

Latex hypersensitivity: a case study

Susan N. Mathew, MD; Alton L. Melton, Jr, MD; and William O. Wagner, MD

We report 16 cases of latex allergy and the diagnostic methods used to determine sensitivity. By history, eight had usually experienced anaphylaxis during operative procedures, and eight experienced contact urticaria. Skin prick tests were positive in all subjects and negative in ten controls. In vitro analysis by ELISA for latex-specific IgE was positive in only three subjects. No adverse reactions occurred during testing. We conclude that prick skin testing is the preferred diagnostic method, and that the in vitro method used in this study has an unacceptable lack of sensitivity.

INTRODUCTION

Natural rubber has long been known to cause contact dermatitis due to sensitizing agents used in rubber processing. Recently, several authors have reported intraoperative anaphylactic reactions in adults and children that were directly attributable to the latex itself.²⁻⁵ In these reports, there appears to be a significant risk for latex anaphylaxis in children with spina bifida and congenital urologic abnormalities, and a lesser increased risk in health care workers. After identifying several patients with latex hypersensitivity, we evaluated them to determine the most sensitive diagnostic test and to attempt to determine which predisposing factors may be important in the development of latex allergy.

PATIENTS AND METHODS

Between January and August 1991, we identified 16 patients whose histories were consistent with latex hypersensitivity. They included 12 children and 4 adults with ages ranging from 3 to 35 years (median age = 10.5 years, mean age = 14.7 years). Eleven of the 16 had personal histories of atopy. Eight had experienced anaphylaxis (seven intraoperative) and eight had experienced contact urticaria. Signs and symptoms of anaphylaxis included respiratory (asthma, stridor), cardiovascular (hypotension, shock), and cutaneous (diffuse urticaria-angioe-

dema) reactions. Ten controls were selected from the adult and pediatric allergy clinic population, none of whom had any history of reactions to latex.

Skin prick testing was performed with latex in three different forms and appropriate positive and negative controls in all subjects and controls. Testing was carried out on the skin of a distal extremity with a sterile bifurcated needle (Allergy Labs of Ohio, Inc, Columbus, OH). Testing materials included histamine phosphate 1 mg/mL as a positive control, albumin/saline solution (Hollister-Stier, Spokane, Washington) as a negative control, solid latex rubber (prepared by exposing 3 mL of ammoniated latex concentrate to room air for greater than 72 hours), latex extract (prepared by incubating a 1 × 1 inch cube of solid latex in 5 mL of albumin/saline solution for greater than one hour), and undiluted liquid ammoniated latex concentrate (gift of Goodyear Tire Co., Akron, OH). Prick testing was read 15 minutes after application and results were expressed on a 4-point scoring system: 0 = negative, equal to negative control; 1+ = negative, wheal diameter less than 3 mm; 2+ = weakly positive, wheal diameter greater than 3 mm, but significantly smaller than histamine control; 3+ = positive, wheal diameter equal to positive control ± 2 mm; 4+ = strongly positive, wheal diameter significantly greater than positive control. Because we were testing subjects with histories of anaphylaxis with a

relative uncharacterized antigen, appropriate measures to treat anaphylaxis were immediately available. Also, the testing area is contained in the same facility as the hospital and intensive care unit.

In vitro analysis was performed on all subjects and controls to measure latex specific IgE concentrations in the serum. This was performed by the ELISA method with a paper disk solid-phase and beta-galactosidase as the enzyme (Phadezym RAST method: Pharmacia, Uppsala, Sweden). Results were scored on a 4-point system as follows: class 0 = less than 0.1 (undetectable) Phadezym RAST Unit (PRU)/mL; class I/O = (negative) 0.1–0.34 PRU/mL; class I (very low) 0.35–0.74 PRU/mL; class II (low positive) 0.71–3.4 PRU/mL; class III (moderately positive) 3.15–17.5 PRU/mL; class IV (strongly positive) greater than 17.5 PRU/mL. For our study, only ELISA scores of class II or higher were considered positive.

