

Short communication

The prevalence of latex allergy in children seen in a university hospital allergy clinic

Novembre E, Bernardini R, Brizzi I, Bertini G, Mugnaini L, Azzari C, Vierucci A. The prevalence of latex allergy in children seen in a university hospital allergy clinic.

Allergy 1997; 52: 101–105. © Munksgaard 1997.

Natural rubber latex allergy is responsible for a wide spectrum of clinical symptoms, ranging from rhinoconjunctivitis to severe anaphylaxis, in both adults and children. An association between allergy to latex and allergy to various fruits has been reported. This study investigated the prevalence and clinical significance of latex sensitization in children seen in a university hospital allergy clinic. A total of 453 consecutive children were screened in a 7-month period. A detailed clinical history with particular attention to the past surgical history and the eventual presence of latex- or food-induced allergic symptoms was obtained. Skin prick tests (SPT) for the more important inhalant allergens and foods were performed on all children. In patients with positive latex SPT, latex challenge and additional SPT for some fresh foods (avocado, pineapple, apricot, grape, banana, pear, apple, orange, almond, and chestnut) were also performed. RAST for the same food antigens, as well as patch test with latex and a standard battery of contact allergens, was also done. Of 326 atopic children, 10 (3%) presented positive skin test to latex, but only five (1.5%) also had a positive clinical history to latex exposure. Latex challenge was positive in 3/9 positive-latex-SPT children. None of the nonatopic children had positive skin test to latex or symptoms to latex exposure. A history of previous surgery was found in 5/10 positive-latex-SPT children, in 63/316 negative-latex-SPT atopic children ($P < 0.05$), and in 23/127 nonatopic children. RAST to latex was positive in 5/10 positive-latex-SPT children. Associated fruit-specific IgE (SPT and/or RAST) were found in all latex-symptomatic children and in 2/5 latex-asymptomatic children. Apple, kiwi, and chestnut were the most common SPT-positive foods. Only one patient with clinical allergy to latex and positive skin tests to fruits had a history of clinical symptoms after ingestion of kiwi and orange. The natural history of the positive-latex-SPT children without clinical reactions to latex exposure and the clinical significance of the association of latex and fruit sensitivity require further studies.

E. Novembre, R. Bernardini, I. Brizzi, G. Bertini, L. Mugnaini, C. Azzari, A. Vierucci

Allergy and Clinical Immunology Unit,
Department of Pediatrics, University of
Florence, Florence, Italy

Key words: children; fruit allergy; latex allergy;
skin prick test.

Elio Novembre, MD
Allergy and Immunology Unit
Department of Pediatrics
A. Meyer Hospital
Via L. Giordano 13
Florence
Italy

Accepted for publication 2 August 1996

Natural rubber latex allergy is responsible for a wide spectrum of clinical symptoms, ranging from rhinoconjunctivitis to severe anaphylaxis. Workers in the latex industry, health-care workers, patients with spina bifida, and atopic patients are considered more at risk of this kind of sensitization (1). In this study, we investigated latex sensitivity in children evaluated for atopic diseases in our allergy clinic.

Material and methods

Subjects

A total of 453 children (287 male and 166 female, aged 3–16 years, mean 7 years and 2 months), evaluated for the first time by the same operator (E.N.) for inhalant and/or food allergy in a university outpatient allergy clinic between May and November 1994, were studied. These children were

representative of the allergy clinic population seen in 1 year (2500 children), coming mostly from Florence (55%), Tuscany (32%), and other Italian regions (13%). Some 249 children (55%) lived in urban and 204 (45%) in rural areas. None were enrolled in this study at their school or elsewhere. None were referred for latex allergy. Children were referred for one or more of these symptoms: asthma (225 cases [49%]); rhinitis (210 [46.3%]); conjunctivitis (125 [27.5%]); atopic dermatitis (70 [15.4%]); urticaria (45 [9.9%]); chronic cough (40 [8.8%]); recurrent infection (12 [2.6%]); and other symptoms such as colic, diarrhea, vomiting, and poor growth (60 [13.2%]).

