Prevention of IgE Sensitization to Latex in Health Care Workers After Reduction of Antigen Exposures

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Objective: To investigate occupational latex allergy in health care workers (HCWs) before and after an intervention designed to reduce latex allergen exposure from gloves. **Methods:** Latex antigen concentrations in work area air ducts were measured before the intervention. Symptoms and latex sensitization were monitored annually before and after the intervention in 805 HCWs, using questionnaires and skin prick testing. **Results:** The prevalence of latex sensitization before the intervention correlated with air duct latex antigen measurements, for HCWs exposed to low (9/413, 2%), intermediate (23/292, 8%), and high (11/67, 16%) antigen levels, $P < 0.0001$. After the intervention, new latex sensitization rates declined 16-fold, and 25% of previously sensitized employees reverted to negative skin tests. **Conclusion:** Airborne antigen exposure is a major source of latex sensitization among HCWs. Use of powder-free latex gloves markedly reduces the risk of sensitization.

Clinicians observed the rapid emergence of symptomatic latex allergy across the world after a single case report of contact urticaria to rubber in 1979.[1] Numerous studies subsequently demonstrated an increasing prevalence of latex-specific IgE antibody in health care workers (HCWs) but differences in study methods and design led to controversies.[2–5] Researchers hypothesized that new onset sensitization to latex proteins was a result of a marked increase in latex glove use in health care, a high latex allergen content of the gloves, and/or airborne exposure to cornstarch powder with adsorbed allergen from powdered latex gloves. This led to recommendations and implementation of strategies to lower glove allergen content, reduce the use of powdered latex gloves, and use nonlatex gloves where appropriate.[6–8] This proactive approach was based on existing science and prudent public health actions but did not necessarily imply that latex gloves were the single agent associated with the emergence of this disease in HCWs.

Previous studies of latex sensitization have used varying methodologies and have shown inconsistent results. Some studies using skin prick testing (SPT) in the general population in Europe and Canada demonstrated a low prevalence ($\leq$1%) of latex sensitization. Other published studies using serologic testing of random or sequential convenience samples from the general public have found up to an 8.2% prevalence of latex-specific IgE antibody. Most but not all studies in HCWs showed an elevated prevalence using skin prick test (SPT) and serologic methodologies.[9–13]

The strength of conclusions about the prevalence and causes of latex allergy in many US studies is limited by the variation in serologic test kits and the absence in the United States of a reagent cleared by the Food and Drug Administration for latex allergy skin testing.[14–16]

Another suggested explanation for the discrepancy is the serologic cross-reactivity of latex allergens with proteins commonly found in various fruits. Nevertheless, several studies have shown HCWs with a low prevalence of antibodies to these fruit proteins.[17]

A study of incident latex allergy in two hospitals in Canada demonstrated a weak association between exposure to powdered latex gloves and development of a positive SPT.[18] In contrast, several published studies have documented reductions in symptoms and sensitization after interventions directed at reducing latex glove antigen exposures.[19–22] To further address the relationship between occupational allergy and antigen exposures from natural latex gloves, we performed a prospective study of latex allergen exposure and sensitization to latex-specific SPT reagents among HCWs before and after an intervention to reduce exposure to latex allergen from gloves. We first sought to document a quantitative relationship between workplace latex antigen exposure and the prevalence of sensitization, and subsequently evaluated the degree of risk reduction after recommended preventive measures were initiated.

METHODS

The study took place from June 1998 to December 2002 and was approved by the institutional review boards at Children's Hospital of Wisconsin (CHW), Froedtert Memorial Lutheran Hospital (FMLH), the Medical College of Wisconsin, the Food and Drug Administration, and the Human Subjects Review Board at the Centers for Disease Control/National Institute for Occupational Safety and Health. Employees who worked with latex gloves in two hospitals were studied prospectively over 4.5 years. HCW symptoms and sensitization to latex were monitored for approximately 12 months before and an average of 33 months after both hospitals changed the type of latex gloves used. The glove interventions took approximately 6 months to fully implement. A quantitative estimate of each HCW's latex exposure was obtained using antigen levels in dust from air handling unit ducts in the individual's principal work area.

