

Prevalence and risk factors of latex sensitization in an unselected pediatric population

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Background: The prevalence of latex sensitization has been investigated in population groups considered at high risk, but it has not been systematically surveyed among the general population.

Objective: We sought to determine the prevalence of and the risk factors associated with latex sensitization in a general pediatric population.

Methods: We investigated 1175 children (mean age $\pm$ SD, 105 ± 17.5 months) in 11 elementary schools in Tuscany (Italy). All parents answered a questionnaire, and children underwent skin prick tests (SPTs) with latex, six aeroallergens (*Dermatophagoides pteronyssinus*, *D. farinae*, cat, grass pollen, *Alternaria tenuis*, and *Parietaria judaica*), three food allergens (milk, egg white, and wheat), and three insect venoms (honeybee, wasp, and *Polistes*).

Results: Eight subjects (0.7%; mean age $\pm$ SD, 123 ± 9.28 months) had positive SPT responses to latex. No children showed allergic reactions to latex. One or more positive SPT responses to aeroallergens were present in 340 children (28.9%); one or more positive SPT responses to food allergens were present in 26 (2.2%); one or more positive SPT responses to aeroallergens, food allergens, or both were present in 353 (30.0%); and one or more positive SPT responses to one or more insect venoms were present in 43 subjects (3.7%). Significant ($p < 0.05$) risk factors associated with latex sensitization included: positive SPT responses to aeroallergens, food allergens, or both; a positive response to one or more insect venoms; a positive response to mite, milk, egg white, wheat, honeybee venom, wasp venom, *Polistes* venom, or a combination thereof; and increased age.

Conclusion: This report shows a very low prevalence of latex sensitization with an absence of clinical symptoms to latex. This study demonstrates a significant association between latex sensitization and the presence of one or more positive SPT responses to aeroallergens, food allergens, or both; one or more positive SPT responses to one or more insect venoms; and increased age. (*J Allergy Clin Immunol* 1998;101:621-5.)

Key words: Latex, sensitization, atopy, prevalence, children

In the last few years, latex allergy has been increasingly recognized as a potential medical problem because of the increase in frequency and potential severity of

Abbreviation used

SPT: Skin prick test

latex-induced reactions.¹ Health care workers,² rubber industry workers,³ and patients with spina bifida⁴ are considered population groups at high risk. Limited data are available on the prevalence of latex allergy in the general population, which seems to be less than 1%.^{5,6} On the other hand, Ownby et al.⁷ have found a 6.4% prevalence of seropositivity for anti-latex IgE antibodies in 1000 volunteer blood donors. The latex allergy risk seems to be higher among atopic than among nonatopic subjects. In fact Liebke et al.⁸ found a high prevalence of latex sensitization (20.8%) in atopic children. We had demonstrated that latex sensitization in children referred to our clinic for allergic evaluation was present in a small proportion (3%) of atopic children, whereas it was absent in nonatopic children. Half (1.5%) of the children with a positive skin test response to latex had clinical reactions to latex.⁹

Therefore the aim of this study was to evaluate the prevalence of and the risk factors associated with latex sensitization in an unselected general population (elementary schools) so as to understand better the true importance of this problem outside of recognized risk groups.

METHODS

This study was carried out in four small towns (Pontedera, Calcinaia, Bientina, and Buti) near Pisa in Tuscany (Italy) between February and May 1997. All 1452 children of the 11 elementary schools were invited to participate in an epidemiologic study on the prevalence of latex sensitization and allergy on the basis of a questionnaire and a skin prick test (SPT).

Questionnaire

Parents answered a questionnaire that evaluated whether the child had had any clinical reactions to rubber or previous surgical procedures. Other elements investigated were rhinoconjunctivitis and wheezing, as well as any previous reaction after Hymenoptera sting.

The questions used were as follows: (1) Has your child ever had any clinical reactions (urticaria, angioedema, rhinitis, conjunctivitis, asthma, anaphylactic shock, or other latex symptoms) regarding rubber latex products (baby bottle nipples, pacifiers, balloons, rubber toys, surgical or household gloves, etc.)? (2) Has your child undergone any surgical procedures?