Patients and/or children were asked about latex allergy by means of a detailed clinical history with particular attention to their surgical history, as well as the use of baby bottle nipples or pacifiers in the first 2 years of age. The possibility of symptoms induced by rubber balloons or other latex objects (household gloves, footwear, sports equipment) was also investigated. Informed consent was obtained from children and/or parents. None of the patients had spina bifida or other deformities which have been considered to be a risk for latex allergy.

Skin prick test (SPT) with commercial extract

The subjects were tested with glycerinated extracts (1/20 w/v) of the more important foods (milk, egg, peanut, tomato, wheat, potato, rice, codfish, and soybean) and the most common inhalant substances (*Dermatophagoides pteronyssinus*, grass pollen, *Parietaria officinalis*, *Artemisia vulgaris*, olive pollen, cat dander, dog dander, and *Alternaria tenuis*) (Bayropharm, Milan, Italy).

The extract of latex was supplied by Lofarma Allergeni (Milan, Italy): briefly, an ammoniated latex extract was diluted with phosphate-buffered saline (PBS), mixed for 24 h, and centrifuged at 30 000 g at 4°C for 30 min. 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 µg/ml.

Skin prick tests (SPT) were done on the volar side of the forearm with a lancet (Dome-Hollister Stier, Slough, UK) (1-mm tip), pricking through a drop of extract, which was immediately removed. The SPT results were assessed according to recommendations of the European Academy of Allergy and Clinical Immunology (EAACI) (2). The average diameter of each wheal was established by measuring the longest diameter and the diameter perpendicular to it. Positivity was rated 4+ in the presence of a wheal double the size of the wheal

induced by histamine 10 mg/ml, 3+ in the presence of a wheal with the same diameter as the wheal induced by histamine, and 2+ if the average diameter was half that of the wheal induced by histamine. Only wheals 2+ or more were considered positive.

SPT with fresh foods (FFSPT)

FFSPT were carried out only on latex-SPT-positive subjects, by the Dreborg & Foucard prick+prick technique (3), with the following foods: avocado, pineapple, apricot, grape, banana, pear, apple, kiwi, orange, almond, and chestnut. Each piece of fruit was cut, and the lancet was pressed into the pulp and then immediately used to prick the skin. The results of FFSPT were calculated by the same method as the SPT with commercial extracts.

Latex challenge

The latex challenge was performed in children with positive latex SPT as follows: a fingertip was cut from a surgical glove (Le Petit, Grandate, Como, Italy), dampened with water, and placed on one finger for 15 min. At the same time, one vinyl glove finger dampened with water was placed on a finger of the other hand as control. Urticaria on the finger/hand exposed to latex was regarded as a positive reaction.

Patch test

The patch skin test were carried out on eight positive-latex-SPT subjects with the latex extract (Lofarma, Milan, Italy) and with a standard battery of contact allergens (Pharmacia, Uppsala, Sweden) including the rubber additives thiuram mix, mercapto mix, and carba mix (True Test). The results were evaluated 48 and 72 h after the application.

Laboratory evaluation

The laboratory evaluation included measurement of serum specific IgE (to latex, avocado, banana, kiwi, apple, pear, orange, grape, chestnut, almond, and pineapple) by CAP RAST (Pharmacia, Uppsala, Sweden). Results were expressed in kU/l. A result of >0.35 kU/l was considered positive. Specific IgE were measured only in children with a positive latex SPT.

Statistical analysis

A personal history of previous surgery as well as the use of baby bottle nipples or pacifiers in

latex-SPT-positive or -negative subjects, was analyzed by Fisher's exact test.

Results

Of 453 children, 326 (71.9%) presented one or more positive SPT to common inhalant and/or food antigens and were considered atopic. Ten (3%) of these atopic children had positive SPT to latex extract, and seven also presented positive cutaneous reactions when pricked through a surgical glove. Five children (1.5%) had a positive clinical history after latex exposure (mostly when touching rubber balloons or gloves) (Tables 1 and 2). None of the 316 atopic latex-negative children or 127 nonatopic children had a history of symptoms after latex exposure.