Participants

All employees, especially those who regularly used gloves at both hospitals were asked to participate. The FMLH employed approximately 3483 persons including 1019 nurses during the period of the study, while CHW employed 3152 persons including 1209 nurses. A total of 805 (12.13%) employees who used medical gloves were recruited from the two hospitals among 6635 total employees. Job descriptions suggested that approximately 65% of employees in these hospitals worked in a job category that might include the use of latex gloves. Individuals with environmental allergies were encouraged to participate because this is a recognized risk for developing latex allergy. Informed consent was obtained before participation

Facilities

The CHW and FMLH are free-standing academic hospitals affiliated with the Medical College of Wisconsin. The two facilities have separate heating, ventilation, and air conditioning (HVAC) systems but are connected by three corridors. The FMLH supplies

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personnel and materials (gloves) to two adult units within the CHW facility.

Skin Prick Testing

All participants underwent SPT with Clone 600 nonammoniated latex in duplicate (two latex SPTs were placed simultaneously on the same arm) yearly for the duration of the study. (Reagent provided courtesy of Greer Laboratories, Inc., Lenoir, NC.) Every SPT on each participant was performed by the same individual (M. K.) to prevent any bias or variation in testing technique, and each round of testing thus took several months to complete. Testing was performed, and interpreted as positive or negative, under Food and Drug Administration Investigational New Drug approval #4920 using the previously published methodology.[16]

The SPT wheal and flare reactions were outlined in black ink on the forearm of the subject. Clear tape was placed on the outline to transfer ink to the tape. To reduce observer bias, the tape was then used to transfer the outline of the reactions to paper and assessed by an independent investigator, not present at the time of the SPT. Skin prick testing was performed using serial dilutions of latex with close observation, and thus required 1 to 2 hours per person at each visit. A physician was readily available if any adverse event required intervention. For this study, an individual was considered to be allergic to latex at a specific visit if they were SPT positive on both of the duplicate tests performed using the published methodology.

At the first visit, all participants were also skin prick tested with a panel of seasonal and perennial aeroallergens using Multitest™ (Lincoln Diagnostics, Inc., Decatur, IL). A positive test was determined when the wheal was 3 mm or greater than a wheal from a saline control. The allergens used included ragweed pollen, grass pollen, tree pollen, house dust mite, cat, dog, *Alternaria*, and *Cladosporium*. An individual was considered to be atopic if a SPT was positive to one or more of the environmental allergens. SPTs to commercial food extracts of banana, avocado, potato, lobster, and shrimp were also obtained at baseline.

Both CHW and FMLH allowed participating employees to complete skin prick testing during work hours.

Questionnaires

All participants filled out questionnaires yearly to characterize various potential exposures, including type of work in the hospital, patterns of occupational and household glove use, smoking, previous surgeries and deliveries, use of latex condoms or diaphragms, and contact with household pets. Participants recorded symptoms and medical conditions, including presence of asthma or other medical conditions that are associated with latex sensitivity (eg, spina bifida or bladder catheterization), environmental allergies, food allergies, and skin or respiratory tract symptoms at or away from work, and symptoms triggered by contact with any latex products or soaps. They also estimated the number of gloves typically used during a working shift. Age, race, sex, and tenure in health care work were documented.

If an individual tested positive to latex, he or she was immediately instructed to use nonlatex gloves and avoid direct contact with latex products. Nonlatex gloves were provided at work to these individuals by their employer. This approach was taken whether or not the employee reported symptoms from latex contact, for safety reasons. Nevertheless, since the hospital-wide glove intervention was not immediate, the time spent in the workplace before completing the glove intervention was included in the pre-intervention period.

