

Longitudinal study on latex sensitization in children with spina bifida

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The course of latex sensitization is rarely documented, and only a few reports about the influence of prophylaxis in the occupational environment have been published concerning health care workers. Therefore we did a follow-up study in the high risk group of patients with spina bifida and evaluated the efficacy of latex prophylaxis. For this purpose we measured IgE antibodies (FEIA) against latex and inhalative allergens in the sera of 67 patients with spina bifida and reevaluated them 0.6 to 4.1 years later, having instructed the patients about prophylactic measures and established a latex-free environment for surgery of all spina bifida patients in our hospital. 37% of the patients did not develop latex antibodies during the follow-up period, 27% showed decreasing levels of antibodies (12% to non-detectable levels), 19% had an increase in latex sensitization (6% newly sensitized), and 9% showed no change in levels of latex antibodies. From our data it may be concluded that surgery without strict latex prophylaxis is the main cause of new sensitization and worsening of preexisting latex antibody levels. Mild sensitization can be reduced by prophylactic measurements to non-detectable antibody levels. With consistent prophylaxis, even symptomatic patients can be operated without risk of allergic complications or increasing antibodies.

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The course of natural rubber latex sensitization and allergy has been described by some longitudinal studies in health care workers (1–4), but to our knowledge there has been no follow-up study of the group with the highest risk of latex allergy, children with spina bifida. In such patients, a rate of sensitization of up to 70% has been documented in several studies (5, 6). Multiple surgery and a history of atopy are identified as risk factors for latex allergy (6) and an association to HLA-DR phenotypes has been demonstrated for the sensitization against hevein, a well-defined allergenic latex protein (7). To minimize the risk for these patients recommendations for prophylactic measures have been published (8, 9), but the efficacy of primary, secondary or tertiary prophylaxis has still to be evaluated. As it is very difficult to establish a completely latex-free environment, it is important to identify which conditions are associated with the greatest risk of sensitization.

Methods

Patients

Sixty-seven patients (age range 1.2 to 25.1 years, mean 11.2 years, median 11.2 years; 37 males, 30 females) from the outpatient clinic for spina bifida in

the Cologne Children's Hospital were included in the follow-up study after informed consent had been obtained from their parents. By a questionnaire, the number of previous operations and their complications, known allergies and atopies, clinical symptoms of latex allergy and their daily contacts with latex products were compiled. All patients with intermittent (self-)catheterization were equipped with latex-free material when they learned this method, so no additional latex contacts were given by this procedure.

In the serum, the total IgE, the specific IgE against natural rubber latex and a screening test for inhalant allergens (SX1: rye, birch, *Phleum pratense*, *Artemisia vulgaris*, cat's and dog's epithelium, *Dermatophagoides pteronyssinus*, *Cladosporium herbarum*) were determined by fluorescence enzyme immuno assay (FEIA, CAP-System, Pharmacia, Uppsala, Sweden). Patients with antibodies in the SX1 test were taken as atopic. The results were classified as shown in Table 1.

Patients with latex antibodies were instructed about prophylactic measures and received an emergency document according to the task force recommendations of the AAAI (9). Simultaneously we were able to establish that in the Cologne Children's Hospital, surgery on all spina bifida patients was

done in a latex-free environment regardless of patients' latex antibodies.

The antibody status was reevaluated up to three times (mean 2.2 tests per patient) after varying periods (minimum 0.6 years, maximum 4.1 years, mean and median 1.9 years) and the patients were asked for details of any operations and symptoms of latex allergy experienced between these evaluation points.

Statistics

The statistical analysis was done by calculating the data with the Statview program on an Apple Macintosh computer. A univariate analysis (counting of frequencies, means) was performed, the statistical differences of variables were analyzed by the chi-square test for qualitative items and by the Mann-Whitney U-test for quantitative items.

