

Latex Allergy in Pediatric Surgery Is Dependent on Repeated Operations in the First Year of Life

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Background/Purpose: Patients with spina bifida represent the highest risk group for hypersensitivity to latex. Recognized risk factors for these patients are repeated surgery and an atopic disposition. Little is known about children operated on in the first year of life for reasons other than spina bifida.

Methods: Eighty-six patients (mean age, 10.2 years) with gastrointestinal or urologic surgery were investigated for the number, type, and date of surgical interventions. Additionally, skin prick tests and provocation tests were performed to classify sensitized and symptomatic latex-allergic individuals.

Results: Twenty-seven patients were regarded as sensitized to latex (31.4%). Twenty patients were classified as being atopic (25.6%). Atopic patients were significantly more often sensitized and provocation positive compared with nonsen-

sitized and provocation-negative ones ($P < .01$). Children already operated on in the first year of life ($n = 44$) with a positive provocation showed significantly higher latex-specific IgE-values than individuals with a negative outcome ($P < .0001$). The total number of operations and degree of sensitization showed a significant correlation; more than 8 surgical interventions during the first year of life significantly increased the risk of clinically relevant allergy to latex.

Conclusion: This study emphasizes that individuals undergoing surgical interventions during infancy should be handled latex free from the very beginning of life.

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INDEX WORDS: Allergy, dialysis, latex, operation, provocation test, surgery, urology.

ALLERGY TO NATURAL rubber latex (NRL) has increasingly become a health concern in defined risk groups such as patients with spina bifida. The prevalence of sensitization to latex in patients who have spina bifida ranges from 29% to 64.5%.¹⁻⁷ Previously known risk factors for developing hypersensitivity to latex include atopic disposition^{4,8-10} and frequent surgery.^{1-4,7,11,12} Clinical symptoms of latex allergy vary from local urticaria to severe anaphylaxis, including life-threatening intraoperative anaphylactic reactions.^{13,14}

Although the effects of one surgical operation seem to be sufficient to induce latex-specific IgE antibody production,¹⁵ there is a correlation between the number of operations and the degree of sensitization and allergy to latex in patients with spina bifida.^{4,12} However, not only the number, but also the type of surgical procedures seem to influence the risk of developing hypersensitivity to latex.⁸

One may hypothesize that contact of latex on the meninges may have an especially strong sensitizing potential, whereas other routes (eg, intraperitoneal) may be less important. Our aim was therefore to study the influence of surgical interventions during the first year of life as an independent risk factor.

MATERIALS AND METHODS

Patients

Eighty-six patients (30 girls, 56 boys) aged from 2 months to 24 years (mean, 10.2 years) who underwent at least one surgical procedure

between 1979 and 2000 were included. Sixteen children were operated on because of gastrointestinal malformations (eg, laparoschisis) and 70 children because of urologic malformations (eg, urethral valves, obstruction of the ureteropelvic junction; Fig 1). None of these operations was performed latex free.

Study Design

Details of the date and type of previous surgical interventions were collected. In a structured interview, patients (or parents) were asked about clinical symptoms caused by latex exposure in daily situations (eg, inflating a balloon) and during medical interventions (eg, surgery). Additionally, skin prick tests and provocation tests were performed and a blood sample was taken. The local ethics committee approved the study, and patients (or parents) gave their informed consent.

Skin Prick Testing

Skin prick tests (SPT) were performed with low ammoniated raw and unfinished natural rubber latex milk (Ansell, Munich, Germany). Skin test responses were assessed as positive if the maximum wheal diameter was 3 mm or greater without reaction to a negative control (saline) and the skin index was ≥ 0.6 . The skin index was calculated as

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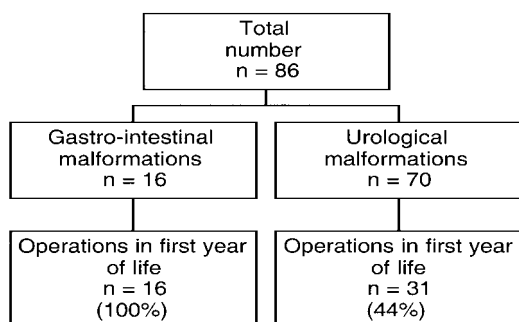


Fig 1. Kinds of surgery and interventions in the first year of life.

the ratio of the diameter of the allergen wheal to the histamine (positive control) wheal.