Workplace Latex Antigen Measurements

Samples for analysis of latex allergen were collected from the HVAC system return air ducts at each hospital, to determine whether detectable aeroallergen was being circulated within each participant's specific work area. Return ducts from multiple air handling units at both hospitals were sampled. Each hospital's engineering department identified the specific ducts for sampling as those returning the air from work areas where clinical glove use occurred. Allergen in the return duct leading away from the work area was considered to be a marker for airborne latex exposures over time. Wipe samples from the lowest interior duct surface were collected on filter paper and weighed and stored in labeled plastic bags at 4°C until extracted. Dust latex allergen content was analyzed by an experienced investigator (Marc Swanson, Mayo Clinic) who was blinded to the source of the samples, using published techniques.[23] The collected dust was sieved and extracted (1:5 w/v) in 0.1 mol/L of phosphate-buffered saline containing 0.2% bovine serum albumin, 0.05% Tween 20, and 0.01% sodium azide. The extracts were centrifuged and assayed immediately or stored until analysis at −20°C. Airborne dust was also obtained using area air samplers operating at 1 L/s for 4 hours. Area sampling devices were located in selected workspaces, with equipment placed to be reasonably representative of general breathing zone air while not interfering with essential patient care or other work functions. Particulates were collected onto polytetrafluoroethylene filters rated more than 99% efficient for particles more than 0.3 μm in diameter. The exposed filter membrane was delaminated from the polyester spun backing and directly extracted in 0.25 to 1.0 mL of buffer. Latex allergen in ducts and air was measured using an IgE inhibition immunoassay.[23] Appropriate blanks and calibration samples were analyzed with each batch of measurements. Allergen content in duct samples was reported in micrograms per gram of dust.

Hospital Glove Use

Purchasing units in both hospitals kept records of the types of gloves used before and after the intervention. (Table 1) At both hospitals, 90% of the gloves used were examination gloves. For more than 5 years before the study, CHW had provided only nonlatex examination gloves, after a cluster of anaphylaxis from latex allergy in patients with spina bifida.[24] Powdered latex gloves at CHW (representing 10% of glove use) were used predominately in the operating rooms, intermediate care, and intensive care units, and included surgical gloves and single latex gloves included in prepackaged device kits (eg, suction catheters). In contrast, at FMLH, powdered latex gloves represented 100% of gloves used before the study, including examination and surgical gloves as well as gloves in prepackaged kits.

Intervention

All participants were requested to complete the questionnaire, latex SPT, and serologic testing twice in the pre-intervention stage (at baseline and 12 months), and then yearly after implementation of the glove interventions. The glove interventions took up to 6 months

TABLE 1. Gloves Used in the Two Study Hospitals Before and After an Intervention in Glove Type

	Pre-intervention	Post-intervention
Children's Hospital of Wisconsin		
Surgical gloves	Non-Powdered Latex	Non-Powdered Latex
Examination gloves	Non-Latex*	Non-Latex*
Gloves in kits	Powdered Latex	Non-Powdered Latex
Froedtert Memorial Lutheran Hospital		
Surgical gloves	Powdered Latex	Non-Powdered Latex
Examination gloves	Powdered Latex*	Non-Powdered Latex*
Gloves in kits	Powdered Latex	Non-Powdered Latex

*90% of gloves used were examination gloves verified by buying records of both institutions.

to fully implement (Table 1). CHW removed all prepackaged kits containing powdered latex gloves and substituted kits containing either nonlatex or powder-free latex gloves. At FMLH, all surgical gloves, examination gloves, and prepackaged kit gloves were replaced with powder-free latex gloves. To control any exposure differences due to glove variation, both institutions agreed to buy gloves from one manufacturer. The purchasing departments and investigators worked closely with that company to assure that all powder-free latex gloves used were from the same lots throughout the study period. For each subject, the duration of pre-intervention exposure was characterized as the months of glove use starting from the initial SPTs until the date of completion of the intervention, and findings were compared with post-intervention glove exposure in months calculated as the time from the completion of the intervention until the date of the specific follow-up SPT.