RESULTS

Among the 12 children involved in the study, eight had spina bifida, two had congenital urologic abnormalities, and two had neither, but did have indwelling gastrostomy tubes. These latter two had developed respiratory reactions when playing with rubber toys in addition to intraoperative anaphylaxis. Three children developed urticaria and angioedema during dental procedures. One of these had tested negative on a prior evaluation for

Received for publication March 9, 1992.
Accepted for publication October 6, 1992.

possible local anesthetic allergy (including subcutaneous challenge), and was later found to be latex sensitive. Six of the 12 children had experienced contact urticaria to balloons, some accompanied by asthma while inflating the balloons. All children had histories of early and frequent operations or of indwelling rubber urinary catheters or gastrostomy tubes (Table 1).

The four adult subjects had prolonged exposure to latex rubber products through health care occupations (EMS, occupational therapist, dental assistant, and chemotherapy nurse). In each case this mainly involved the use of latex gloves on a regular basis for at least 3 years. Two of these people also suffered from hand eczema. The EMS worker had to change his career because of recurrent episodes of latex-induced anaphylaxis, once involving touching the steering wheel of the EMS vehicle which had glove powder on it from the previous driver.

Skin prick testing was positive (score = 2 or greater) in all 16 subjects and negative in all ten controls. Raw liquid ammoniated latex was positive in all 16 subjects (100%), latex extract was positive in 14/16 (88%) subjects, and the solid rubber was positive in 9/16 (56%). There were no local or systemic adverse reactions to skin prick testing observed in any of the study subjects or controls. In vitro testing by ELISA for latex-specific IgE in serum was positive (class II or greater) in only three out of 16 subjects (19%). Even if equivocal class I concentrations were considered positive, 6/16 would have been considered negative (Table 1). All ten controls had values below class II, with two in the class I/O range.

DISCUSSION

Natural rubber is derived from the milky sap of the rubber tree, *Hevea brasiliensis*, found originally in the Amazonian region.⁶ Today most natural rubber comes from Malay-

Table 1. Patient Characteristics* and Test Results

Patient	Primary Diagnosis/ Employment	Mode of Latex Exposure	Clinical Presentation	Skin Prick Testing	Phadezym-RAST
1	Spina Bifida (SB)	EFSP; FUC >3 yr	Intraoperative anaphylaxis (IA)	NH3 latex: 4 Latex ext: 4 Solid latex: 2	Class III (6.6 PRU/mL)
2	SB	EFSP; FUC >3 yr	IA	NH3 latex: 4 Latex ext: 4 Solid latex: 2	Class I (0.48 PRU/mL)
3	SB	EFSP; FUC >3 yr	Contact urticaria (CU)	NH3 latex: 4 Latex ext: 3 Solid latex: 3	Class II (1.03 PRU/mL)
4	SB	EFSP; FUC >3 yr	CU	NH3 latex: 4 Latex ext: 3 Solid latex: 2	Class I (0.46 PRU/mL)
5	SB	EFSP	CU and angioedema	NH3 latex: 4 Latex ext: 4 Solid latex: 1	Class I (0.35 PRU/mL)
6	SB	EFSP	CU	NH3 latex: 4 Latex ext: 3 Solid latex: 2	Class I (0.62 PRU/mL)
7	SB	EFSP; FUC >3 yr	CU	NH3 latex: 3 Latex ext: 3 Solid latex: 2	Class 0 (0 PRU/mL)
8	SB	EFSP; FUC >3 yr	CU	NH3 latex: 2 Latex ext: 1 Solid latex: 0	Class I/O (0.11 PRU/mL)
9	Congenital Urogenital Anomaly (CUA)	EFSP; FUC >3 yr	IA	NH3 latex: 4 Latex ext: 3 Solid latex: 0	Class I/O (0.21 PRU/mL)
10	CUA	EFSP	IA	NH3 latex: 4 Latex ext: 3 Solid latex: 1	Class III (4.42 PRU/mL)
11	Cerebral palsy and chronic GER	Indwelling G-Tube	IA	NH3 latex: 4 Latex ext: 4 Solid latex: 3	Class I (0.68 PRU/mL)

