

Diagnostic evaluation of type I latex allergy

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Background: Latex hypersensitivity affects a significant number of health care workers. No universally accepted method for the diagnosis of latex allergy is currently available in the United States.

Objective: Determine the accuracy of clinical assessment in predicting type I latex allergy, and compare the ability of various latex skin test preparations and in vitro assays in confirming the diagnosis of latex allergy.

Methods: Subjects were classified into "history positive," "history ambiguous," or "history negative" based on reports of clinical symptoms. Skin prick tests were performed with ammoniated latex and glove extracts. Sera were analyzed for latex-specific IgE using the Pharmacia CAP and DPC AlaSTAT assays.

Results: A total of 207 subjects had histories taken, skin testing, and blood drawn. Out of 49 type I latex-allergy "history positive," 42 (86%) were skin test positive, and 24 (49%) were serum positive. Fifty-nine subjects were latex allergy "history ambiguous." In this group, skin testing showed 19 (32%) positives, and latex-specific IgE were detected in 10 (17%). Out of 99 latex "history negative," 9 (9%) were skin test positive, and 11 (11%) were positive for latex-specific IgE. Out of the 61 subjects with IgE symptoms following latex exposure who were skin test positive, a positive in vitro assay was found in 32 (52%).

Conclusions: Skin testing is more likely to confirm a positive latex allergy history. Use of raw ammoniated and glove skin testing preparation sources combined adds to the diagnostic sensitivity. AlaSTAT and CAP correlate well with each other and have good negative predictive value, but lack the sensitivity of skin testing. Use of AlaSTAT and CAP assays combined raises the diagnostic sensitivity as compared to using one in vitro test alone.

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INTRODUCTION

A clinical history of type I latex allergy especially, but not necessarily, when associated with risk factors like spina bifida or occupational exposure requires special attention.¹⁻³ Type I hypersensitivity to hevea latex (also known as natural rubber latex) is the result of latex protein-specific IgE antibodies that are capable of inducing histamine release from sensitized mast cells and basophils.⁴ Patients who have this allergy experience symptoms of

IgE-mediated disease that vary from localized hand symptoms such as itching and urticaria, to a wide range of systemic symptoms including generalized urticaria, sneezing, tearing, cough, wheezing, hypotension, and shock.⁴⁻⁶

The diagnosis of type I hypersensitivity to natural rubber latex is currently confirmed by in vivo skin testing with raw latex or glove extracts, or by commercially available in vitro assays that measure latex-specific IgE.⁷ A glove "use test" first described by Turjanmaa et al may be performed for cases when there is discrepancy between skin test results and clinical history or when in vitro studies are positive in otherwise asymptomatic subjects.⁸ Bronchial provocation testing with aerosolized latex has recently been described.^{4,9,10} Other research-based in vitro tests of latex allergy include ELISA, immunoblots, cellular

proliferation assays, basophil histamine release, and flow cytometry.¹¹⁻¹⁶

In this study we evaluated how clinical assessments based on patient histories compare with test results from ammoniated and glove latex prick skin testing preparations and two commercially available in vitro latex-specific IgE assays.

MATERIALS AND METHODS

The study was approved by the Institutional Review Board of Long Beach Memorial Hospital. Study population consisted of all patients (mostly health care workers) referred to our office for latex evaluation between February 1994 and December 1996. In addition, subjects were recruited during Long Beach Memorial's annual safety fairs in 1995 and 1996. All study subjects were required to sign a consent form detailing the study and potential risks prior to enrollment. Enrollment was contingent upon subject's approval to undergo both skin and blood testing.

Study Questionnaire

Patients were interviewed by study investigators and assigned an overall pre-testing clinical impression of being type I latex allergy "history positive," "history negative," or "history ambiguous," as shown in Table 1. "History positive" patients were defined as those consistently having urticaria, bronchospasm, anaphylaxis, or rhinoconjunctivitis less than one hour following latex exposure. Patients were given a "history ambiguous" labeling for having the above symptoms occur inconsistently, in the presence or absence of exposure to latex. A "history ambiguous" patient is defined as somebody with pre-existing asthma or allergic rhinitis with inconsistent worsening around latex, or a patient having delayed onset (more than 60 minutes) of IgE symptoms following latex exposure. "History negative" patients

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Table 1. Pre-Testing Clinical Classification of Study Participants

	Positive*	Ambiguous*	Negative*
IgE-mediated symptoms following latex exposure	Any or all of: rhinoconjunctivitis, urticaria, bronchospasm, anaphylaxis	Any or all of: rhinoconjunctivitis, urticaria, bronchospasm, anaphylaxis	None
Onset following latex exposure	Less than one hour, usually in minutes	More than one hour	N/A†
Frequency following latex exposure	Almost always	Occasional or intermittent	N/A†
Improvement with avoidance of latex	Almost always	Occasional or intermittent	N/A†
Irritant or contact dermatitis	Possible	Possible	Possible

* Classification was done prior to any skin or blood testing and refer to type I latex allergy.

