

Inhalation challenge testing of latex-sensitive health care workers and the effectiveness of laminar flow HEPA-filtered helmets in reducing rhinoconjunctival and asthmatic reactions

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Background: There are few data relating latex aeroallergen concentrations to biologic responses in latex-sensitized persons. **Objectives:** We sought to investigate acceptable latex aeroallergen concentrations below which latex-sensitive health care workers do not experience symptoms and to study the effect of high-efficiency particle arrest (HEPA)-filtered laminar flow helmets in preventing latex-induced symptoms.

Methods: Under challenge chamber conditions, latex-sensitive health care workers underwent 7 sequential inhalation challenge tests by donning and discarding either vinyl gloves (challenge 1), low latex-allergen powder-free gloves (challenge 2), or high latex-allergen powdered gloves (challenges 3 to 7) for up to 1 hour. Volunteers wore a laminar flow helmet during all challenges; HEPA filters in the helmet were in place only during challenges 3 and 4. Flow-volume loops, symptom scores, and latex aeroallergen concentrations were measured before and during each test.

Results: At 60 minutes, latex aeroallergen concentrations during challenges 3 to 7 (mean, 7600 ng/m³; range, 93 to 54,000 ng/m³) were significantly higher than during challenges 1 or 2 (mean, 65 ng/m³; range, nondetectable to 100 ng/m³) ($P < .001$). During challenges 5 and 6, mean maximum percent falls in FEV₁ (-16% and -11%, respectively) were significantly greater compared with those measured during challenges 3 and 4 (-3% and -1%, respectively) ($P = .03$). Mean maximum change from baseline symptom scores during challenges 5 and 6 was significantly higher than that during challenges 3 and 4 ($P = .006$). During challenges with high latex-allergen gloves, 4 volunteers had reproducible FEV₁ falls of 20% or greater at cumulative inhaled latex aeroallergen doses ranging from less than 100 ng to 1500 ng.

Conclusion: The laminar flow helmets were effective in reducing latex-induced symptoms. Only 1 volunteer exhibited a fall in FEV₁ of 20% or greater after a cumulative inhaled latex

aeroallergen dose of less than 100 ng, and no volunteer showed a decline in FEV₁ after exposure to powder-free low allergen gloves. (*J Allergy Clin Immunol* 1998;102:998-1004.)

Key words: Latex allergy, inhalation challenge tests, latex aeroallergens, health care workers

Occupational allergy to natural rubber latex (NRL) is being recognized with increasing frequency among health care workers. Latex aeroallergens can be quantitated immunochemically; the highest concentrations occur in medical care delivery settings where powdered rubber gloves are frequently donned and discarded. Heilman et al¹ showed that latex aeroallergen concentrations were strongly correlated with the total number of powdered, high-allergen gloves used. However, there are few published data regarding acceptable latex aeroallergen concentrations below which latex-sensitive persons do not experience symptoms or, conversely, data regarding the latex aeroallergen concentrations that frequently elicit symptoms in individual latex-sensitive persons. We report a prospective, single-blind, pilot study in which inhalation challenge tests were performed in latex-sensitive health care workers with histories of occupational asthma when exposed to high-allergen powdered NRL gloves. Additionally, we studied the protective effect of laminar flow helmets in reducing latex-induced episodes of asthma, rhinitis, and conjunctivitis in these subjects.