Table 1. Patient Characteristics* and Test Results (cont'd)

Patient	Primary Diagnosis/ Employment	Mode of Latex Exposure	Clinical Presentation	Skin Prick Testing	Phadezym-RAST
12	Chronic GER	Indwelling G-Tube	IA	NH3 latex: 3 Latex ext: 2 Solid latex: 0	Class I/O (0.13 PRU/mL)
13	Occupational therapist	Hand gloves >3 years	IA & CU	NH3 latex: 3 Latex ext: 1 Solid latex: 1	Class I (0.44 PRU/mL)
14	EMS/fireman	Hand gloves >3 years	Anaphylaxis	NH3 latex: 3 Latex ext: 3 Solid latex: 1	Class I/O (0.19 PRU/mL)
15	Dental assistant	Hand gloves >3 years	CU	NH3 latex: 4 Latex ext: 3 Solid latex: 2	Class I (0.5 PRU/mL)
16	Chemotherapy nurse	Hand gloves >3 years	CU and hand eczema	NH3 latex: 3 Latex ext: 4 Solid latex: 3	Class I/O (0.15 PRU/mL)

* EFSP = early and frequent surgical procedures, FUC = Foley urinary catheterization, NH₃ = ammoniated, GER = gastroesophageal reflux, Ext = extract, SB = spina bifida, IA = intraoperative anaphylaxis, CU = contact urticaria, and CUA = congenital urogenital anomaly.

sia. The sap is filtered and then collected into a vessel containing a preservative, such as ammonia. This product is concentrated and then shipped to rubber refineries, where it is processed for use in manufacturing rubber products such as tires, balloons, elastic thread, rubber adhesives, condoms, and surgical gloves.³

During the past several years, increasing numbers of reports of patients with latex hypersensitivity and anaphylaxis have been published. Turjanmaa et al screened 512 hospital employees for latex allergy and found 2.9% to be latex sensitive by prick skin testing, while 0.8% of a control group of 130 subjects had positive tests.² Slater et al found a prevalence of 45% (5 of 11 patients) in a spinal bifida population by history and in vitro testing.³ Gold et al described 15 patients with

spina bifida or congenital urologic abnormalities who had experienced 19 intraoperative anaphylactic reactions.⁴ Meerpol et al reported a latex allergy prevalence of 18% to 28% in patients with spina bifida.⁵

Frequent and early exposure to latex appears to represent a significant risk factor for the development of latex hypersensitivity. Frequent and early intraoperative exposure was present in 10/16 of our cases. Strict avoidance of latex product use in the operating room has allowed four of our subjects to undergo subsequent surgery without reaction, and without premedication. For two of our subjects, complete latex avoidance has become nearly impossible because of regular treatment with intravenous hyperalimentation and intravenous gamma globulin.

In our series, prick skin testing

represented the superior method for latex allergy testing. The sensitivity was far greater than that of the Pharmacia ELISA, even when equivocal class I ELISA results are considered positive. Of the latex skin test reagents used, the raw ammoniated latex sap was the most sensitive, followed by the aqueous extract, which gave equivocal 1⁺ reactions in two subjects. Testing with solid latex was negative in three of our subjects and equivocal in four more. None of the control subjects reacted to these antigens. It is our understanding that other investigators have induced anaphylaxis during prick skin testing with latex glove extracts.¹ We have no explanation for the disparity between their results and ours. We have not had any adverse reactions to prick skin testing and consider this to be the preferred method of testing. Clearly, the ELISA used in this study displays an unacceptable lack of sensitivity.

Considering the high prevalence of latex hypersensitivity in patients with spina bifida and congenital urologic abnormalities, we now routinely screen all such individuals for latex allergy prior to any anticipated surgical procedure and institute strict latex avoidance in the operating room if testing is positive. One might argue that all procedures in the at-risk population should be performed with strict latex avoidance to prevent possible future development of sensitivity. We have no basis for such a recommendation at this time. Because of the concern over potential adverse experiences with latex skin testing, we recommend using extreme caution before performing such testing in routine allergy practice.

