

Development of latex allergy in children up to 5 years of age – a retrospective analysis of risk factors

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The aim of the study was to investigate possible associations between the time course of early sensitization to latex and various life style factors. Of the 398 children from a prospective birth cohort study, 20 (5%) showed specific serum IgE to latex at the age of 5 years. Sensitization started beyond the first year of life and 19 out of 20 sensitized children showed increasing specific IgE-values over time. All 20 sensitized children were atopic ($p < 0.00000$). Total IgE was significantly higher in the sensitized group (median 394.5 kU/l) than in the non-sensitized group (median 39.2 kU/l) ($p < 0.00001$). Comparing the latex-sensitized group with the non-sensitized children, there were significantly more operations in the latex group ($p < 0.05$) during the first 5 years of life. Medical history, certain foods, the use of pacifiers, mattress composition and socio-economic data proved not to be significant risk factors. From our study we conclude that – besides the number of operations and an atopic predisposition – no other definite risk factor for developing sensitization or allergy to latex (such as everyday household objects) can be identified in children up to 5 years of age.

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Within the last 10 years, immediate type allergy to natural rubber latex has become an increasing and clinically important problem in childhood. Several case reports about severe and even fatal incidents in children have been published (1–7). Groups at exceptional risk of latex allergy in childhood include those with spina bifida and urogenital malformations (8–11).

While it is well known that an atopic disposition plays a key role for developing sensitization and clinical symptoms to latex, there is no information about the beginning of sensitization and risk factors during the first years of life. We therefore studied not only the point prevalence of the 5-year-old children from our Multicentre Allergy Study, but also looked retrospectively at the stored sera of the first years and investigated possible associations between sensitization and various life style factors by means of a questionnaire.

Material and methods

Subjects

This investigation was part of our Multicentre Allergy Study (MAS). In this prospective and observational birth cohort study, 1314 children, born in 1990, were followed up at the ages of 1, 3, 6, 12, and 18 months and 2, 3, 4, and 5 years. At the age of 5 years, 1004 children were still in the study. In 1995, questionnaires were sent to all families; 590 families returned the questionnaire, blood samples could be obtained from 642 children. Questionnaires and blood samples were available from 398 children (222 boys, 176 girls) who were included in this study.

Methods

The questionnaire inquired about clinical symptoms (e.g. urticaria, eczema, wheezing, anaphylaxis)

upon contact to latex in the daily environment (e.g. balloons, pacifiers, sports equipment, toys, cross-reacting foods) and to medical equipment (e.g. during surgery, anaesthesia, gloves, plasters).

Total IgE and specific IgE to latex was determined from sera by the solid-phase immunoassay (FEIA), the Pharmacia CAP-system (PCS) (Pharmacia, Uppsala, Sweden) (12). Inhalant (SX1) and nutritional (fx5) allergens were investigated by screening tests using the same automated IgE assay (13). SX1 contains the allergens timothy, birch, mugwort, house-dust mite, cat, dog and *Cladosporium herbarum*. Fx5 contains milk, egg, fish, soy, wheat and peanut. None of these is known to cross-react with latex. The detection limit was 0.35 kU/l IgE; children were regarded as sensitized if specific IgE was above detection limit.

Study design

The whole cohort of children was followed from birth on; however, the latex part of the study was investigated retrospectively, starting at the age of 5 years. Only patients for whom questionnaires and blood samples were available at that age were included in the study. Blood samples from the previous years (1, 2 and 3 years of age) were analyzed retrospectively. The study protocol was approved by the local Ethics Committee.

Statistical analysis

The statistical analysis was performed using SPSS/PC version 7.0. The chi-square test, the Fisher's exact test, the test for linear trend association and Mann-Whitney-U-test were used to test for differences between latex-sensitized and non-sensitized children.

Results

Of the 398 5-year-old children, 20 (5%) showed specific IgE to latex in serum, 378 did not. Total IgE ranged from < 0.35 kU/l to 6020 kU/l (median 39.2 kU/l) in the non-sensitized group and from 97.1 kU/l to more than 10 000 kU/l (median 394.5 kU/l) in the sensitized group ($p < 0.00001$). One hundred and forty-nine children were defined as atopic; all 20 sensitized children were atopic, i.e. also showed specific IgE to at least one other inhalant or nutritional allergen ($p < 0.00000$). Therefore, 13.4% of the atopic children were sensitized to latex.

