

The prevalence of anti-latex IgE antibodies in 1000 volunteer blood donors

Dennis R. Ownby, MD,^a Helen E. Ownby, PhD,^b Judith McCullough, BA,^a and A. William Shafer, MD^b Detroit, Mich.

Background: Latex allergy has been recognized as a medical problem with increasing frequency since the mid 1980s. Although certain groups of individuals, such as health care workers, have been recognized as having increased risk for latex allergy, little is known about the prevalence of latex allergy in the general population.

Methods: To estimate the prevalence of latex allergy among healthy adults, we measured anti-latex IgE antibodies in residual serum samples from 1000 volunteer Red Cross blood donors. The 1000 samples were from a sample of blood units collected from workplace mobile sites throughout Southeastern Michigan. Samples collected from mobile sites operating at health care institutions were excluded to minimize sampling of health care workers. Anti-latex IgE antibodies were measured by using the AlaSTAT assay (Diagnostic Products Corp., Los Angeles, Calif.) according to the manufacturer's directions. Samples with anti-latex IgE concentrations of 0.35 IU/ml or greater were classified as positive and samples with IgE concentrations of 1.50 IU/ml or greater were classified as strongly positive. All positive samples were assayed a second time to confirm the result. All positive samples were also measured with the CAP assay (Pharmacia Diagnostics, Dublin, Ohio).

Results: The samples tested were from donors with a mean age of 37.8 years, and 47% were women. Sixty-four (6.4%, 95% confidence interval = 4.9-8.1%) of the samples were confirmed as repeatedly positive for anti-latex IgE, and 23 of the 64 positive samples were strongly positive (2.3% of the 1000). Sixty-one percent of the samples positive as determined by the AlaSTAT assay were also positive as determined by the CAP assay. Samples from male donors were more likely to be positive than those from female donors (8.7% vs 4.1%, $p = 0.003$). Prevalence of positive samples was not related to age or race.

Conclusions: We conclude that the prevalence of detectable anti-latex IgE antibodies, in a large and relatively unselected adult population, is higher than previous estimates have suggested. Although the clinical significance of these observations needs further evaluation, the data suggest that latex allergy is not confined to individuals in previously recognized high-risk groups. (*J Allergy Clin Immunol* 1996;97:1188-92.)

Key words: Latex allergy, anti-latex IgE antibodies, prevalence, volunteer blood donors

During the last decade, latex allergy has been increasingly recognized as a potential medical problem. Allergic reactions to latex have ranged from mild local urticaria to fatal anaphylaxis.¹⁻³ Because latex allergy has only recently been rec-

ognized, limited data are available concerning the extent of this problem. Several studies have shown that certain groups of individuals, with frequent exposure to latex, have a relatively high prevalence of latex allergy including children with spina bifida, health care workers, and rubber plant workers.⁴⁻⁹

Few studies have been done on the prevalence of latex allergy in individuals outside of recognized risk groups. Some have estimated the prevalence of latex allergy in the general population as less than one per thousand, and at least one study from Finland substantiates this estimate.^{10, 11} However, a few small studies of relatively unselected children suggest that the prevalence may be higher.^{12, 13} Our own experience with latex-induced reactions during barium enema examinations (six reactions of

From ^aAllergy Research Laboratory, Henry Ford Hospital; and ^bAmerican Red Cross Blood Services, Southeastern Michigan Region.

Supported in part by Diagnostic Products Corporation and Fund for Henry Ford Hospital.

Received for publication Apr. 20, 1995; revised July 27, 1995; accepted for publication July 27, 1995.

Reprint requests: Dennis R. Ownby, MD, Division of Allergy, Henry Ford Hospital, 2799 West Grand Blvd., Detroit, MI 48202.

Copyright © 1996 by Mosby-Year Book, Inc.
0091-6749/96 \$5.00 + 0 1/1/68120

5554 procedures) suggested that the prevalence of clinically significant latex sensitivity in the population of southeastern Michigan could be as high as one per thousand.¹ If the estimate of one severe latex-induced reaction per thousand population were accurate, the prevalence of any latex sensitivity in the general population would be expected to be substantially greater than one per thousand.

It is difficult to obtain a large study population of individuals who are representative of the general population of a region. We believed that the study population that would best represent the general population of healthy adults in Southeastern Michigan was a sample of volunteer Red Cross blood donors.

METHODS

Serum samples

Samples were collected from residual serum tubes of 1000 blood donations over a 3-week period. All donations were from workplace mobile collection sites, excluding sites at health care institutions. To obtain a sample broadly representative of the population, no more than 30 samples per day were accepted from a single mobile unit. All donors were informed that a sample of the donated blood might be used for additional tests or to evaluate experimental blood tests, unless they objected. Strict confidentiality was maintained by identifying samples only by code numbers, which were matched with limited demographic data for analysis. It was not possible to ask the blood donors any questions about their personal allergic histories or potential risk factors for latex allergy.

