



ORIGINAL CONTRIBUTIONS

Latex Sensitization in Health Care Workers and in the US General Population

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Sensitization to natural rubber latex is a prerequisite to type I immediate hypersensitivity reactions (urticaria, angioedema, anaphylaxis, and allergic rhinitis) that result from subsequent latex exposure. This study examines occupations in which latex glove use is common to determine whether it is associated with increased prevalence odds of latex sensitization (measured by latex-specific immunoglobulin E antibodies) by using data from 5,512 adults aged 17–60 years from the Third National Health and Nutrition Examination Survey (1988–1991). After other factors associated with latex sensitization were controlled for, there was a nonsignificant association between longest-held jobs in health care and latex sensitization (odds ratio (OR) = 1.49, 95 percent confidence interval (CI): 0.92, 2.40). For current occupations, latex sensitization was not associated with health care work in which gloves were used (OR = 1.17, 95 percent CI: 0.51, 2.65) or with other occupations in which latex glove use is common (OR = 1.01, 95 percent CI: 0.49, 2.07) compared with other occupations. Current health care workers who reported not using gloves were at increased risk of latex sensitization, both among those without a history of childhood atopy (OR = 2.30, 95 percent CI: 1.04, 5.13) and those with such a history (OR = 28.04, 95 percent CI: 3.64, 215.97). This odds ratio heterogeneity suggests that subjects with childhood atopy may be at high risk of latex sensitization. *Am J Epidemiol* 2001;153:515–22.

asthma; IgE; latex; latex allergy; rhinitis, allergic, perennial

Allergic reactions to natural rubber latex are a concern in the health care industry. Among health care workers, the prevalence of latex sensitization has been estimated at 3–22 percent (1–12), depending on the population studied, the definition of sensitization used, and the selection criteria for inclusion of subjects in the study. Among the general population, the prevalence has been estimated at 6–12 percent (13–16). However, in spite of the numerous studies that have examined either the seroprevalence of latex-specific

immunoglobulin E (IgE) antibodies or skin prick reactivity to extracts from latex gloves, direct comparisons between health care workers and comparable general populations have not been made. Thus, it is not established that the prevalence of latex sensitization is higher in health care workers than in the general population. It is desirable that the prevalence of latex sensitization be measured accurately in exposed and comparable referent groups in to identify the latex products and circumstances of use that are associated with sensitization.

Latex sensitization refers to the presence of latex-specific IgE antibody. It is postulated that both dermal contact and inhalation of airborne glove powder in health care settings may sensitize nonallergic individuals (17–19), which has led to recommendations for changes in glove use (20). Among sensitized individuals, reexposure to latex antigens may result in IgE-mediated clinical allergies (21, 22), which include anaphylaxis, urticaria, angioedema, asthma, and allergic rhinitis (23).

Our investigation examined the data collected by the Third National Health and Nutrition Examination Survey (NHANES III) regarding the seroprevalence of latex-

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Abbreviations: CDC, Centers for Disease Control and Prevention; CI, confidence interval; IgE, immunoglobulin E; NHANES III, Third National Health and Nutrition Examination Survey; OR, odds ratio.

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specific IgE antibodies in the US general population. The purpose of this study was to examine whether work in health care jobs is associated with increased risk of latex sensitization and to determine whether other factors (such as glove use, atopy, age, sex, and race) affect this association.

MATERIALS AND METHODS

We used data from the Third National Health and Nutrition Examination Survey, phase I, which was conducted by the National Center for Health Statistics between October 1988 and October 1991 (24, 25). The data were obtained on a public-use CD-ROM provided by the National Center for Health Statistics (26). The NHANES III data, when used with sampling weights to correct for different sampling probabilities, noncoverage, and nonresponse, provide estimates of the health status of the civilian, noninstitutionalized population of the United States aged 2 months and older (24). A 15 percent random sample of participants aged 17–60 years was tested by the Centers for Disease Control and Prevention (CDC) for latex-specific IgE antibodies. Subjects were chosen for laboratory analyses without knowledge of their occupation, symptoms, latex sensitization status, or other factors associated with latex sensitization.

Questionnaire data regarding health conditions, allergies, and demographic factors were obtained from the same individuals. The variables we considered as potential explanatory factors were occupation (current occupation, ever wear protective equipment, ever wear protective gloves, how long worked at job, longest-held occupation), demographics (sex, race, ethnicity, age, urban/rural residence), family history of allergic conditions (parental asthma or hay fever), smoking (ever smoked cigarettes, smoke cigarettes now, anyone in the home smoke cigarettes, quit smoking because of health problems), allergic conditions (ever asthma, ever bronchitis, ever hay fever, age at diagnosis of asthma, age at diagnosis of bronchitis, age at diagnosis of hay fever, current asthma, current bronchitis, current hay fever), respiratory and allergic conditions (wheezing or whistling in the chest; stuffy nose; watery, itchy eyes; symptoms brought on by exercise; symptoms brought on by animals; symptoms brought on by work environment; symptoms brought on by pollen), and frequency of visiting a dentist.