ACKNOWLEDGMENTS

The authors thank Lovetta Larkins and Lori Ziegler for assisting in the preparation of this manuscript.

REFERENCES

- Spaner D, Dolovich J, Tarlo S, et

- al. Hypersensitivity to natural latex. *J Allergy Clin Immunol* 1989;83:1135-7.
2. Turjanmaa K. Incidence of immediate allergy to latex gloves in hospital personnel. *Contact Dermatitis* 1987;17:270-5.
3. Slater JE, Shaer C, Mostello L, et al. Rubber-specific IgE in children with spina bifida [Abstract]. *J Allergy Clin Immunol* 1990;85:293.
4. Gold M, Swartz JS, Braude BM, et al. Intraoperative anaphylaxis: an association with latex hypersensitivity. *J Allergy Clin Immunol* 1991;87:662-6.
5. Meerpol E, Kelleher R, Bell S, et al. Allergic reactions to rubber in patients with myelodysplasia [Letter]. *N Engl J Med* 1990;323:1072.
6. Moralex CA, Bosomba A, Carreira J, et al. Anaphylaxis produced by rubber glove contact: case reports and immunological identification of the antigens involved. *Clin Exp Allergy* 1989;19:425-30.
7. Axelsson JGK, Johansson SGO, Wrangsjö K. IgE-mediated anaphylactoid reactions to rubber. *Allergy* 1987;42:46-50.

Request for reprints should be addressed to:
 Alton Melton, MD
 The Cleveland Clinic Foundation
 9500 Euclid Ave
 Desk A72
 Cleveland, OH 44195

GENETIC RISK FOR ASTHMA, ALLERGIC RHINITIS, AND ATOPIC DERMATITIS

The authors determined the genetic risk for allergic disorders (asthma, allergic rhinitis, atopic dermatitis) from 6665 questionnaires completed by the parents of German schoolchildren 9-11 years of age in a population based cross sectional survey. Children with at least one of these atopic diseases had positive first degree family histories in 55% of cases compared with 35% for children with no atopic disease ($P < .001$). Allergy in both parents was associated with an allergy in the child in 56% of cases (77/137); allergy in more than two first degree relatives, in 67% (109/163).

Allergic rhinitis occurred in 16% of the children with one allergic parent; 25%, with two. In families with one allergic parent allergic rhinitis was most frequent in the child when the parent also had allergic rhinitis (19%). Asthma occurred in 9% of the children with one allergic parent; 16%, with two. In families with one allergic parent asthma was most frequent in the child if the parent also had asthma (13%). Atopic dermatitis increased with the number of first degree relatives with allergy from 26% with one parent with allergy to 40% for two allergic parents and 46% with more than two allergic first degree relatives. In families with one allergic parent risk of atopic dermatitis was greatest when that parent also had atopic dermatitis (39%).

In families with one allergic parent the risk of asthma in the child was increased if the parent had asthma (odds ratio 2.6, 95% CI 1.7 to 4.0) but not if the parent had allergic rhinitis or atopic dermatitis. The risk of allergic rhinitis in the child was highest if the one parent had allergic rhinitis (odds ratio 3.6, 95% CI 2.9 to 4.6); that for atopic dermatitis, if the one parent had atopic dermatitis (odds ratio 3.4, 95% C.I. 2.6 to 4.4).

When two first degree relatives had allergy the odds ratio for asthma in the child was greatest when both relatives had asthma (5.2, 95% CI 2.5 to 10.8); that for allergic rhinitis was greatest when both had allergic rhinitis (5.7, 95% C.I. 4.2 to 7.8); that for atopic dermatitis, when both had atopic dermatitis (4.1, 95% C.I. 3.0 to 5.7).

These results confirm other data that suggest asthma, allergic rhinitis, and atopic dermatitis are multifactorial diseases that result from interaction of genetic and environmental factors.

—RMS

Dold S, Wjst M, von Mutius E, et al. Genetic risk for asthma, allergic rhinitis, and atopic dermatitis. *Arch Dis Child* 1992;67:1018-22.