† Not applicable.

were defined as those having no evidence of type I symptoms following latex exposure. Patients reporting irritant or contact dermatitis to latex exposure could be in any of the three groups as the presence of these symptoms had no bearing on their type I classification.

Skin Prick Test

Skin testing was performed on all consenting participants. Testing was done by the epicutaneous method on the forearm with two groups of latex testing materials. The first group consisted of three separate batches of unmodified raw ammoniated latex (two batches from Johnson and Johnson, New Brunswick, NJ, and one batch from ALK Laboratories, Wallingford, CT). The second skin testing group consisted of three latex glove extracts (DigitCare, Los Angeles, CA; Safeskin, Boca Raton, FL; and VHA-Ansell, Eatontown, NJ) prepared as previously described.¹⁷

IBT Reference Laboratories (Lenexa, KS) measured the latex allergen content using an ELISA inhibition assay developed from pooled latex-allergic patient sera. The milligram of allergen per milliliter of the skin prick extracts were (1) ammoniated batch #1 (Johnson & Johnson), 2.61, (2) ammoniated batch #2 (Johnson & Johnson), 3.64, (3) ammoniated batch #3, (ALK Laboratories), 2.22, (4) Digitcare glove extract, 2.49, (5) Safeskin glove extract, 2.55, and (6) VHA glove extract, 2.91.

Skin testing was done by the punch technique, using the DermaPIK (Greer Laboratories, Lenoir, NC) and read 15 minutes after application.¹⁸ Histamine phosphate 1 mg/mL was used as positive control, and albumin-saline solution as negative control (Hollister-Stier, Spokane, WA). Results were considered positive if the largest wheal diameter was 50% or greater than that of the histamine control, and at least 3

mm larger than the negative saline control.

A positive raw skin test was defined as a positive result to at least one of the three raw testing materials. Similarly, a positive glove skin test was defined as a positive result to at least one of the three glove prick test materials. The overall skin prick test was defined as positive if at least one of the raw or glove skin pricks was positive. Medications to treat adverse reactions were readily available.

Latex-Specific IgE

Blood was obtained by peripheral venipuncture from all consenting subjects. Serum was separated and analyzed for latex-specific IgE using two FDA (Food and Drug Administration, USA) approved assays, the CAP (Pharmacia Biotech, Uppsala, Sweden) and AlaSTAT (Diagnostic Products Corp, Los Angeles, CA) assays. Either test was defined as positive if the result was class I or higher. The overall blood test was defined as positive if one or both tests was(were) positive.

RESULTS

Study Questionnaire Results

A total of 207 patients had extensive histories, skin tests, and blood drawn. Based on clinical history and prior to any diagnostic testing, 49 (24%) patients were coded as "latex history positive," and 99 (48%) were coded as "latex history negative." Fifty-nine patients (29%) were labeled as "history ambiguous" due to inconsistent or delayed (more than one hour) IgE-related symptoms following latex exposure (Table 1). Rhinoconjunctivitis and urticaria (systemic or local) were the most commonly reported IgE-related symptoms, occurring in 76 (37%) and 39 (19%) of the 207 patients, respectively (Table 2). Asthmatic symptoms were less common (12%), however they were more likely to occur in the clinically "positive" group versus other clinical classifications ($P \leq .001$). There was no statistically significant difference between the "history positive" and "history ambiguous" groups with regard to rhinoconjunctivitis. Ur-

Table 2. Clinical Symptoms of Study Population Following Latex Exposure

	Clinical Diagnosis of Type I Latex Allergy		
	Positive (n = 49)	Ambiguous (n = 59)	Negative (n = 99)
IgE symptoms	49	59	0
Urticaria	24	15	0
Rhinoconjunctivitis	36	40	0
Asthma	22	2	0
Anaphylaxis	6	0	0
Contact dermatitis	24	30	40

ticaria was more commonly reported in the "history positive" group than in the "history ambiguous" group. Anaphylaxis was the least common IgE-mediated symptom, and although it always resulted in a "history positive" labeling, the number of patients with this symptom was too small to achieve statistical significance. Overall, contact dermatitis was the most common symptom reported by study participants (45%) and was reported with nearly equal frequency in all clinical groups.

Skin Prick Test Results

Out of the 49 patients coded latex "history positive," 42 (86%) were skin test positive (Fig 1a) versus only 9 of 99 (9%) of those coded "history negative." Latex skin test was positive in 19 of 59 (32%) "history ambiguous" patients. Ammoniated raw latex was more likely than glove-based preparations to yield a positive prick test result in all clinical groups, as shown in Figure 1a, with the ammoniated raw extract picking up 81.4% of the positive skin tests and glove extracts picking up 74.3%. There was no significant difference between the individual testing materials within each group of the latex preparations used in this study (data not shown). Adverse reactions to skin testing were limited to rhinoconjunctivitis in three subjects. All three patients were treated uneventfully with an oral antihistamine.