The CDC used the AlaSTAT test (Diagnostics Products Corporation, Los Angeles, California) to test for latex sensitivity (27). In the AlaSTAT test, 50 μ l of serum is mixed with 100 μ l of latex allergen reagent. After an hour of incubation, an antilgand reagent is added to capture latex-specific IgE bound to the latex reagent. After washing, an enzyme-anti-IgE reagent is added to react with IgE that has bound the latex allergen. After another wash, substrate is added, and color development is stopped after precisely 15 minutes by the addition of sulfuric acid. The absorbance at 492 nm of each latex allergen test is compared with a reference curve, and values of latex-specific IgE are interpolated. For the purposes of these analyses, values below 0.35 IU/ml were classified as negative, values from 0.35 to 1.50 IU/ml were classified as positive, and those at and above 1.50 IU/ml were classified as strongly positive. These cutpoints and

ranges are commonly regarded as differentiating between negative, positive, and strongly positive, latex-specific IgE antibody concentrations (15, 16).

NHANES III contained information on the current occupation, including questions about whether gloves were ever worn in the subject's current job. Subjects were grouped by occupation according to the following definitions:

- Health care workers were defined as subjects who reported their current occupation as one of the health diagnosing, assessment, and treatment occupations or as one of the health service occupations. A total of 109 health care workers reported using gloves, and 65 reported that they did not use gloves at work.
- Other jobs with glove use were defined as those involving subjects who worked in occupations other than health care in which latex glove use is common and who reported using gloves at work. These were food handlers and cooks (28, 29), private household workers (29), protective service workers (law enforcement, ambulance attendants, and firefighters) (29), cleaning occupations, and nursery farmers (30).
- Nonhealth-care workers, nonglove users were defined as subjects who reported any other current occupation.

NHANES III also contained information about the longest-held occupation of each subject. This information was of interest in this study because of the possibility that latex-sensitized subjects might have left exposed jobs preferentially compared with nonsensitized subjects. If this were true, the longest-held occupation might be less subject to any differential selection bias out of health care occupations. Subjects were grouped according to the longest-held occupation using the definitions above, except that information on glove use was not collected in the NHANES III survey.

Because the NHANES III data were derived from a stratified sample of the US population, the weight assigned to each subject was also used in the analyses. Of the 5,524 subjects tested for IgE, 12 subjects were excluded because they had been examined in their homes rather than in mobile examination centers, leaving 5,512 subjects available for the analyses. Information on glove use was missing for three subjects, leaving 5,509 in the analyses by current occupation. Information on longest-held occupation was missing for 290 subjects, leaving 5,222 subject in the analyses by longest occupation.

To assess the possibility of selection bias, we examined whether the study results were influenced by different serum selection probabilities with respect to work in health care, other factors associated with latex sensitization, and demographic factors (age, sex, ethnicity). The prevalence of latex sensitization was compared between occupation groups by using a contingency table. Prevalence odds ratios and 95 percent confidence intervals were calculated by using weighted ordinal logistic regression in which the outcome variable was latex sensitization classified as a three-level variable: negative (<0.35 IU/ml), positive (0.35 to <1.50 IU/ml), and strongly positive (≥ 1.50 IU/ml). Demographic variables, allergic conditions, history of atopy, and other factors were added sequentially to identify the best model (judged by the -2 log-likelihood ratio test). Effect modifica-

tion was examined by the addition of interaction terms, and when odds ratio heterogeneity was detected, the strata were kept separate in further analyses.

Assessing the role of atopy was an important issue, insofar as atopic conditions (e.g., asthma and hay fever) are both recognized risk factors for latex sensitization and may also be consequences of latex sensitization. To differentiate whether atopy was antecedent to health care work or may have been a consequence of health care work, we examined the association between latex sensitization and health care work separately for subjects who reported childhood asthma and hay fever (onset before age 18 years) and those who did not and for those who reported the onset of asthma or hay fever prior to starting their current job and those who did not.