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TABLE I. General and clinical features of 1175 children

Sex	
F	587 (49.96%)
M	588 (50.04%)
Mean $\pm$ SD age (mos)	105 $\pm$ 17.51 (range, 74-162)
Previous surgical procedures	230/1175 (19.57%)
Rhinoconjunctivitis	244/1162 (21%)
Current wheezing	114/1166 (9.7%)
Any reaction after Hymenoptera sting (honeybee, wasp, <i>Polistes</i>)	228/1175 (19.4%)
Positive SPT response to latex	8/1175 (0.68%)
Positive SPT response to one or more aeroallergens	340/1175 (28.94%)
Positive SPT response to one or more food allergens	26/1175 (2.21%)
Positive SPT response to one or more insect venoms	43/1175 (3.66%)
Positive SPT response to one or more aeroallergens, food allergens, or both	353/1175 (30.04%)

Different denominators indicate lack of information for some patients.

(3) Has your child had any attacks of rhinoconjunctivitis (sneezing or running or blocked nose, sometimes with itchy/watery eyes or nose, that was not associated with a cold)? (4) Has your child had wheezing or whistling in the chest in the last 12 months? (5) Has your child ever had a reaction immediately after an insect sting (honeybee, wasp, or *Polistes*)? If yes, what kind of reaction, local or generalized (urticaria or angioedema, breathlessness, dizziness, or loss of consciousness)?

Skin testing

SPTs were performed in the schools during school hours and carried out on the volar side of the forearm with a plastic lancet (1 mm tip) from Laboratorio Lofarma (Milan, Italy).

A commercial latex extract (Laboratorio Lofarma) was used as previously reported.⁹ Briefly, an ammoniated latex extract was diluted with phosphate-buffered saline, mixed for 24 hours, and centrifuged at 30,000 g at 4° C for 30 minutes. The rubbery supernatant was discarded, and the yellow aqueous layer was filtered and then dialyzed in normal saline. The protein concentration of this latex extract was 12.5 μ g/ml.

Every child also underwent SPTs with commercial extracts of house dust mite (*Dermatophagoides pteronyssinus* and *D. farinae*), *Alternaria tenuis*, cat, grass pollen, *Parietaria judaica*, milk, egg whites (Neo-Abello, Milan, Italy), wheat (Bayer, Milan, Italy), honeybee venom, wasp venom, and *Polistes* venom (Laboratorio Lofarma). Each lyophilized venom was tested at a 100 μ g/ml concentration and prepared extemporarily according to the manufacturer's instructions. A positive control with 10 mg/ml histamine was included.

SPT results were assessed as positive (wheal response $\geq 2+$) according to the recommendations of the European Academy of Allergy and Clinical Immunology.¹⁰

Statistical analysis

The data of this study were analyzed with Windows software Intercooled Stata 4.0 (Stata Corp., College Station, Tex.). Associations between the various assembled variables were

TABLE II. Positive SPT responses to latex and to various aeroallergens, food allergens, and insect venom allergens in 1175 children

Allergen	No. of positive responses (n = 1175)
Latex	8 (0.68%)
Mite	268 (22.81%)
Cat	98 (8.34%)
Grass pollen	132 (11.23%)
<i>Alternaria tenuis</i>	77 (6.55%)
<i>Parietaria judaica</i>	31 (2.64%)
Milk	13 (1.11%)
Egg white	9 (0.77%)
Wheat	10 (0.85%)
Honeybee venom	35 (2.98%)
Wasp venom	17 (1.45%)
<i>Polistes</i> venom	12 (1.02%)

analyzed with univariate logistic regression and Fisher's exact test when needed (*p* values < 0.05 were considered significant).

RESULTS

One thousand one hundred ninety (81.95%) of the 1452 children participated in this study, and a formal written consent was obtained. Fifteen children were excluded on the basis of incomplete compilation of the questionnaire, cutaneous dermatographism, or absence during administration of the SPTs. One thousand one hundred seventy-five of 1452 children (80.92%; mean age $\pm$ SD, 105.09 $\pm$ 17.51 months; age range, 74 to 162 months) completed the study.

Latex sensitization (positive SPT response) and clinical reactions to latex

Eight of 1175 children (0.68%; six boys and two girls; mean age $\pm$ SD, 123.75 $\pm$ 9.28 months; age range, 109 to 134 months) had positive latex SPT responses. No SPT side effects were noted. All subjects had a negative history of latex symptoms.