Statistical Analysis

Statistical analysis was performed using the SAS® v9.0 software package (SAS/STAT user's guide, version 9, 2002; SAS Institute, Inc., Cary, NC) Group comparisons of participant characteristics; latex SPT results; glove use; glove-related hand, respiratory, or systemic symptoms; and latex dust exposure were made between the two hospitals and between SPT positive and negative HCWs, using *t* tests for continuous variables, and chi-square tests for dichotomous variables, or by Mantel-Haenszel chi-square test for comparisons of more than two groups.

The conversion of SPT results from positive to negative, or negative to positive was evaluated for the pre- to post-intervention phases among participants who had at least two and up to four SPT results. For those who started with positive SPT results, the converting rate of SPT positive to negative was calculated as the number of conversion cases divided by the total time of glove use during either the pre- or the post-intervention phases (months between the SPT day and the date of intervention). The converting rate of SPT negative to positive was similarly determined among the participants who started with negative SPT results, and was calculated as the number of conversion cases divided by the months of glove use during pre- and post-intervention.

The statistical significance of the difference in the converting rates across the two exposure periods of pre- and post-intervention was tested by using the Poisson regression for categorized time-to-event data analysis approach (SAS Proc Genmod, SAS Institute, Inc.).[25]

RESULTS

Cross-sectional Analysis

A total of 805 volunteers were recruited into the study, predominantly nurses and patient care assistants (69%). The demographics of the participants are shown by facility in Table 2. As expected, female HCWs represented 91% of the population studied. The mean age of the workers at the FMLH facility was significantly greater than at CHW, but the difference (2.6 years) was considered of little practical relevance. Both groups demonstrated a high prevalence of rhinitis and/or asthma, reflecting our encouragement of atopic HCWs to enroll in the study. CHW workers reported more asthma and rhinitis than the FMLH workers (48.7% vs 41.6%) (Table 2). Participants at FMLH reported significantly greater use of latex gloves than at CHW, consistent with the glove purchasing practices at the two hospitals (Table 1).

Atopic HCWs were recruited at a higher rate than reported in general populations,[26] with more than 60% of the participants having a positive aeroallergen test and more than 55% reporting a history of asthma, allergic rhinitis, or eczema, and more than 10% showing SPT reactivity consistent with food allergy (Table 3).

TABLE 2. Demographics and Medical History of Participants

	CHW, $N = 305$	FMLH, $N = 500$
Age, yr, mean (SD, range)	37.7 (8.5, 21–63)	40.3 (9.3, 19–66)**
Female sex, *n* (%)	281 (92.1)	452 (90.4)
Race/Ethnicity, *n* (%)		
White	265 (87.2)	431 (86.2)
African American	24 (7.9)	49 (9.8)
Other	8 (2.6)	5 (1.0)
Hispanic	7 (2.3)	15 (3.0)
Atopic history (rhinitis, asthma)	148/304 (48.7)	208/500 (41.6)*
Dermatitis on hands	49/304 (16.1)	63/500 (12.6)
Food allergy (self-reported)	17/304 (5.6)	32/500 (6.4)
Job function		
Direct patient care	263/304 (86.5)	421/499 (84.3)
Indirect patient care	30 (9.9)	63 (12.6)
No patient care	11 (3.6)	16 (3.2)
Glove user		
Medical gloves in work	238/304 (93.1)	459/500 (91.8)
Latex examination gloves, powdered	62/304 (20.4)	278/500 (55.6)***
Sterile latex surgical, powdered	93/304 (30.6)	188/500 (37.6)*
Latex examination, non-powdered	27 (8.9)	298 (59.6)***
Nonlatex examination, non-powdered	103 (33.9)	234 (46.8)**
Sterile latex surgical, non-powdered	43 (14.1)	130 (26.0)***
Chemical protect latex, non-powdered	2 (0.7)	38 (7.6)***

Enrolled into the study, $N = 805$.
*$P < 0.05$; **$P < 0.001$; ***$P < 0.0001$.
CHW, Children's Hospital of Wisconsin; FMLH, Froedtert Memorial Lutheran Hospital.