A final model, which included occupation group, age, sex, race, and physician-diagnosed asthma or hay fever, was chosen to represent the association between each measure of latex sensitization and each occupation group. This model was compared with a reduced model, which excluded physician-diagnosed asthma or hay fever, to examine whether a history of atopy altered the associations between latex sensitization and occupation. All analyses were performed using SAS version 6.12 (SAS Institute, Inc., Cary, North Carolina) (31) and SUDAAN version 6.04 (Research Triangle Institute, Research Triangle Park, North Carolina) (32), which allows estimation of complex sample variances in the presence of stratified and clustered survey data (33).

RESULTS

There were no appreciable differences (and no statistically significant differences) between subjects whose latex-specific IgE was measured and those who were excluded from the IgE analysis, in terms of sex, race/ethnicity, age, the proportion who worked in health care, the proportion with physician-diagnosed asthma or hay fever, or the proportion of smokers. Thus, there was no evidence of selection bias in the testing of subjects for latex-specific IgE.

The best model for each combination of latex sensitization and occupation group contained the same set of explanatory variables (age, race, sex, and physician-diagnosed asthma or hay fever), and the regression coefficients for these variables were relatively stable across these models. For example (table 1), the model indicates that after controlling for all other factors, subjects who reported that their longest job was in health care were at 1.49 times higher odds of latex sensitization (both a positive and strongly positive IgE response vs. a negative response) than were nonhealth-care workers (95 percent confidence interval (CI): 0.92, 2.40). Females were at significantly lower odds than were males (odds ratio (OR) = 0.58, 95 percent CI: 0.45, 0.75), Black non-Hispanics (OR = 1.41, 95 percent CI: 1.10, 1.80) were at significantly increased odds compared with White non-Hispanics, and older ages were at significantly reduced odds (for subjects aged 50–60 years compared with those aged 19 and under (OR = 0.61, 95 percent CI: 0.43, 0.86)). Subjects with physician-diagnosed asthma or hay fever were at significantly increased odds (OR = 2.53, 95 percent CI: 2.12, 3.02) compared with those without these conditions.

TABLE 1. Proportional logistic regression analyses of factors associated with latex sensitization*, including longest-held occupation in health care, United States general population, 1988–1991

Variable	OR†	95% CI†
Longest occupation in health care		
No	1.00	
Yes	1.49	0.92, 2.40
Sex		
Male	1.00	
Female	0.58	0.45, 0.75
Race		
White Non-Hispanic	1.00	
Black Non-Hispanic	1.41	1.10, 1.80
White Hispanic	1.08	0.77, 1.50
Black Hispanic and other	2.25	1.27, 3.98
Age group (years)		
≤19	1.00	
20–29	1.16	0.78, 1.72
30–39	0.74	0.46, 1.21
40–49	0.57	0.31, 1.06
50–60	0.61	0.43, 0.86
Physician-diagnosed asthma or hay fever		
No	1.00	
Yes	2.53	2.12, 3.02

* Latex sensitization defined as negative (<0.35 IU/ml), positive (0.35 to <1.50 IU/ml), or strongly positive (≥1.50 IU/ml).

† OR, odds ratio; CI, confidence interval.

Table 2 presents the results for the occupations in two different models: a model containing occupation group and demographic variables (sex, race, age) and a final model containing the same set of predictor variables with atopy (asthma or hay fever) added. Comparison of these models allows an assessment of whether there is any appreciable confounding by atopy after controlling for sex, race, and age. The final model indicates that there was a weak association between latex sensitization and the longest-held job in health care (OR = 1.49, 95 percent CI: 0.92, 2.40) and no association between latex sensitization and work in other jobs in which glove use is common (OR = 1.07, 95 percent CI: 0.75, 1.53). In each instance, comparison of the full model and the reduced model indicated that adjustment for atopy did not appreciably alter any of the associations between occupations and latex sensitization.

For current occupations (table 2), there was no association between latex sensitization and health care work with glove use (OR = 1.17, 95 percent CI: 0.51, 2.65). Among health care workers who denied using gloves, there was a moderate association with latex sensitization (OR = 2.53, 95 percent CI: 1.21, 5.29). However, there was odds ratio heterogeneity when these results were stratified on childhood atopy (for those with childhood atopy, OR = 28.04, 95 percent CI: 3.64, 215.97; for those without childhood atopy,

TABLE 2. Prevalence of latex-specific immunoglobulin antibody in subjects who reported that their occupation was health care worker vs. nonhealth care worker in the United States general population, 1988–1991