In vitro assays

The AlaSTAT assay (Diagnostic Products Corp., Los Angeles, Calif.) was used for measuring anti-latex IgE antibodies according to the manufacturer's instructions. Previous experience with this assay suggested that it offered maximal sensitivity with good specificity.¹⁴ Briefly, 50 μ l aliquots of serum from each donor was added to duplicate assay tubes along with the liquid latex matrix. After a 1-hour incubation, the anti-ligand solution was added. This solution contains avidin, which binds the biotin on the liquid latex matrix to the biotin-coated walls of the assay tubes. The tubes were then washed three times to remove all unbound serum proteins. IgE that bound to the liquid matrix was detected by the addition of an enzyme-labeled anti-human IgE, followed by washing and the addition of a chromogenic substrate. The amount of IgE bound in the tube was determined by extrapolation from a standard curve. Samples with IgE concentrations of 0.35 IU/ml or greater were graded as positive. We arbitrarily chose to grade samples with concentrations of 1.50 IU/ml or greater as strongly positive. All positive samples were assayed a second time in another AlaSTAT assay to

TABLE I. Comparison of the AlaSTAT and CAP class scores in the 64 sera positive in the AlaSTAT assay

	CAP class				Total
	0	I	II	III	
AlaSTAT class					
0	0	0	0	0	0
I	25	10	5	1	41
II	3	4	6	0	13
III	3	0	5	2	10
Total	31	14	16	3	64

verify the positive result, and only samples positive in both assays were considered as positive in the analysis.

Because of the limited experience with in vitro tests for anti-latex IgE antibodies, we also re-assayed all positive samples, with sufficient serum, in the CAP assay (Pharmacia Diagnostics, Dublin, Ohio). The CAP assay was performed according to the manufacturer's instructions. Samples with IgE concentrations of 0.35 kU/L or greater were graded as positive. The CAP assay was chosen as a secondary comparison method because many investigators have found that the CAP assay has performed well with other allergens.^{15, 16} It was not possible to evaluate all 1000 samples in the CAP assay.

Both the AlaSTAT and CAP results can be converted into class scores on the basis of reference curves. The criteria for the AlaSTAT classes are: 0, 0.00 to 0.29; 0/I, 0.30 to 0.34; I, 0.35 to 1.49; II, 1.50 to 2.99; III, 3.00 to 14.9; and IV, ≥ 15.0 IU/ml. The criteria for the CAP classes with traditional scoring are: 0, <0.35 ; I, 0.35 to 0.7; II, 0.7 to 3.5; III, 3.5 to 17.5; IV, 17.5 to 50; V, 50 to 100; and VI, >100 kU/L. The nominal criterion for classifying a sample as positive is the same, 0.35 U/ml or greater, in both assays, but the criteria for the classes are otherwise different.

RESULTS

The 1000 samples tested came from donors with a mean age of 37.8 years (range, 17 to 66 years). Four hundred seventy (47%) of the donors were women; and 879 of the donors described themselves as white, 80 as black, and 41 as belonging to other racial groups. These proportions are similar to those of all blood donors in southeastern Michigan. No information concerning the occupations or personal allergy histories of the donors was obtained.

We first compared the results of the AlaSTAT and CAP assays in the 64 sera that were repeatedly positive according to the AlaSTAT. The results are shown in Table I. Overall, 39 (61%) of the 64 AlaSTAT-positive samples were also positive in

TABLE II. Distribution of positive test results for anti-latex IgE among 1000 study subjects by sex, age, and race

	AlaSTAT		Total (%)	p Value*	1990 Census (%)†
	Negative	Positive			
Sex					
Male	485	45	530 (53)	0.014	47.0
Female	451	19	470 (47)		53.0
Age					
<45 yr	665	41	706 (70.6)	0.14	
≥45 yr	271	23	294 (29.4)		
Race					
White	829	50	879 (87.9)	0.039	77.0
Black	70	10	80 (8.0)		20.6
Other	37	4	41 (4.1)		2.6

*p Values were determined by using the chi square statistic.

†Data from Census of Population and Housing 1990: Summary Tape File 1 on CD-ROM (Michigan), prepared by the Bureau of the Census. Washington, DC, 1991.

the CAP assay. The major differences in the results of the two assays are the 31 sera that were positive in the AlaSTAT and negative in the CAP, including six sera that were class II or III according to the AlaSTAT assay but negative according to the CAP assay. However, if the 23 sera with class II or III AlaSTAT results are considered, 17 of the 23 (74%) are positive according to the CAP assay.