METHODS

Subjects

We recruited 11 nonsmoking Mayo Medical Center female employees with clinical histories of occupational asthma (cough, wheeze, and/or shortness of breath) after latex exposure, all of whom had previously documented positive puncture skin test responses to NRL, elevated latex-specific serum IgE antibodies, or both (Table I). Because of institutional purchasing policies instituted in December 1993, volunteers were exposed to lower occupational latex aeroallergen levels after that date. We excluded from study any pregnant or lactating women, any volunteer with a history of latex-induced laryngeal edema or hypotension, or persons whose baseline FEV₁ was less than 80% of predicted value. Participants were not receiving regular asthma or allergy medications and were instructed to withhold inhaled bronchodilators beginning 6 hours before challenge. Written informed consent was obtained

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TABLE I. Study group characteristics

Volunteer no	Age (y)	Work location	Atopic	Puncture skin test (mm wheal diameter)		
				Histamine	Latex	
				1 mg/mL	0.25 mg/mL	2.5 mg/mL
1	35	Allergy/immunization Clinic	Yes	4 × 4	13 × 12	ND
2	31	Radiology records	Yes	4 × 4	0	10 × 7
3†	33	Rehabilitation	No	5 × 5	13 × 7	ND
4	51	Transfusion medicine	Yes	6 × 6	0	4 × 5
5	35	Transfusion medicine	Yes	5 × 5	5 × 6	ND
6†	34	Surgical trauma ICA/ICU	Yes	3 × 3	0	8 × 7
7†	34	Cardiovascular radiology	No	5 × 5	5 × 10	ND
8†	31	Surgical trauma ICA/ICU	No	4 × 4	15 × 7	ND
9	26	Colon-rectal surgery	Yes	4 × 4	5 × 5	ND
10*	33	Nursing float pool	Yes	3 × 3	0	4 × 5
11*	37	Transfusion medicine	No	5 × 5	3 × 4	6 × 6

ND, Not done; 0, negative.

*Withdrew early from study; data from these subjects were not included in the analysis.

†FEV₁ drop greater than 20% during challenges with high allergen powdered latex gloves.

Abbreviations used

EU: Endotoxin unit
HEPA: High efficiency particle arrest
LAL: Limulus ameobocyte lysate
NRL: Natural rubber latex
PBZ: Personal breathing zone

from all volunteers, and the study was approved by the Mayo Institutional Review Board.

Latex aeroallergen chamber

A stainless steel walk-in cold room was used (3.3 × 2.85 × 2.1 m or 19.75 m³) for performing latex aeroallergen challenge testing; the refrigeration unit was not used. This room was located inside a larger storage area in a research building removed from patient care or laboratory areas. A 4 × 4 inch hole was made on a corner of the ceiling to vent CO₂ accumulation into the larger room during the challenge test; no other ventilation was used. Temperature, CO₂, and humidity were measured during the test; these ranged from 21°C to 28°C, 0.1% to 0.3%, and 19% to 22%, respectively. The room was cleaned thoroughly after each challenge test.

Gloves used for challenge tests

Latex aeroallergen was generated by having volunteers don and discard 1 pair of gloves every 3 minutes. Between each glove change, the volunteers alternately "snapped" the gloves being worn once each minute in an attempt to release additional allergen. Gloves used were chosen on the basis of previous measurements of their NRL allergen content and were from a single lot. Glove types used were as follows: vinyl gloves (Handies, Technical Inc, Stow, Ohio), low-allergen powder-free examination gloves (Safeskin Corp), or high-allergen powdered examination gloves (Royal Med, Redline Healthcare Corp, Golden Valley, Minn). During each challenge, unused gloves from each box were randomly set aside and later tested to verify their latex allergen contents.

Latex aeroallergen challenge protocol

Challenges were conducted between January and May 1997. Volunteers wore a laminar flow helmet (Racal Airstream AH₃ High-

Efficacy Air Purifying [HEPA] System, Frederick, Md), lab coat, disposable cap, shoe booties, and vinyl undergloves during each of the 7 challenges to minimize transfer of NRL allergen to their skin or clothing. Each volunteer underwent inhalation challenge testing inside the challenge chamber for up to 1 hour on 6 occasions at least 1 day apart and, to assess the possible priming effect of prior challenges, on a seventh occasion approximately 10 days after the sixth test (Table II). During the first challenge, vinyl gloves were changed; this was a negative control test. During the second challenge, powder-free low-allergen latex exam gloves were used with no HEPA filters in the laminar flow helmet. Rubber gloves with high-latex allergen were used for all subsequent challenges. During the third and fourth challenges, the HEPA filters in the helmet were installed and operating; on the subsequent 3 occasions, the filters were removed. The volunteers were not aware whether the filters were in place.

