

Anaesth Intensive Care 2001; 29: 393-399

Latex Hypersensitivity in Spinal Cord Injured Adult Patients

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SUMMARY

Latex hypersensitivity is a major cause of anaphylaxis during anaesthesia. Patients with spina bifida, health care or rubber industry workers have been considered at risk for latex sensitization. By analogy, the existence of other at-risk subsets of patients with latex exposure due to frequent surgical procedures has been suggested.

The aim of this study was to evaluate the prevalence of latex sensitization in a cohort of adult patients with spinal cord injury and repeated latex exposure.

Forty-two adult patients with spinal cord injury were studied and retrospectively compared to a group of 30 children with spina bifida evaluated using a similar protocol.

Patients were administered a questionnaire concerning history of latex hypersensitivity, atopy, and surgical procedures. Latex sensitivity was investigated by skin prick-tests and latex-specific IgE assay. The search for atopy was based on in vivo and in vitro tests against a panel of environmental allergens.

No chronic spinal cord injured patient had a history of latex allergy. When compared with spina bifida, the number of surgical procedures was not statistically different. Although not significantly different, the prevalence of atopy was higher in spina bifida patients. The high level of latex sensitization in spina bifida patients contrasted sharply with the absence of sensitization observed on both skin and in vitro tests in patients with spinal cord injury ($P < 0.0001$).

This study confirms that adult patients with chronic neurologic defects resulting from spinal cord injury exhibit a low risk of latex sensitization. These results suggest that considering adult patients with repeated surgical procedures as a group at risk for latex sensitization because of a high degree of latex exposure should be re-examined.

Key Words: ALLERGY: latex, neurologic defects, skin test, adults, anaesthesia

Over the last two decades, latex hypersensitivity has emerged as a major cause of anaphylaxis during anaesthesia¹⁻⁷. Several distinct populations have been considered at risk, leading to detailed recommendations concerning the diagnosis of sensitization and the prevention of adverse reactions before anaesthesia and surgery⁸. Among these populations are

patients who have been repeatedly exposed to latex, such as patients with spina bifida^{4,9-15}, health care¹⁶⁻¹⁸ or rubber industry workers¹⁹. A history of atopy^{2,14,16,17,20} has been recognized as an additional risk factor for latex sensitization in these populations.

As with all allergens, the longer the exposure, the greater the number of sensitized individuals¹⁸. Thus, among the various risk factors proposed for latex sensitization in children with spina bifida, the frequency of latex exposure during multiple surgical procedures, bladder catheterization or rectal disimpaction has been incriminated¹⁵. Based on these observations, the existence of other at-risk subsets of patients who undergo frequent surgical or medical procedures such as haemodialysis²¹ or supportive procedures in chronic neurologic defect conditions²² has been suggested. Nevertheless, recent studies aimed at confirming this increased risk for latex sensitization remained negative^{23,24}. Several reasons could explain these negative results including the different at-risk populations studied, or the methods used to detect sensitization. This could be the case in the series of adult patients suffering from acquired neurologic

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Accepted for publication on March 9, 2001.

Anaesthesia and Intensive Care, Vol. 29, No. 4, August 2001

defects reported by Konz et al, where latex sensitization assessment was limited to latex-specific IgE antibody titre determination²³.

It is important to precisely define at-risk populations in order to improve the efficacy and cost-effectiveness policy concerning preoperative allergy assessment, surgery in latex-free environment or reduced latex exposure. The aim of this study was to evaluate the prevalence of latex sensitization assessed by combined skin and in vitro immunologic tests in a cohort of adult patients with spinal cord injury. These results were compared with those previously obtained in a series of children with spina bifida evaluated according to a similar protocol¹⁴.

PATIENTS AND METHODS

Forty-two adult patients, paraplegic or quadriplegic as a result of spinal cord injury and admitted to the neurologic rehabilitation unit or the neurosurgical department of the Nancy University Hospital, were involved in the study between July 1, 1994 and September 1, 1997. This protocol was approved by the local Ethical Committee. Informed consent was obtained from each patient.

These patients were retrospectively compared with a group of 30 children with spina bifida evaluated according to a similar protocol¹⁴.

Basic Information

Patients were administered a questionnaire which elicited an overview of the patient's medical condition and assessed the history of latex hypersensitivity including itching, hives, rhinoconjunctivitis, bronchospasm, angioedema or anaphylaxis. The questionnaire also documented the number of surgical procedures, as well as the frequency of bladder and rectal manipulations with latex devices (e.g., catheterization and rectal disimpaction). Coexisting atopic conditions, including history of allergies, asthma, allergic rhinitis, rhinoconjunctivitis, atopic dermatitis, and food sensitivity were also recorded.