Provocation Tests

After having washed their hands, patients put one wet hand into a latex glove (Sempermed classic, Lot YE5F7; Semperit, Vienna, Austria) and, as a control, put the other wet hand into a neoprene glove (Dermaprene; Ansell, Munich, Germany). After wearing these gloves for 30 minutes (or on showing clinical symptoms), the gloves were taken off, and possible clinical reactions were assessed by a physician. Hands were washed again. The single-blind test response was assessed as positive if typical immediate-type clinical reactions (eg, urticaria or Quincke's edema) occurred. Care was taken under continuous observation that children did not rub the glove onto other parts of the body.

In Vitro Testing

Total IgE and specific IgE to latex in the serum specimens were determined by a commercially available ELISA (FEIA, Pharmacia CAP-system; Pharmacia Upjohn, Uppsala, Sweden).¹⁶ In 3 of these a serum sample was refused, and these patients could not be considered for calculations concerning serum IgE. To establish atopic status, we performed a screening test for inhalant (SX1) and nutritional (fx5) allergens using the same automated IgE assay.¹⁷ Atopy was defined as SX1- or fx5-values ≥ 0.35 kU/L.

Statistical Analysis

Results were calculated with the SPSS package for Windows 10.0. The Mann-Whitney U-test and the χ^2 test were used. *P* values less than .05 were considered significant.

RESULTS

Allergologic Findings

Total IgE ranged from less than 0.35 kU/L (detection limit) to greater than 2915.0 kU/L (mean, 147.6 kU/L).

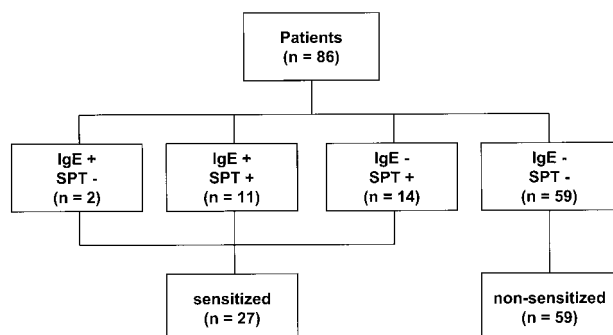


Fig 2. Diagnostic classification of sensitization.

Latex-specific IgE in serum ranged from less than .35 kU/L to greater than 35.8 kU/L (mean, 0.39 kU/L). Thirteen patients (15.6%) showed specific IgE to latex in serum. Twenty-five patients (29.1%) were skin prick test positive concerning natural rubber latex milk. Patients were regarded as sensitized to latex if they were positive to either specific IgE in serum or in the skin prick test ($n = 27$, 31.4%). In 11 patients SPT plus specific serum IgE to latex were positive, in 59 patients (68.8%) both parameters were negative (Fig 2).

Provocation Tests

Of all patients, 11 of 86 (12.8%) showed clinical symptoms on provocation (local urticaria [$n = 6$], generalized urticaria [$n = 3$], allergic rhinoconjunctivitis [$n = 2$]). Of the sensitized patients, 8 of 27 (29.6%) were provocation positive. Patients with a positive provocation showed significantly higher latex-specific IgE values (median 7.3 kU/L) than individuals with a negative outcome (median, 1.0 kU/L; $P < .0001$). Considering only the 44 children operated on in the first year of life, we observed nearly identical data (3.2 kU/L v less than .35 kU/L; $P < .001$; Fig 3).

Number of Surgical Interventions

All 86 patients had undergone at least one operation. Table 1 lists the first surgical intervention, and Table 2

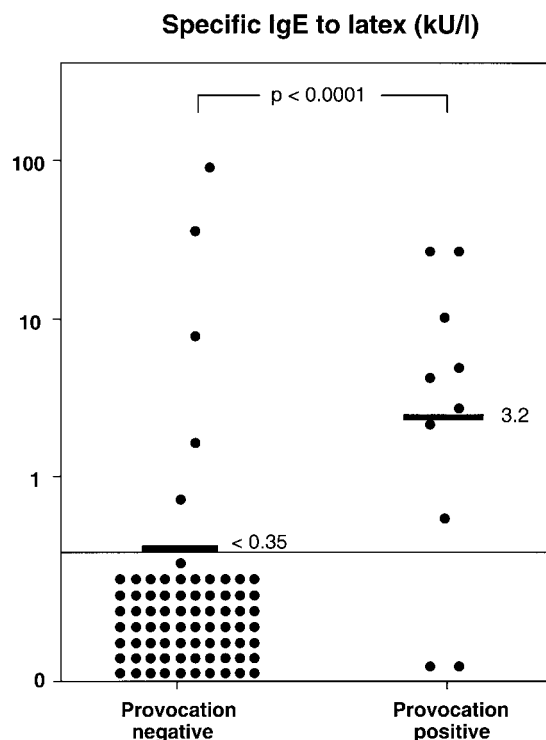


Fig 3. Specific IgE to latex in provocation-negative ($n = 76$) and provocation-positive ($n = 10$) latex-sensitized children operated on in the first year of life. Bars represent median values.

