Anesthesiology
1997; 86:599-602

Association between Latex Sensitization and Repeated Latex Exposure in Children

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Background: **Children with spina bifida are at greater risk for latex and ethylene oxide sensitization. The authors' aim in this study was to evaluate the role of previous surgical procedures in the development of sensitization to latex and ethylene oxide.**

Methods: **The authors investigated 80 children 1–16 yr old, separated into 3 groups. Two groups had a history of 3 or more general anesthetics: 29 children had spina bifida (spina bifida group) and 31 had undergone multiple surgeries for another disease (multiple surgeries group). A control group of 20 children had undergone less than 1 anesthetic. Clinical manifestations with latex, perioperative anaphylactic reactions, and number of previous anesthetics were recorded. Skin prick tests with a commercial extract of latex, four common inhalant allergens, and radioallergosorbent test to latex and ethylene oxide were performed.**

Results: **The three groups did not differ significantly with respect to age, sex, and atopic status. Mean number of anesthetics was comparable in the spina bifida and the multiple surgeries group. Latex sensitization was common in the spina bifida group (59%) and in the multiple surgeries group (55%) but not in the control group (0%, $P < 0.05$). Ethylene oxide sensitization was significantly more frequent in the spina bifida group than in the multiple surgeries group (44% *vs.* 19%; $P = 0.052$) and strongly associated with latex sensitization. Mean number of previous anesthetics was greater in children sensitized to latex (8.4 *vs.* 3.9; $P < 0.05$).**

Conclusion: **Results suggest that it is the number of surgical procedures rather than spina bifida *per se* that is related to sensitization to latex. (Key words: Allergens: ethylene oxide; latex. Diseases: ethylene oxide sensitivity; latex allergy; multiple surgeries; spina bifida.)**

LATEX allergy is thought to be responsible for 70% of anaphylactic reactions occurring in anesthetized children.†† Children with spina bifida are known to be at increased risk for latex and ethylene oxide (EO) sensitization.[1,2] This sensitization could be explained by multiple surgical procedures or repeated bladder catheterizations these patients undergo.[3] However, the possibility of a genetic predisposition in children with spina bifida[2] also has been suggested.

The following study was undertaken to compare sensitization to latex and EO in children with and without spina bifida undergoing multiple surgical procedures.

Methods

After approval from the Ethics Committee and informed parental consent, we investigated 80 children 1–16 yr old. Twenty-nine children had spina bifida and a history of three or more general anesthetics for surgical procedures. Thirty-one children did not have spina bifida but had undergone multiple surgeries for other problems, including urinary malformations (eight cases), bone malformations, or neurologic or other diseases (multiple surgeries group). Twenty children with one or no previous general anesthetics were included in the study as the control group. They were outpatients seen before a first or second surgical procedure.

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Received from the Hospital Sainte-Marguerite, Marseille, France. Submitted for publication June 21, 1995. Accepted for publication November 25, 1996. Supported by grants from Assistance Publique à Marseille and ADEREM 001. Presented at the American Academy of Allergy and Clinical Immunology meeting in 1995, and the National Congress of the Societé Française d'anesthesie reanimation, September, 1995.

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†† United States Food and Drug Administration: Allergic reactions to latex containing medical devices. FDA Medical Bulletin. July 2–3, 1991.

Table 1. Characteristics of the Three Groups of Children

	Spina Bifida (n = 29)	Multiple Surgeries (n = 31)	Control (n = 20)
Male sex [no. (%)]	12 (41)	20 (65)	12 (60)
Age (yr) (mean ± SD)	9.8 ± 4.1	9.2 ± 4.6	7.4 ± 4.1
Previous anesthetic (n)	7.5 ± 3.7	7.7 ± 4.3	0.4 ± 0.5
History of atopy [no. (%)]	8 (28)	6 (19)	3 (15)

In a questionnaire, parents were asked to identify clinical manifestations during contact with items made of latex, such as balloons. The number of previous general anesthetics and anaphylactic peroperative reactions also were recorded. To diagnose the atopic status, prick tests with four common inhalant allergens (Laboratoire des Stallergènes, Paris, France) were performed. These allergens were dermatophagoïdes pteronyssinus (100 index reactivity [IR]/ml), cat (100 IR/ml), dog (100 IR/ml), and grass pollen (100 IR/ml). Atopic status was defined as one or more positive test to these allergens. Latex sensitization was evaluated for all children by a skin prick test with a commercial extract of a 1/100° solution of natural latex (Laboratoire des Stallergènes, Paris, France) and measurement of specific immunoglobulin E to latex using the radioallergosorbent test (RAST; Laboratoire Pharmacia, Sweden). The RAST was considered positive if greater than 0.35 Pharmacia RAST units (PRU)/ml. A subject was considered sensitized when the prick test or the RAST was positive. Ethylene oxide sensitization was evaluated by the RAST.

