

Prevalence of latex-specific IgE antibodies in patients being evaluated for allergy

Gary Reinheimer, MD and Dennis R. Ownby, MD

Objective: The purpose of this study was to determine the prevalence of detectable latex-specific IgE in patients being evaluated for allergy.

Methods: The AlaSTAT assay was used to test for latex-specific IgE in 200 consecutive serum samples sent to our laboratory for total IgE levels. Samples sent for latex-specific IgE were excluded. The population studied included 87 males and 113 females ranging in age from 1 to 82 years of age. Inhibition studies with a latex extract were performed on all positive samples. Chart reviews and questionnaires provided information regarding risk factors for latex allergy and reactions to latex.

Results: Twenty-four (12%) subjects were positive for latex-specific IgE. Seventeen of the 24 positive subjects (70.8%) were <18 years of age and *all* of the strongly positive subjects (7 or 3.5%) were <18 years of age. The geometric means for total IgE for the latex positive and negative subjects were 351 IU/mL and 80 IU/mL respectively, $P < .001$. The mean percent inhibition with latex was 66%. Chart reviews and questionnaires revealed only 2 of 24 positive subjects were in high risk groups, none of the positive subjects had any history of reactions to latex, and 22 (91.6%) had evidence of atopic disease.

Conclusion: *In vitro* tests may detect latex specific IgE in atopic individuals, especially children, with no history of recurrent latex exposure and no history of adverse reactions to latex.

INTRODUCTION

Latex allergy has recently been recognized as a cause of reactions ranging from localized urticaria to anaphylaxis.¹⁻⁶ Multiple deaths from latex exposure have also been reported.^{7,8} Groups known to be at risk for latex sensitivity include rubber industry workers, children with spina bifida, persons requiring multiple operative procedures, and health care workers.⁹⁻¹² Atopy is common among latex sensitive individuals, and may be an additional risk factor.^{13,14} The purpose of this study was to determine the prevalence of detectable latex-specific IgE in patients being evaluated for atopic diseases and to determine what factors may be related to the development of latex-specific IgE antibodies.

METHODS

Two hundred consecutive serum samples sent to our laboratory for total IgE measurement, but not for latex-specific IgE testing, were screened for latex specific IgE. The total IgE result did not influence sample selection. The primary reason serum samples are sent for total IgE measurement is as a screen for allergic disease, although samples may have been submitted for many other reasons. Latex-specific IgE was measured using the AlaSTAT assay (Diagnostic Products Corporation, Los Angeles, California). The AlaSTAT assay is an enzyme-linked immunometric assay that uses liquid-phase polymerized allergens and monoclonal antibodies to measure specific IgE.

Briefly, ligand-labeled latex antigen matrix and individual serum samples are mixed in ligand-coated tubes and allowed to incubate. This allows any latex-specific IgE to bind to the latex matrix. A multivalent anti-ligand is then added which creates a bridge be-

tween the IgE/latex matrix and the ligand coated tube. The unbound IgE is then removed by washing. Horseradish peroxidase-labeled monoclonal anti-IgE is then added to the tubes, incubated, and then washed. A chromogenic substrate is added and color development is terminated after 15 minutes. The resulting color is directly related to the amount of latex-specific IgE which is interpolated from a standard curve. All samples and reference standards were run in duplicate. Results were accepted only if the coefficient of variation was <15% for duplicates. Details of the AlaSTAT assay are discussed elsewhere.^{15,16} Specific IgE to latex was reported using International Units (IU). These results were then divided into classes (Table 1). All samples in class 0/I or above were repeated to confirm the results. Samples reported Class 0 to 0/I were considered negative, samples reported as Class I were considered positive, and samples reported as Class II or above were considered strongly positive.

After obtaining approval for the study from the Institutional Human Rights committee, the medical charts of subjects with serum samples testing positive for anti-latex IgE were reviewed. The age, sex, atopic status, past surgical history, history of food allergies, and total IgE were recorded. The presence of atopy was defined as 2 or more positive prick or intradermal skin tests, if the patient had been skin

Table 1. AlaSTAT Class Distribution

Class	Range
Class 0	0.00-0.29 IU/mL
Class 0/I	0.30-0.34 IU/mL
Class I	0.35-1.49 IU/mL
Class II	1.50-2.99 IU/mL
Class III	3.00-14.99 IU/mL
Class IV	>15 IU/mL

From the Henry Ford Health System, Detroit, Michigan.