The numbers of participants who completed one, two, three, and four latex SPT sessions during the 5 years of study were 282, 94, 149, and 280, respectively, resulting in a total of 2037 SPT sessions of which 107 were interpreted as positive. The prevalence of a positive SPT to latex at the first test was 18 of 305 or 5.8% at CHW and 22 of 500 or 4.4% at FMLH, which is not statistically different. In the pre-intervention phase, the majority of participants who demonstrated a positive latex SPT reacted at low concentrations of latex (1 μg/mL and 100 μg/mL). A total of 49 participants were SPT positive to latex at any time during the study, each demonstrating at least one and up to four positive results.

Questionnaires at baseline (Table 4) documented 45 of 805 (5.6%) participants with urticaria from gloves; 123 of 805 (15.7%) with dermatitis; and 136 of 805 (16.9%) with asthma, but only 10 of 805 (1.2%) identified gloves as an inciting factor for their asthma. Latex SPT positive participants were significantly more likely to report urticaria, asthma, rhinitis, wheezing, cough, conjunctivitis, food allergy, and glove-related dermatitis than SPT negative participants. None of the 805 study participants reported previous anaphylactic reactions to latex at baseline, although two individuals reported such events during the pre-intervention phase of the study.

TABLE 3. Skin Prick Testing to Clone 600 Nonammoniated Latex and Allergen Panel* at Study Entry Among 805 Health Care Workers

Test	CHW† ($N = 305$)	FMLH‡ ($N = 500$)	*P*
Latex SPT +	18 (5.9%)	22 (4.4%)	0.3415
Latex SPT + @ 1 μg/mL	5 (1.6%)	3 (0.6%)	0.1632
Latex SPT + @ 100 μg/mL	11 (3.6)	17 (3.4)	0.8767
Latex SPT + @ 1.0 mg/mL	2 (0.7)	2 (0.4)	0.6363
Multitest™ + to ≥1 aeroallergens (≥grade 1)	183 (60)	309 (62)	0.5917
Multitest™ + to ≥1 foods (≥grade 1)	24 (7.9)	60 (12.1)	0.0619

*Ragweed pollen, grass pollen, tree pollen, house dust mite, cat, dog, *Alternaria*, *Cladosporium*, banana, avocado, potato, lobster, and shrimp.

CHW, Children's Hospital of Wisconsin; FMLH, Froedtert Memorial Lutheran Hospital; SPT, skin prick test.

Exposure Measurements

During the pre-intervention study period, samples were collected from 71 representative HVAC return ducts, and latex allergen measurements in these ranged from 0.01 to 411.06 μg/g. On the basis of each individual participant's usual work location, we were able to assign a representative work area return duct latex allergen measurement to 772 of the 805 participants; whereas for 32 participants with varying work locations (eg, float nurses, patient transport, etc), the assignment of a specific latex antigen exposure level was not applicable. Exposure concentrations to latex allergen in HVAC ducts were considered low if less than 10 μg/g of workplace dust, intermediate if between 10 and 100 μg/g, and high if more than 100 μg/g. Airborne latex antigen levels from 180 area samples were uniformly below the limit of quantitation, and were not further evaluated.

Relationship Between Latex Skin Prick Test Results and Risk Factors

Exposure to latex allergen in work area return air ducts was significantly higher among HCWs with at least one positive latex SPT (Table 4). The proportion of HCWs sensitized to latex increased with the concentration of latex allergen in the work area ducts, for participants exposed to low (9/413, 2.18%), intermediate (23/292, 7.88%), and high (11/67, 16.42%) quantities of latex allergen, $P < 0.0001$ by Mantel-Haenszel chi-square test. For 32 of the participants, work locations were variable (eg, float nurses, patient transport, etc) and assignment of a latex antigen exposure level from a single hospital HVAC duct was not appropriate. Interestingly, the proportion of latex sensitized individuals in this group with varying work locations (6/32, 18.8%) was much greater than among the group of HCWs with consistent work locations (43/772, 5.6%; $P < 0.01$).

