

# A hooded exposure chamber method for semiquantitative latex aeroallergen challenge

Kenneth M. Kurtz, MD,<sup>a</sup> Robert G. Hamilton, PhD,<sup>a</sup> John A. Schaefer, CIH,<sup>b</sup> and N. Franklin Adkinson, Jr, MD<sup>a</sup> *Baltimore, Md*

**Background:** Allergen challenges are useful in adjudicating discordant clinical histories and skin test responses, serologic test responses, or both, as well as in determining the degree of allergic reactivity. Latex allergen challenges have been developed but have limitations that reduce their usefulness.

**Objective:** We sought to develop a novel hooded exposure chamber (HEC) system to allow safe, sensitive, and semiquantitative evaluation of respiratory latex allergy.

**Methods:** The HEC system uses an impinger to produce a particle cloud of cornstarch isolated from powdered latex gloves. The particles are air driven into a face shield and hood to simultaneously challenge the subject's conjunctiva, nose, and lungs during 3 minutes of normal tidal breathing. A cloud of respirable latex allergen-associated cornstarch particles (LACs) is consistently produced in the HEC during challenges. Twenty-three subjects with latex allergy (history and positive skin test response, positive serologic test response, or both) and 3 atopic control subjects not allergic to latex (history and negative skin test response, negative serologic test response, or both) were sequentially exposed to air, control cornstarch, and then progressive 2-fold increments of LACs in a single-masked fashion. A positive challenge result was defined as (1) a peak expiratory flow rate decline of 15% or greater from baseline; (2) a peak expiratory flow rate decline of 10% or greater and an increase of either the rhinoconjunctivitis or chest symptom score scale of 3 or more points from baseline; or (3) an increase of either the rhinoconjunctivitis or chest symptom score scale of 6 or more points from baseline.

**Results:** Twenty-two of the 23 subjects with latex allergy reached threshold criteria for a positive challenge at LAC titers of 1:8 or greater, giving a sensitivity of 0.96. Challenge endpoints were moderately corrected with skin test sensitivity ( $r_s = -0.55$ ,  $P = .01$ ) but not with RAST reactivity. None of the 3 control subjects responded to LACs at the 1:8 dilution. No patient or control subject responded to the air or control

cornstarch control exposures. All responses were confined to mild symptoms of allergic rhinoconjunctivitis, asthma, or both that either resolved spontaneously or were easily reversed with inhaled albuterol. No subject experienced a systemic or late-phase reaction.

**Conclusion:** The HEC procedure is a safe, sensitive, and specific method for masked semiquantitative latex aeroallergen challenges that mimic occupational latex exposure to powdered latex gloves. (*J Allergy Clin Immunol* 2001;107:178-84.)

**Key words:** Latex allergy, aeroallergen challenge, occupational allergy, occupational asthma

Allergic sensitivity to natural rubber latex has become a major health hazard for health care workers and patients with repetitive latex exposures.<sup>1-9</sup> Allergenic proteins from the rubber tree *Hevea brasiliensis* cause allergic reactions in sensitized individuals after direct exposure to the skin or exposure of the conjunctiva and respiratory tract to airborne latex allergen. Latex allergen associated-cornstarch particles (LACs) become airborne when powdered latex gloves are used, with resulting latex allergen exposure to the conjunctiva, upper airway, and lower airway.<sup>10,11</sup>

The diagnosis of latex allergy begins with a clinical history linking latex exposure and symptoms of allergy. A suggestive history is then supported by confirmatory skin and serologic test responses for latex-specific antibodies.<sup>12-14</sup> When the clinical history and IgE antilatem test results are discordant, provocation procedures have been used to adjudicate patients' true latex sensitivity status. Such procedures can also measure the degree of latex sensitivity if a dose-response relationship can be defined.

A number of procedures have been previously described to expose individuals safely to airborne latex allergen. Challenges with latex extracts have been developed but do not simulate natural exposures.<sup>15,16</sup> A number of glove use challenges have also been described, but most have significant limitations, including difficulties with subject masking, variability of latex glove allergen content, and inability to quantify latex allergen exposure.<sup>17-26</sup>

The purpose of this study was to develop a safe, sensitive, specific, and natural method for latex aeroallergen challenge that addresses some of the limitations of the challenge procedures previously reported. The hooded exposure chamber (HEC) method described here has the advantages of allowing masking of the subject (and the investigator if desired) and providing a semiquantitative

From <sup>a</sup>the Department of Medicine, Division of Allergy & Clinical Immunology at the Johns Hopkins Asthma and Allergy Center, Baltimore; and <sup>b</sup>Occupational Health and Safety, Johns Hopkins University, Baltimore.

Supported by National Institutes of Health grants AI43654 and AI31867 and a Glaxo Wellcome Allergy Fellowship Research Award to Dr Kurtz.

Received for publication May 5, 2000; revised September 12, 2000; accepted for publication October 5, 2000.