Other variables

Table I summarizes the general and clinical features of the 1175 children studied. Table II regards the presence of positive SPT responses to latex and to the aeroallergens, food allergens, and insect venom allergens tested.

Statistical analysis showed a significant association between latex sensitization and the presence of one or more positive SPT responses to aeroallergens (*p* = 0.049); one or more positive SPT responses to food allergens (*p* < 0.001); one or more positive SPT responses to aeroallergens, food allergens, or both (*p* < 0.001); one or more positive SPT responses to one or more insect venoms (*p* < 0.001); a positive SPT response to mite (*p* = 0.018), milk (*p* = 0.003), egg white (*p* < 0.001), wheat (*p* < 0.001), honeybee (*p* < 0.001), wasp (*p* < 0.001), and *Polistes* allergens (*p* < 0.001); and an

TABLE III. Statistical comparison of variables among eight children with positive latex SPT responses and 1167 children with negative latex SPT responses in a general population

	Subjects with positive latex SPT responses (n = 8)	Subjects with negative latex SPT responses (n = 1167)	Statistics
Sex			
M	6	582	p = NS*
F	2	585	
Mean ($\pm$ SD) age (mos)	123.7 $\pm$ 9.2	104.9 $\pm$ 17.5	p = 0.005†
Previous surgical procedures	1	229	p = NS*
Rhinoconjunctivitis	1	243	p = NS*
Current wheezing	3	323	p = NS*
Any reaction after Hymenoptera sting (honey bee, wasp, <i>Polistes</i>)	1	227	p = NS*
Positive SPT response to one or more aeroallergens	5	335	p = 0.049*
Positive SPT response to one or more food allergens	5	21	p < 0.001*
Positive SPT response to one or more insect venoms	6	37	p < 0.001*
Positive SPT response to one or more aeroallergens, food allergens, or both	8	345	p < 0.001*

NS, Not significant.

*p value determined by two-sided Fisher's exact test.

†p value determined by Student's t test.

association with increased age ($p = 0.005$) (Tables III and IV).

DISCUSSION

In the literature there are several reports of injury and death associated with latex allergy.¹¹ In fact the international scientific community has felt the need to publish guidelines for the identification and care of people with latex allergy.¹ There is also an association (A.L.E.R.T., P.O. Box 23722, Milwaukee, WI 53223-0722) founded by a group of health care workers affected by latex allergy, which provides information about latex hypersensitivity and supports individuals allergic to natural rubber latex. Latex allergy is indeed considered an important medical problem in the world. Three groups (children with spina bifida, workers with industrial exposure to latex, and health care workers) are considered at a higher degree of exposure to natural rubber latex with a probable consequent higher risk for latex sensitization than the rest of the population.¹ However, contact with latex products,¹² as well as the inhalation of latex allergens extractable from rubber tire fragments,¹³ are frequent also in the general population. One might therefore expect sensitization to latex to be quite common, even if not as marked as in the groups at risk.¹³

Our study, carried out in an unselected pediatric population, nevertheless shows a very low prevalence of latex sensitization. In fact only eight (0.68%) of the 1175 children had a positive latex SPT response. Moreover, all of the 1175 patients had a negative history of latex symptoms. These findings demonstrate that latex sensitization and latex allergy only play an important role in selected groups of the population.¹ A possible explanation for these findings is that because latex sensitization was significantly associated with increased age, repeated latex exposure might be an important factor for latex

TABLE IV. Statistical comparison of positive SPT responses to various aeroallergens, food allergens, and insect venom allergens among eight children with positive latex SPT responses and 1167 children with negative latex SPT responses in a general population

	Subjects with positive latex SPT responses (n = 8)	Subjects with negative latex SPT responses (n = 1167)	Statistics
Mite	5	263	p = 0.018*
Cat	2	96	p = NS*
Grass pollen	1	131	p = NS*
<i>Alternaria tenuis</i>	0	77	p = NS*
<i>Parietaria judaica</i>	1	30	p = NS*
Milk	2	11	p = 0.003*
Egg white	4	5	p < 0.001*
Wheat	3	7	p < 0.001*
Honeybee venom	4	31	p < 0.001*
Wasp venom	3	14	p < 0.001*
<i>Polistes</i> venom	6	6	p < 0.001*

NS, Not significant.