Results

The data of the latex IgE antibody values at the first measurement are shown in Table 1. 55% of the spina bifida patients had antibodies above the cut-off level of >0.35 kU/l, and 48% above the cut-off level of >0.7 kU/l. Fifteen of 67 (22%) patients showed symptomatic latex allergy with all degrees of allergic reactions up to intraoperative anaphylaxis in 5 patients. These symptomatic patients had high levels of latex antibodies (at least CAP class 2; 12 patients with CAP classes 4 to 6).

Atopy

Twenty-eight (42%) had a positive SX1 test on inhalative allergens, 18 (27%) patients presented with a personal history of atopy (eczema, asthma, rhinoconjunctivitis). All but 2 patients (with allergy against animal antigens not contained in SX1) with a personal history of atopy were also positive in the SX1 test. 75% of patients with a positive SX1 test showed positive latex antibodies (>0.35 kU/l), compared with 52% of patients with a negative SX1 test ($p>0.05$). Two of the new sensitized patients were positive in the SX1 test. On the other hand, 52% of the latex IgE positive patients were also positive in the SX1 test, compared with 29% in latex negative patients ($p>0.05$).

Surgery

Four hundred and thirty-eight operations had been done on the 67 patients (mean 6.5, minimum 1, maximum 30) before the first measurement of latex antibodies. Latex-sensitized patients had significantly more surgery than non-sensitized patients (mean 8.1 vs 4.2, $p=0.002$).

Table 1. Distribution (absolute numbers and relative percentages) of IgE antibodies against latex in patients with spina bifida at the beginning of the study. Classification according to results in fluorescence enzyme immuno assay (FEIA, CAP system)

Patients with IgE antibodies against latex			
CAP class	kU/l	n	%
0	<0.35	30	44.7
1	$0.35-0.7$	5	7.5
2	$0.7-3.5$	10	14.9
3	$3.5-17.5$	6	9.0
4	$17.5-50$	8	11.9
5	$50-100$	4	6.0
6	>100	4	6.0
Σ		67	100
Patients with IgE ≥ 0.35 kU/l		37	55.2

Between the first and following (second to fourth) measurements of latex antibodies, 21 patients (31%) underwent 38 operations (3 patients with 2 operations, 1 patient with 3, 4 or 5 operations): 15 operations of the shunting system, 18 orthopedic operations, 3 urological operations, and 1 operation of a spinal dermoid cyst. There were no reports of allergic complications during these operations, even 4 symptomatic children (1 with previous anaphylaxis) underwent surgery without allergic symptoms under the precautions of tertiary latex prophylaxis.

Follow-up of latex IgE antibodies

Twenty-six of 67 (39%) patients persisted without latex antibodies (Fig. 1), although 7 patients underwent 13 operations (2 patients had 2 operations, 1 patient had 5 operations). These operations were performed in our own hospital, by our consultant orthopaedic surgeon, or in a center for neuro-urology especially instructed in intra- and perioperative latex prophylaxis.

In 18 of 67 (27%) patients, latex antibodies decreased. Only 3 of these children underwent an operation, 1 of them in our hospital with a remarkable decrease from more than 100 kU/l to 64.8 kU/l after the operation. Five of 67 (7%) patients had no latex antibodies further detectable at the second to third test, 3 of them started with a low sensitization of CAP class 1 antibodies (1 operation in 1 patient), 2 with CAP class 2 (Table 2).

Only in 6 of 67 patients (9%) did latex antibodies remain at a stable level (within the assay variability) between the tests. Four operations in 3 patients with former symptoms of latex allergy and high levels of latex IgE antibodies (CAP class 6 in 2 patients, class 5 in 1 patient) were tolerated without allergic symptoms.

Patients ($n = 26$) without development of latex antibodies (CAP latex < 0.35 kU/l)

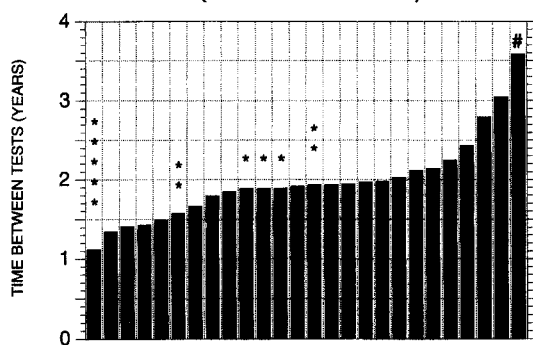


Fig. 1. Time interval without development of latex antibodies (CAP latex < 0.35 kU/l) in 26 patients.