Baseline clinical signs and symptoms of wheezing, shortness of breath, cough, stuffy nose, sneeze, runny nose, and ocular symptoms (itching, lacrimation, and redness) were recorded by using a semi-quantitative (0 to 3) scale. Symptom scores were also recorded every 15 minutes during the challenge and also on the evening of each challenge day. A baseline composite symptom score was calculated as the mean of the 7 individual baseline symptom scores. For each individual symptom, the maximum score obtained during the challenge was used to calculate the maximum composite symptom score. The change in symptoms from baseline was calculated by subtracting the baseline composite symptom score from the maximum composite symptom score. Flow volume loops and FEV₁ were also measured just before the volunteer began donning and discarding gloves and every 15 minutes thereafter until the challenge test was stopped.

We attempted to estimate the time required for the FEV₁ to fall by 20% or greater for each challenge. We stopped the challenge if (1) the individuals experienced troublesome cough, wheeze, chest tightness, or shortness of breath; (2) the FEV₁ decreased by 20% or more from baseline levels; or (3) the volunteer had been inside the chamber for 60 minutes. If the volunteer experienced troublesome symptoms or the FEV₁ decreased 20% or more from baseline level, they were treated with nebulized or inhaled bronchodilator.

Pulmonary function testing

We followed the testing protocol recommended by the American Thoracic Society.² To minimize the volunteer's exposure to

TABLE II. Inhalation challenge test protocol

Challenge no	Day no	Gloves used	Helmet HEPA filter
1	1	Vinyl glove — Handies*	Removed
2	2	Powder-free latex exam gloves — Safeskin†	Removed
3	3	Lightly powdered latex exam gloves — Royal Med‡	In place
4	4	Lightly powdered latex exam gloves — Royal Med‡	In place
5	5	Lightly powdered latex exam gloves — Royal Med‡	Removed
6	6	Lightly powdered latex exam gloves — Royal Med‡	Removed
7	16	Lightly powdered latex exam gloves — Royal Med‡	Removed

*Lot GJ 2683 Technical Inc (Stow, Ohio).

†Lot 6207-A13 Safeskin Corp (San Diego, Calif).

‡Lot 1310523 Redline Health Care Corp (Golden Valley, Minn).

ambient NRL aeroallergen during the pulmonary function testing, the volunteers were asked to inhale to total lung capacity and then to hold their breath while the pulmonary function technician flipped up/down the laminar flow helmet face shield and placed/removed the nose clip and mouthpiece. The spirometer and the disposable flow sensor element were mounted outside the challenge chamber and connected to the volunteer by means of large diameter corrugated tubing through the wall of the challenge chamber. For each individual challenge, the maximum percent change from baseline FEV₁ was calculated by using the reproducible FEV₁ measured during the challenge.

Air samplers

Personal breathing zone (PBZ) samples (5 L/min) were collected by volunteers during all challenges from the outside of the helmet (sampling ambient air) and from inside the helmet (sampling filtered or unfiltered air). An area sampler (1 L/s) was operated inside the challenge chamber 15 minutes before the challenge test to determine any baseline aeroallergen level. The filters in the area sampler were changed every 15 minutes thereafter. The PBZ samples were collected only during the time the volunteers began to don and discard the gloves.