Reprint requests: N. Franklin Adkinson, Jr, MD, Professor of Medicine, Johns Hopkins Asthma & Allergy Center, 5501 Hopkins Bayview Circle, Room 2A62, Baltimore, MD 21224.

Copyright © 2001 by Mosby, Inc.

0091-6749/2001 \$35.00 + 0 1/86/112125

doi:10.1067/mai.2001.112125

#### Abbreviations used

- CC: Control cornstarch
- HEC: Hooded exposure chamber
- LAC: Latex allergen-associated cornstarch particle
- PEFR: Peak expiratory flow rate
- PST: Puncture skin test

estimation of latex allergen sensitivity. In addition, the HEC challenge mimics occupational exposure to latex aeroallergen from powdered latex gloves.

## METHODS

### LAC preparation

The interior of powdered latex examination gloves (Baxter HealthCare) from a single lot determined by means of aqueous extraction assay to have a high allergen content were individually washed out with 15 mL of PBS 3 times. The glove effluent was centrifuged (1000g for 3 minutes), and the supernatant was decanted. The resulting LAC slurry was then dried by suctioned air through an 8- $\mu$ m milipore filter (Milipore Corporation). This process yielded about 1 g of LACs for each 25 harvested gloves. Two-fold dilutions were made from the dried LACs by using control cornstarch (CC) not associated with latex allergen (Roquette America, Inc) in advance of the challenge tests. The latex allergen potency of the glove-derived LACs was standardized between preparations by using a solid-phase RIA.<sup>27</sup> Briefly, LACs were used as the allergosorbent, and increasing amounts of an IgE anti-latex human serum pool were used to quantify allergen bound to the cornstarch. Two LAC preparations were used in this study. Both were derived from a single lot of gloves (Lot D9B219X) manufactured in 1989.

### Serologic measurement of latex-specific IgE

The level of latex-specific IgE in the serum of patients and control subjects was initially determined by using an agarose-based RAST.<sup>27</sup> These results were reported in nanograms per milliliter and later converted to kilo international units of allergen per milliliter by using cross-validation. Later, the level of latex-specific IgE in the serum of patients and control subjects was determined by using the Pharmacia CAP System and reported in kIUa per milliliter.<sup>28</sup>

### Latex skin tests

Duplicate serial latex puncture skin tests were carried out on the volar aspect of the arm by using a nonammoniated latex skin test reagent (Greer Laboratories, under IND 7883) diluted in 50% glycerin-water to concentrations of 1, 10, 100, and 1000  $\mu$ g/mL. A bifurcated needle was used to puncture the skin, as previously described.<sup>12</sup> A positive puncture skin test response was defined as a wheal 2 mm or larger than that produced by the negative control and erythema of 5 mm or larger than that produced by the negative control. For the purposes of comparative analysis, the concentration of nonammoniated latex necessary to produce a wheal 8 mm larger than that produced by the negative control was interpolated or extrapolated from a graph of the log concentration versus wheal size. Histamine (1.8 mg/mL) and glycerinated diluent skin tests were used as positive and negative controls, respectively.

### Subjects

Patients with latex allergy ( $n = 23$ ) and control subjects not allergic to latex ( $n = 3$ ) were recruited from the patient populations of the Johns Hopkins Health System and the University of Maryland

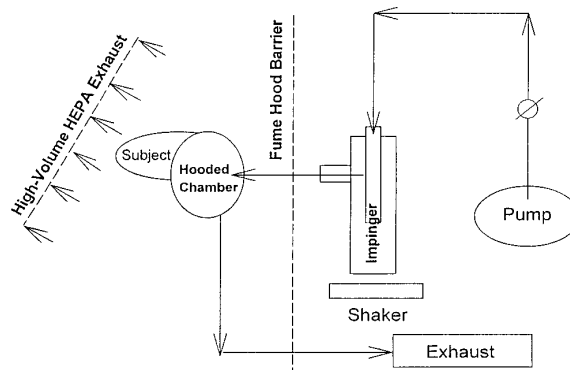


FIG 1. Schematic of the HEC system. HEPA, High-efficiency particulate air.

Health System and from posted and circulated advertisements. The patients and control subjects were men and women between the ages of 18 and 60 years with either (1) respiratory latex allergy (clinical history of latex allergy manifested by upper, lower, or both types of airway symptoms and a positive latex skin response, positive serologic test response, or both) or (2) no latex allergy (no clinical history of latex allergy and a negative latex skin test response). Exclusion criteria were as follows: pregnancy; severe skin disease with compromise of the integument barrier; unstable asthma symptoms; peak expiratory flow rate (PEFR) less than 80% of personal best on the challenge day; symptomatic rhinitis or conjunctivitis at baseline on the challenge day; history of cardiac arrhythmia or coronary artery disease; requirement for continuous therapy with antihistamines, therapy with astemizole or hydroxyzine within 12 weeks of the challenge day, or therapy with any other medication with antihistaminic properties within 7 days of the challenge day; change in anti-inflammatory nasal sprays or inhaled medications within 1 month of the challenge day; or concurrent  $\beta$ -blocker drug therapy. The study protocol was approved by the Johns Hopkins Bayview Institutional Review Board. All patients and control subjects gave written informed consent.

