

# Relation of latex-specific IgE titer and symptoms in patients allergic to latex

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**Background:** The relation between latex-specific IgE titer and the type or total number of latex-induced symptoms has not been previously investigated.

**Objective:** We sought to determine the association of latex-IgE in vitro assay results with the type, number, or severity of symptoms in patients allergic to latex.

**Methods:** Ninety-one patients with positive histories and positive skin test responses were identified as having type I allergy. Data was collected for reported symptoms after latex exposure. Symptom severity was quantitated by 2 scores: (1) the total number of symptoms to latex exposure and (2) a symptom severity score (3 = anaphylaxis, 2 = asthma, and 1 = rhinoconjunctivitis, urticaria, or both). All subjects underwent AlaSTAT and CAP tests.

**Results:** AlaSTAT class was associated with total number of symptoms ( $r = 0.32$ ,  $P < .001$ ) and severity score ( $r = 0.33$ ,  $P < .002$ ). Similarly, CAP class was associated with both number of symptoms ( $r = 0.32$ ,  $P < .0001$ ) and severity score ( $r = 0.31$ ,  $P < .001$ ). Among the symptoms reported, asthma had the strongest association with a positive in vitro IgE assay (odds ratio = 6.7 [95% confidence interval = 1.9, 25.6]), followed by urticaria (odds ratio = 1.9 [95% confidence interval = 0.8, 4.6]). Contact dermatitis had no statistical association with in vitro assays in this study. AlaSTAT and CAP class correlated together significantly ( $r = 0.58$ ,  $P < .001$ ).

**Conclusion:** Patients allergic to latex with higher AlaSTAT or CAP class were more symptomatic. Increasing class or titer also predicted more severe symptoms. Higher class of either the AlaSTAT or CAP assay to latex was strongly associated with latex-related asthma and urticaria and marginally associated with latex-related rhinoconjunctivitis. (*J Allergy Clin Immunol* 1999;103:671-7.)

**Key words:** Latex allergy, in vitro IgE assay, asthma, AlaSTAT, CAP

It is now well established that proteins derived from natural rubber latex can cause a type I hypersensitivity reaction that is mediated by IgE antibodies specific to latex proteins.<sup>1,2</sup> The types of symptoms that can be pre-

### Abbreviations used

CI: Confidence interval

OR: Odds ratio

cipitated by latex exposure can vary from mild immediate contact and local urticaria to more severe and systemic reactions, such as systemic urticaria, allergic rhinoconjunctivitis, asthma, and even anaphylaxis.<sup>3-5</sup> Airborne latex allergens have been shown to be a cause of occupational asthma in health care workers allergic to latex.<sup>6,7</sup> However, establishing a causal relationship between latex exposure and asthmatic symptoms in patients allergic to latex may prove difficult and may require bronchial provocation testing.<sup>8</sup>

The use of clinical assessment in combination with skin testing and commercially available RAST assays provides the current basis in making the diagnosis of latex allergy.<sup>9-11</sup> In a study by Hadjiliadis et al<sup>10</sup> with commercially available latex skin prick test material, the size of the skin prick test response in patients allergic to latex correlated with the severity of latex-induced clinical allergic responses. Similarly, a recent study by Beebe and Sullivan<sup>12</sup> indicated that health care workers allergic to latex with a history of anaphylaxis, asthma, allergic rhinitis, or condom reactions were more likely to express IgE to latex when measured by in vitro assays.

AlaSTAT and Pharmacia CAP are 2 recently approved in vitro assays in the United States for diagnosis of latex allergy. The correlation between these in vitro assays and the total number or severity of latex-induced symptoms has not been previously investigated. In this study we analyze the relation between the class of the in vitro assays for latex-specific IgE and clinical symptoms of patients who have latex allergy as determined by clinical history and confirmatory skin tests.