Quantitation of latex aeroallergen

Both air samplers collected air particles onto polytetrafluoroethylene filters (Quan-Tec-Air, Inc, Rochester, Minn), from which allergens were extracted in 100 mmol/L phosphate buffer (pH 7.5) containing 0.2% BSA and 0.01% sodium azide. The filter extracts were tested for latex allergen content by a previously described inhibition immunoassay.³ Briefly, a solid-phase allergen was prepared by adsorbing a concentrated extract of highly allergenic powdered latex examination gloves to the wells of microtiter plates. The assay was performed by adding several 3-fold dilutions of reference standard or filter extract with fixed quantities of a latex-specific IgE antibody pool. Results were expressed as mass units of protein per cubic meter of air on the basis of the protein content (BCA determination) of the assay standard (7 mg/mL). Because of the relatively short sampling periods used in this study, the lower limit of aeroallergen detection was only 55 ng/m³ for the area samples and 167 ng/m³ for the PBZ samples.

Endotoxin assay

Twenty-one Safeskin powder-free gloves and 21 Royal Med powdered gloves were selected from the middle of a box of 100 and randomly redistributed into 7 samples of 3 gloves each. Endotoxin content was measured by the kinetic chromogenic limulus amoebocyte lysate (LAL) test (Nelson Labs, Salt Lake City, Utah).⁴ The specificity of the LAL results was confirmed by the End-X endo-

toxin removal system at the same laboratory by using 2 samples of each brand of gloves.

Statistical analysis

Aeroallergen concentrations measured from the area sampler and PBZ samplers were analyzed by using a log transformation. For analysis purposes, nondetectable aeroallergen concentrations from the area sampler and PBZ samplers were assigned values of 55 ng/m³ and 167 ng/m³, respectively. By using data from the PBZ samples, the maximum percent change from baseline FEV₁, and the maximum composite symptom score, repeated measures ANOVA was used to assess the efficacy of the Racal helmet HEPA filter. This analysis was restricted to challenges 3 and 4 (HEPA filters in place) and challenges 5 and 6 (HEPA filters removed). Separate analyses were performed for the aeroallergen concentrations inside and outside the helmet. The percent efficiency of the HEPA filter was calculated for each individual trial by subtracting the latex aeroallergen concentration inside the helmet from the aeroallergen concentration outside the helmet, dividing by the aeroallergen concentration outside the helmet, and multiplying by 100.

In addition to repeated measures ANOVA, other statistical methods included use of the paired *t* test, 1-way ANOVA, and 2-sample rank-sum test. In all cases 2-sided tests were used, with *P* values of 0.05 or less used to denote statistical significance.

RESULTS

Safety

Eight volunteers completed all 7 challenge tests. A ninth volunteer completed 6 challenge tests, and the other 2 volunteers withdrew from the study after the second and third challenge tests (1 because of a family emergency and 1 fearing more severe reactions with future challenges). Data from the latter 2 subjects were excluded from all analyses. One volunteer (number 4), who had moderate positive latex skin test responses 6 years previously, now showed only a minimal positive skin test response, but she was included in the study to provide a broad range of sensitivity among the volunteers. Among 67 challenge sessions done in this study, there were 10 challenge sessions (all but one during either challenges 5, 6, or 7) in which volunteers developed allergy symptoms and needed to stop the challenge before 1 hour. No volunteer had anaphylaxis or needed oral prednisone during or after the challenge study. Six volunteers required

inhaled bronchodilator, ipratropium bromide nasal spray, or oral antihistamine after the challenge.

Latex aeroallergen concentrations

We confirmed that the extractable latex allergen contents of the “low-allergen” gloves used during the study were indeed low (mean = 259 AU/mL, median = 273 AU/mL, range = 145 to 352 AU/mL; $n = 21$) and that the allergen contents of the “high-allergen” gloves were elevated (mean = 23,700 AU/mL, median = 22,600 AU/mL, range = 2100 to 42,200 AU/mL; $n = 73$) ($P < .001$). During tests with high-allergen gloves and the area sampler, latex aeroallergen concentrations increased from less than 60 ng/m³ at baseline to a mean of 2800 ng/m³ by 15 minutes and remained elevated (range = 93 ng/m³ to 54,000 ng/m³) at 60 minutes (Fig 1). Latex aeroallergen concentrations generated during challenge 2 were slightly higher than those during challenge 1, but this difference was not statistically significant. The mean aeroallergen concentrations generated during challenges 3, 4, 5, 6, and 7 were significantly higher than those during challenges 1 or 2 ($P < .001$) (Table III).