A number of factors were not found in this study to be associated with latex SPT results, including previous surgery, sex, and smoking.

Longitudinal Analysis

Latex SPT conversion rates were evaluated among participants who had at least two and up to four SPT results ($N = 523$). During the pre-intervention phase of the study, defined by the time between the first SPT and the date when the glove change intervention was completed, a total of seven participants (two CHW and five FMLH HCWs) converted their latex SPT from negative to positive (Table 5A). The total exposure time was 6644 months with a rate of conversion of 0.105% per month. This represented a conversion rate of one in every 79 latex SPT negative participants per year of work.

In the post-intervention phase of the study, as defined by the time between the date of completion of the glove change and the date of subsequent SPTs, only one participant converted his own latex SPT from negative to positive. The total exposure time during the post-intervention phase was 15,807 months with a conversion

TABLE 4. Characteristics at Study Entry of Participants by Clone 600 Skin Prick Test Response

Characteristics	Latex SPT +, $n = 49$	Latex SPT–, $n = 755$*	*P*
Age, yr, mean (SD)	37.7 (9.5)	39.1 (8.9)	0.3254
Sex: M/F, *n* (%)	6 (8.3) / 43 (5.9)	66 (91.7) / 689 (94.1)	0.4053
Race and ethnicity (W/AA/O/H), %	42/4/0/3	654/69/13/19	0.3796
Ever smokers, *n* (%)	18 (36.7)	246 (32.6)	0.5487
Symptoms and medical conditions. *n* (%)			
Rhinitis/latex gloves	15 (30.6)	51 (6.8)	<0.0001
Conjunctivitis/latex gloves	16 (32.7)	45 (6.0)	<0.0001
Cough with latex or nonlatex gloves	7 (14.3)	14 (1.9)	<0.0001
Wheeze with latex or nonlatex gloves	6 (12.2)	10 (1.3)	<0.0001
Asthma	16 (32.7)	120 (15.9)	0.0024
Asthma with glove exposure	4 (8.2)	6 (0.8)	0.0020
Dermatitis from any medical gloves	25 (51.0)	99 (13.1)	<0.0001
Food Reaction—self-reported	11 (22.5)	38 (5.0)	<0.0001
Latex dust exposure assessment			
Medical gloves used at work	48 (98.0)	694 (91.9)	0.1247
Air duct allergen detected at work location (latex dust >0.5 μg/g), *n*/*N* (%)	37/523 (7.1)	6/249 (2.4)	0.0082
Air duct latex allergen exposure, μg/g, mean (SD)	78.5 (75.5)	37.2 (55.4)	0.0010

*One missing questionnaire.

AA, African American; H, Hispanic; O, other; SPT, skin prick test; W, white.

TABLE 5A. Rates of Conversion of Subject From Latex Skin Prick Test Negative to Positive and Positive to Negative Before and After Glove Interventions to Reduce Latex Allergen Exposure Among Those With at Least Two and Up to Four Skin Prick Test Results

	Participants		
$N = 523$	CHW	FMLH	Combined Hospitals
Pre-intervention			
SPT + to SPT −	0/12	0/14	0/26
SPT − to SPT +	2/155	5/290	7/445
Post-intervention			
SPT + to SPT −	2/15	5/13	7/28
SPT − to SPT +	0/202	1/264	1/466

CHW, Children's Hospital of Wisconsin; FMLH, Froedtert Memorial Lutheran Hospital; SPT, skin prick test.