## METHODS

The Institutional Review Board of Long Beach Memorial approved the study. Study population consisted of all patients (mostly health care workers) referred to one of the authors for latex evaluation between February 1994 and December 1996 as previously reported.<sup>9</sup> In addition, subjects were recruited during Long Beach Memorial's annual safety fairs in 1995 and 1996. All subjects were required to sign a consent form detailing the study and potential risks before enrollment. Only subjects with histories consistent

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**TABLE I.** Correlation of latex diagnostic tests with number of symptoms and severity score

|                       | Spearman's correlation coefficient (rho value) |                |
|-----------------------|------------------------------------------------|----------------|
|                       | Symptoms*                                      | Severity score |
| AlaSTAT               |                                                |                |
| Class $\geq 1$        | 0.32†                                          | 0.33†          |
| Class $\geq 3$        | 0.46†                                          | 0.41†          |
| CAP                   |                                                |                |
| Class $\geq 1$        | 0.32†                                          | 0.31†          |
| Class $\geq 3$        | 0.38†                                          | 0.33†          |
| Overall in vitro test |                                                |                |
| Class $\geq 1$        | 0.25‡                                          | 0.25‡          |
| Class $\geq 3$        | 0.52†                                          | 0.47†          |

\*Total number of symptoms after latex exposure.

† $P < .01$ .‡ $P < .05$ .

with type I allergic symptoms to latex (rhinoconjunctivitis, urticaria, asthma, or anaphylaxis) who had positive latex skin prick test responses were included in this study.

### Skin prick tests

Skin testing was performed on all consenting participants. Testing was done by the epicutaneous method on the forearm with 2 groups of latex-testing materials, consisting of raw latex (ammoniated latex and nonammoniated latex, Johnson and Johnson), and Soluprick (ammoniated latex from ALK Laboratories), and 3 latex glove preparations (DigitCare, Los Angeles, Calif; Safeskin, Boca Raton, Fla; and VHA-Ansell, Eatontown, NJ). Glove extracts were prepared as previously described.<sup>13</sup> ELISA-inhibition studies (IBT Reference Laboratories, Lenexa, Kan) with pooled sera from patients allergic to latex confirmed the presence of allergenic latex proteins in all preparations before testing as previously described.<sup>9</sup> Skin testing was done by the punch technique with the DermaPIK (Greer Laboratories, Lenoir, NC), and results were read 15 minutes after application.<sup>14</sup> Histamine phosphate 1 mg/mL was used as positive control, and albumin-saline solution was used as negative control (Hollister-Stier, Spokane, Wash). Results were considered positive if any of the latex skin tests resulted in a wheal response 50% or greater in diameter than that of the histamine control and at least 3 mm larger than that of the negative saline control. The overall skin prick test response was defined as positive if 1 or more of the raw or glove skin prick responses was positive. All measures 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 by using the CAP (Pharmacia Biotech, Uppsala, Sweden) and AlaSTAT (Diagnostic Products Corp, Los Angeles, Calif) assays. Results were recorded as class 0 through class 6 in accordance with each of the manufacturer's recommendations.

### IgE symptom score

Data from patients allergic to latex was collected for IgE symptoms reported with latex exposure (rhinoconjunctivitis, urticaria, asthma, or anaphylaxis). The total number of latex symptoms reported varied between 1 and 4. A symptom severity score was calculated in order of decreasing severity as follows: 3 = anaphylaxis, 2 = asthma, and 1 = rhinoconjunctivitis, urticaria, or both. Individ-

uals were always assigned the most severe symptom severity score among their reported symptoms. For example, a patient with latex-induced anaphylaxis and latex-induced rhinoconjunctivitis was assigned a score of 3. Anaphylaxis was strictly defined as documented hypotension (drop of greater than 20 mm Hg from baseline) or a systemic reaction to latex that was severe enough to require emergent care that included epinephrine.

### Data analysis

Microsoft Excel 97 for Windows 95 and SPSS 7.5 for Windows 95 were used for data analysis. Spearman's rank correlation, a measure of the association between rank orders that does not require normality, was used for analysis of the relation between in vitro tests and symptom number and severity. Risk for having the various symptoms in relation to in vitro assay class was calculated by using the odds ratio (OR) and 95% confidence interval (CI). Statistical significance was measured by using the chi-square and Fisher's exact tests.