There was a similar use of baby bottle nipples or pacifiers in the first 2 years of age in atopic (positive or negative latex SPT) and nonatopic children. A history of previous surgery was found in 5/10 positive-latex-SPT children (three with a positive and two with a negative clinical history), in 63/316 negative-latex-SPT atopic children ($P < 0.05$), and in 23/127 nonatopic children. The total number of operations was six, 68, and 28, respectively. No patient had more than two operations. Only one (V.F.) of the three latex-allergic

children who had had surgery manifested mild urticaria/angioedema 10 min after the operation.

RAST to latex was positive in only 5/10 positive-latex-SPT children. Latex challenge was positive in 3/9 of the children tested.

Associated fruit-specific IgE (SPT and/or RAST) were found in all five latex-symptomatic children: (kiwi, apple, and chestnut in four cases; avocado, pineapple, orange, pear, almond, and grape in three cases; banana in two cases; apricot in one case) and in 2/5 latex-asymptomatic children (chestnut and pear in two cases; avocado, banana, apple, apricot, orange, almond, pineapple, and grape in one).

Only one patient with clinical allergy to latex and positive FFSPT presented a history of clinical symptoms after ingestion of kiwi and orange. None of the five latex-SPT-positive children with no symptoms after latex exposure had a history of fruit-allergic reactions.

The patch tests to latex and other contact allergens were negative in all the positive-latex-SPT patients tested, except for two who had a reaction (one to thiuram mix, and one to nickel).

Discussion

The prevalence of latex allergy apparently varies widely, depending on the population examined (8–17% of exposed health-care workers and 10–65% of children with spina bifida) (4–8).

Studies evaluating the prevalence of latex allergy in children are limited: Shield & Blaiss (9) studied 80 children who were referred to a university clinic for allergic evaluation and found positive skin tests to latex in 3/44 atopic subjects (6.8%). All three had multiple positive skin tests to inhalant antigens and respiratory symptoms (rhinitis and/or asthma).

Table 1. Sensitization to latex in 453 children

	n (%)	Positive skin tests to latex	Symptoms to latex
All children	453 (100%)	10 (2.2%)	5 (1.1%)
Nonatopic subjects	127 (28.03%)	—	—
Atopic subjects	326 (71.94%)	10 (3.06%)	5 (1.53%)

Table 2. Characteristics of patients skin-prick-test positive to latex

Subjects	Sex/years of age	No. of previous surgical operations/type	Age at symptom presentation (years)	Circumstances of symptoms	Clinical history of latex exposure	Latex ST		Latex RAST (kU/l)	Latex challenge
						CE	GP		
1 (M.C.)	F/4	—	3	Rubber balloons	U	4+	3+	18.9	Positive
2 (D.B.)	M/9	1/calcanoevalgus feet	9	Rubber balloons Dentist's gloves	R, As, C	4+	3+	80.2	Positive
3 (M.M.)	M/5	2/hydrocele	5	Rubber gloves	A, C, D, As	4+	3+	13.1	Negative
4 (C.S.)	F/9	—	8	Rubber balloons	C	3+	2+	<0.35	Negative
5 (V.F.)	M/5	1/phimosis	4	Surgery	U, A, C, D	3+	3+	55.2	Positive
6 (L.P.)	M/9	—	—	—	None	3+	2+	<0.35	Negative
7 (A.M.)	M/9	1/varicocele	—	—	None	3+	3+	1.72	Negative
8 (L.B.)	F/9	—	—	—	None	3+	0	<0.35	ND
9 (E.M.)	M/10	1/adrenoidectomy	—	—	None	2+	0	<0.35	Negative
10 (L.D.)	F/8	—	—	—	None	2+	0	<0.35	Negative

ST: skin test; R: rhinitis; C: conjunctivitis; As: asthma; D: dermatitis; U: urticaria; A: angioedema; CE: commercial extract; GP: glove pricking; ND: not done.