*p value determined by two-sided Fisher's exact test.

sensitization. In fact health care workers,² rubber industry workers,³ and patients with spina bifida⁴ are groups of the population with higher and longer exposure to natural rubber latex, with a probable consequent higher risk for latex sensitization¹ than our pediatric population. Therefore it is very likely that the low prevalence of latex sensitization shown in this study might have been higher had an adult population been investigated. However, it is also probable that this low latex prevalence might be unchanged in an older population because latex exposure appears to be high only in well-defined

population groups.¹⁴ In any case, epidemiologic studies in older populations are necessary to clarify this problem.

The SPT method in this epidemiologic study was used for various reasons. It is a rapid, economic, and safe test, even if rare anaphylactic reactions after latex SPTs^{15, 16} have been observed. However, special considerations regarding the safety of SPTs (with latex as well as other antigens) should be reserved only for patients with a previous clinical history of anaphylactic reactions.¹⁷ Latex extract was also used in a previous study on the prevalence of latex sensitization in a selected pediatric population⁹ during which no side effects of latex SPTs were noted.

Epidemiologic studies of latex sensitivity based on serologic tests (e.g., RAST) are very difficult to perform in a pediatric population because parents rarely consent to having their children's blood drawn. Also, use of RAST is an expensive and not always very sensitive diagnostic method. In fact only 60% to 83% of persons with positive SPT responses to latex had a positive RAST result.⁴

In this study one or more positive SPTs to aeroallergens, food allergens, or both (atopy) were associated with latex sensitization (Table III). All children with latex sensitization were atopic, whereas only 345 of the other 1167 subjects had one or more positive SPT responses to aeroallergens, food allergens, or both (Table III). It is therefore likely that the higher and easier production of specific IgE to latex is due to not only a high degree of latex exposure but also to atopic status. Various studies have demonstrated that atopy is associated with a higher probability of latex sensitization.^{4, 8, 9} In our study in the general population, latex sensitization was only present in atopic subjects who were older than subjects not sensitized to latex, suggesting that atopic status and older age (longer latex exposure) are risk factors for latex sensitization. However, without longitudinal data, the possibility that latex sensitization precedes or is concomitant with sensitization to aeroallergens, food allergens, or both cannot be excluded.

Sensitizations to milk, egg white, or wheat (Tables III and IV) are significant risk factors for latex sensitization. Other studies have shown that patients with latex sensitization had specific IgE to various foods,¹⁸ but this is the first report on a significant association between latex sensitization and sensitization to one or more food allergens such as milk, egg white, or wheat. Latex and the foods tested may share allergen epitopes, but further studies on the cross-reactions between latex and these foods are necessary to confirm this hypothesis. On the other hand, we cannot exclude the possibility that the presence of food sensitization to the most important food antigens represents a more sensitive marker of atopy.

We have also shown a significant association between latex sensitization and the presence of one or more positive SPT responses to one or more insect venoms (honeybee, wasp, or *Polistes*). Terrados et al.¹⁹ have

demonstrated that an SPT with penicillin performed in subjects with latex allergy may show false-positive results as a consequence of latex contamination of the penicillin extract. Therefore a contamination of the insect venom extract with a latex protein during preparation might explain this significant association. However, because RAST and RAST inhibition to study latex contaminants were not performed, a cross-reaction between Hymenoptera venoms and latex antigens cannot be excluded.

In conclusion, this study on the prevalence of latex sensitization in an unselected pediatric population shows a very low prevalence of latex sensitization (0.68%) and an absence of clinical symptoms to latex. These data show that latex hypersensitivity is not a very important problem in the pediatric population. There is a significant association between latex sensitization and the presence of one or more positive SPT responses to aeroallergens, food allergens, or both (atopy); one or more positive SPT responses to one or more insect venoms (honey bee, wasp, or *Polistes*); and older age. Finally, latex sensitization was present only in atopic children. Therefore it would seem unnecessary to call latex sensitization into question when a patient has negative SPT responses to common aeroallergens, food allergens, or both.

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