Immunologic Studies

Latex sensitivity testing was carried out using both in vivo and in vitro methods. The investigation included prick-tests with three different varieties of latex: an ammoniated natural rubber latex emulsion (Porges S.A., Sarlat, France), and two commercial fresh natural rubber latex extracts (Stallergenes SA, France and Allerbio, France). Skin prick testing was performed according to standard procedures on the volar side of the forearm. A 9% (w/vol) solution of

codeine phosphate was used as a positive control, and saline solution as a negative control. A test was considered positive if the saline test used as control was negative and the diameter of the wheal after 15 minutes was at least half that obtained with the positive control.

In vitro testing for latex-specific IgE was carried out using RAST (Pharmacia Cap System™, Pharmacia, France) according to manufacturer's instructions. Values of allergen-specific IgE above 0.35 kU/l were considered to be positive.

The search for atopy was based on in vivo and in vitro tests. Skin-prick tests were performed with common inhalant allergen extracts (house dust mites: *Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*, cat and dog epithelia, gramineae pollens, Stallergenes SA, France). In addition, an in vitro test for common inhalants-specific IgE was systematically carried out (Phadiatop®, Pharmacia, Sweden). Atopy was diagnosed by the presence of one or more positive prick tests of common inhalant allergens and/or positive Phadiatop® test.

Statistical Analysis

Statistical analysis was performed with the Staview IV® software (Abacus Concepts, Berkeley, CA, U.S.A.). Results are presented as mean and range. Comparisons between groups were achieved by the Fisher exact test. The criterion of significance was $P < 0.05$.

RESULTS

The main results are summarized in Table 1. These results were compared with data obtained in a series of 30 spina bifida children investigated with a similar protocol and previously published by our group¹⁴.

TABLE 1
Patient characteristics

	Spinal cord injury	Spina bifida
Number of patients	42	30
Age	33 (20-64)	10 (5-16)*
Surgical procedures	6 (1-23)	9 (5-21)
Atopy	12 (29%)	14 (46%)
Latex intolerance	2	1
Latex sensitization	0	12 (40%)*

Results are presented as mean (range).

* $P < 0.05$.

As expected, a significant difference was observed between the two groups regarding the age. The mean age of the adult patients was 33 years (range 20 to 64), when it was only 10 years (range 5 to 16) in spina bifida children.

The clinical evaluation revealed that none of the

adults had a history of latex allergy. A clinical latex intolerance (contact urticaria) was suspected in two adults, and in only one of the children.

The prevalence of atopy, based on the questionnaire and skin and in vitro tests results, was estimated at 29% (12/42). Four patients had a history of asthma, five had a history of aeroallergy, and three had a history of dermatitis. Skin prick-tests were positive in all cases of atopy, when specific IgE assay for inhalant allergens were positive in seven atopic subjects, and negative in the remaining atopic patients. Although not significantly different, the prevalence of atopy was higher in spina bifida patients 40% (12/30). Moreover, atopy was present in 10 out of 12 spina bifida patients sensitized to latex (83%).

The number of surgical procedures was not statistically different between the two series of patients. Patients with spinal cord injury averaged six operations after the initial trauma, with the number of operations ranging from one to 23, whereas patients with spina bifida had an average of nine operations with a range from five to 21. Bladder catheterization was performed in all adult patients (mean cumulative duration four years [range 1 to 24]), and in half of the spina bifida children. No differences were observed regarding the presence of catheterization in spina bifida children with respect to latex sensitization.

No adverse reactions were reported during the skin-testing procedures in either group. Both skin and in vitro tests for latex sensitization were negative in all adult spinal cord-injured patients. On the contrary, there was a high level of sensitization in spina bifida patients (12 out of 30), which contrasted sharply with the absence of sensitization toward latex in patients suffering from spinal cord injury ($P < 0.0001$).

DISCUSSION

This study confirms that adult patients with chronic neurologic defects resulting from spinal cord injury, despite recurrent and sustained latex exposure through surgical interventions and prolonged urinary catheterization, exhibit a significantly lower risk of latex sensitization, when compared with a group of spina bifida children. These results underline the need for carefully defining an at-risk population, prior to recommending any systematic preoperative allergy assessment before anaesthesia. The definition of patients with repeated surgical procedures as a group at risk of latex sensitization extrapolated from observations on spina bifida children or other groups considered at risk because of a high degree of latex exposure should be re-examined.

Our results further confirm those previously reported by Konz et al, who found a significantly lower rate of sensitization against latex in patients suffering from spinal cord injury, when compared with a group of children with spina bifida²³. However these observations were based on responses to a questionnaire and on latex-specific IgE antibody evaluation, without reported skin testing of latex antigen in the spinal cord injured group, raising the question of a possible underestimation of latex sensitization.