Table 1 and Fig. 1 show the time course of the specific IgE values from 1 to 5 years of age. None of the 13 children for whom values could be determined was sensitized to latex at 1 year of age. Sensitization started around the second year of life, but many of the children (10/20) were sensitized be-

Table 1. Specific IgE to latex in serum (kU/l)

ID number	1 year of age	2 years of age	3 years of age	5 years of age
604321	< 0.35	4.7	n.d.	26.6
408441	< 0.35	< 0.35	< 0.35	11.0
307611	n.d.	3.3	5.3	7.5
605441	< 0.35	< 0.35	n.d.	4.3
103211	< 0.35	< 0.35	1.4	4.1
406181	n.d.	n.d.	2.6	4.0
505161	< 0.35	0.9	1.5	3.8
208231	n.d.	n.d.	< 0.35	3.6
106481	n.d.	n.d.	< 0.35	1.8
305611	< 0.35	n.d.	< 0.35	1.7
501891	< 0.35	< 0.35	n.d.	1.4
501981	< 0.35	n.d.	n.d.	1.2
506021	< 0.35	< 0.35	< 0.35	1.0
208581	n.d.	n.d.	0.8	0.66
401211	n.d.	n.d.	n.d.	0.64
306981	< 0.35	n.d.	< 0.35	0.6
307311	< 0.35	< 0.35	< 0.35	0.55
205801	< 0.35	n.d.	< 0.35	0.51
301991	< 0.35	< 0.35	< 0.35	0.49
210351	n.d.	n.d.	< 0.35	0.46
% positive	0/13 (0%)	3/14 (21%)	6/16 (33%)	20/20 (100%)

Legend: n.d. = not determined, < 0.35 = specific IgE to latex below detection limit.

tween 3 and 5 years of age. Except for patient 14, who had slightly lower values at the second time-point investigated, all patients showed increasing specific IgE-values over time. Point prevalence rates rose from 0% at 1 year of age, to 30% at 2 years of age, to 36% at 3 years of age and finally to 100% (by definition) at 5 years of age (Table 1).

Comparing the latex-sensitized group ($n=20$) with the non-sensitized group ($n=378$), there were significantly more operations in the latex-sensitized group ($p < 0.05$) during the first 5 years (Table 2).

Evaluating the history of clinical symptoms on contact with materials containing latex revealed that the history was not helpful in distinguishing the two groups: in general, parents of non-sensitized children reported most of the positive reactions to latex. Only the history of symptoms to other foods than avocado, banana, kiwi or milk revealed a statistically significant association with both the chi-square and the Fisher's exact test, ($p < 0.03$ and $p < 0.04$, respectively).

The question concerning the composition of the mattress in the children's beds was asked at 3 months and 3 years of age. At 3 months only 4/398 children slept on a latex mattress so that a statistical analysis was not possible. At the age of 3 years, 21 children slept on latex mattresses: 6.6% of the latex-sensitized and 6.7% of the non-sensitized children (NS). The age of the mattress had no influence (data not shown).

Specific IgE to latex (kU/l)