To assess the efficiency of the Racal helmet HEPA filter, we compared the latex aeroallergen concentration measured inside and outside the helmet during challenges 3 and 4 (HEPA filter in place) with that measured during challenges 5 and 6 (HEPA filter removed). By using repeated measures ANOVA, the mean latex allergen concentration outside the helmet was not significantly different across these 4 challenges. However, the mean latex allergen concentration inside the helmet was significantly lower during challenges 3 and 4, with the filter in place, compared with challenges 5 and 6, with the filter removed ($P = .011$). The median percent efficiency of the HEPA filter helmet was 96.5% (range, 29% to 100%).

Latex aeroallergen concentrations measured from the PBZ samples outside the helmet were predictably higher than latex aeroallergen concentrations measured from area samples. The aeroallergen concentration measured from the PBZ sample inside the helmet was always lower or equal to the aeroallergen level measured from the PBZ sampler outside the helmet, even when the filter was removed (challenges 5 and 6). During challenges 3 and 4, with the HEPA filter in place, low concentrations of aeroallergen were detected from the PBZ sample collected inside the helmet if there were very high aeroallergen concentrations generated inside the room.

Pulmonary function tests

There were no significant falls ($>20\%$) in FEV₁ during challenges 1 and 2. Although the mean maximum percent fall in FEV₁ during challenge 3 was slightly greater than that during challenges 1 or 2 (Fig 2), the difference was not statistically significant. During challenges 5 and 6, the mean maximum percent falls in FEV₁ (-16% and -11% , respectively) were significantly greater compared with those measured during challenges 3 and 4 (-3% and -1% , respectively) ($P = .03$). There was no statistical difference in mean maximum percent fall in FEV₁ during

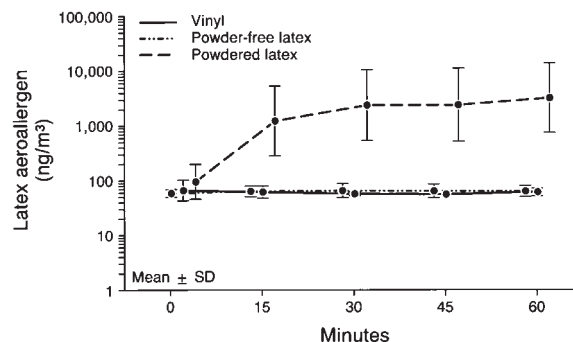


FIG 1. Latex aeroallergen level (mean $\pm$ SD) measured every 15 minutes with a high-volume area sampler during the 60-minute challenge. For calculation of mean and standard deviation, non-detectable aeroallergen levels were assigned a value of 55 ng/m³. For vinyl gloves (challenge 1) and powder-free latex gloves (challenge 2), the sample size is 9 at all time periods. For powdered latex gloves (challenges 3 to 7) the sample size is 44, 44, 40, 37, and 35 at baseline, 15, 30, 45, and 60 minutes, respectively.

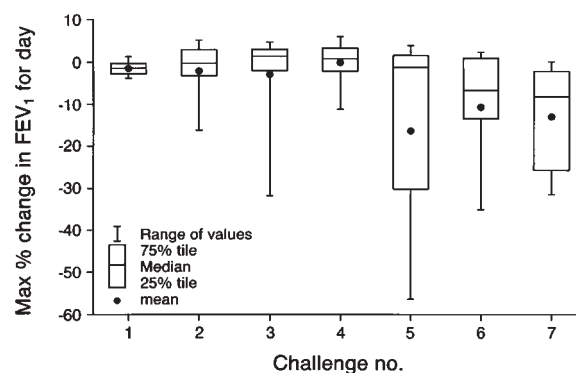


FIG 2. Maximum FEV₁ percent change from baseline was calculated for each subject by using the lowest FEV₁ measured during the 60-minute challenge period. The distributions of maximum FEV₁ during challenges 5 and 6 (powdered latex gloves with HEPA filter removed) were significantly greater than those for challenges 3 and 4 (powdered latex gloves with HEPA filter in place) ($P = .030$, repeated measures ANOVA).