The prevalence of anti-latex IgE antibodies according to the AlaSTAT assay was 64 of 1000 or 6.4% (95% confidence interval = 4.9-8.1%). Twenty-three of the 64 samples were strongly positive (IgE ≥1.50 IU/ml). As shown in Table II, positive samples were significantly more frequent in men than in women and in blacks compared with whites or others. Age did not appear to influence the prevalence of seropositivity. The composition of the entire five-county population, from which the studied blood samples were drawn, is also shown in Table II. The male-to-female ratio in the blood donors is the opposite of the ratio in the population, and whites are overrepresented among the blood donors.

DISCUSSION

We have found a 6.4% prevalence of seropositivity for anti-latex IgE antibodies in 1000 Red Cross volunteer blood donors from whom serum samples were obtained during 1993 in Southeastern Michigan. Units collected at health care institution sites were excluded to minimize the possibility of obtaining a spuriously high prevalence estimate because of the inclusion of a large num-

ber of health care workers. Because it was not possible to directly question the blood donors, we cannot exclude the possibility that some of them may have been occupationally exposed to latex, either as health care workers or in other occupations. The overall prevalence of seropositivity for anti-latex IgE antibodies remains high, even if the only samples considered positive are those that were strongly positive (2.3%) or those that were positive according to both the AlaSTAT and CAP assays (3.9%). The prevalence of 6.4% is consistent with our previous experience of approximately one latex-induced reaction per 1000 patients during barium enema examinations.¹ In comparison with the 6.4% prevalence in this population of blood donors, we found an 8.8% prevalence of anti-latex antibodies, by using the same AlaSTAT assay and criteria for a positive test result, in a population of 741 inpatient registered nurses.¹⁷

The major strengths of this study are the large number of serum samples drawn from a population of relatively healthy adults and the objective measurement of anti-latex IgE antibodies. Some studies have relied on history of symptoms associated with latex exposure, which is an unreliable method of determining sensitivity.^{3, 6, 7}

Concerns about confidentiality made it impossible to obtain any information directly from the donors about possible risk factors for latex allergy or clinical reactivity to latex. Lacking this information, we were not able to evaluate questions about specific risks for latex sensitivity. We speculate that blood donors, and others without recognized oc-

cupational exposure to latex, may become sensitized by latex contact with household rubber products or by contact with latex during routine medical care.

The 6.4% prevalence of detectable anti-latex IgE antibodies may initially appear to be unreasonably high, but this prevalence is low compared with the prevalence of anti-Hymenoptera venom IgE found in population surveys. Stuckey et al.¹⁸ used the Pharmacia RAST to measure anti-honeybee IgE in 3439 subjects and found a RAST score of 2 or greater in 542 (15.8%) of the subjects. Of the 542 positive RAST test results, 450 (83%) occurred in individuals who did not have histories of adverse sting reactions.¹⁸ Similar data were obtained by Golden et al.¹⁹ in a study of a stratified sample of 320 employees representative of 2097 electric plant employees. Seventeen percent of workers had positive skin test results and 24% had positive in vitro test results in response to either or both honeybee and yellow jacket venoms. Only 3.3% of the workers had a history of systemic reactions after insect stings. These studies demonstrate that the prevalence of venom-specific IgE in unselected adults is relatively high, even though reported episodes of anaphylaxis are infrequent. Compared with these studies of the prevalence of venom-specific IgE, the 6.4% prevalence of anti-latex IgE antibodies found in our study is modest and consistent with the relatively infrequent reports of systemic reactions associated with latex exposure.

Another concern about the results of our study is whether the AlaSTAT assay is specific for anti-latex IgE. The small quantities of serum available precluded performing inhibition assays with the positive sera; however, we have performed multiple inhibition assays in the past, and we have always been able to inhibit positive AlaSTAT test results with latex extracts.^{12, 14} We also believe that the positive AlaSTAT test results accurately indicated the presence of anti-latex IgE antibodies because the CAP assay produced similar positive results in 61% of the AlaSTAT-positive sera. The discrepancy between the AlaSTAT positive results and negative CAP results in 31 sera may be due to several factors. We have observed similar discrepancies between AlaSTAT and CAP results with sera from individuals with histories highly suggestive of latex allergy, and we believe that the criteria for a positive CAP result may be unduly conservative, even though the criteria for a positive test result in both assays is 0.35 IU/ml specific IgE. Another possible explanation is that the relative

concentrations of various latex proteins differ between the solid phases of the two assays. Differences in solid-phase latex protein concentrations are likely to affect the detection of anti-latex IgE antibodies. The two assays may also differ in the detection of IgE cross-reactivity between latex and other allergens. Because we did not test all samples in the CAP assay and we did not obtain histories or skin test data on the blood donors, we cannot comment on the relative diagnostic value of either test.