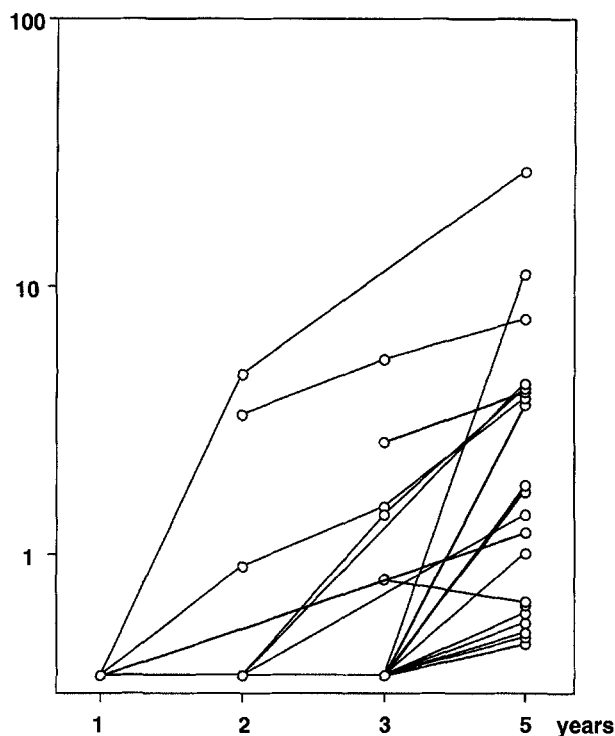


Fig. 1. Development of specific IgE to latex (kU/l) during the first 5 years of age (n=20).

Socio-economic data, such as sex ($p=0.394$), educational level of the parents ($p=0.298$), duration of breast feeding ($p=0.672$) or the family history of atopy ($p=0.139$), did not show any statistically significant differences in the latex-sensitized compared to the non-sensitized group of children.

Discussion

In our study, 5% of the 5-year-old children were sensitized to latex. This prevalence is somewhat lower than in a previous study of our group in which 609 sera (303 of non-atopic and 306 of atopic children) from 4.5-year-old children were screened for IgE antibodies to latex and an overall prevalence of 10% was found (14). However, this 10% prevalence may have been due to a higher proportion of atopic children (50%), compared to the general pediatric population or this cohort study. In the literature, varying prevalence rates of sensitization to latex are reported in children: 19% in children suspected of having allergic diseases (15) and 7% in a random sample of 80 children (16). Overall, numbers between 5% and 10% may be realistic for the general pediatric population, while between 10% and 20% must be expected in atopic children (14). In this

Table 2. Number of operations before 5th birthday

	No operations	1 operation	2 operations	Total
Latex-sensitized children	15 (75%)	4 (20%)	1 (5%)	20
Non latex- sensitized children	332 (87.8%)	43 (11.4%)	3 (0.8%)	378
	347	47	4	398

Legend: linear-by-linear association $p<0.05$.

study, 13.4% of the atopic children were sensitized to latex. This number is lower than in our previous study (14), in which 20.8% were sensitized. The most probable explanation for this difference is the high prevalence of children with atopic dermatitis in the previous study.

The time course of sensitization started around the second year of life, but many of the children were sensitized between 3 and 5 years of age. Point prevalence rates in this group rose from 0%, 30%, and 33% to 100% at 1, 2, 3, and 5 years of age respectively (Table 1). Because 16/20 children (80%) first had negative results, the beginning of sensitization can be assessed in these patients. It remains unclear at what time a maximum point prevalence would generally occur. Follow-up studies with longer observation periods are therefore needed. On the other hand, there were only six children with complete blood samples at 1, 2, 3, and 5 years of age, and it therefore cannot be excluded for sure that there were patients who were already sensitized at the age of 1 year (e.g. patients 307611 and 208581). Seven out of twenty patients had specific IgE values to latex of <0.7 kU/l at the age of 5 years. Because of the lack of provocation tests, it remains unclear whether these low values are of clinical relevance.

As in other studies, it could be confirmed in this investigation that the two most important risk factors for developing sensitization and allergy to latex are: (1) the number of operations (11, 17–20), and (2) an atopic disposition (14, 21). Latex allergy, however, also occurs in children with no known risk factor (22).

While there is an intriguing hypothesis for the especially high prevalence of sensitization and allergy to latex in spina bifida, namely that these children undergo operations on the first day of life, thereby experiencing extraordinary and early exposure to long-term effects from allergen depots on the mucosa of glove powder containing latex, as well as the booster effect of many operations in the following years. We were unfortunately unable to discover relevant life style factors such as contact with cross-reacting foods (e.g. banana, avocado, kiwi), the use of pacifiers, the composition of the mattress or socio-

economic data in the children of our cohort study. This may partly be due to statistical problems because of the low number of sensitized children. Therefore, prospective, long-term studies are warranted to further unravel the mysteries of early latex sensitization.

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