challenges 5 and 6 compared with challenge 7. During challenges 5, 6, and 7, there were 4 volunteers whose FEV₁ fell 20% or greater. The maximum percent change in FEV₁ and cumulative inhaled latex allergen doses each day were reproducible in these 4 volunteers (Fig 3). The cumulative latex allergen doses to which the volunteers were exposed were calculated from the PBZ sampler data, assuming a tidal volume of 7 mL/kg and a respiratory rate of 18/min. The cumulative inhaled latex doses that caused FEV₁ falls of 20% or greater ranged from 110 ng to 1500 ng in these 4 volunteers. There were 5 volunteers who did not experience a 20% or greater fall in FEV₁, including the 1 volunteer who was minimally reactive to latex by skin testing. The cumulative inhaled latex dose in this group was nearly identical, ranging from 100 ng to 1400 ng. During challenge 7, declines in

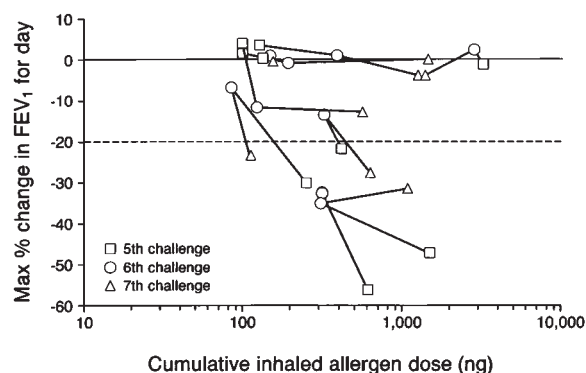


FIG 3. Maximum FEV₁ percent change from baseline for each subject during challenges 5, 6, and 7 according to cumulative inhaled allergen dose. Maximum FEV₁ percent change from baseline was calculated for each subject by using the lowest FEV₁ measured during the 60-minute challenge period. The 3 challenge results for each patient are connected by lines.

FEV₁ were not evoked by lower cumulative latex aeroallergen doses than those during challenges 5 and 6 (Fig 3), indicating that there was no increased airway reactivity or "priming" effect produced by the previous challenges.

Symptom scores

The mean maximum change from baseline symptom scores during challenge 2 did not differ significantly from that during challenge 1, nor did mean maximal changes from baseline during challenges 3 and 4 differ significantly from those during challenges 1 or 2. The maximum changes from baseline symptom scores during challenges 5 and 6 (mean = 0.9, range = 0 to 2.3) were significantly higher than those during challenges 3 and 4 (mean = 0.2, range = -0.1 to 1.0) ($P = .006$). The maximum changes from baseline symptom scores during challenge 7 did not differ significantly from those recorded during challenges 5 and 6. The maximum changes in pulmonary and rhinoconjunctivitis symptom scores are listed for each volunteer and each challenge session in Table IV. Even volunteers who did not have a greater than 20% fall in FEV₁ during challenges 5, 6, and 7 had significant increases in symptom scores compared with challenges 1, 2, 3, and 4.

Endotoxin levels

Endotoxin levels measured from the outside of the Safeskin gloves (mean = 2.1 endotoxin units (EU)/g glove weight, median = 2.0 EU/g, range = 0.43 to 3.3 EU/g) were significantly lower than those measured from Royal Med gloves (mean = 233 EU/g, median = 228 EU/g, range = 172 to 332 EU/g) ($P < .001$, rank-sum test). There was a significant reduction in the detection of endotoxin (73% to 100% reduction) after the gloves were treated with the endotoxin removal system, confirming the specificity of the LAL test.

