
Prevalence of latex sensitization in a hospital employee population

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Background: Immediate-type allergic reactions to latex products have become increasingly recognized in hospital workers.

Objective: This study was designed to assess the prevalence of latex sensitization by skin testing and specific IgE testing in a group of hospital employees and compare these with each subject's self-reported allergic history.

Methods: Volunteers were recruited from selected departments. Each was tested with epicutaneous skin test with latex glove extract and commercial environmental allergens, had blood drawn for latex-specific IgE testing (AlaSTAT brand of ELISA), and was given a questionnaire for general and latex allergy history.

Results: There were 135 participants. Eleven (8.2% of sample, 95% confidence interval 3.4% to 13.0%) were skin test positive for latex reagent, and seven of these (5.2% of sample) reported allergic symptoms to latex contact. Testing for latex-specific IgE (ELISA) showed 6.7% with class II or higher reaction. There was high correlation of the two tests, with ELISA showing a sensitivity of 63.6% and a specificity of 98.4% with reference to skin testing. In this sample, 16% reported some upper respiratory symptoms in association with latex contact, although only one-third of this group was skin test positive. Past history of allergic or atopic disease was poorly predictive of skin or blood test reactivity. A reaction to a greater number of environmental allergens was associated with positive latex skin test reactivity.

Conclusion: Testing for latex sensitivity in this hospital sample revealed more than 5% of workers developed clinical allergies to latex and continued to remain occupationally in contact with latex. In vitro testing is a potential substitute for the more technically difficult skin testing.

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INTRODUCTION

Natural rubber has long been known to cause contact dermatitis.¹ IgE-mediated allergy to latex has been recognized only since the late 1970s when severe allergic reactions, including anaphylaxis and death, have been reported.^{2,3} Allergic reaction reports occurred most commonly in patients with recurrent mucosal or internal exposure to latex products. Examples of these were patients who underwent several intra-abdominal or urologic procedures,⁴ or barium enemas using latex-tipped balloons.⁵ Others with less in-

tense exposures, such as workers in medical and dental professions, have been reported to be at increasing risk.⁶ The increased use of latex to comply with universal blood and body fluid precautions has made this even more problematic.

Diagnostic tools to confirm latex allergy have not been easily available in the United States. Soluble extract from latex gloves is used in many allergists' offices for epicutaneous testing. Turjanmaa⁷ found the prevalence of latex sensitization by skin prick testing to be 2.5% of general hospital workers, and later studies have placed this prevalence between 4.7%⁸ and upward of 17% in selected groups.⁹ Enzyme-linked assay for specific IgE to latex (ELISA) is available, although previous reports did not show as high a

sensitivity of this method when compared with skin testing.^{10,11} Improved testing using liquid-phase allergens (AlaSTAT) have yielded results comparable to RAST¹² although it showed a high degree of reactivity to latex among atopic patients without significant latex exposure.¹³ There have been no studies to date of an occupationally exposed population of healthcare workers demonstrating prevalence of sensitization to latex by both ELISA and skin testing. This study sought to determine these prevalences and compare latex sensitization with questionnaire history of atopy and allergic events.

METHODS

The study sample was drawn from an employee population in a 900-bed general hospital. The protocol was approved by the hospital's Institution Review Board, and signed consent was obtained from each subject before participation. Prior requisitions for supplies were used to determine usage rate of gloves and the departments for study were chosen to include higher-use and lower-use departments. Volunteers were solicited from these departments to participate. Subjects accepted were non-pregnant adults with some regular occupational exposure to latex products. Questionnaires were administered to participants eliciting information about past history of atopic symptoms, medications, surgery, and possible allergic events. A history of latex allergy was accepted as the self-reported presence of "sneezing spells, runny or stuffy nose, watery or itchy eyes, coughing, wheezing or shortness of breath from working with latex gloves," or "working in patient care areas."

Epicutaneous testing was administered to these volunteers with reagents

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of common environmental allergens and two latex reagents. One latex reagent was obtained from a commercial source (Bencard Corp, Toronto, Ontario, Canada). The other was prepared from latex gloves by incubating latex examination gloves in normal saline for four hours and passing the solution through a 0.45-micron filter. The protein concentration of the solution was measured by a Kodak XR 700 (dry slide biurette reaction) automated analyzer and diluted with normal saline to a final concentration of 200 ng protein/mL. An initial group of 55 participants was tested with both reagents. At a later date the Bencard reagent was unusable and subsequent testing was performed with the latex glove extract alone.