### RESULTS

Ninety-one patients with histories consistent with type I allergic symptoms to latex (rhinoconjunctivitis, urticaria, asthma, or anaphylaxis) who had positive latex skin prick test response were included in the final analysis. Severity scores ranged from 1 (lowest score) to 3 (highest score). AlaSTAT results were positive in 40 of 91 (44%) subjects, and Pharmacia CAP results were positive in 47 of 91 (52%). Fifty-seven of the 91 (63%) had a positive response to at least 1 in vitro assay. The relatively low positive in vitro assay rate may be a function of comparing the in vitro assays to the relatively strong concentrated skin test reagent and may be a result of multiple (ie, 6) latex skin test reagents being used. A total of 25 subjects (28%) had a class 3 or higher result on at least 1 assay (AlaSTAT = 19 [21%]; CAP = 17 [19%]).

Rhinoconjunctivitis was the most common reported symptom in 61 of 91 subjects (67%), followed by contact dermatitis and urticaria in 39 (43%) and 38 (42%) subjects, respectively. Twenty-six subjects (29%) reported asthmatic symptoms in relation to latex exposure, and 8 (9%) reported a history of latex-related anaphylaxis.

A positive AlaSTAT or CAP test response correlated with both total number of symptoms and severity score (Table I). A class 3 response or above on either test had an overall higher correlation, with total number and severity of symptoms reported. AlaSTAT class and CAP class correlated well against each other ( $r = 0.58$ ,  $P < .001$ ).

Asthmatic symptoms and urticaria were strongly associated with both AlaSTAT and CAP assays (Fig 1). Asthma had the strongest association with a positive in vitro IgE assay result (OR = 7.0 [95% CI: 1.9, 25.6];  $P < .0001$ ) followed by urticaria (OR = 1.9 [95% CI: 0.8, 4.6];  $P < .001$ ). A class 3 response or above on 1 or both tests was significantly associated with reporting of asthmatic symptoms (OR = 10.0 [95% CI: 3.5, 28.7];  $P < .0001$ ) and urticaria (OR = 7.8 [95% CI: 2.7, 22.6];  $P < .0001$ ). Furthermore, asthmatic symptoms and urticaria correlated well with each other ( $r = 0.45$ ,  $P < .0001$ ). Patients