### HEC system

The HEC system (Fig 1) is comprised of an electric-powered air-purifying respirator (0.5 cubic feet per minute) with a fitting face shield and hood (Neotecick Care-flo; Fig 2). A particle cloud is produced by using an impinger that passes air through 17 g of powdered CC or LACs and introduces the particles into the airstream distal to the pump. Separate impingers were used for each CC or LAC dose. Particle counts are measured by using a laser particle counter (MET ONE), which was calibrated to measure particles in the respirable range (1-10  $\mu$ m in diameter). Contamination of the ambient air in the test room with LACs is minimized by placing the impinger apparatus in an externally ventilated fume hood and by using a high air flow HEPA filter (Enviro Care, HospiGuard) in the exposure room.

### Challenge protocol

Single-masked challenges were conducted with controls of both air only and CC. The subject is unaware of how many (if any) LACs are administered. The challenges proceed as a series of consecutive iterations (Fig 3). The subject breathes through the mouth and nose at normal tidal volume within the HEC for 3 minutes, followed by 15 minutes of observation. After each 3-minute exposure, the airflow is turned off, and the hood is removed. The subject is monitored for an additional 3 minutes and then assessed according to symptom inventory and PEFR. The subject is then monitored for 12 more minutes, and the assessment is repeated. After this, the subject again dons the



FIG 2. Photograph of a human subject volunteer installed in the HEC system.

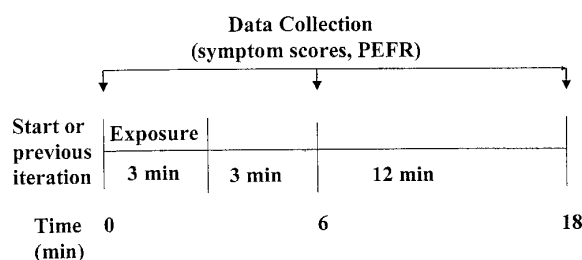


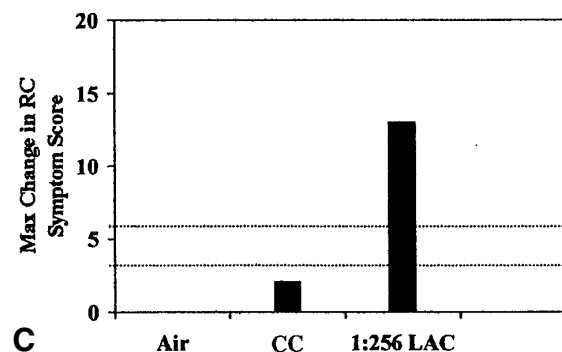
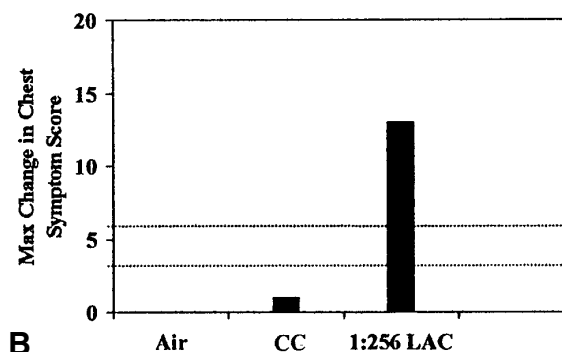
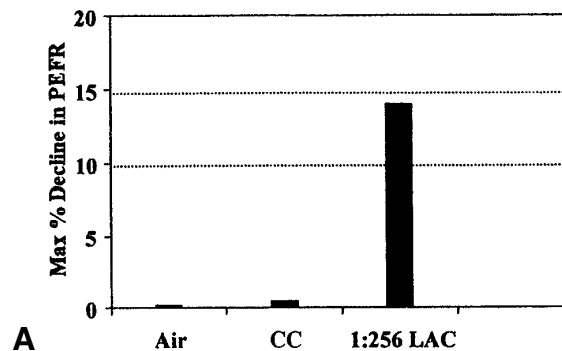
FIG 3. Schematic of HEC challenge iterations.

HEC for the next iteration of the challenge. The first iteration uses air only, with no particles. The second iteration uses CC only, with no latex allergen. Subsequent iterations use increasingly potent 2-fold dilutions of LACs starting with a 1:128 or higher dilution (ie, 1 part LACs and 127 parts CC) and proceeding to a positive endpoint or the 1:8 dilution, which is the maximum practical exposure. All 17 g of CC or LACs is aerosolized during the 3-minute exposure. The subject is discharged 30 minutes after the final iteration. All subjects were asked to report any delayed reactions or symptoms.