The most important feature of this study is that it provides a baseline estimate of latex sensitization in a relatively unselected adult population. Because latex allergy has only recently been commonly recognized and because latex use and manufacturing are rapidly changing, it will be valuable to resurvey similar populations in the future to determine whether the prevalence of latex sensitization in the adult population of the United States changes with time. It is also useful to have a baseline estimate of latex allergy in a general population to compare against estimates of the prevalence of latex sensitization in high-risk populations. Without an estimate of allergy in the general population, it is impossible to accurately estimate the magnitude of increased risk associated with belonging to the high-risk population.

REFERENCES

1. Ownby DR, Tomlanovich M, Sammons N, McCullough J. Anaphylaxis associated with latex allergy during barium enema examinations. *Am J Roentgenol* 1991;156:903-8.
2. Sussman G, Tarlo S, Dolovich J. The spectrum of IgE-mediated responses to latex. *JAMA* 1991;265:2844-7.
3. Bubak ME, Reed CE, Fransway AF, et al. Allergic reactions to latex among health-care workers. *Mayo Clin Proc* 1992;67:1075-9.
4. Vandenplas O, Delwiche J-P, Evrard G, et al. Prevalence of occupational asthma due to latex among hospital personnel. *Am J Respir Crit Care Med* 1995;151:54-60.
5. Meeropol E, Frost J, Pugh L, Roberts J, Ogden JA. Latex allergy in children with myelodysplasia: a survey of Shriners hospitals. *J Pediatr Orthop* 1993;13:1-4.
6. Lagier F, Vervloet D, Lhermet I, Poyen D, Charpin D. Prevalence of latex allergy in operating room nurses. *J Allergy Clin Immunol* 1992;90:319-22.
7. Berkey ZT, Lucianc WJ, James WD. Latex glove allergy. A survey of the US Army Dental Corps. *JAMA* 1992;268:2695-7.
8. Slater JE, Mostello LA, Shaer C. Rubber-specific IgE in children with spina bifida. *J Urol* 1991;146:578-9.
9. Tarlo SM, Wong L, Roos J, Booth N. Occupational asthma caused by latex in a surgical glove manufacturing plant. *J Allergy Clin Immunol* 1990;85:626-31.
10. Tomazic VJ, Withrow TJ, Fisher BR, Dillard SF. Latex-associated allergies and anaphylactic reactions. *Clin Immunol Immunopathol* 1992;64:89-97.

11. Turjanmaa K, Makinen-Kiljunen S, Reunala T, Alenius H, Palosuo T. Natural rubber latex allergy, the European experience. *Immunol Allergy Clin N Am* 1995;15:71-88.
12. Reinheimer G, Ownby DR. Prevalence of latex-specific IgE antibodies in patients being evaluated for allergy. *Ann Allergy* 1995;74:184-7.
13. Shield SW, Blaiss MS. Prevalence of latex sensitivity in children evaluated for inhalant allergy. *Allergy Proc* 1992;13:129-31.
14. Ownby DR, McCullough J. Testing for latex allergy. *J Clin Immunoassay* 1993;16:109-13.
15. Williams PB, Dolen WK, Koepke JW, Selner JC. Comparison of skin testing and three *in vitro* assays for specific IgE in the clinical evaluation of immediate hypersensitivity. *Ann Allergy* 1992;68:35-45.
16. Kleine-Tebbe J, Eickholt M, Gätjen M, Brunnée T, O'Connor A, Kunkel G. Comparison between Magic Lite and CAP system: two automated specific IgE antibody assays. *Clin Exp Allergy* 1991;22:475-84.
17. Grzybowski MK. The prevalence of latex allergy among a nursing population. Ann Arbor: University of Michigan; 1994. Thesis.
18. Stuckey M, Cobain T, Sears M, Cheney J, Dawkins RL. Bee venom hypersensitivity in Busselton [Letter]. *Lancet* 1982;2:41.
19. Golden DBK, Marsh DG, Kagey-Sobotka A, et al. Epidemiology of insect venom sensitivity. *JAMA* 1989;262:240-4.

Availability of Journal Back Issues

As a service to our subscribers, copies of back issues of The Journal of Allergy and Clinical Immunology for the preceding 5 years are maintained and are available for purchase from the publisher, Mosby-Year Book, Inc., at a cost of \$10.50 per issue. The following quantity discounts are available: 25% off on quantities of 12 to 23, and one third off on quantities of 24 or more. Please write to Mosby-Year Book, Inc., Subscription Services, 11830 Westline Industrial Dr., St. Louis, MO 63146-3318, or call (800) 453-4351 or (314) 453-4351 for information on availability of particular issues. If unavailable from the publisher, photocopies of complete issues are available from University Microfilms International, 300 N. Zeeb Rd., Ann Arbor, MI 48106 (313) 761-4700.