The environmental reagents were obtained from a commercial source (Greer Labs, Lenoir, NC). This panel consisted of Timothy grass, *Cladosporium*, ragweed, *Alternaria*, tree mix, and two mite extracts, *D. farinae* and *D. pteronyssinus*. Banana extract was also included to evaluate reports of cross-reactivity. Dermapik (Greer Laboratories, Lenoir, NC) skin prick devices were used for epicutaneous testing with normal saline and histamine controls. The Dermapik device was dipped into the test reagent, applied to the volar forearm, and gently rotated one-quarter turn. A reaction was considered positive if the wheal at 20 minutes was at least 3 mm greater than saline control. Subjects were excluded from skin test interpretation if nonreactive to histamine control. Results were graded 0 to +4¹⁴ as shown on Table 1.

Venous blood samples were obtained by venipuncture, which were spun after clotting to remove serum within two hours. Frozen serum sam-

ples were mailed on dry ice for testing by ELISA technique, known as AlaSTAT EIA (Diagnostic Products Corporation, Los Angeles, CA), by the manufacturer. This is an enzyme-labeled immunometric assay used to detect allergen-specific IgE, performed as follows. Liquid allergens were formed by covalently binding allergen extracts to a soluble polymer/co-polymer matrix which was labeled with the same ligand used for coating the reaction tubes. After an initial incubation of liquid allergen with patient sera, multivalent anti-ligand was added to create a bridge between the allergen-IgE complexes formed with the patient sera and the ligand-coated tube. Specific IgE was detected using an enzyme-labeled anti-IgE antibody and substrate, o-phenyldiamine. Responses were compared with a response curve created with timothy allergic sera and timothy allergen. Results were classified from class 0 to IV (Table 2).

Data analysis was performed by personal computer using SYSTAT (SPSS, Inc, Chicago, IL) program. Statistical tests on ordinal data with one comparison were by Mann-Whitney U test, and on ordinal data with more than one comparison were by Kruskal-Wallis one-way analysis of variance.

RESULTS

In this study 135 employees participated in the above protocol. Demographic distribution of the sample is given in Table 3. The first 55 subjects were tested with both latex reagents and three showed a positive reaction to both reagents, and the other 52 reacted to neither. The remaining 80 subjects were tested to the same concentration of glove extract only. There were no adverse reactions to skin testing. One

subject showed no reaction to histamine and was excluded from skin-testing data analysis. Eleven of the remaining 134 (8.2%, 95% confidence interval 3.4% to 13.0%) were skin test positive to latex reagents. Seven of these individuals (5.2% of sample) reported mild reactions to latex contact (rhinitis, conjunctivitis, and/or sneezing, one reported shortness of breath) and four denied any latex-associated symptoms. Of the eleven, seven were nursing staff, and the remainder included two respiratory therapists, a phlebotomist and a surgery resident physician.

Specific IgE testing showed 19 subjects to have positive ELISA of class I or higher. Ten had a class I reaction, of whom only one had a positive latex skin test, and eight of the remaining nine reported no latex-associated symptoms. For greater specificity, an ELISA of class II or higher was considered positive for this data analysis.

There was high correlation of latex skin and ELISA testing (Table 4). Mann-Whitney U test showed highly significant association of the two tests ($P < .0005$).

Calculating the precision of ELISA with skin testing as the reference, the sensitivity of ELISA testing was 63.6%, and the specificity was 98.4%; if class I reactions had been considered positive, these would have been 72.7% and 91.1%, respectively. The predictive value of a positive test was 77.8% and of a negative test 96.8%; if a test of class I been considered as positive, these would have been 42% and 97% respectively.