*Surgery at the Children's Hospital or by the consultant orthopaedic surgeon.

Surgery outside the Children's Hospital.

In 4 patients (6%) with 3, 4, 5 and 8 operations before the first latex antibody testing, a new sensitization to latex was detectable (Fig. 2). All of these patients had additional operations outside our hospital: the patient with the strongest new sensitization had undergone 4 shunt revisions and an untethering surgery of the spinal cord within 2 weeks; each of the other 3 patients had 1 to 3 orthopedic operations between the first and second measurement of latex antibodies.

Table 2. Patients ($n=18$) with decreasing values of specific IgE against latex (CAP system) during the observation period, arranged by initial IgE value

Patient ID	Values of specific IgE against latex (kU/l)			Time between tests (years)	
	Test				
	1	2	3	1-2	1-3
CH	>100*	64.8	59.3	0.9	2.0
JK	>100	20.7		2.7	
TO	49.6	37.8		1.9	
SH	36.4	15.4	7.9	0.4	1.4
SD	34.7	20.6		1.3	
MM	15.8	12.6		1.3	
FW	14.0	11.4		1.5	
IS	9.3	2.7	3.9	0.2	1.4
SE	3.2	1.0		0.8	
IB	2.8#	1.5		0.8	
AW	2.4	1.9	0.8	0.8	3.4
DK	2.3	<0.35	<0.35	0.7	2.0
JM	1.7	0.7		2.0	
JH	1.3	0.4		1.7	
DK	0.7	0.5	<0.35	1.0	3.1
DT	0.5	<0.35		1.4	
CW	0.5	<0.35		2.4	
TS	0.4#	<0.35		1.5	

Patient ID bold and in italics: children with symptoms of latex allergy.

*Surgery at the Children's Hospital after the test.

#Surgery outside the Children's Hospital after the test.

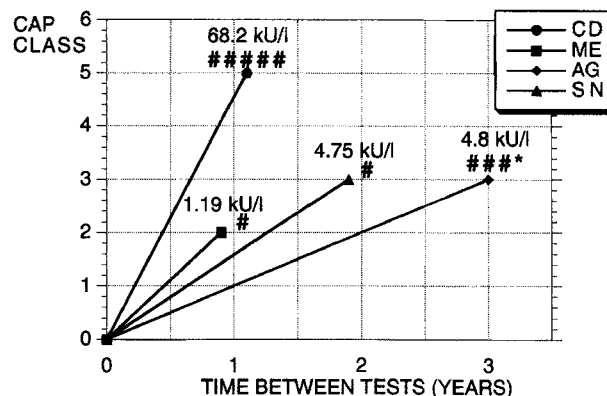


Fig. 2. New sensitization to latex documented by an increase in specific latex IgE values in the follow-up of 4 patients.

*Surgery at the Children's Hospital or by the consultant orthopaedic surgeon.

Surgery outside the Children's Hospital.

In 13 (19%) patients, the increase of latex antibodies is assumed to be an indication of stronger sensitization (Table 3). Four of these patients had undergone 1 to 3 operations outside the Children's Hospital. Patient CS had an operation in our hospital, before strict prophylaxis could be guaranteed.

In the symptomatic sensitized group, no patient lost latex antibodies (CAP class 0), but in 6 patients the latex antibody values decreased, remaining stable on a high level (CAP class 6 in 2 patients, class 5 in 1) in 3 patients. In 4 patients latex antibodies increased. In 5 symptomatic patients an operation could be carried out without allergic symptoms under latex prophylaxis regardless of the course of the latex antibodies.