TABLE III. Area latex aeroallergen concentrations at 60 minutes

Challenge no	n	Latex aeroallergen concentrations at 60 minutes			
		Mean (ng/m ³)	Median (ng/m ³)	Range (ng/m ³)	SD
1	9	62	ND	ND-85	11
2	9	65	ND	ND-100	18
3-7	35	7600	2900	93-54,000	11,000

ND, Not detectable; values below the detection limit were assigned a value of 55 ng/m³ for the calculation of the mean and standard deviation.

DISCUSSION

On the basis of feedback provided by our institutional review board, the experimental design of our pilot study was chosen to maximize safety to the participants. Thus the order of testing the gloves was not randomized, and each subject was exposed to lower aeroallergen doses first (helmet filters in place) and higher aeroallergen doses later (helmet filters removed). Also, because the challenge chamber had not been used for previous studies, it was necessary to document the reproducibility of the latex aeroallergen generation method. Therefore the final protocol included use of the laminar flow helmets, yet blinded the volunteer subjects with respect to the gloves being used and the integrity of the helmet filtration system, limited the duration of allergen exposure to 1 hour, and included replicate challenges on separate days.

In this study we confirmed previous findings that the use of powder-free gloves⁵ or gloves containing low concentrations of latex allergen¹ is associated with significant reductions in latex aeroallergen concentrations. The results of this study show that exposure to cumulative inhaled latex allergen of less than 100 ng over 1 hour induced a greater than 20% fall in FEV₁ in only 1 of our 9 latex-sensitive volunteers. However, at cumulative inhaled doses of greater than 100 ng for less than 60 minutes, 4 of 9 latex-sensitive volunteers experienced asthma symptoms and a fall of 20% or greater in FEV₁ within 1 hour. More precise estimates of cumulative inhaled latex doses that consistently elicit asthma symptoms in latex-sensitive persons are dictated by a wide range in individual reactivity. Our estimates are limited by number of volunteers studied and the inclusion of the helmet for safety.

The HEPA-filtered helmet did demonstrate both mechanical efficiency and clinical effectiveness in reducing latex-induced occupational asthma, rhinitis, and conjunctivitis. Symptoms scores and changes in FEV₁ during challenges with high allergen gloves with the helmet HEPA filter in place did not differ statistically from values measured during challenges with synthetic gloves. However, when the helmet filters were removed, aeroallergen concentrations inside the helmet were still consistently lower than the levels outside the helmet. This was

TABLE IV. Maximum change from baseline for pulmonary symptom scores (wheezing, dyspnea, and cough) and rhinoconjunctivitis scores (stuffy nose, sneezing, rhinorrhea, ocular itching, and redness) for each volunteer during each of the 7 challenge tests