Latex Allergy Diagnosis

The diagnosis of IgE-mediated latex hypersensitivity is based on clinical history and the demonstration of an IgE-mediated pathogenesis by specific immunologic tests²⁵. Careful history taking is essential when diagnosing latex allergy. Unfortunately, even a thorough questionnaire will not identify all latex allergic patients^{26,27}. Therefore, additional immunological investigations are required.

At present, in vitro measurement of serum latex-specific IgE can be performed by RAST, AlaSTAT, various Elisa methods and other IgE-binding techniques such as immunoelectrophoresis, immunospot and immunodotblotting. However, the sensitivities and specificities of these tests vary and are not optimal, possibly due to deficiencies and biological variations in natural latex allergen sources, cross-reactivity with other IgE antibodies or an improperly selected threshold of the assay^{25,28}. In addition, their sensitivity and specificity have been reported to be highly dependent on the population being studied²⁹. Unfortunately, there is no universally accepted standardized serum test to assess Type I latex allergy. Nevertheless, a recent report has indicated some advantages of the test used in the present study, in anaesthesia personnel³⁰.

Because latex-specific IgE assay sensitivity has been reported to be low in some studies^{16,31}, intradermal skin testing of latex antigen is usually regarded as the most useful confirmatory test^{25,32}. High sensitivity and specificity levels ranging from 93 to 100% and 82 to 99% respectively have been reported^{22,28,33,34}. Nevertheless, latex allergy stems from a large variety of proteins, which could differ in their relative antigenicity and could vary widely in their relative abundance in the preparations used for skin testing. Recently, Hamilton et al³⁵ in a phase I/II clinical study, observed equivalent diagnostic accuracy (sensitivity and specificity) with natural latex, ammoniated latex, and rubber glove extracts skin test reagents. Nevertheless, in this study, dif-

ferent sources of latex allergen were used to further enhance skin-prick test sensitivity. Finally, if anaphylactic events after epicutaneous skin testing have been previously reported³⁶⁻³⁹, in more recent studies^{28,33,35} adverse effects were absent or only rarely observed, and were not observed in the patients reported in the present study.

Differences Between Spinal Cord-Injured Patients and Other At-Risk Populations

It is widely acknowledged that patients having undergone multiple surgical procedures, as well as atopic individuals, should be considered as groups at risk for latex sensitization⁸. This may have important consequences via the extension of recommendations for systematic screening for latex sensitization before surgery in multi-operated patients. These considerations mainly rely on observations made in well-defined risk groups with a high degree of exposure to latex such as health care workers^{16,27,40,42}, or patients with myelomeningocele^{9,14,15,43-47}.

In the health care workers group, a prevalence of latex sensitization ranging from 2.6 to 12.1% based on latex skin-prick testing has been observed⁴⁸⁻⁵². This sensitization was associated with a high frequency of work-related symptoms⁵¹, and in particular with latex-induced occupational asthma confirmed with specific inhalation challenge documented in 2.5% of health care workers⁵³.

Atopy is also usually regarded as an important predisposing factor for latex sensitization. A cumulative risk for an IgE-mediated latex allergy has been observed in atopic health care workers^{16,20,40,48,54}, atopy ranging from 58 to 67% in latex-sensitive hospital personnel^{16,55}. It has been estimated that the presence of atopy increases the risk of latex sensitization from a factor ranging from 4.4¹⁷ to 25²⁰.

Our results indicate important differences when compared with the above-mentioned at-risk groups. In our series, despite a documented high degree of latex exposure, latex sensitization was undetectable both on skin and specific-IgE testing. These results are similar to those previously reported in unselected patients prick-tested before surgery (0.12%)⁵⁶. The differences we observed persist even when atopic subjects were considered. In our study, atopic patients do not exhibit sensitization towards latex.

Moreover, the observation of higher levels of latex sensitization in the general population than previously expected^{57,58}, compared with a low rate of perioperative reaction to latex, has already raised questions regarding the need for systematic screening in atopic patients. In addition, sensitization without

symptoms of latex allergy does not mean that an allergic reaction will occur⁵⁹. The clinical significance of prick tests and specific IgE to latex has also been questioned. Their positivity reflect an IgE-dependent sensitivity but does not necessarily indicate a clinical allergy^{20,56}. Therefore, in our opinion, on the basis of the results reported here, the interest in systematic preoperative screening for latex sensitization in adult patients having experienced multiple surgical procedures, even in the case of atopy, should be reconsidered.

Finally, the differences observed between our patients and health care workers suggest that other factors such as the route of exposure and the number of particles can contribute to latex sensitization. Health care workers might share an increased risk when compared to multioperated patients because of a greater exposure to inhaled latex particles in contaminated operating-room air, or because of repeated exposition to non-reusable latex products resulting in higher exposure to free latex particles.