### Subject response assessment

The subjects' responses to the exposures were evaluated by measuring PEFr (Wright Mini-peak Flow Meter) and symptom inventories. Separate symptom score scales for rhinoconjunctivitis and chest symptoms were adopted from previously successful airway challenge models.<sup>29</sup> There are 5 subscales for rhinoconjunctivitis (nasal itching, congestion, and running; ocular itching and tearing) and 4 subscales for chest symptoms (chest tightness, shortness of breath, cough, and wheezing). Each 6-point subscale is additive because subjects report different symptoms. Separate indices are maintained for rhinoconjunctivitis (maximum score, 30) and chest symptoms (maximum score, 24).

The challenge proceeds until (1) a positive result is observed, (2) the highest practical LAC dose of 1:8 is achieved, or (3) the physician or patient decides not to continue because of intensive or cumulative discomfort. The criteria for a positive challenge are (1) a PEFr decline of 15% or greater from baseline; (2) a PEFr decline of 10% or greater from baseline and an increase in either the



### Exposure

FIG 4. Representative subject results. **A**, Percentage decline in PEFr; **B**, increase in chest symptom score; **C**, increase in rhinoconjunctival (RC) symptom score. The dotted lines represent the threshold criteria for a positive challenge response either singly (upper lines) or in conjunction (lower lines). This subject met the criteria for a positive challenge at the 1:256 LAC endpoint dilution.

rhinoconjunctivitis or chest symptom score scale of 3 or more points from baseline; or (3) an increase in either the rhinoconjunctivitis or chest symptom score scale of 6 or more points from baseline. The higher of the 2 scores from the 6- and 18-minute observation points was used to apply the threshold criteria.

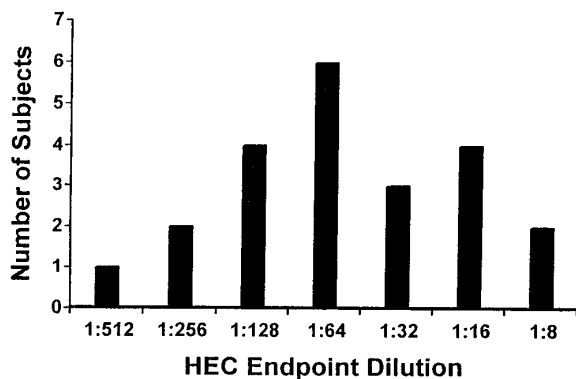


FIG 5. Frequency distribution of LAC endpoint dilutions for positive HEC challenge responses ( $n = 22$ ).

### Statistical methods

The Spearman rank correlation coefficients (nonparametric) for the relationship between the challenge endpoints and the skin and serologic test results were calculated by using standard methods.<sup>30</sup>

## RESULTS

### Particle cloud production

When ambient air alone is present in the impinger, particle counts remain low ( $27 \pm 3$  [mean  $\pm$  SEM] particles of 1-10  $\mu\text{m}$  in diameter per milliliter;  $n = 17$ ). When CC is present in the impinger, particle counts were higher ( $22,296 \pm 698$  particles of 1-10  $\mu\text{m}$  in diameter per milliliter). The within-iteration coefficient of variation for serial measurements of a single particle cloud was 2.3% ( $n = 49$ ). The between-iteration coefficient of variation for measurements of different particle clouds produced by identical methods was 7.0% ( $n = 5$ ). When LACs were present in the impinger, particle counts were not different from those observed when CC was used.

### Sensitivity

Twenty-three subjects with latex allergy have undergone the HEC challenge procedure (Table I). Twenty-two of these subjects had a positive challenge result. Of the 22 positive results, criteria were achieved at 6 minutes for 2 subjects and at 18 minutes for 20 subjects. None of the positive challenges involved criteria 1 alone, 9.1% met criteria 2 alone, 54.5% met criteria 3 alone, 4.5% met criteria 1 and 2, 4.5% met criteria 1 and 3, 8.2% met criteria 2 and 3, and 9.1% met criteria 1, 2, and 3 (see the "Subject response assessment" section). These results indicate that the sensitivity of the HEC challenge procedure is 22 of 23 or 0.96. The one subject who did not respond at the highest LAC concentration (ie, the 1:8 LAC dilution) had a clinical latex allergy history that was dominated by contact dermatitis rather than conjunctival and respiratory symptoms. In addition, this subject had low-level latex sensitivity, as determined by skin test and serologic assay (Table I). Fig 4 shows the response of a

