

Ventricular shunts and the prevalence of sensitization and clinically relevant allergy to latex in patients with spina bifida

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Patients with spina bifida represent the highest-risk group for developing hypersensitivity to latex. Recognized risk factors for these patients are repeated surgery and an atopic disposition. Our aim was to study the influence of a ventricular shunt as an independent risk factor. One hundred and sixty-one patients with spina bifida (median age 10 years) were investigated for the presence of a shunting device and the number, type and date of previous surgical interventions. Additionally, skin-prick tests and provocation tests were performed in order to classify sensitized and symptomatic latex-allergic individuals. Eighty-eight patients (54.7%) were sensitized; 55 (34.2%) were provocation-positive. Patients with a shunt system had undergone a significantly higher number of surgical procedures ($p < 0.0001$) and showed significantly higher levels of immunoglobulin E (IgE)-antibodies to latex ($p < 0.0001$) than patients without a shunting device. The total number of operations correlated significantly with the level of IgE-antibodies to latex in serum ($p < 0.0001$), whereas the number of shunt operations in patients with a ventricular shunt did not significantly correlate with the degree of sensitization. In conclusion, patients with spina bifida who have a ventricular shunt are at particularly high risk because they undergo a significantly higher number of operations than patients without a ventricular shunt. However, the ventricular shunt does not seem to be an independent risk factor. Furthermore, this study emphasizes that individuals at high risk, such as patients with spina bifida, should be handled latex-free from the very beginning of life.

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Latex allergy has increasingly become a health concern in defined risk groups such as patients with spina bifida and health care workers. The prevalence of sensitization to latex in patients who have spina bifida ranges from 29% to 64.5% (1–7), with the exception of only 4.3% in Venezuela (8). Clinical symptoms vary from local urticaria to severe anaphylaxis, including life-threatening intraoperative anaphylactic reactions (9, 10). Previously known risk factors for developing hypersensitivity to natural rubber latex (NRL) include atopic disposition (4, 11–13) and frequent surgery (1–4, 7, 14).

Although one surgical operation seems to be sufficient to induce latex-specific immunoglobulin

E (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, 14). However, not only the number, but also the type of surgical procedures seems to influence the risk of developing hypersensitivity to latex (11), as some authors have described a correlation between the presence of a ventricular shunt in children with spina bifida and the prevalence of IgE-antibodies to latex (5, 16–18).

Because 75% of children with spina bifida have a ventricular shunt system (14), it raises the question of whether latex allergy is due to meningeal exposure or to the high total number

of surgical interventions in these patients. Our aim was therefore to study the influence of a ventricular shunt as an independent risk factor.

Patients and methods

Patients

One hundred and sixty-one patients (85 female, 76 male) with spina bifida, aged from 4 months to 33 years (median age 10 years), were included. Two patients with known previous anaphylactic reactions to latex were excluded.

Study design

Patients' data on the presence of a ventricular shunt system and date and type of previous surgical interventions were collected. In a structured interview, patients (or parents) were asked about clinical symptoms owing to latex exposure in daily situations (e.g. inflating a balloon) and during medical interventions (e.g. 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 were performed with low-ammoniated raw and unfinished NRL milk (Ansell, Munich, Germany). Skin-test responses were assessed as positive if the maximum wheal diameter was 3 mm or greater without reaction of negative control (saline), and the skin index was greater than 0.6. The skin index was calculated as 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 min (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 (e.g. 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) (19). To establish atopic status, a screening test for inhalant (SX1) and nutritional (fx5) allergens was performed using the same automated IgE assay (20). Atopy was defined as SX1-and/or fx5-values ≥ 0.35 kU/l.

Statistical analysis

Ordinal data were calculated using the Mann–Whitney test (comparison of two independent groups) or with the Kruskal–Wallis test (comparison of more than two independent groups), nominal data with the chi-square test. For calculation of odds ratios the logistic regression and chi-square tests were used (95% confidence intervals were added in brackets). *p*-values < 0.05 were considered significant.

Results

Allergological findings

Seventy-eight patients (47.6%) showed a positive skin-prick test to NRL milk, 81 patients (50.3%) showed specific IgE-antibodies to latex. Eighty-eight patients (54.7%) were sensitized to latex in terms of a positive skin-prick test and/or specific IgE to latex in serum.

As shown in Fig. 1, 55/161 (34.2%) patients and 54/88 (61.4%) sensitized patients showed clinical symptoms on provocation [(local urticaria ($n = 55$), mild generalized urticaria ($n = 1$), allergic rhinoconjunctivitis ($n = 7$)]. The median time between the beginning of the challenge and the onset of symptoms was 10 min. Patients with a positive provocation showed significantly higher latex-specific IgE values (median 12.1 kU/l) than individuals with a negative outcome (median 1.0 kU/l) ($p < 0.0001$, Mann–Whitney *U*-test).