Discussion

Many prevalence studies have revealed the high risk status of patients with spina bifida, which our data were also able to confirm. In follow-up studies, an increase of latex sensitization could be documented for nursing students (3) and students of dentistry (2). The use of latex gloves was found to be the main source of allergen in health care workers, either by direct skin contact or by inhaling allergens bound to the glove powder (10). So it is not surprising that the use of non-latex gloves reduced the latex antibody values by more than 50% in 7 of 10 latex allergic patients (1). In the group investigated by Zeldin et al. (4) only total consistency in changing to a latex-free environment led to improved skin prick test results and diminished symptoms of latex allergy, whereas simply avoiding latex contacts in a latex-containing environment led to subjective improvement in only 8 of 17 health care workers. In contrast to health care workers, where hevein was identified as the major latex allergen, in spina bifida patients the latex protein Hev b 1 (rubber elongation factor)

Table 3. Patients (n=13) with increasing values of specific IgE against latex (CAP system) during the observation period, arranged by initial IgE value

Patient ID	Values of specific IgE against latex (kU/l)				Time between tests (years)		
	Test						
	1	2	3	4	1-2	1-3	1-4
LV	95.2	>100			0.8		
RR	67.3	>100			1.2		
RE	44.4	31.0	97.4	90.4	1.3	3.2	4.1
CS	37.8*	>100	29.1		1.0	2.7	
MP	29.7#	46.6			2.2		
TY	23.8	32.2	64.4	20.1	0.5	2.6	3.4
JS	18.5#	27.4			2.7		
CY	10.5#	32.7			1.0		
SF	5.2	9.1			1.7		
SJ	2.1	4.8			1.7		
SV	1.0	4.22			1.6		
IB	0.7#	10.3	0.7		0.8	3.1	
AS	0.4	0.9	2.8		0.5	2.2	

Patients ID bold and in italics: patients with symptoms of latex allergy.

*Surgery at the Children's Hospital after the test.

#Surgery outside the Children's Hospital after the test

is the major allergen (11, 12). This protein, with a high molecular weight of 14 kD, is allergenic by direct mucosal contact and not by inhalation, as is the much smaller hevein. Prophylactic regimens for spina bifida patients therefore have to minimize the amounts of Hev b 1 incorporated, especially during surgery. To our knowledge this is the first follow-up study in children with spina bifida.

Much more attention should be paid to the details of anesthesiologic and surgical equipment, to avoid anaphylactic reactions despite latex prophylaxis (13). Our data confirm the need for strict latex prophylaxis, as 4 patients without measurable sensitization following up to 8 surgical operations developed latex antibodies after the next 1 to 5 surgical operations outside our hospital. Under our own latex-free conditions we noted an increase of latex antibodies (to more than 100 kU/l) in 1 patient (CS) only, who was highly sensitized (CAP class 4) before the last operation, and which took place before we had established a latex-free environment for spina bifida patients. 12% of all patients showed an increase in latex antibodies without intervening surgery despite our advice on prophylactic latex avoidance under home conditions. This fact shows how difficult it is to establish a latex-free environment outside the operating theater in the hospital, or even outside the hospital, if the latex content of many materials is hidden and unknown, as there is no requirement to declare latex in Germany. We conclude that the sensitization of patient RE increased during multiple stays in hospitals outside the Cologne Children's Hospital.

Patients with low sensitization (up to CAP class 2) can decrease their latex antibodies to undetectable

levels by prophylaxis. It must be emphasized that there was no new sensitization without surgical operations in our study. In 37% of our patients new sensitization could be avoided by prophylactic measures.

Even in patients with known latex allergy surgery can be done without anaphylactic reactions when a latex-free environment in the operating theater and perioperatively has been established. We were able to demonstrate this in 4 patients with symptomatic latex allergy and 6 additional patients with asymptomatic latex sensitization. In the symptomatic patients, no desensitization could be monitored, indicating a need for a permanent tertiary prophylaxis.

We conclude that meticulous latex prophylaxis, especially during surgery, can avoid sensitization even in patients with spina bifida.

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