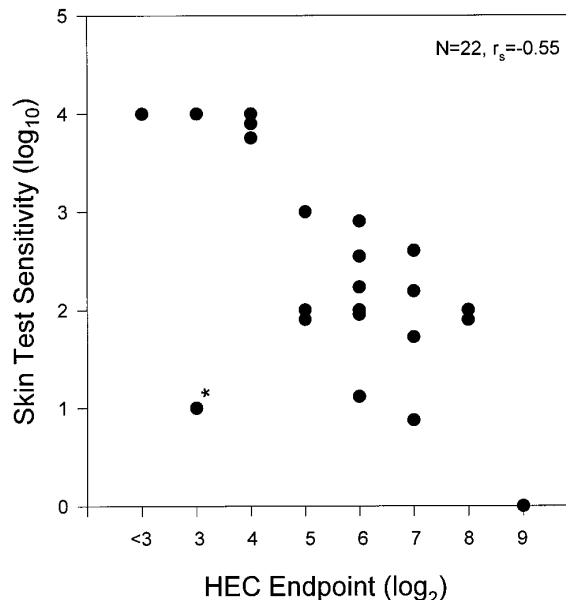


FIG 6. Correlation between the HEC endpoint and skin prick test results in micrograms per milliliter of latex protein for an 8-mm wheal response ( $r_s = -0.55$ ,  $P = .01$ ). \*Outlier (subject 4, Table I).

representative patient to the air, CC, and LAC challenges. This subject met the criteria for a positive challenge at an LAC dilution of 1:256. Initial positive challenge responses by subjects with latex allergy were observed at dilutions ranging from 1:512 to 1:8 (Fig 5).

### Specificity

The specificity of the HEC challenge procedure was addressed in 2 ways. First, all of the subjects with latex allergy were challenged with air and CC control iterations before LACs were administered. None of the subjects responded to these masked controls. Second, 3 atopic control subjects not allergic to latex have undergone CC and LAC challenges in the HEC. Two of these control subjects had histories of allergic rhinoconjunctivitis alone, and the other had a history of allergic rhinoconjunctivitis and asthma. None of the control subjects responded to air, CC, or LACs at the maximum latex exposure of 1:8 LAC dilution.

### Correlation between the HEC endpoint and the skin tests and serologic tests for latex allergy

There was a significant correlation between the HEC endpoint and skin test results ( $r_s = -0.55$ ,  $P = .01$ ; Fig 6) but not the serologic test results ( $r_s = 0.29$ ,  $P = .19$ ). Skin test sensitivity and RAST values were moderately correlated ( $r_s = -0.51$ ,  $P = .02$ ).

### Safety

All positive challenge reactions were confined to mild symptoms of allergic rhinoconjunctivitis and asthma. All reactions resolved either spontaneously or after treatment

**TABLE I.** Demographic, skin test, serologic test, and HEC challenge result data on the 23 latex-sensitive subjects enrolled in the study

| Subject   | Age (y) | Sex | Occupation            | Nonlatex atopy | Latex skin test result* ( $\mu\text{g/mL}$ ) | Latex-specific IgE (kIUa/mL) | HEC challenge result |
|-----------|---------|-----|-----------------------|----------------|----------------------------------------------|------------------------------|----------------------|
| 1         | 36      | F   | Florist               |                | 100                                          | 17.2 <sup>‡</sup>            | Positive             |
| 2         | 30      | F   | Medical technician    |                | Positive <sup>†</sup>                        | Not done <sup>§</sup>        | Positive             |
| 3         | 42      | F   | Nurse                 |                | 1000                                         | 15.2 <sup>‡</sup>            | Positive             |
| 4         | 26      | F   | Laboratory technician |                | 10                                           | 41.2 <sup>‡</sup>            | Positive             |
| 5         | 32      | M   | Laboratory technician | RC, AS         | 155                                          | 2.47                         | Positive             |
| 6         | 31      | F   | Nurse practitioner    | AS             | >1000                                        | 0.54                         | Negative             |
| 7         | 45      | F   | Medical technician    | RC, AS, FA     | 100                                          | 11.2                         | Positive             |
| 8         | 41      | F   | Nurse                 | AS             | 53                                           | 58.7                         | Positive             |
| 9         | 49      | F   | Nursing assistant     |                | 350                                          | 1.66                         | Positive             |
| 10        | 27      | F   | Microbiologist        | RC, AS         | >1000                                        | 1.31                         | Positive             |
| 11        | 29      | F   | Nursing assistant     | RC, FA         | <1                                           | 7.12                         | Positive             |
| 12        | 55      | F   | Nursing assistant     |                | 90                                           | 4.05                         | Positive             |
| 13        | 29      | F   | Nurse                 | RC, AS, FA     | 400                                          | 2.17                         | Positive             |
| 14        | 27      | M   | Laboratory technician | RC, AS         | 100                                          | 29.0                         | Positive             |
| 15        | 50      | F   | Nurse                 |                | 80                                           | 1.35                         | Positive             |
| 16        | 49      | F   | Medical technician    |                | >1000                                        | 41.2 <sup>‡</sup>            | Positive             |
| 17        | 57      | F   | Nurse                 | RC             | 800                                          | 0.46                         | Positive             |
| 18        | 35      | F   | X-ray technician      |                | >1000                                        | <0.35 <sup>  </sup>          | Positive             |
| 19        | 38      | F   | Nursing assistant     | RC, AS, FA     | 170                                          | 5.17                         | Positive             |
| 20        | 51      | F   | Nursing assistant     | RC, FA         | 100                                          | 6.62                         | Positive             |
| 21        | 32      | M   | Dentist               | RC, AS, FA     | 13                                           | 4.38                         | Positive             |
| 22        | 27      | M   | Laboratory technician |                | >1000                                        | <0.35 <sup>  </sup>          | Positive             |
| 23        | 49      | F   | Nurse                 |                | 7.5                                          | 7.03                         | Positive             |
| Control 1 | 50      | F   | Clerical worker       | RC             | Negative                                     | <0.35 <sup>  </sup>          | Negative             |
| Control 2 | 57      | F   | Nurse                 | RC, AS         | Negative                                     | <0.35 <sup>  </sup>          | Negative             |
| Control 3 | 52      | F   | Nurse                 | RC             | Negative                                     | <0.35 <sup>  </sup>          | Negative             |