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tested. A positive prick skin test was defined as >2 cm of erythema in the presence of a negative saline control. A positive intradermal test was defined as a wheal >0.5 cm with >2 cm of erythema. Past surgical histories and occupation were also noted. Total serum concentrations of IgE were measured by a previously reported enzyme-linked immunosorbent assay (ELISA).¹⁷

A telephone survey was then conducted by one author. The strongly positive patients, or their parents, were contacted. Verbal consent was obtained prior to administering the survey. Information regarding occupation, atopic history, reactions to household or medical items containing latex, food allergies, number of exposures to latex containing devices during medical or dental procedures, premature births, and number of hospital and intensive care unit admissions was obtained.

Inhibition studies with latex extract were performed on all positive samples to test assay specificity. Each assay included a standard inhibition curve using a crude extract of ammoniated latex. The class 1 samples were inhibited with 20 μ L of latex extract in 180 μ L of serum and the class 2 and above samples were inhibited with 50 μ L of latex extract in 150 μ L of serum. The mixture of serum and latex extract were incubated overnight. The following day, the sera were assayed for latex specific IgE. Percent inhibition was calculated by first determining the percent bound (mean absorbance of the serum with inhibitor divided by the mean absorbance without the inhibitor) and then subtracting the percent bound from 100 to obtain the percent inhibition. Greater than 25% inhibition was considered significant.¹⁸

STATISTICAL ANALYSIS

The patients, with and without, detectable anti-latex IgE were compared with respect to age, gender distribution, and total IgE values. Total IgE and age were analyzed using the Wilcoxon two-sample rank sum test. Likelihood ratio chi-square was also used

to compare gender distribution between the two groups.

RESULTS

The 200 sera studied came from 87 males and 113 females ranging in age from 1 to 82 years of age, with 89 (44.5%) subjects being <18 years of age. Twenty-four (12%) sera were positive for latex-specific IgE (11 females and 13 males) (Tables 2 and 3). Seventeen of the 24 latex positive sera (70.8%) were from patients <18 years of age, while children <18 years of age made up only 40.9% (72/176) of the sero-negative study population. The increased proportion of latex reactivity from those less than 18 years of age was statistically significant, $P = .005$. We also found that all of the strongly positive patients (7% or 3.5%) were <18 years of age. The total IgE geometric mean for the latex positive patients was 351 IU/mL and the geometric mean for the negative group was 80 IU/mL, $P < .001$.

All of the sera with detectable anti-latex antibodies showed significant inhibition when pre-incubated with latex extract. The latex inhibition studies revealed strong inhibition (>85%) in five of the seven strongly positive sera. The inhibition results for the class I sera varied from 33% to 100% inhibition with a mean of 68% (Table 3).

Five of the seven strongly positive subjects, or their parents, responded to the questionnaire. None of these subjects had a history of reactions to latex products, or more than one exposure to latex products in a medical or surgical setting. Similarly, there were no histories of any adverse reactions to foods thought to crossreact with a latex, in-

cluding banana, avocado, kiwi, or chestnut. A chart review of the remaining 19 positive patients revealed similar findings, except for patients 16 and 19. Patient 16 had had 2 cesarean sections and patient 19 is an operating room nurse who has had a cholecystectomy, tonsillectomy, and ophthalmologic surgery on two occasions, but no known reactions to latex.

Sixteen of the 24 latex-positive patients had previously been skin tested using panels of common allergens and 15 (62.5%) were positive to two or more common inhalants supporting a diagnosis of atopy. One patient, who was dermatographic, had in vitro tests performed for common inhalants and all were negative. Seven subjects (29.2%), not skin or in vitro tested, had total IgE levels greater than two standard deviations above the mean for age, suggesting atopic disease. The two remaining subjects had histories of recurrent exposure to latex, but no evidence of atopic disease based on total IgE levels, skin or in vitro testing.

DISCUSSION

Twelve percent of 200 individuals suspected of having allergic disease had detectable levels of latex-specific IgE, and detectable latex-specific IgE was more prevalent in children than adults. Atopy has been frequently found in latex allergic patients. This was confirmed in our study with 62.5% of the latex-positive individuals being atopic. If subjects with significantly elevated IgE levels are included among those defined as atopic, the percentage increases to 91.6%. All but one of the seven strongly positive subjects were atopic by skin testing, and of all the

Table 2. Characteristics of Study Population

Characteristic	Latex Positive	Latex Negative	P Value
Total (%)	24 (12)	176 (88)	—
Sex M/F	13/11	74/102	—
Age, mean (range)	21 (3–68)	29 (1–82)	—
Age <18 yrs (%)	17 (70.8)	72 (40.9)	0.005
Total IgE* (IU/mL)	351†	80‡	0.001

* Geometric mean.

† 95% confidence interval 24 to 5136 IU/mL.