Latex-Specific IgE Results

Of the 49 "history positive" subjects, 22 (45%) were AlaSTAT positive (class I or higher), and 17 (35%) were CAP positive (Fig 1b). In the 59 "history ambiguous" group the AlaSTAT and CAP were positive in 8 (14%) and 6 (10%), respectively. Out of 99 patients coded "history negative," 11 (11%) were positive for latex-specific serum IgE. Nine (9%) of these 99 were also skin test positive.

History and Skin Test Versus In-Vitro Assay Results

Out of the 61 subjects with IgE symptoms following latex exposure ("history positive" or "history ambiguous")

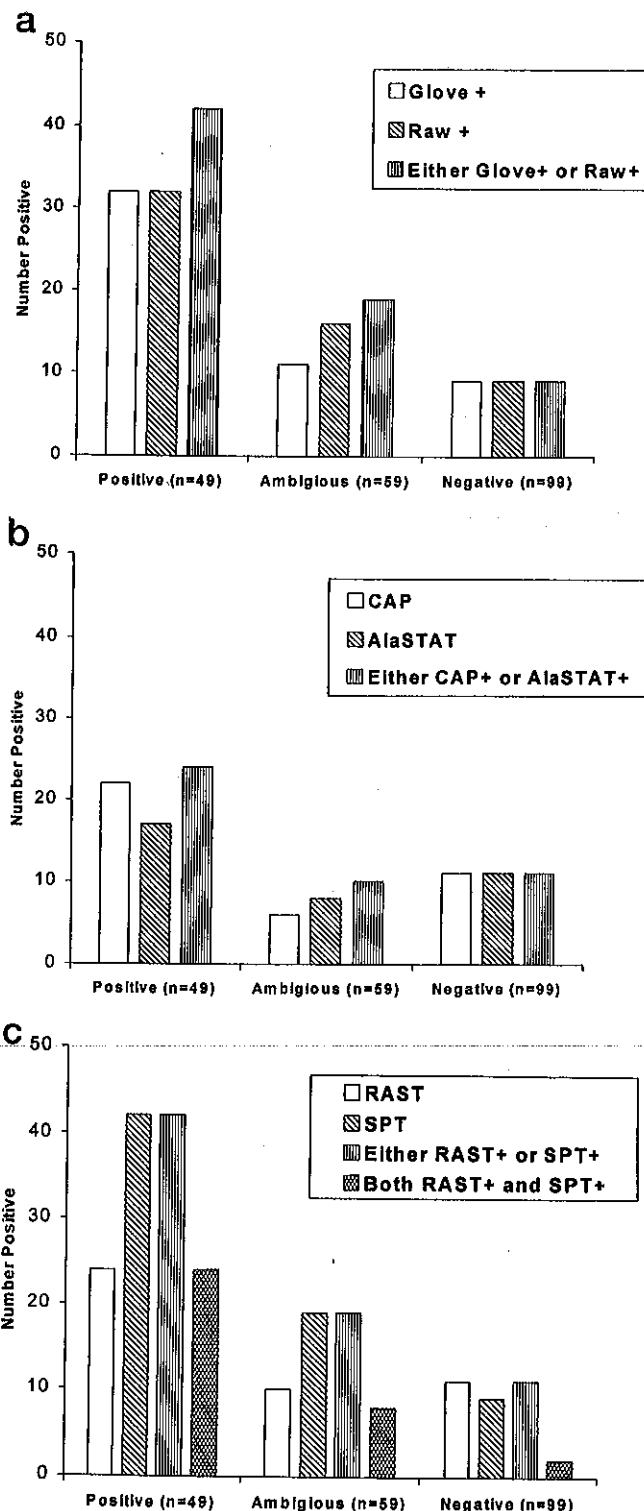


Figure 1. Latex skin prick and latex-specific serum IgE test results according to pretesting classification: (a) skin prick, (b) latex specific IgE, and (c) skin prick and latex specific serum IgE.

tex glove use test and/or a bronchial provocation with aerosolized latex can be particularly useful.^{9,19} Challenge testing would be useful for a patient who has a convincing history of type I latex allergy but who is otherwise negative by both skin testing and in vitro assays. A negative challenge test under these circumstances makes it highly unlikely that this patient has true type I latex hypersensitivity.⁹

Similarly, challenge procedures can be used in patients who are asymptomatic but have a positive latex skin prick test or a positive in vitro assay to distinguish between those with false-positive tests from those who are truly latex allergic but are not yet symptomatic. When provocation testing is not done, these patients should be managed as if they were latex allergic since their next latex exposure could result in a life-threatening reaction.²⁸ In the future a standardized challenge procedure should help establish a gold standard definition of a type I latex-allergic patient.

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