RC, Rhinoconjunctivitis; AS, asthma; FA, food allergy.

\*This indicates the interpolated or extrapolated concentration of nonammoniated latex extract inducing a wheal 8 mm greater than that induced by the glycerin-saline control, as determined by using puncture skin tests.

†This subject had a positive latex puncture skin test response at the 1  $\mu\text{g/mL}$  concentration. Serial dilution skin testing was not carried out, and thus this value could not be ascertained.

‡These values are reported in kIUa per milliliter after conversion from nanograms per milliliter.

§This specimen was not collected.

||These subjects had negative serologic test responses for latex-specific IgE.

with albuterol, which was administered by metered-dose inhaler after 14 of 58 challenge studies in subjects with latex allergy. The maximum decline in PEFr by any subject was 33% below baseline. No subject experienced a systemic allergic reaction or reported a delayed reaction.

## DISCUSSION

Definitive diagnosis of latex allergy has been constrained by the unavailability of a well-characterized, Food and Drug Administration–approved, latex skin test reagent and a 25% false-negative rate for all 3 Food and Drug Administration–cleared, latex-specific, IgE antibody serologic assays.<sup>28</sup> A sensitive, reproducible, and safe provocation test is needed to clarify the latex allergy status when the results of IgE tests are discordant with the patient's history. Reported glove provocation procedures have differed in terms of the type of glove used, the method of exposing the patient, the time of application, and the method of scoring reactions.<sup>17-26</sup> Many of the procedures are difficult to replicate from the vague descriptions of these methods, and they often involve donning gloves in a manner that produces a primarily

skin contact exposure. In cases in which aerosolized allergen is produced, its concentration is highly variable and uncontrolled. No procedure reported to date provides a technology for controlled inhalation exposure of increasing amounts of aerosolized latex allergen to sensitized individuals.

The data reported in this article indicate that the HEC challenge apparatus reproducibly generates a cloud of glove-derived LACs in the respirable range. We also found that the challenge procedure is safe, sensitive, and specific. The distribution of the endpoint LAC dilutions indicates that there is at least a 64-fold range in individual respiratory sensitivity to airborne latex allergen by this method.

The correlation between the challenge endpoint and serial-dilution skin test midpoints reported here is consistent with data from other studies. Our previous studies of a nasal provocation model of ragweed pollinosis found comparable significant correlations ( $r_s = 0.54$ ) between early nasal response and skin test titration.<sup>31</sup> Also, skin sensitivity to ragweed allergen has been shown to be moderately associated with respiratory sensitivity by bronchial challenge ( $r_s \sim 0.65$ ).<sup>32</sup> Thus provocation mod-

els of respiratory allergy appear to be driven by immunologic sensitivity, suggesting an immunologic mechanism for the clinical responses described in this article.

Weaker correlations between challenge endpoints and serologic test results have been previously observed.<sup>31</sup> Serologic tests for latex-specific IgE are known to be less sensitive than latex skin testing<sup>29</sup>; this could be one factor. Another possibility is that biologic tests may incorporate a component of releasability, which is the intrinsic cellular property that translates the IgE-dependent signal into cellular activation.<sup>33</sup> Whatever the explanation, it is clear from the current results and those of other challenge models of respiratory allergy that skin test endpoints are better than serologic tests in predicting provocation results.

The single outlier subject shown in the skin test versus challenge endpoint plot (subject 4 in Fig 6) had ongoing daily exposure to powdered latex gloves, which may explain her relatively high latex sensitivity shown by skin and serologic tests. On the other hand, her clinical history of latex allergy was largely confined to skin symptoms, and she had no history of nonlatex-induced asthma or allergic rhinitis, which may explain her relatively low respiratory latex sensitivity determined by using the HEC method. As such, she did not strictly meet the entry requirements for the study.

The single subject with latex allergy who did not respond to LACs (subject 6) had a clinical history dominated by skin symptoms, with only mild respiratory symptoms after latex glove use. In addition, this individual had low-level latex sensitivity, as assessed by skin and serologic tests. This subject may have responded at a more intense LAC exposure had this been possible. Whether similar subjects with clinical histories of mild respiratory reactions to latex allergen and low-level IgE-mediated sensitivity to latex will have positive HEC challenges remains to be determined, as a larger number of subjects are evaluated.