Similarly, our results suggest that other additional important factors must be taken into account to explain the sharp differences we observed between adult patients with spinal cord injury and spina bifida patients. In this later group, latex-sensitization frequency ranges from 32 to 64.5% in skin prick test screenings^{20,60} and from 34 to 72% in serologic IgE measurements^{12,23}. In contrast to these studies, a low prevalence rate of 4.3% was reported in Venezuelan children with spina bifida⁶¹.

Various hypotheses have been proposed to explain the patient-specific rate of latex sensitization in spina bifida patients. Apart from the high degree of latex exposure (gloves, catheters), the existence of group-specific risk factors has been hypothesized. The fact that patients with spina bifida are sensitized to latex protein fractions that are different from those of health care workers has suggested that they are a unique group^{34,62-67}. A genetic predisposition, as well as possible neurologic and immunologic systems interactions to the development of latex allergy has been suggested^{23,68}.

A further question is whether or not the age of exposure to latex allergen may predispose an individual to the development of hypersensitivity. It has been suggested that children exposed to latex through surgery during the first days of life may also preferentially produce IgE antibody to latex antigen, resulting in clinical sensitivity^{23,69}. This could partly explain the differences observed in our series, since the mean age of the spinal cord injury patients we investigated was significantly higher than those of spina bifida

patients. However, the prevalence of latex allergy and sensitization seemed to be a function of advancing age and possibly of more surgical procedures⁷⁰, rather than age at exposure³⁴. Moreover, when compared with multi-operated children, the prevalence of immediate latex hypersensitivity in children with spina bifida is clearly higher⁴⁵. Nevertheless, the prevalence of latex sensitization reported in multi-operated children or in patients suffering from spinal cord injury remains higher than the prevalence observed in our patients.

Atopy is usually considered as a risk factor, in particular in spina bifida patients. In our series, although not statistically significant, atopy in spinal cord injured patients was less prevalent than in spina bifida patients. Moreover, atopy was present in 83% of the spina bifida patients sensitized to latex.

Patients with spina bifida have been considered as a unique population in their tendency to develop atopy by some authors²³. However, the role of latex sensitization in the development of atopy through sustained production of cytokines produced by activated mast cells and basophils^{71,72}, which in turn might have influenced the polarization of naive T cells into the Th2 development pattern, has been proposed. It has been suggested that this phenomenon could produce more environmental allergy and atopy manifesting at younger age in these patients³⁴. The recent report of a normal prevalence of atopy in subjects with spina bifida having little latex exposure would support this mechanism⁶¹.

Study Limits

The main limitation of this study is the use of an historical cohort of spina bifida patients. This is due to the dramatic reduction in the incidence of spina bifida in France, resulting from the wide use of systematic screening for this pathology during pregnancy. This renders the constitution of a large cohort of new spina bifida cases difficult. One might speculate that the relatively recent awareness of latex allergy might have led to changes in practice over time. Nevertheless, the present study was initiated to specifically address the question of the need to develop a policy in the reduction of latex exposure in chronically latex-exposed adult patients. As a result, in the absence of any scientific evidence for an increased risk of latex sensitization in this patient group, and after approval of our Ethics Committee, no modifications in the usual practice were recommended. In particular, latex urinary catheters or gloves were obtained from the same manufacturers.

However, it is obvious that latex exposure was not

strictly comparable between both groups. Urinary catheterization was present in all spinal cord injured patients, whereas it was only present in half of the spina bifida patients. In addition, the type of surgery was obviously not the same in spina bifida and spinal cord injured patients.

In terms of diagnostic procedures, the tests used in both cohorts of patients were similar. Although latex extracts could differ in their relative antigenicity and could vary in their relative abundance in the preparations used for skin testing, in both cohorts, three different sources of latex allergen, provided by the same manufacturers were used to further enhance skin-prick test sensitivity.

Therefore in our opinion, despite the evident limitations raised by the use of historic spina bifida controls, these are not sufficient enough to discard the wide differences between latex sensitization in spina bifida and spinal cord injured patients, as we observed.

Finally, the results observed in this group of adult spinal cord injured patients indicates that one should consider the need for reassessing the definition of multi-operated adult patients, even in case of atopy, as a specific group at risk for latex sensitization. Therefore, systematic allergologic assessment in the absence of clinical symptoms of sensitization against latex will be of questionable interest.

ACKNOWLEDGEMENTS

We would like to thank Dan Longrois, M.D., Ph.D. for his help in reviewing this manuscript, and William Canada, M.D. for reviewing the English version of the manuscript.

Financial support was from Centre Hospitalier et Universitaire de Nancy, France.

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