A positive control test and a negative control test were performed with a 9% codeine phosphate solution and a coca solution, respectively. Coca solution is the diluent solution used in the Stallergène commercial extract. Prick tests were considered positive if the wheal measured was greater than half the wheal induced by the positive control and greater than the wheal induced by the negative control. All these tests were performed in our allergy department.

All medical material known to contain latex such as gloves, catheters, facial mask, and tracheal tube was avoided during surgery when a child was diagnosed as sensitized to latex. To avoid EO in children sensitized to this gas, medical material sterilized with EO was washed with sterile water before use.

Statistical Analysis

Results were expressed as mean ± SD. Two-tailed chi-square analysis and the Mann-Whitney test were used to compare results in the three groups.

Table 2. Comparison of Sensitization to Latex (Positive ST and/or Positive RAST) and Ethylene Oxide (Positive RAST) in the Three Groups

	Spina Bifida [no. (%)]	Multiple Surgeries [no. (%)]	Control
Positive skin test to latex	12 (41)	9 (29)	0*
Positive RAST to latex	16 (55)	13 (31)	0*
Sensitization to latex	17 (59)	17 (55)	0*
Positive RAST to ethylene oxide	13 (44)	6 (19)†	0*

* $P < 0.05$.

† $P = 0.052$ comparing spina bifida with multiple surgeries.

Results

The three groups of children did not differ significantly with respect to age, sex, and atopic status. The number of previous anesthetics and the number of perioperative anaphylactic reactions were comparable in the spina bifida group and in the multiple surgeries group (table 1).

A large prevalence of latex sensitization was observed in the spina bifida group (59%) and in the multiple surgeries group (55%). No case of sensitization was found in the control group (table 2). We found a discrepancy between the results of the RAST and the skin tests: 13 children had positive RASTs but negative skin tests, whereas 2 children had positive skin tests with a negative RAST. In 16 children, both tests were positive. The RAST was not performed in three children with positive skin tests.

The difference between EO sensitization in the spina bifida group (44%) and in the multiple surgeries group (19%) approached statistical significance ($P = 0.052$). Ethylene oxide sensitization was strongly associated with latex sensitization: among the 19 children with a RAST test positive for EO, 17 (90%) were sensitized to

Table 3. Characteristics of Children Sensitized to Latex

	Spina Bifida (n = 17) [no. (%)]	Multiple Surgeries (n = 17) [no. (%)]
Male sex	7 (41)	10 (59)
No. of previous anesthetics (mean ± SD)	8.7 ± 3.8	8 ± 5
Clinical manifestations to latex	5 (29)	3 (18)
Perioperative anaphylactic reactions	5 (29)	4 (24)
History of atopy	6 (35)	4 (24)

Table 4. Comparison between the Children Sensitized to Latex and Those Not Sensitized to Latex*

	Sensitized to Latex (n = 34)	Not Sensitized to Latex (n = 46)
Age (yr)	8.1 ± 4.2	9.1 ± 4.5
Male sex [no. (%)]	17 (50)	27 (59)
No. of previous anesthetics	8.4 ± 4.4	3.9 ± 3.9†
History of atopy [no. (%)]	10 (29)	7 (15)

* Plus–minus values are mean ± SD.

† $P < 0.05$ comparing two groups.

latex (table 2). Ethylene oxide sensitization was not associated with the number of surgeries undergone. Mean number of general anesthetics in children with a RAST positive for EO was 7.2 ± 3.4, and 7.3 ± 3.7 in children with a negative RAST.

The number of previous anesthetics and prevalence of atopy were not different in children sensitized to latex in the spina bifida group and the multiple surgeries group (table 3). In the spina bifida group, five children had experienced a reaction during a previous surgery: two cases of urticaria, one bronchospasm, one erythema and dyspnea, and one not specified. All had specific immunoglobulin E to latex and four had a prick test positive for latex, suggesting that these previous peroperative reactions were caused, in part, by contact with latex during the procedure. In the multiple surgeries group, four children had experienced a perioperative anaphylactic reaction: one circulatory collapse, two with Quincke edema, and one with urticaria. They also were sensitized to latex. Among these nine children who had experienced an anaphylactic reaction during surgery, seven had also a RAST positive for EO.

There was a significant difference between the number of operative procedures in children sensitized to latex (8.4 ± 4.4) and children not sensitized (3.9 ± 3.9) (table 4).

Discussion

The high prevalence of latex sensitization in spina bifida was first reported by Slater *et al.*[4] They found RASTs positive for latex in 10 of 32 children with spina bifida. Moneret-Vautrin *et al.*[5] found skin tests positive for latex in 8 of 25 children with spina bifida. In other studies, the rate of sensitization was greater: 60% of children studied by Ellsworth *et al.*[6] were sensitized to latex and 72% of those in Konz *et al.*'s study.[7] We also found that 59% of children with spina bifida were sensitized to latex.