The HEC challenge method appears to be safe, sensitive, and specific. It has the advantages of allowing for masking of the subject (and the investigator if desired) and provides a semiquantitative measure of latex allergen sensitivity. It also mimics occupational exposure to powdered latex gloves. In addition, the semiquantitative nature of the HEC method would allow the serial use of this test for natural history and intervention studies.

The HEC challenge technique does have limitations. There is considerable variation in the latex allergen potency of LACs derived from different glove sources. This can pose a difficulty with standardization, when it is necessary to acquire more LACs. In this study all of the LACs were harvested from a single lot of powdered latex gloves. Although 2 preparations of this lot were used in this study, only a single allergen preparation was used for any given subject. The relative allergen potency of sequential LAC preparations can be adjusted after comparison with solid-phase RIA. In addition, the glove-washing procedure may yield LACs that do not contain the full repertoire of allergens that becomes airborne with the use of powdered latex gloves. The observation that 22 of 23 subjects with latex allergy responded to LAC challenges used in this study

suggests, however, that the LAC allergens are broadly representative of those encountered naturally and probably display adequate amounts of the clinically important latex antigens. Other practical limitations include labor-intensive acquisition of the LACs, the requirement for special equipment and laboratory space, and the time required to reach an endpoint in individual patients (up to 4 hours). Nevertheless, this technique, once established, becomes a valuable research tool for semiquantitative assessment of clinical sensitivity to latex.

We have some limited clinical experience in using the HEC challenge procedure to adjudicate discordant clinical histories of latex allergy and measures of latex-specific IgE by skin tests, serologic tests, or both. The HEC challenge procedure was successfully used to study 2 patients with clinical histories consistent with latex allergy but negative latex skin and serologic test responses.<sup>34</sup> In both cases the patient had subjective symptoms of asthma after exposure to CC but not in response to the preceding air exposure. One of the subjects had an accompanying 15% decline in PEFR, whereas the other had no change in PEFR. Given the specificity of the HEC challenge procedure, we were able to conclude that the patients' symptoms were not mediated by a latex-specific mechanism.

The HEC challenge procedure may be useful as a semiquantitative estimate of the clinical sensitivity of individuals with latex allergy. Studies of the reproducibility of the HEC method are now underway. If HEC challenges are found to be reproducible, then the method may be usefully used in studies of the natural history of latex allergy and in studies of interventions for latex allergy, such as avoidance or immunotherapy.

## REFERENCES

1. Charous BL, Hamilton RG, Yunginger JW. Occupational latex exposure: characteristics of contact and systemic reactions in 47 healthcare workers. *J Allergy Clin Immunol* 1994;94:12-8.
2. Beaudouin E, Pupi P, Jacson F, Laxenaire DA, Moneret-Vautrin DA. Allergie professionnelle au latex. *Rev French Allergol* 1990;30:157-67.
3. Lagier F, Vervloet D, Lhermet I, Poyen D, Charpin D. Prevalence of latex allergy in operating nurses. *J Allergy Clin Immunol* 1992;90:319-22.
4. Slater JE. Rubber anaphylaxis. *N Engl J Med* 1989;320:1126-30.
5. Turijman K. Incidence of immediate-type allergy to latex gloves in hospitalized personnel. *Contact Dermatitis* 1987;17:270-5.
6. Brown B, Schauble J, Hamilton RG. Prevalence of latex allergy among anesthesiologists. *Anesthesiology* 1998;89:292-9.
7. Ber DJ, Munemasa KH, Hamilton RG, Cornish K, Klien DE, Settepane GA. Allergy to latex [abstract]. *J Allergy Clin Immunol* 1993;91:521A.
8. Meeropol E, Kelleher R, Bell S, Leger R. Allergic reactions to rubber in patients with myelodysplasia. *N Engl J Med* 1990;323:1072.
9. Slater JE, Trybul DE, Shaer C. Rubber specific IgE in children with spina bifida. *J Urol* 1991;146:578-9.
10. Beezhold D, Beck WC. Surgical glove powders bind latex antigens. *Arch Surg* 1992;127:1354-7.
11. Tomazic VJ, Shampaine EL, Lamna A, Withrow TJ, Adkinson NF, Hamilton RG. Cornstarch powder on latex products is an allergen carrier. *J Allergy Clin Immunol* 1994;92:751-8.
12. Hamilton RG, Adkinson NF. Natural rubber latex diagnostic skin testing reagents. Comparative performance on non-ammoniated latex, ammoniated latex, and latex rubber glove extracts. *J Allergy Clin Immunol* 1996;98:872-83.
13. Hamilton RG, Charous BL, Adkinson NF, Yunginger JW. Serological methods in the laboratory diagnosis of latex rubber allergy: study of non-

