this population.

Most of the 36 patients with positive SPT responses (72%) were well aware of their sensitivity to latex, although there were some with exposure to latex through multiple operations or through the workplace who were unaware of sensitization or only became aware of latex sensitivity after an anaphylactic reaction. We have recently reported the results of routine latex SPTs in our hospital-based outpatient allergy and asthma clinic.³⁰ We identified 4.5% of that population as having previously unsuspected 2+ or greater positive responses to latex. In such a population, in which atopy is

relatively common and the skin test can be easily and safely added to routine testing, it is likely to be cost-effective and to prevent severe clinical responses. However, the predictive value for latex skin prick testing in determining the development of anaphylaxis or respiratory allergy has not been prospectively determined.

Assessment of the value of preoperative screening for latex allergy by using the latex SPT has not been reported, but our findings show that large SPT responses likely increase the risk of anaphylaxis with latex exposure during surgery. Therefore we consider it justifiable to offer such screening to patients undergoing multiple surgical procedures, patients with congenital urologic abnormalities, and health care workers. In additions, the high risk previously reported in patients with spina bifida¹⁷⁻¹⁹ justifies the routine avoidance of latex products for such patients.

It has been previously noted that banana and latex share some cross-reactive antigens³⁵⁻³⁹; therefore, some patients who are sensitive to latex also describe a banana sensitivity. In this study the incidence of historical banana sensitivity was higher in the group with a larger SPT response to latex. Other food-attributed symptoms were not more common in the groups with larger latex SPT responses, but specific food skin tests were not performed in this study to determine whether responses were truly IgE-mediated.

In summary, this study establishes a relationship between the extent of a latex SPT response and clinical symptoms caused by latex exposure. Our findings suggest that this test should be used to identify subjects at risk of severe allergic reactions to latex.

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