The high prevalence of sensitization in spina bifida patients could be due to repeated exposure to latex during surgical procedures and bladder catheterizations, or to a genetic predisposition.[1] In our study, in which we compared children with spina bifida with either children having undergone multiple surgeries for another disease or a control group of children who had undergone one or no surgery, we demonstrated that the former hypothesis is the most likely. Indeed, we found the same rate of sensitization in the spina bifida and the multiple surgeries group, and the mean number of anesthetics in children sensitized to latex was greater than in nonsensitized children. Cawley *et al.*[8] confirmed these results: in children with myelodysplasia, latex sensitization was greater in those who had more than six surgical procedures. Kelly *et al.*[9] found a significant risk for perioperative anaphylactic reaction in children with spina bifida who had nine or more prior surgical procedures.

Atopy is a risk factor for latex allergy and increases the risk for latex allergy in exposed subjects.[5,10–12] In our study, although the difference was not significant, the incidence of atopy, as in the latex-sensitized group, was twice that in the nonsensitized group. The lack of statistical significance may be related to the small size of the study groups. Atopy was diagnosed using skin prick tests. We tested only four major antigens (two dust mites, grass pollen, and cat dander) for two reasons. First, some children were young, and it was difficult to perform more skin tests. Second, it has been shown, in epidemiologic studies, that more than 85% of atopic patients can be identified by testing only these antigens.[13]

Clinical manifestations of latex allergy had a high positive predictive value for true latex sensitization. All eight children who complained of allergic symptoms after latex exposure were, indeed, sensitized. Symptoms included facial edema and urticaria when inflating balloons. Seven had a skin test positive for latex. Six had a RAST positive for latex and, among these six, five had a class 4 positive RAST. In this group of children allergic to latex (clinical manifestations and presence of a positive RAST or a positive skin test), 60% were atopic. Atopy could facilitate the sensitization, and latex could be considered a common allergen. However, in this study, prevalence of atopy is not statistically different in the latex-sensitized children as compared with control subjects and cannot be considered a risk factor.

Another study confirmed that latex allergy is an important risk factor for perioperative anaphylactic reactions in children.[14] In this study, conducted by the French association of pediatric anesthesiologists and including 162,551 general anesthetics in children, 20 cases of anaphylaxis were re-

corded. In 70% of these cases, the etiology was latex allergy. In our study, all five children of the spina bifida group and four children in the multiple surgeries group who experienced anaphylactic reactions during anesthesia were allergic to latex. Only two of the five children in the spina bifida group had clinical manifestations of latex allergy. In 1991, the Food and Drug Administration suggested that questions about latex sensitivity should be included in the preanesthetic evaluation in children with multiple operations and indwelling catheters.§ Therefore, it is advisable to screen, for latex sensitization, by skin test or RAST, all children who have undergone multiple procedures before another surgery. Such screening also was proposed by Beaudouin *et al.*[3] for children with spina bifida. Conversely, Slater and Mostello[15] did not agree with this proposal.

Ethylene oxide is a gas frequently used to sterilize medical material, including urinary catheters, that cannot withstand high temperatures. Ethylene oxide sensitization has been described in children with spina bifida experiencing perioperative anaphylactic reactions, always in association with a latex sensitization. In our study, we found that 32% of the children in the spina bifida and multiple surgeries groups were sensitized to EO. In 90% of these cases, this sensitization was associated with a latex sensitization. The rate of EO sensitization was significantly greater in children with spina bifida (44%) than in others (19%), perhaps due to a high frequency of bladder catheterizations in children with spina bifida. We cannot prove this hypothesis because the bladder catheterization rate was not studied in our children, though only one of seven children in the group undergoing multiple surgeries for uropathy was sensitized to EO. This is comparable to the rate of sensitization in the multiple surgery group without uropathy. Ethylene oxide could act in association with latex to induce an anaphylactic reaction in children sensitized to both allergens. Among the nine children who experienced a perioperative reaction, seven were sensitized to EO. No publication has reported perioperative anaphylaxis caused only by EO.

In conclusion, children with a history of multiple surgeries are at high risk for latex sensitization. Children with latex sensitization had a higher mean number of procedures than those without latex sensitization. Children with spina bifida are often sensitized to EO, but generally in association with a latex sensitization. The majority of anaphylactic reactions during anesthesia in children is related to latex allergy. Therefore, in all children with a history of multiple surgeries, we advise a systematic preoperative screening for latex allergy before anesthesia, first by asking for specific symptoms of clinical latex allergy, and second by using skin prick tests or RAST, except if there is a clear history of latex allergy. However, the best prevention would be latex avoidance from the first surgical procedure in all children who might undergo multiple surgical procedures because of spina bifida or another serious disease.

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