Volunteer no	Challenge 1	Challenge 2	Challenge 3	Challenge 4	Challenge 5	Challenge 6	Challenge 7
1. Pulmonary	0.00	0.00	0.00	0.00	0.00	0.33	0.67
Rhinoconjunctivitis	0.00	0.00	0.00	0.50	1.00	0.75	0.25
2. Pulmonary	0.67	-0.33	1.00	0.67	0.00	1.67	0.33
Rhinoconjunctivitis	0.25	-0.25	0.50	0.75	1.50	0.25	0.50
3. Pulmonary	0.00	0.00	0.00	0.00	3.00	1.00	2.00
Rhinoconjunctivitis	0.00	0.00	0.00	0.00	1.50	0.25	1.00
4. Pulmonary	0.00	0.00	0.00	0.00	0.00	0.33	0.00
Rhinoconjunctivitis	0.00	0.00	-0.25	0.00	0.00	0.00	0.00
5. Pulmonary	0.00	0.00	0.00	0.00	0.00	0.33	1.00
Rhinoconjunctivitis	0.00	0.00	0.00	0.00	1.25	1.25	0.75
6. Pulmonary	0.00	0.00	0.33	0.00	2.00	2.00	2.33
Rhinoconjunctivitis	-0.25	0.00	0.00	0.00	0.00	-0.25	0.25
7. Pulmonary	0.00	1.00	2.00	0.67	2.33	2.00	ND
Rhinoconjunctivitis	0.00	0.00	0.25	-0.25	0.00	0.25	ND
8. Pulmonary	0.00	0.00	0.00	0.00	2.33	3.00	1.67
Rhinoconjunctivitis	0.00	0.00	0.50	0.00	2.25	1.25	1.25
9. Pulmonary	0.00	0.00	0.00	0.00	1.00	0.00	1.67
Rhinoconjunctivitis	0.00	0.00	0.00	0.25	1.25	0.75	1.00
10. Pulmonary	0.00	0.00	ND	ND	ND	ND	ND
Rhinoconjunctivitis	0.00	0.00	ND	ND	ND	ND	ND
11. Pulmonary	0.33	0.0	0.0	ND	ND	ND	ND
Rhinoconjunctivitis	0.00	1.25	1.00	ND	ND	ND	ND

ND, Not done.

because the particles bearing latex allergen settle rapidly,³ and the larger particles could be trapped along the tubing and inside the helmet. Even with the helmet filters in place during challenges with high allergen gloves, there were measurable allergen concentrations inside the helmet, most likely because some allergen could enter the breathing zone when the face shield was raised for performing pulmonary function tests.

To our knowledge, our study was the first conducted wherein the latex aeroallergen was generated under simulated work conditions during which latex aeroallergen concentrations were measured during a provocation test. In a recent cross-sectional study of 32 health care delivery sites involving 145 workers, Baur et al⁶ noted a significant association between self-reported allergy symptoms and latex aeroallergen concentrations of 0.6 ng/m³ or greater. However, participants did not undergo inhalation challenge testing to determine the range of aeroallergen concentrations required to elicit symptoms in individual subjects. Our findings also extend those of previously published studies^{7,8} involving fewer latex-sensitive health care workers who underwent graded bronchial provocation testing with nebulized extracts prepared from corn starch powder or surgical gloves.

In another study by Brugnami et al,⁹ 4 latex-sensitive nurses underwent inhalation provocation testing by handling latex gloves for varying periods of time. Although latex aeroallergen levels were not measured, all of the volunteers recorded measurable asthma or allergy symptoms on at least 1 evening after a challenge. These findings sug-

gest that latex allergens can elicit a late asthmatic response without producing an early asthmatic response. In our study we measured only symptom scores in the evening of each challenge day. Further studies may also need to include measuring any late asthmatic responses.

Williams and Halsey¹⁰ have measured high levels of endotoxin in latex gloves, especially in powdered, non-sterile examination gloves. We also found high endotoxin levels in the powdered Royal Med examination gloves used in our study. Endotoxin may be important in triggering respiratory tract inflammation¹¹ and could potentiate asthma symptoms in latex-sensitive health care workers.¹²

We concluded that the quantity of latex aeroallergen required for asthma symptom provocation varies widely from person to person. In our study only 1 volunteer exhibited a fall of greater than 20% in FEV₁ after cumulative inhaled aeroallergen doses of less than 100 ng, and no volunteer showed a greater than 15% decline in FEV₁ after exposure to powder-free low allergen gloves. We also showed that HEPA-filtered laminar flow helmets, as used in this study, were effective in reducing the symptoms of latex-induced asthma, rhinitis, and conjunctivitis. However, a comparable reduction in symptoms could be achieved simply by substituting powder-free low allergen latex gloves for powdered high allergen latex gloves. Having demonstrated the safety of the challenge protocol and the good reproducibility of the aeroallergen generation by individual subjects, we can proceed with additional studies that include greater numbers of latex-sensitive persons and tests of nonspecific bronchial reactivity.

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