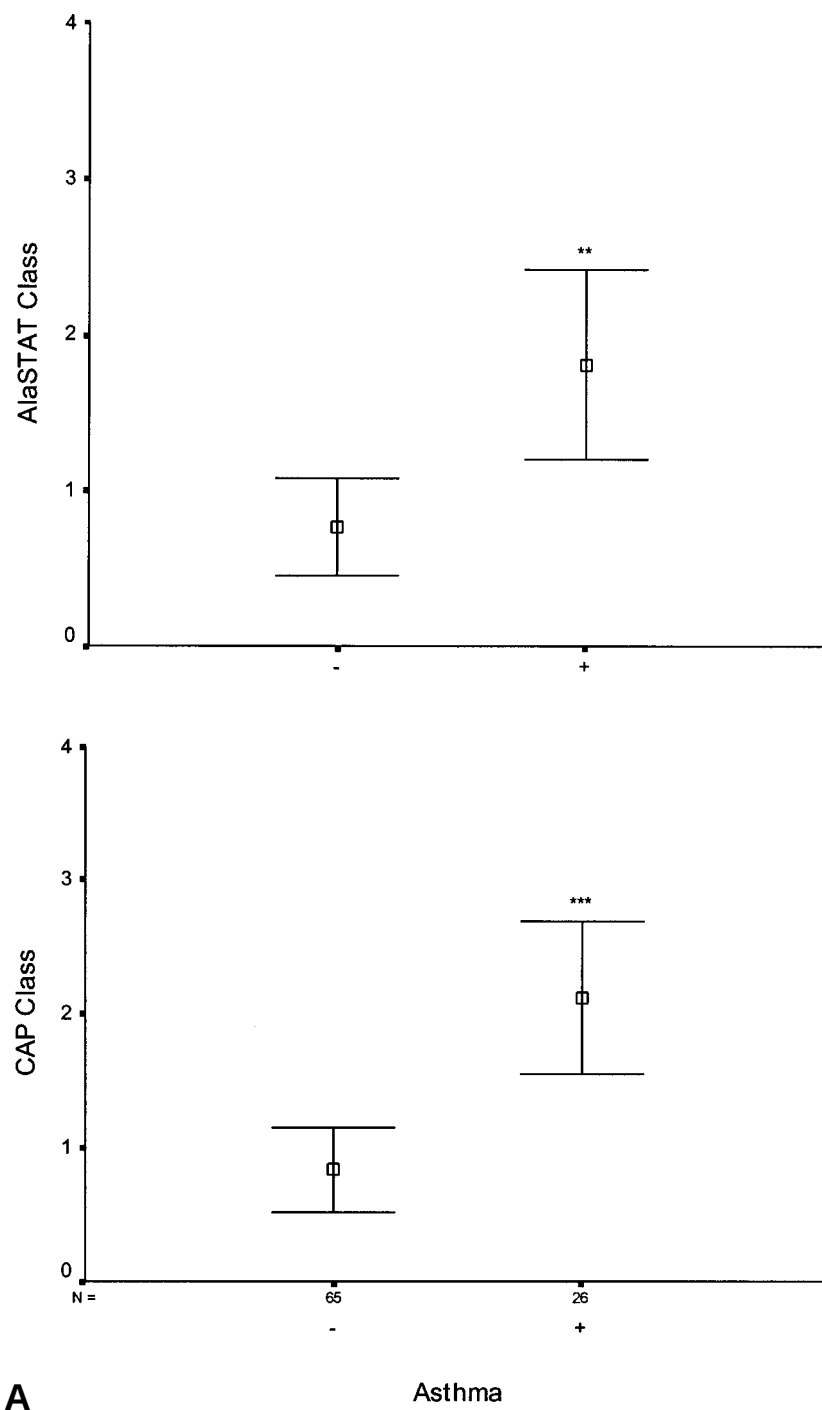


**FIG 1.** AlaSTAT and CAP class results in relation to asthmatic symptoms (**A**), urticaria (**B**), rhinoconjunctivitis (**C**), and eczema (**D**) after latex exposure. Number of patients reporting anaphylaxis was too small to allow for analysis. Error bars represent 95% CI from the mean. \* $P < .05$ , \*\* $P < .01$ , \*\*\* $P < .001$ .

having a history of urticaria were more likely to have asthmatic symptoms (OR = 8.7 [95% CI: 3.0, 25.1];  $P < .0001$ ). The number of patients with anaphylaxis was too small to reach statistical significance. As expected, contact dermatitis, which is not IgE mediated, had no correlation with in vitro assays in this study.

## DISCUSSION

A strong clinical history of latex allergy with a positive skin prick test response to latex is sufficient to label an individual as having latex allergy. However, the severity of latex allergy can vary among those affected. In a