On the other hand, none of the 36 nonatopic children had positive latex skin tests. Reinheimer & Ownby (10) tested latex-specific IgE in 200 consecutive serum samples sent for total IgE levels and found 24 positive subjects (12%); 17 of the 24 positive subjects (70.8%) were under 18 years of age, and all of the seven strongly positive subjects were under 18 years of age. Again, 22/24 (91.6%) of the latex-positive subjects had evidence of atopic disease. Chart reviews and questionnaires, however, revealed that none of the positive subjects had any history of reactions to latex.

In this study, we found that 10/326 (3%) atopic children referred to our clinic for allergic evaluation had positive skin tests to latex. Symptoms to latex were present in only five subjects (1.5%); all these subjects were SPT positive to latex, while only four were RAST positive. On the other hand, RAST positivity seems to correlate with clinical symptoms to latex better than SPT, as 4/5 (80%) latex-symptomatic children were RAST positive, while only 1/5 (20%) latex-asymptomatic children were RAST positive (Table 2). In this respect, these data agree with those of Sorva et al. (11), who found their 11 latex-allergic children all positive to latex IgE by the CAP System, while only 8/11 were also SPT positive. However, the presence of serum specific IgE to latex also in subjects with negative clinical history (7, 10) suggests that both tests should be used in assessing latex allergy. Latex challenge was positive in only 3/5 of children with positive clinical history to latex exposure and negative in 4/4 children with negative clinical history (Table 2). This confirms that, even if the specificity is very high, the sensitivity of this test, as well as other tests in the diagnosis of latex allergy, needs to be studied (11). The main problem in detecting latex allergy with common procedures (SPT, RAST, challenge test) is that the antigenic molecule profiles differ among the products used and also between the finished products and the raw material. In addition, the specificities of the anti-latex IgE antibodies have varied among the sensitized persons; therefore, the evaluation of latex sensitivity and specificity is strongly limited to the extract used (12).

An obvious limitation of this study is that the sample studied (children seen in an allergy clinic) is not representative of the general population. However, none of the 127 nonatopic children had positive skin tests to latex. Therefore, our data confirm that latex sensitivity in children is strongly associated with the atopic status, while the prevalence (3%) is less than that reported in adults (4, 13).

The degree of atopy also seems to correlate with latex allergy; in fact, it has been demonstrated that

children with high IgE serum levels (more than 1000 U/ml) more frequently had serum specific IgE to latex than children whose serum IgE was less than 1000 U/ml (14). None of the patients studied presented significant local or systemic reactions after skin test or pricking with latex.

Some authors were concerned about recent recommendations (6) that latex be included in a routine SPT series of inhalant allergens, due to the possibility of SPT-induced anaphylactic shock (15, 16). It would probably be sufficient to reserve special considerations regarding the safety of SPT (with latex as well as other antigens) for patients with a clinical history of previous anaphylactic reactions (17).

Although the usefulness of a routine screening is questionable, the presence in our group study of an equal number of asymptomatic and symptomatic patients with specific IgE to latex suggests that further studies are needed. In fact, we do not know whether the asymptomatic SPT-positive children are to be considered a group "at risk" of developing latex allergy at a later time. A delayed SPT was not seen in this group and patch tests were negative.

A history of previous surgery was found significantly increased in positive-latex-SPT atopic children, when compared with negative-latex-SPT atopic children and nonatopic children. Only 1/5 positive-latex-SPT children who had undergone previous surgery had had more than one operation, suggesting that even a single operation is associated with latex sensitization. The use of baby bottle nipples or pacifiers in the first 2 years of age does not appear to influence latex sensitization.

The association between an allergy to latex and one to various fruits (banana, avocado, kiwi, and chestnut, but also potato and tomato) has been recently described, suggesting that they may share antigenic determinants (18).