	No. of subjects in each category of antibody concentration			Model including HCW* and demographics†		Model including HCW, atopy, and demographics‡	
	<0.35	0.35–<1.50	≥1.50	OR*	95% CI*	OR	95% CI
Longest held occupation							
Health care workers	197	28	17	1.52	0.93, 2.47	1.49	0.92, 2.40
Other jobs with glove use	617	97	60	1.07	0.75, 1.54	1.07	0.75, 1.53
Nonhealth care workers, no glove use	3,673	520	303	1.00		1.00	
Current occupation							
Health care workers who use gloves	90	13	6	1.22	0.52, 2.85	1.17	0.51, 2.65
Health care workers who do not use gloves	47	9	9	2.61	1.22, 5.62	2.53	1.21, 5.29
Other jobs with glove use	140	29	10	1.05	0.52, 2.12	1.01	0.49, 2.07
Nonhealth care workers, no glove use	4,208	593	355	1.00		1.00	

* HCW, health care workers; OR, odds ratio; CI, confidence interval.

† Model includes health care work, sex, race, age as predictors of latex-specific immunoglobulin E antibody status.

‡ Model includes health care work, sex, race, age, and physician-diagnosed asthma or hay fever as predictors.

OR = 2.30, 95 percent CI: 1.04, 5.13). This interaction suggests that health care workers who denied glove use and who have a history of childhood atopy may be at substantially higher risk of latex sensitization than those without such a history. There was no clear evidence of odds ratio heterogeneity for any of the other current or longest-held job groups. Other current jobs in which latex glove use is common were not associated with latex sensitization (OR = 1.01, 95 percent CI: 0.49, 2.07).

It is possible that the lack of association between current health care work with gloves and latex sensitization is due in part to movement of sensitized workers out of jobs in which they would be exposed to gloves. To evaluate this possibility, we analyzed information on whether subjects had ever changed jobs because of health problems. Current health care workers who did not use gloves were not appreciably different from nonhealth-care workers with respect to such job changes (12.1 vs. 11.8 percent, respectively, $p = 0.96$). These findings suggest that subjects had not moved to health care jobs in which gloves were not used because of allergies or other health problems.

The prevalence of latex sensitization was calculated for each of 39 different longest-held occupational groups (figure 1). Figure 1 shows that health care workers were not unusual with respect to other occupations when ranked by the prevalence of sensitization at 0.35 to less than 1.50 IU/ml, when ranked by the prevalence of sensitization at 1.50 IU/ml or more, or when both categories were summed. Other occupations in which latex gloves are used frequently, such as miscellaneous food workers, cooks, private household workers, protective service workers (law enforcement, ambulance attendants, and firefighters), cleaning occupations, and nurs-

ery farmers, tended to be in the upper half of the distribution but were not at clearly higher risk than other occupations.

DISCUSSION

The results in table 2 suggest that there may be an association between long-term work in health care and latex sensitization. Insofar as the information about the longest-held jobs does not contain information about glove use, it cannot be determined whether these associations are explained by glove use or by other factors. However, the findings for current jobs suggest that glove use may not be associated with increased risk of sensitization either among health care workers or in other jobs in which latex glove use is common. They also indicate that work in health care jobs in which gloves are not used is moderately associated with latex sensitization. The associations between occupations and latex sensitization were not appreciably altered by adjustments for asthma and hay fever. This suggests that these conditions were not consequences of sensitization, but rather were predictors of sensitization that are independent of occupation (and latex exposure). However, a history of childhood atopy was a strong effect modifier in current health care workers who denied glove use. Although this observation suggests that people with childhood atopy may be at high risk of latex sensitization, the data in our study are too small to draw any firm conclusions on this point. This effect was not seen in the other current or longest-held job groups.

In the aggregate, these results provide little support for the conclusion that glove use is associated with latex sensitization either in health care workers or in other jobs in