Surgical interventions

All 161 patients had undergone at least one operation (primary correction on the first day of life). The number of operations ranged from 1 to 20 (median 6). Individuals with more than eight surgical procedures had a significantly higher risk of developing sensitization, those with more than nine operations had a significantly higher risk of developing a clinically relevant allergy to latex ($p < 0.0001$, Mann–Whitney *U*-test) (Fig. 1). More than three surgical interventions during

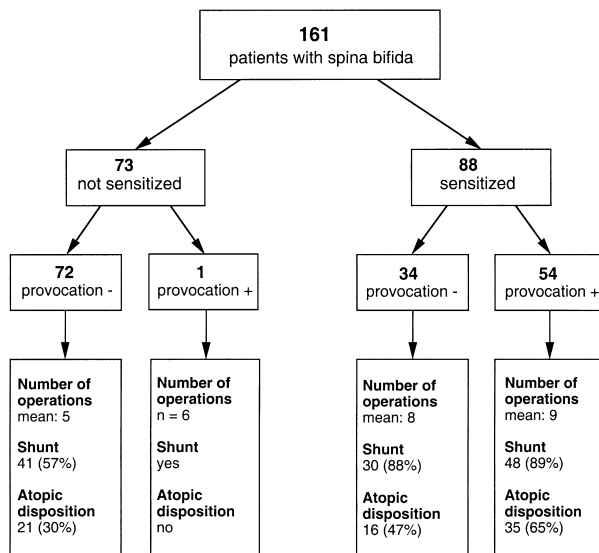


Fig. 1. Flow chart summarizing the outcome of investigations.

the first year of life significantly increased the risk of sensitization ($p < 0.005$), more than four operations during the first year significantly increased the risk of clinically relevant allergy to latex ($p < 0.0001$, Mann–Whitney U -test).

Ventricular shunt

One hundred and twenty patients (74.5%) had a ventricular shunt owing to hydrocephalus. Patients with a shunt showed a significantly higher number of previous surgical interventions (median 7 operations) than patients without a shunt (median 3 operations) ($p < 0.0001$, Mann–Whitney U -test). Within the group of nonsensitized individuals, 57% had a ventricular shunt; within the latex-sensitized, provocation-negative group, 88% had a ventricular shunt; and within the latex-sensitized, provocation-positive group, 89% had a ventricular shunt (Fig. 1). Accordingly, patients with a ventricular shunt were significantly more often sensitized and provocation-positive than individuals without a shunt ($p < 0.0001$, chi-square test). Patients with a ventricular shunt also showed significantly higher values of IgE-antibodies to latex (mean 10.2 kU/l) than individuals without a shunt system (mean 2.8 kU/l) ($p < 0.0001$, Mann–Whitney U -test) (Fig. 2). The odds ratio for the existence of a shunt system in terms of a positive provocation response was 3.9 (95% CI: 1.5–10.1, $p < 0.003$).

In the group of patients with spina bifida and a ventricular shunt ($n = 120$), the total number of operations showed a significant correlation with the concentration of IgE-antibodies to latex ($p < 0.01$). However, the number of shunt-

related operations in these patients did not significantly correlate with CAP-classes ($p = 0.17$, Kruskal–Wallis test for CAP 0–5) (Fig. 3). Only one patient showed a CAP-class 6: he had undergone 11 surgical interventions of which six were shunt-related.

Discussion

Allergological findings

This study indicates that 54.7% of patients with spina bifida are sensitized to latex. Interestingly, 61.4% of sensitized patients had a positive provocation and may therefore be at risk of developing symptoms on contact with latex in daily life or during medical interventions. During 161 skin-prick and provocation tests, no significant side-effects were noted. However, two additional patients with known anaphylactic reactions to latex had been excluded from testing. Skin-prick testing with NRL and glove tests may be regarded as safe diagnostic procedures in patients without a known risk for anaphylactic reactions. History of patients or their parents concerning symptoms on contact with latex had a sensitivity of 54.5% and a specificity of 94.3% and is therefore not a reliable diagnostic procedure.