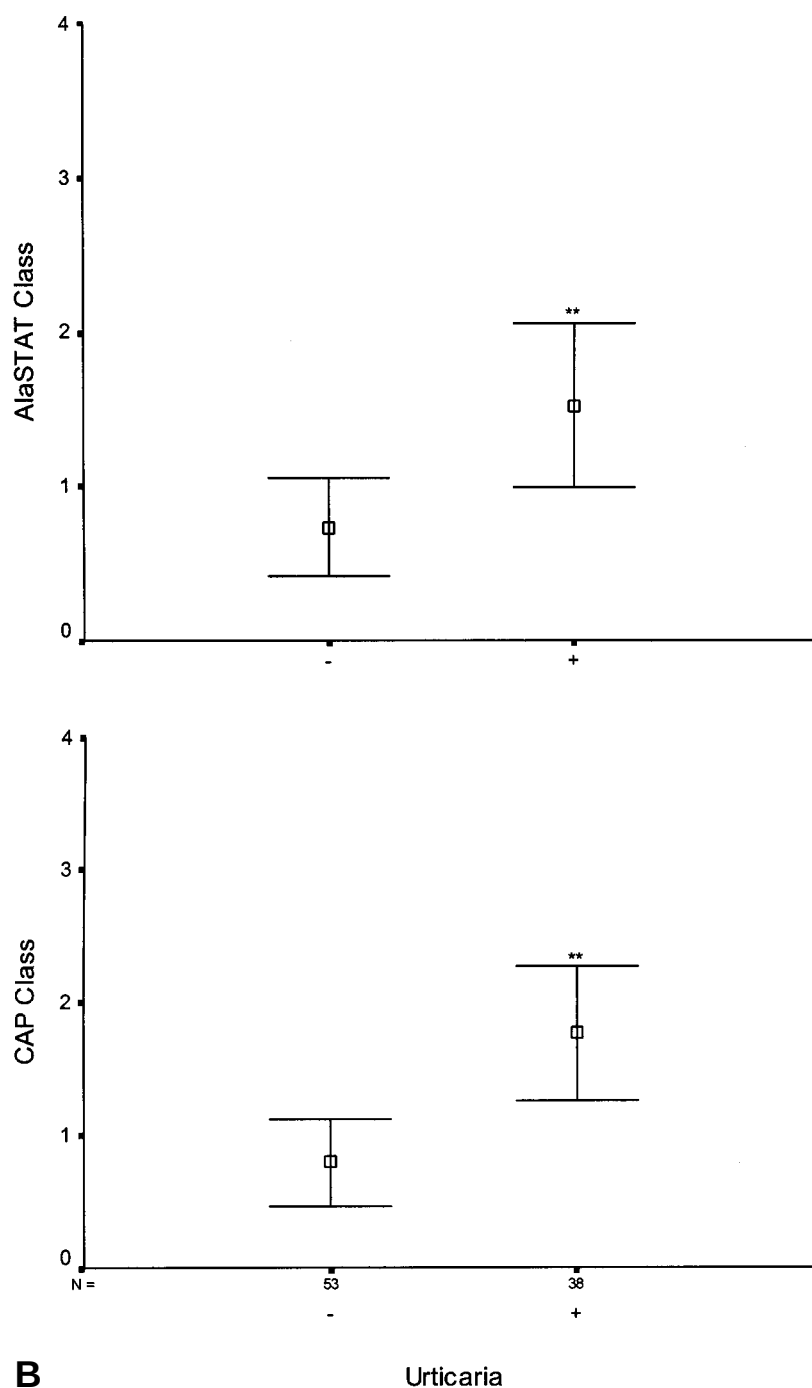


FIG 1, CONT. B

study by Hadjiliadis et al<sup>10</sup> the size of reaction to latex on skin prick testing with commercially available skin test material in Canada showed strong correlation with the severity of latex allergy.

The diagnostic ability of currently available in vitro assays for latex-specific IgE has been previously reported,<sup>9</sup> but it is not the purpose of the data analysis presented here. In this article we explore whether in-

creasing titers of 2 recent Food and Drug Administration–approved in vitro latex assays (Pharmacia CAP and DPC AlaSTAT) correlate with the severity of latex allergy. For that purpose, a symptom severity score was used in which anaphylaxis was given the highest score of 3 followed by asthma (score = 2) and rhinoconjunctivitis, urticaria, or both (score = 1). Severity scores ranged from 1 to 3. From our data, we concluded that individuals