Table 1. List of First Surgical Intervention (n = 86)

Surgical Intervention	No.
Abdominal wound closure	16
Peritoneal dialysis catheter	15
Pyeloplasty	14
Abdominal intervention (excluding Pd-catheter)	11
Arterio-venous fistula	8
Urethral valve resection	8
Antireflux surgery	7
Kidney transplantation	4
Reconstruction of bladder	3

the surgical interventions and number of operations. The total number of operations ranged from 1 to 20 (mean, 4.4). The total number of operations and degree of sensitization in terms of a positive skin index showed a trend (Fig 4), but, because of large variations, values did not reach statistical significance. Individuals with more than 8 surgical procedures had a statistically significant elevated risk of a clinically relevant allergy to latex (Fig 5).

Forty-four patients (51.0%) had undergone at least one operation during the first year of life. The number of operations during the first year ranged from 1 to 7 (mean, 1.2). All sensitized children (n = 27) were operated on during the first year of life. Again, more than 8 surgical interventions in children operated on during the first year of life significantly increased the risk of clinically relevant allergy to latex (Fig 5).

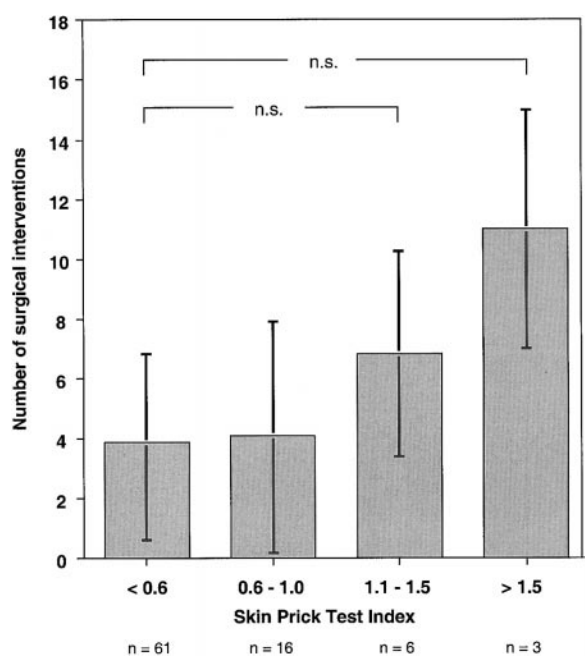


Fig 4. Correlation of specific IgE to latex in serum and total surgical procedures. Values refer to patients without specific IgE to latex (CAP 0). Data are presented as mean values $\pm$ 1SD. ns, not significant.

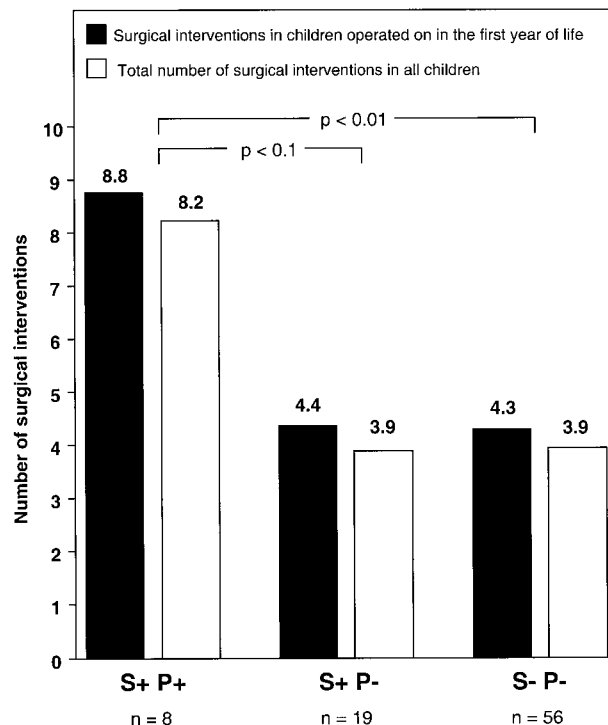


Fig 5. Association of total number of operations and operations during the first year of life and state of sensitization or the occurrence of clinical symptoms. S, sensitization; P, provocation positive.