‡ 95% confidence interval 5 to 1296 IU/mL.

positive subjects, only two were confirmed as nonatopic by skin or in vitro testing. Both of these patients had histories of recurrent exposure. The AlaSTAT assay was specific for anti-latex IgE since all of the positive sera showed significant inhibition. Higher levels of inhibition would probably have been found if sufficient serum had been available to perform complete inhibition titration studies.

The most striking finding in this study was the discovery that children (<18 years of age) were significantly more likely than adults to be seropositive for anti-latex IgE antibodies. Children with spina bifida have been reported to have a high prevalence of latex allergy, but none of the positive sera in this study came from children with spina bifida or other congenital abnormalities. Occupational exposure to latex has also been postulated to increase the risk of latex allergy, but if occupational exposure were a major cause of latex allergy, we should have found a greater prevalence of latex allergy in adult sera. The higher prevalence of positive sera among children suggests that children are more frequently exposed to latex than adults, that children are more likely to become sensitized by any latex exposure or that both statements are true. Previous studies of skin test reactivity to common allergens have shown a peak prevalence in early adolescence and this peak of prevalence may also be true for latex sensitivity.

Patient surveys and chart reviews were only able to identify recurrent latex exposure in two patients. Recurrent latex exposure was defined as two or more surgical procedures or regular exposure to latex products. These data suggest that either latex exposure is more common than expected, or that the antigens found in latex may be cross reactive with other antigens. The latter may indeed be the case based on a recent study by Appleyard et al who reported cross reactivity between latex, ragweed, and blue grass allergens.¹⁹ Atopy has been considered a risk factor for latex sensitivity even without known exposure.²⁰ Cross reacting al-

Table 3. Characteristics of Latex-Specific IgE-Positive Patients

Subject	Sex	Age, yr	Total IgE, IU/mL	Latex Class	% Inhibition	Atopic*
1	F	15	2891†	4	97	NA
2	F	09	752†	3	58	Y
3	F	16	142	3	97	Y
4	M	02	569†	3	45	Y
5	M	14	285†	3	93	Y
6	F	09	45	3	94	Y
7	M	11	450†	2	86	Y
8	M	68	1028†	1	42	NA
9	M	37	460†	1	77	NA
10	M	06	248†	1	33	Y
11	F	26	240	1	94	Y
12	M	06	859†	1	56	NA
13	M	14	179†	1	53	Y
14	F	17	875†	1	41	NA
15	M	09	35	1	76	Y
16	F	40	64	1	100	N
17	M	09	222†	1	87	NA
18	M	11	238†	1	48	Y
19	F	51	246	1	90	N
20	M	27	253†	1	40	Y
21	F	12	45	1	100	Y
22	F	78	589†	1	100	NA
23	F	16	11722†	1	46	Y
24	M	03	1355†	1	79	Y

* Defined as 2 or more positive skin tests.

† >2 SD above mean for age.

NA = not available.

lergens may partially explain these findings. If these results can be confirmed by others, screening for latex allergy with currently available latex extracts may result in false positive tests, especially in patients with atopy and no history of frequent latex exposure. If it becomes appropriate to use in vitro tests to screen for latex allergy pre-operatively in individuals with histories of recurrent latex exposure or atopy, positive individuals with atopy and no history of recurrent exposure may need additional evaluation. Skin tests with latex extracts have also produced positive results in children having no known risk factors for latex allergy and no history of allergic reactions from latex.²¹

CONCLUSION

In vitro tests may detect latex-specific IgE in atopic persons with no history of recurrent latex exposure and no history of adverse reactions to latex. Cross reactive allergens may account for positive tests in these individuals.

Alternatively, latex sensitization may be much more common than previously suspected. The clinical significance of positive in vitro tests for anti-latex IgE needs to be determined.

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Request for reprints should be addressed to:
 Dennis R. Ownby, MD
 Henry Ford Hospital
 2799 W. Grand Boulevard
 Detroit, MI 48202

EVIDENCE FOR HUMAN MAST CELLS AS A SOURCE FOR IL-4, IL-5, IL-6, AND TUMOR NECROSIS FACTOR- α

Because the cytokines IL-4, IL-5, IL-6, and TNF- α are considered important in the mediation of airway inflammation in asthma this study was undertaken to investigate their cellular distribution in bronchial biopsies from 22 mild atopic asthmatic patients and 13 normal control subjects. Localization of cytokines was done using a variety of monoclonal antibodies.

Mucosa from both asthmatic patients and normals contained numerous mast cells (identified by monoclonal Ab to tryptase) staining for all four cytokines as well as eosinophils (identified by EG2 antibody) containing some IL-5. There was an increased number of mast cells staining for TNF- α and IL-4 in the specimens from the asthmatic subjects compared with normals.

The authors conclude that these findings document mast cells along with T cells as important sources of these cytokines in the inflammatory process in asthma.

—JGE

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