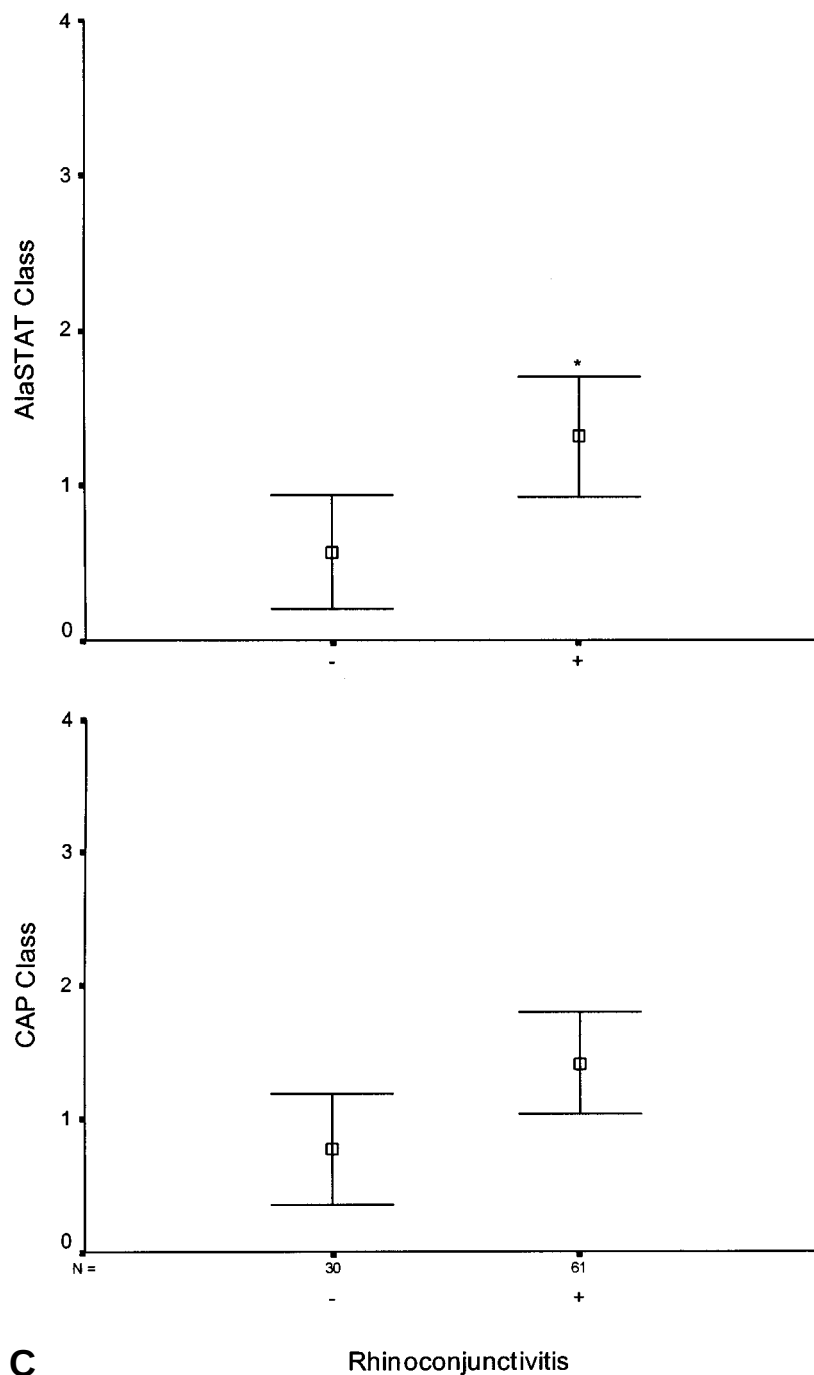


FIG 1, CONT. C

allergic to latex with a positive in vitro test response to latex were more likely to have a greater number of symptoms and higher severity scores. An AlaSTAT class correlated with total number of symptoms and severity score. Similarly, a CAP class correlated with both number of symptoms and severity score. Asthmatic symptoms and, to a lesser extent, urticaria after latex exposure were more likely to be present in those subjects with positive in vitro test responses. This was especially evident

in the subgroup of patients with a class 3 or above on either test.