In this sample, 31 (23%) self-reported latex-associated symptoms. A large group of these (9 of 31) had hand symptoms only. None of these nine had either test positive, which raises doubt that these were type I allergic events but rather contact dermatitis or other irritation, which the questionnaire alone could not discriminate. If hand-only events were excluded, 22 (16.3%, SE 3.2%) reported rhinitis, conjunctivitis, sneezing, or lower respiratory symptoms (Table 5). It was found that less than one-third (7 of 22)

Table 1. Grading of Skin Test Reactions

Grade	Wheal, mm	Flare, mm
0	<3	0-5
+1	3-5	0-10
+2	5-10	5-10
+3	10-15	>10
+4	>10 with pseudopodia	>20

Table 2. Classification of ELISA (AlaSTAT) to Latex

Class	
Class 0	<0.34 IU/mL
Class I	0.35-1.49 mL
Class II	1.50-2.99 mL
Class III	3.00-14.99 mL
Class IV	15.00 IU/mL and greater

Table 3. Sample Demographics

	n	%	SE
Sex			
Male	14	10	2.6%
Female	121	90	
Race			
White	116	86	4.5%
Black	12	9	
Oriental	5	4	
Age mean 37 years (SD 9.2) range 20-64 years			
Job Category			
Registered nurse	66	49	
Other nursing	30	22	
Ancillary	25	19	
Nonclinical	11	8	
Physician	3	2	
Location			
Floor	46	34	
Unit	46	34	
Surgery	28	21	
Other	15	11	
Time in current job mean 9 years (SD 7.2) range 0-37 years			

of these were skin test positive. The same proportion (7/22) were ELISA positive, and the two tests agreed in six of the seven. The presence of any symptoms with latex use was associated with a positive skin test (Mann-Whitney U test statistic 1286, $P = .001$), and with a positive ELISA ($P = .017$).

The relation of past history of general allergies and presence of latex sensitization was explored. Simple regression modeling did not demonstrate a significant association between the number of allergic history factors and a positive latex skin test. Step-wise regression modeling demonstrated that

only family history of allergies was somewhat predictive of a positive latex skin test ($P = .084$) and other history of hayfever did not provide significant additional correlation in this model. Nonparametric testing did not show any association with number of allergic symptoms and a positive skin test for latex.

Skin testing for environmental allergies showed an association between the number of allergen reactions and latex reactivity. A regression model using the number of environmental allergens positive to skin testing as the grouping variable showed a significant prediction of latex skin test reactivity ($P < 0.001$). Partitioning the group into high (four or more reactive allergens) and low (3 or less) showed significant association with latex reactivity (Mann-Whitney U test statistic = 1622, $P = .002$). There was a similar significant association between the presence of four or more reactive allergens and a positive ELISA. There was a significant association between skin test reactivity for latex and banana reagents ($P = .03$), and between banana and more than three environmental allergens ($P < .001$).

There was no significant difference between latex reactors and nonreactors regarding sex, age, race, job title, length of service, work location, or number of prior surgeries.

DISCUSSION

Incidence of allergy to latex varies widely depending on the population under consideration. Our study showed that in hospital personnel the prevalence of positive skin testing for latex was approximately 8%. This result

agrees with the studies quoted above. In this study, however, selection bias may have occurred; it is plausible that those who suspected that they were allergic were more likely to volunteer, biasing the prevalence estimate upward. This was somewhat controlled by limiting volunteers to the selected departments.

Skin testing with glove extract in a limited sample agreed with latex extract available commercially in Canada. The glove extract method remains very cost-effective since the extract is inexpensive to prepare and skin prick testing is a very sensitive and specific way to establish the diagnosis of latex allergy. It still remains difficult to apply in the hands of the general practitioner.

Latex-specific IgE testing has not been as useful as skin testing in prior studies^{8,9} but a good correlation with skin prick testing was observed using the AlaSTAT test if the class I reactors were considered negative. It remains somewhat less sensitive at detecting latex sensitization than skin testing but with a comparable specificity, especially in the presence of clinical symptoms. This generation of ELISA may prove to be a suitable in vitro substitute. Further testing of a clinical case population is warranted.

In this sample those with hand symptoms only (no upper respiratory reaction noted) had no objective evidence of latex sensitization. Those with hand symptoms only without clinically apparent urticaria should likely be considered for other sources of their reaction besides type I allergy to latex.