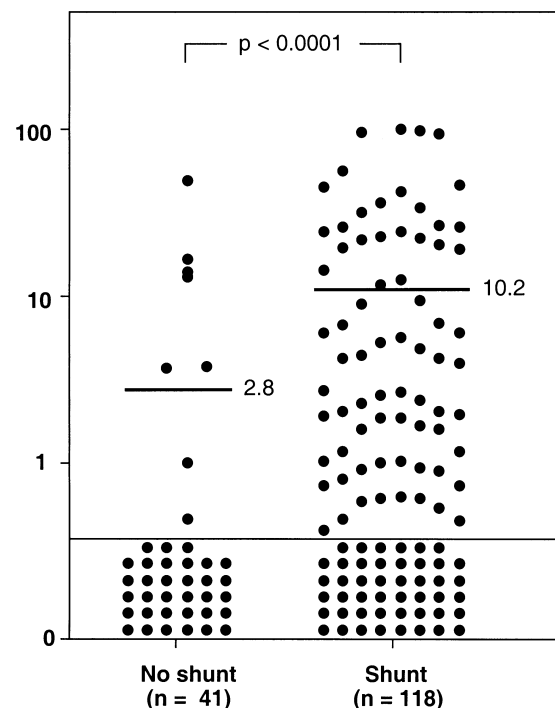


Fig. 2. Specific immunoglobulin E to latex in patients with spina bifida with ($n = 118$) and without ($n = 41$) a ventricular shunt. Bars represent mean values, the horizontal line represents the detection limit. For calculation of statistical significance, the Mann–Whitney U -test was used.

Number of operations

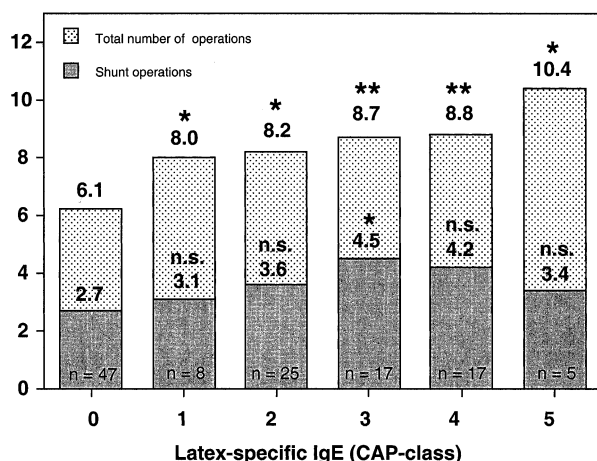


Fig. 3. Correlation of specific immunoglobulin E (IgE) to latex in serum and mean total and shunt-related surgical procedures in patients with spina bifida having a ventricular shunt ($n = 119$). p -values (* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, **** $p < 0.0001$) refer to patients without specific IgE to latex (CAP 0) (Mann-Whitney- U -test). ns, not significant.

Table 1 summarizes data of sensitivity, specificity, positive and negative predictive values for history, specific IgE in serum and skin-prick testing.

Surgical interventions and ventricular shunt

Our findings show that in the group with a ventricular shunt ($n = 120$), the total number of operations significantly correlated with the degree of sensitization to latex, which has been reported by other authors (4, >18), whereas the number of shunt operations did not correlate with the concentration of IgE antibodies to latex (Fig. 3). Patients with spina bifida and a ventricular shunt are at greater risk of developing sensitization to latex because of frequent surgical procedures.

Other patient groups with a ventricular shunt, such as individuals with cerebral palsy, have also been reported to be at risk of developing latex allergy (9, >17). Because shunt systems are latex-free, latex exposure is probably due to glove powder left on the meninges. Furthermore, the presence of latex allergy has been reported not to correlate with the number of intra-abdominal

procedures (21), which again emphasizes that a meningeal contact may be predisposing. This is supported by a current case report in which we presented a boy with local IgE production to latex in the cerebrospinal fluid including meningeal allergic reaction in form of eosinophilia. The child had received a ventriculoatrial shunt at the age of 4 weeks owing to intraventricular hemorrhage (22).

Patients with spina bifida are unique in demonstrating IgE responses to latex contact (23) and have a much higher risk of anaphylactic shock than other patients (10). The prevalence of latex sensitization in patients with spina bifida is significantly higher than in patients with spinal cord injury who had undergone an equal number of operations (23). Children with spina bifida therefore seem to bear a disease-associated propensity for latex sensitization (15).

Another reason for the different prevalence rates of allergy to latex in patients with spina bifida and other patient groups that undergo 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. However, because the pattern was in the same range as for the total number of operations, it is plausible that a high number of operations during the first year of life is an important but not a determining risk factor.

In conclusion, patients with spina bifida and a ventricular shunt are at higher risk of developing hypersensitivity to latex than patients without a shunting device, although there is no significant correlation between the number of shunt operations and the degree of sensitization in patients with a ventricular shunt. Patients with spina bifida who have a ventricular shunt are at particularly high risk because they undergo a significantly higher number of operations than patients without a ventricular shunt. However, the ventricular shunt does not seem to be an

Table 1. Evaluation of the predictive capacity of risk factors for clinically relevant latex allergy

	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Specific IgE in serum	92.7	72.1	63.8	94.9
Skin-prick test	96.4	77.4	68.8	97.6
History of parents/patients	54.5	94.3	83.3	80.7

PPV, positive predictive value; NPV, negative predictive value; IgE, immunoglobulin E.

independent risk factor. Furthermore, our findings emphasize the necessity of latex precautions in patients at risk. Individuals at high risk, such as patients with spina bifida, should be handled latex-free from the very beginning of life.

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