The results suggest that in a patient allergic to latex, a higher class of the in vitro assay may be indicative of more severe symptoms on exposure to latex. A higher class of either assay was most noticeably associated with increased ORs for latex-induced asthmatic and urticarial symptoms. A class of 3 or above on either assay was an even stronger indicator of symptom severity. These

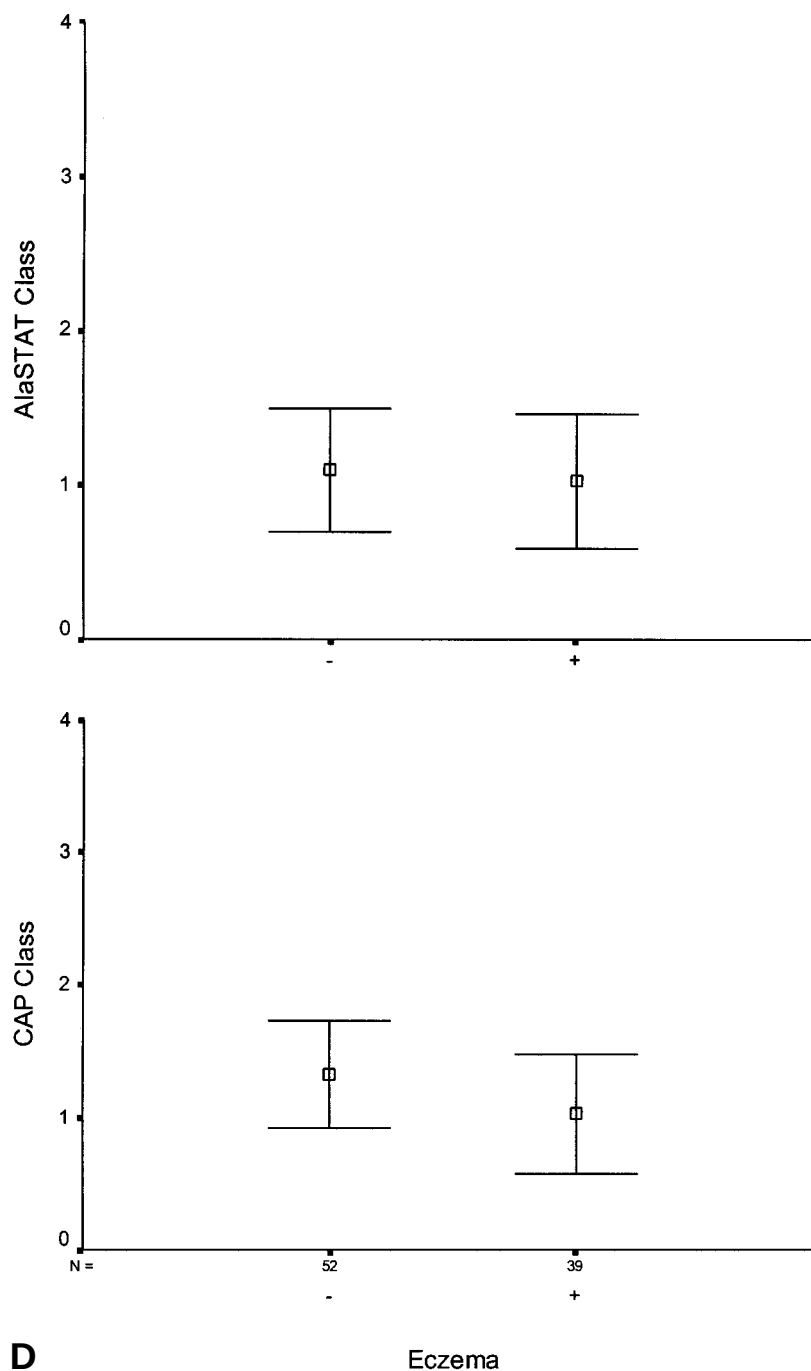


FIG 1, CONT. D

observations may simply be a manifestation of more severe disease. However, it may also be the result of an inherent ability of the *in vitro* assays used in this study to recognize epitopes responsible for the development of asthmatic or urticarial symptoms.<sup>1</sup>

In conclusion, *in vitro* latex-specific IgE assays may play a useful role in determining the severity of latex allergy in patients allergic to latex in addition to their usefulness as diagnostic tests. In particular, they may have a role in the evaluation of work-related asthmatic responses

induced by latex allergy.<sup>15</sup> The importance of determining the severity of latex allergy lies in the ability to provide better medical advice to affected individuals by recommending more strict latex-avoidance measures.<sup>16</sup>

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