Atopy appears to be a somewhat useful factor for predicting latex allergy in prior studies^{6,15}; however, not all studies found a correlation between atopy and allergy to latex. Gold et al⁴ found that atopic disorders were not a significant characteristic of their patients with latex allergy. In the current study historical factors were not correlated with objective evidence of latex allergy. Atopy, as defined by skin testing, did show an association with pos-

Table 4. Latex Skin Test by ELISA

Skin Test	ELISA Class					Total
	0	I	II	III	IV	
0	112	9	1	1	0	123
+1	2	0	0	0	0	2
+2	1	0	0	2	2	6
+3	0	1	1	0	1	3
Total	115	10	3	3	3	134

Table 5. Testing of Subjects with Self-Reported Symptoms

Symptom	Number (%)	n with + Latex Skin Test	n with + ELISA	n with Either Test Positive
Sneeze	12 (8.9)	5	3	5
Rhinitis	14 (10.4)	6	4	6
Conjunctivitis	19 (14.1)	7	5	7
Cough	0	—	—	—
Wheeze	3 (2.2)	2	1	2
Short of breath	0	—	—	—
Hand symptoms Only	9 (6.6)	0	0	0

itive latex testing. These suggest that atopy in only its most pronounced clinical form is a risk factor for developing latex allergy. This agrees with other studies that found atopy does not particularly predispose to occupational sensitization.¹⁶

We conclude that in an occupationally exposed population of hospital clinical employees, over 8% are sensitized to latex products and 5% continue to work despite some form of allergic symptoms to latex. AlaSTAT brand of ELISA testing is a potential substitute for skin testing. Clinically pronounced atopy, such as multiple-reagent skin test reactivity, shows an increased risk of latex sensitization.

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REFERENCES

1. Taylor JS. Rubber. In: Fisher AA, ed. Contact dermatitis, 3rd ed. Philadelphia: Lea & Febiger, 1986; 603–43.
2. Jeager D, Kleinhaus D, Czuppon A, Baur X. Latex-specific proteins causing immediate-type cutaneous, nasal, bronchial and systemic reactions. *J Allergy Clin Immunol* 1992;89:759–68.
3. Fuchs T, Wahl R. Immediate reactions to rubber products. *Allergy Proc* 1992; 13:61–6.
4. Gold M, Swartz J, Braude B, et al. Intraoperative anaphylaxis in association with latex sensitivity. *J Allergy Clin Immunol* 1991;87:662–6.
5. Ownby DR, Tomlanovich M, Sammons N, McCullough J. Anaphylaxis associated with latex allergy during barium enema examinations. *Am J Roentgenol* 1991;156:903–8.
6. Hunt LW, Fransway AF, Reed CE, et al. An epidemic of occupational allergy to latex involving health care workers. *J Occup Environ Med* 1995; 37:1204–9.
7. Turjinmaa K. Incidence of immediate allergy to latex gloves in hospital personnel. *Contact Dermatitis* 1987;17:270–5.

8. Vandenplas O, Delwiche J, Evrard G, et al. Prevalence of occupational asthma due to latex among hospital personnel. *Am J Resp Crit Care Med* 1995;151:54–60.
9. Yassin MS, Lierl MB, Fischer TJ, et al. Latex allergy in hospital employees. *Ann Allergy* 1994;72:245–9.
10. Turjanmaa K, Rasaen L, Lehto MI, et al. Basophil histamine release and lymphocyte proliferation tests in latex contact urticaria. *Allergy* 1989;44: 181–6.
11. Pecquet C, Leynadier F, Dry J. Contact urticaria and anaphylaxis to natural latex. *J Am Acad Dermatol* 1990;22: 631–3.
12. Moneret-Vautrin DA, Halpern GM, Brignon JJ, et al. Food specific antibodies: a comparative study of AlaSTAT Pharmacia RAST Phabedac CAP systems in 49 patients with food allergies. *Ann Allergy* 1993;71: 107–14.
13. Reinheimer G, Ownby DR. Prevalence of latex-specific IgE in patients being evaluated for allergy. *Ann Allergy Asthma Immunol* 1995;74:184–7.
14. Slavin R. 1991. Diagnostic Tests in Allergy. In: Fireman P, Slavin R, eds. Atlas of allergies. Philadelphia: JB Lippincott 3.2.
15. Sussman G, Parlo S, Dolovich J. The spectrum of IgE-mediated responses to latex. *JAMA* 1991;265:2844–7.
16. Roberts DM. The incidence of atopy in a working population. *J Soc Occup Med* 1987;37:106–10.

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