In our study, we found associated fruit-specific IgE (demonstrated by SPT and/or RAST) in all five latex-symptomatic children and in 2/5 latex-asymptomatic ones. Kiwi, chestnut, and apple were the more frequently SPT-positive fruits. Only one of the children who were SPT positive to latex and fruit had clinical symptoms after ingesting kiwi and orange.

In conclusion, in our study, latex-SPT sensitivity was demonstrated in a small proportion of atopic children (3%), while it was absent in nonatopic children. Half of the positive-SPT children also had a positive clinical history after latex exposure; all latex-symptomatic children had specific IgE to some fruit, but only one had symptoms resulting from fruit ingestion. The natural history of the positive-latex-SPT children without clinical

reactions after latex exposure and the clinical significance of the association of latex and fruit sensitivity require further studies.

References

1. Levy DA, Charpin D, Pecquet C, Leynadier F, Vervloet D. Allergy to latex. *Allergy* 1992;47:579-87.
2. Dreborg S, Backman A, Basomba A, Bousquet J, Dieges P, Malling H-I. Skin tests used in type I allergy testing. Position paper prepared by the Subcommittee on Skin Tests of the EAACI. *Allergy* 1989;44 Suppl 10:1-59.
3. Dreborg S, Foucard T. Allergy to apple, carrot, and potato in children with birch pollen allergy. *Allergy* 1983;38:167-72.
4. Moneret-Vautrin DA, Beadouni E, Widmer S, et al. Prospective study of risk factors in natural rubber latex hypersensitivity. *J Allergy Clin Immunol* 1993;92:668-77.
5. Turjanmaa K. Incidence of immediate allergy to latex gloves in hospital personnel. *Contact Dermatitis* 1987;17:270-5.
6. Turjanmaa K, Reunala T. Incidence of positive prick test results to rubber protein. *Contact Dermatitis* 1990;23:79-84.
7. Tosi LL, Slater J, Shaer C, Mostello LA. Latex allergy in spina bifida patients: prevalence and surgical implications. *J Pediatr Orthop* 1993;13:709-12.
8. Slater J, Mostello L, Shaer C. Rubber specific IgE in children with spina bifida. *J Urol* 1991;146:578-9.
9. Shield S, Blaiss MS. Prevalence of latex sensitivity in children evaluated for inhalant allergy. *Allergy Proc* 1992;13:129-31.
10. Reinheimer G, Ownby DR. Prevalence of latex-specific IgE antibodies in patients being evaluated for allergy. *Ann Allergy* 1994;74:184-7.
11. Sorva R, Mäkinen-Kiljunen S, Suvilehto K, Juntunen-Bakman K, Haahtela T. Latex allergy in children with no known risk factor for latex sensitization. *Pediatr Allergy Immunol* 1995;6:36-8.
12. Tomazic VJ, Withrow TJ, Hamilton RG. Characterization of the allergen(s) in latex protein extracts. *J Allergy Clin Immunol* 1995;96:635-42.
13. Fuchs T. Latex allergy. *J Allergy Clin Immunol* 1994;93:951-2.
14. Akasawa A, Matsumoto K, Saito H, et al. Incidence of latex allergy in atopic children and hospital workers in Japan. *Int Arch Allergy Immunol* 1993;101:177-81.
15. Bonnekoh B, Merk HF. Safety of latex prick skin testing in allergic patients. *JAMA* 1992;267:2603.
16. Kelly KJ, Kurup V, Zacharisen M, Resnick A, Fink J. Skin and serologic testing in the diagnosis of latex allergy. *J Allergy Clin Immunol* 1993;91:1140-5.
17. Novembre E, Bernardini R, Bertini G, Massai G, Vierucci A. Skin-prick-test induced anaphylaxis. *Allergy* 1995;50:511-13.
18. Blanco C, Carrillo T, Castillo R, Quirarte J, Cuevas M. Latex allergy: clinical features and cross-reactivity with fruits. *Ann Allergy* 1994;73:309-14.

This document is a scanned copy of a printed document. No warranty is given about the accuracy of the copy. Users should refer to the original published version of the material.