- ammoniated, ammoniated, and glove extracts as allergen reagent sources. *J Lab Clin Med* 1994;123:594-604.
14. Ownby DR, Ownby HE, McCullough J, Shafer AW. The prevalence of anti-latex IgE antibodies in 1000 volunteer blood donors. *J Allergy Clin Immunol* 1996;97:1188-92.
  15. Marcos C, Lazaro M, Fraj J, Quirce S, Hoz B, Fernandez-Rivas M, et al. Occupational asthma due to latex surgical gloves. *Ann Allergy* 1991;67:319-23.
  16. Pisati G, Baruffini A, Stanizzi R. Bronchial provocation testing in the diagnosis of occupational asthma due to latex surgical gloves. *Eur Respir J* 1994;7:332-6.
  17. Baur X, Jager D. Airborne antigens from latex gloves. *Lancet* 1990;4:912.
  18. Brugnamì G, Maribbini A, Siracusa A, Abbritti G. Work-related late asthmatic response induced by latex allergy. *J Allergy Clin Immunol* 1995;96:457-64.
  19. Hamilton RG, Adkinson NF. Validation of the latex glove provocation procedure in latex-allergic subjects. *Ann Allergy Asthma Immunol* 1997;79:266-72.
  20. Jagear D, Kleinhans D, Czuppon AB, Baur X. Latex-specific proteins causing immediate-type cutaneous, nasal, bronchial, and systemic reactions. *J Allergy Clin Immunol* 1992;89:759-68.
  21. Kelly KJ, Kurup VP, Reijula, Fink JN. The diagnosis of natural rubber latex allergy. *J Allergy Clin Immunol* 1994;93:813-6.
  22. Turjanmaa K, Reunala T, Rasanen L. Comparison of diagnostic methods in latex surgical glove contact urticaria. *Contact Dermatitis* 1988;9:241-7.
  23. Vandenplas O, Delwiche J, Evrard G, Aimont P, Brempt X, Jamart J, et al. Prevalence of occupational asthma due to latex among hospital personnel. *Am J Respir Crit Care Med* 1995;151:54-60.
  24. Vandenplas O, Delwiche J, Depelchin S, Sibille Y, Weyer R, Delaunois L. Latex gloves with a lower protein content reduce bronchial reactions in subjects with occupational asthma caused by latex. *Am J Respir Crit Care Med* 1995;151:887-91.
  25. Hamilton RG, Adkinson NF, and the Latex Allergy Task Force. Diagnosis of natural rubber latex allergy: multicenter latex skin testing efficacy study. *J Allergy Clin Immunol* 1998;102:482-90.
  26. Laoprasert N, Swanson MC, Jones RT, Schroeder DR, Yunginger JW. Inhalation challenge testing of latex-sensitive health care workers and the effectiveness of laminar flow HEPA-filtered helmets in reducing rhinoconjunctival and asthmatic reactions. *J Allergy Clin Immunol* 1998;102:998-1004.
  27. Hamilton RG, Adkinson NF. Immunologic tests for diagnosis and management of human allergic disease: total and allergen-specific IgE and allergen-specific IgG. In: Rose NR, Macario EC, Folds JD, Lane HC, Nakamura RM, eds. *Manual of clinical laboratory immunology*. 5th ed. Washington (DC): American Society for Microbiology; 1997. p. 881-92.
  28. Hamilton RG, Biagini RE, Krieg EF, and the Multi-Center Latex Skin Testing Task Force. Diagnostic performance of Food and Drug Administration-cleared serologic assays for natural rubber latex-specific IgE antibody. *J Allergy Clin Immunol* 1999;103:925-30.
  29. Pipkorn U, Granerus G, Proud D, Kagey-Sabotka A, Norman PS, Lichtenstein LM. The effect of a histamine synthesis inhibitor on the immediate nasal allergic reaction. *Allergy* 1987;42:496-501.
  30. Pagano M, Gauvreau K. *Principles of biostatistics*. 1st ed. Belmont (CA): Duxbury Press; 1993. p. 369-71.
  31. Iliopoulos O, Proud D, Adkinson NF Jr, Norman PS, Kagey-Sabotka A, Lichtenstein LM, et al. Relationship between the early, late and rechallenge reaction to nasal challenge with antigen: observations on the role of inflammatory mediators and cells. *J Allergy Clin Immunol* 1990;86:851-61.
  32. Bruce CA, Rosenthal RR, Lichtenstein LM, Norman PS. Quantitative inhalation bronchial challenge in ragweed hay fever patients: a comparison with ragweed-allergic asthmatics. *J Allergy Clin Immunol* 1975;56:331-7.
  33. Kim YK, Cho Sh, Koh YY, Son JW, Lee BJ, Min KU, et al. Linkage between IgE receptor-mediated histamine releasability from basophils and gene marker of chromosome 11q13. *J Allergy Clin Immunol* 1999;104:618-22.
  34. Primeau M-N, Kurtz KM, Hamilton RG, Schaefer JA, Adkinson NF Jr. Masked latex aeroallergen challenge as a diagnostic tool. *J Allergy Clin Immunol* 2000;104:S245.