TABLE 5B. Incident Rates of Conversion From Latex Skin Prick Test Negative to Positive and Positive to Negative Before and After Glove Interventions for Those With at Least Two Tests

	Incident Rates (%) (Cases/mo at Risk)		
Conversion	Pre-intervention, $n = 471$ with 753 tests	Post-intervention, $n = 494$ with 1002 tests	*P*
Negative to positive	0.105 (7/6644)	0.006 (1/15807)	0.0006
Positive to negative	0.000 (0/449)	0.931 (7/752)	0.0105

$N = 523$

rate of 0.006%/month. This represents a conversion rate of one in every 1317 latex SPT negative participants per year of work. The rate of SPT conversion was significantly greater among participants in the pre-intervention phase than in the post-intervention phase of the study ($P = 0.0006$).

None of the 26 participants with an initial positive latex SPT and a follow-up during the pre-intervention phase reverted to negative (Tables 5A and 5B). For analytic purposes, we used 0.001 of 449 (0.00%) reversions per month for the pre-intervention phase rate to compare with the post-intervention phase reversion rate. In the post-intervention phase, among the 28 participants with positive latex SPTs, a total of seven reverted to negative. This represents a latex SPT reversion rate in the post-intervention phase of 7 of 752 (0.931%) reversions per month, which was significantly greater than the pre-intervention rate ($P = 0.0105$). Of the seven subjects whose SPTs reverted to negative, none had demonstrated a positive SPT at a low concentration of latex antigen (1 μg/mL and 100 μg/mL). In addition, a comparison of indicators of atopy was made between these seven workers who lost their sensitization with the 21 who remained sensitized. A history of asthma or rhinitis was reported in 43% (3/7) versus 90% (19/21), $P = 0.0207$. A positive SPT to one or more foods was 3 times more prevalent among those who remained sensitized.

Employee Retention and Latex Skin Prick Test Reactivity

To examine the association of latex sensitization with employee retention, the number of participants who left the workplace within 2 years of skin prick testing was analyzed. Among the 49 individuals who were latex SPT positive at any time during the study, 17 (34.7%) left their current employment within 2 years after detection of latex allergy while 99 of the 756 (13.1%) who were latex SPT negative left the employment of the hospitals ($P < 0.001$). The human resource departments did not reveal the reason for the employee departures and all were aware of their SPT results. Nonetheless, latex sensitized HCWs left their employment at a rate almost 3-fold than HCWs who were not sensitized to latex.

DISCUSSION

We prospectively evaluated natural latex allergen exposures and latex allergies among 805 HCWs at two hospitals before and after an intervention intended to reduce exposure to latex antigen from medical gloves. The results indicated a significant exposure-response relationship between the concentration of latex antigen in dust from work area ventilation ducts and the proportion of HCWs who demonstrate SPT reactivity to a standardized latex antigen. The intervention, which consisted of removing powdered latex medical gloves from the workplace, was followed by a 16-fold reduction in the rate of latex sensitization. The study provides strong evidence that powdered natural latex medical gloves are a key agent responsible for the sensitization of HCWs to latex, with resulting morbidity and economic costs. Study participants were a convenience sample (the first 805 glove users to volunteer were enrolled into the study), but the large reduction in rate of sensitization observed should be relevant to all HCWs who use gloves. Use of powder-free latex gloves was associated with a marked reduction, but not the elimination of new onset latex sensitization.

HCWs in this study who had demonstrated latex sensitization were nearly 3 times more likely to leave their jobs than their non-sensitized coworkers. Also, among HCWs sensitized to latex before the glove intervention, 7 of 28 or 25% lost their SPT sensitization after an intervention that eliminated use of powdered latex gloves and provided nonlatex gloves to sensitized employees.

These are important findings for both affected individuals and for health care facilities, with implications for personal health, employee turnover, and occupational disease disability.

The findings indicate that latex antigen in dust from air ducts is a meaningful surrogate measure for the risk of latex sensitization. Anecdotally, the measurements also helped to identify a work area at one of the hospitals where latex exposures and sensitization were taking place because of unrecognized use of prepackaged kits containing a powdered latex examination glove. During the pre-intervention year of the study, two participants developed systemic anaphylactic reactions when opening suction catheter kits not identified to contain a powdered latex examination glove. The detection of latex allergen in return ducts where these kits were used helped to provide a basis for recognizing and removing these kits from the institution.