Atopic Disposition

On the basis of specific IgE to inhalant or nutritional allergens in serum, 22 of all patients were classified as being atopic (25.6%). Atopic children operated on in the first year of life (n = 16) were significantly more often sensitized plus provocation positive (37.5%; $P < .01$) compared with nonsensitized plus provocation-negative patients (20.0%). Considering all patients, there was only a trend.

DISCUSSION

Allergologic Findings

The results of this study indicate that 31.4% of our young patients who had undergone at least one surgical intervention were sensitized to latex. Interestingly, 29.6% of sensitized patients had a positive provocation and may, therefore, be at risk of symptoms on contact with latex in daily life or during medical interventions. Therefore, in contrast to patients with spina bifida, with about one third of all patients sensitized, and two thirds of sensitized patients testing provocation positive,¹² only a smaller percentage of patients in this general pediatric surgery population was sensitized.

During 86 skin prick and provocation tests, no significant side effects were noted. Skin prick testing with natural rubber latex and glove tests may be regarded as safe diagnostic procedures; however, patients with

Table 2. Surgical Interventions and Number of Operations

Surgical Interventions	Laparoschisis (n = 16)	Lower Obstructive Uropathy (n = 14)	Upper Obstructive Uropathy (n = 14)	Urologic Congenital Malformation (n = 13)	Miscellaneous, Urologic Disorders (n = 29)	Mean (n = 86)
Mean total number of operations	2.9	5.9	3.3	5.5	4.3	4.4
Mean number of operations during the first year	1.3	1.6	1.2	1.6	0.5	1.2
Mean number of operations beyond the first year	1.6	4.3	2.1	3.9	3.8	3.2
Hemodialysis (n)	—	3	—	2	11	16
Peritoneal dialysis (n)	—	8	—	3	21	32
Kidney transplantation (n)	—	7	—	7	25	39

known anaphylactic reactions to latex should be excluded from testing. Three of 11 provocation-positive patients were not classified as sensitized to latex; however, in one of these patients no blood sample was available so that a final statement on sensitization could not be made.

The concordance between skin prick test results and latex-specific IgE values in serum was poor: both results were positive in only 11 patients. This is in contrast to other studies performed in our group showing that serum IgE had a better sensitivity than SPT and that both tests showed a good concordance.^{4,12} A possible explanation for this discrepancy may be that the CAP system uses latex allergens mainly recognized by patients with spina bifida such as Hev b 3. The sensitized patients in the population of children undergoing general surgery investigated in this study may therefore be underrepresented by the assay.

Surgical Interventions

Surgical operations are accompanied by a transient rise in serum total IgE concentration (peak by the fifth postoperative day).¹⁸ This increase can be prevented by preoperative treatment with prednisolone, but not with ranitidine.¹⁹ The unspecific rise of total IgE may reflect involvement of IgE in acute-phase responses to tissue injury.¹⁸

Our findings show that the degree of specific sensitization to latex is significantly correlated with the total number of operations, which has been reported for patients with spina bifida.^{4,11,12,20} Patients with more than 8 surgical procedures had a significantly higher risk of a clinically relevant allergy to latex. These results are identical to the results from studies in children with spina bifida.¹²

Although data are readily available on latex sensitization/allergy and surgical intervention in patients with spina

bifida, little is known about the situation for general pediatric surgical patients. In a large survey of 1,523 pediatric general surgical operations, 11 operations were performed under latex precautions; all of these patients had a preoperative diagnosis of latex allergy.²¹ During the same period of 12 months, intraoperative anaphylactic reactions caused by latex allergy occurred in 2 general surgical patients (0.13%), and 4 additional cases were reported from other study hospitals. None of these patients were suspected of having a latex allergy before their surgery. The investigators conclude that criteria should be defined to identify preoperatively patients at risk of latex sensitization.²¹ In our study, patients with more than 8 surgical procedures had a significantly higher risk of developing a clinically relevant allergy to latex.

The reason patients with spina bifida are at a higher risk of clinically relevant allergy to latex than other patients including anaphylactic shock¹⁴ may be that they are unique in showing IgE responses to latex contact.²² A reason for the different prevalence rates of allergy to latex in patients with spina bifida and other patient groups with frequent surgery may be the early onset of surgical interventions. Patients with spina bifida usually undergo their first operation on the first day of life. The early exposure to latex may predispose to developing hypersensitivity to latex.⁵ We, therefore, looked separately at the number of operations during the first year of life and found a strong correlation between the number of operations during the first year and sensitization/allergy to latex. Furthermore, no children sensitized to latex had not had an operation during the first year of life.

This study emphasizes that individuals undergoing surgical interventions during infancy should be handled latex free from the very beginning of life.

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