The current study has a number of strengths. The study population was relatively large. The longitudinal design assured that the same subjects were tested repetitively over time before and after the glove intervention, and permitted assessment of the timing of outcomes in relation to the intervention. Powder-free latex gloves used after the intervention were from a single lot from one manufacturer. The investigators have extensive experience in the testing methodology, including the safe use of the Clone 600 SPT reagent.[16,17] One individual performed all testing, avoiding the SPT variability in previous studies that resulted from multiple investigators. Large local reactions, mild transient cough, or rhinitis were the only reported

TABLE 6. Characteristics at Study Entry of Participants by Number of Latex SPTs

	1 Skin Prick Test $n = 282$	2–4 Skin Prick Tests $n = 523$	*P*
Female sex, n (%)	248 (88.3)	484 (92.5)	0.0424
Race and ethnicity (W/AA/O/H)	218/45/5/13	478/28/8/9	0.0652
Ever smokers, n (%)	94 (33.5)	170 (32.5)	0.7851
Symptoms and medical conditions, n (%)			
Atopic history (rhinitis, asthma)	109 (38.8)	247 (47.2)	0.0216
Dermatitis on hands	39 (13.9)	73 (14.0)	0.9754
Multitest™ + ≥1 aeroallergens (≥grade 1)	169 (60.6)	323 (62.1)	0.6693
Multitest™ + ≥1 foods (≥grade 1)	27 (9.7)	57 (11.0)	0.5727
Latex SPT +	11 (3.9)	38 (7.3)	0.0569

AA, African American; H, Hispanic; O, other; SPT, skin prick test; W, white.

adverse reactions during skin prick testing, and no anaphylactic reactions occurred. All SPTs were performed in duplicate by the same individual using consistent technique, and results were interpreted independently by another individual, reducing the possibility of observer biases. External validity of the findings is reinforced by the similarity of the conversion rate from latex SPT negative to positive among HCWs reported in a similar longitudinal study by Sussman and colleagues.[18]

The study also has a number of limitations. Participation was limited to less than 20% of employees with potential exposure to gloves, and no information regarding the nonparticipants was available. The longitudinal study design permits each participant to serve as their own control, reducing the potential for participation biases. Nevertheless, due to variable participation within the cohort, longitudinal skin prick testing was only available for 523 of the 805 HCWs in the study. It is theoretically possible that the number of at-risk participants with increased susceptibility to SPT conversion (eg, atopics) was reduced post-intervention by sensitization that occurred in the pre-intervention period or by differential loss to follow-up. To assess this as a possible source of bias, we compared markers of atopy among study participants with at least two SPTs with those who did not have a follow-up SPT. (Table 6) For both symptoms and SPT evidence of atopy, prevalences were in fact slightly higher among those who participated in follow-up, and thus no evidence of differential loss to follow-up was observed. The high proportion (>60%) of atopic subjects in the initial study group (compared with 4.3% atopics in a previous prospective incidence study[18]) ensures that the 16-fold decline in sensitization rates cannot plausibly be explained by a depletion of susceptible participants. All measurements of airborne latex antigen were below the limit of quantitation, nevertheless, air duct dust samples were available for most participants, and appeared to afford quantitative estimates of HCW antigen exposures. Dust samples were collected only during the pre-intervention period and no repeat dust measurements were available post-intervention. Therefore, it is impossible to explore quantitative relationships between reductions in antigen levels and the changes in SPT results.

SUMMARY

This study provides strong evidence that latex allergy in HCWs is caused by exposure to powdered latex gloves. Control of environmental latex allergen through the use of low allergen powder-free latex gloves was associated with a reduction in rates of sensitization, while provision of nonlatex gloves to sensitized employees allowed some exposed HCWs to lose their latex sensitization. These results reinforce the effectiveness of the recommendation to eliminate powdered latex gloves to minimize the risk of latex allergy in the health care workforce.

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