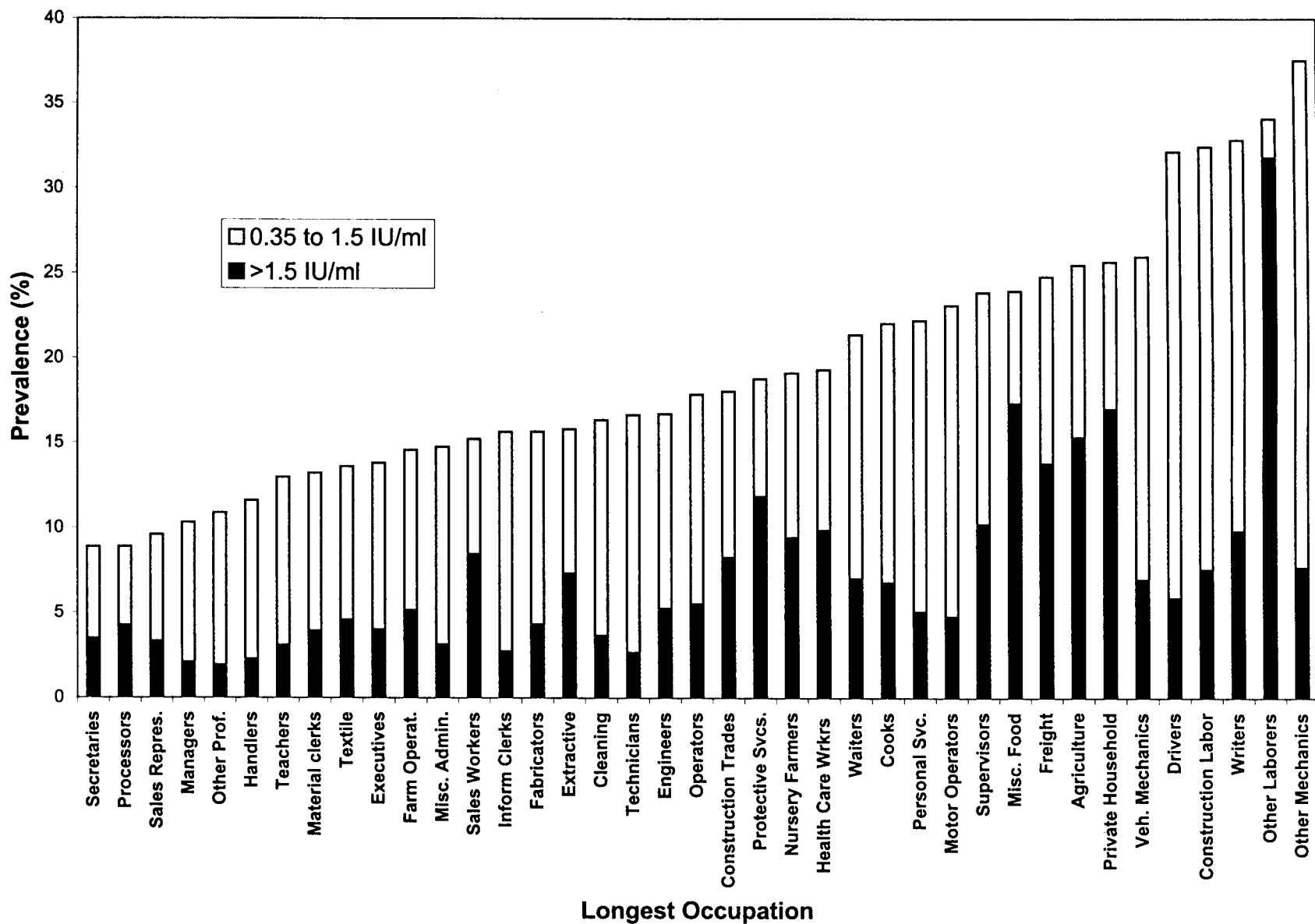


FIGURE 1. Prevalence of latex sensitivity based on latex-specific IgE antibody concentration (IU/ml) by longest occupation, United States general population, 1988–1991.

which latex glove use is common, and they provide weak support for the conclusion that long-term work in health care is associated with sensitization.

It is possible that sensitized subjects selectively leave jobs within health care in which they are exposed to latex gloves, leading to differential exposure misclassification. However, since the majority of subjects who are sensitized to latex are asymptomatic and are unaware of their antibody status (34), such persons would have little reason to change jobs more frequently than those who are not sensitized. In addition, workers who develop clinical allergies to latex gloves typically switch to nonlatex gloves rather than changing jobs, for which there would be an attendant loss of seniority and job skills. In support of this view, we found no evidence that health care workers who used gloves or those who did not changed jobs because of health problems more frequently than did nonhealth-care workers. It is possible, however, that subjects who are sensitized and who continue to suffer from latex-related allergies in spite of attempts to reduce their exposure would preferentially move to nonexposed jobs.

Our findings are consistent with other published studies. Atopy is a strong and consistent risk factor for latex sensitization (1, 4, 5, 8, 10, 13, 16, 21, 35–37). Non-White race has been observed to be a risk factor for latex sensitization in a large study of nurses (5), among surgery patients (13), and among blood donors in the general population (15). Male sex is also a recognized risk factor in some (13, 15), but not all (14), studies. Consistent with our findings, previous studies of health care workers have not demonstrated any consistent pattern of dose response between sensitization and increasing exposure to latex in gloves. Numerous studies have sought, but failed to find, associations between the risk of latex sensitization and the following exposure metrics 1) the duration of exposure to latex gloves or the duration of work in health care (2, 12, 38); 2) the duration of latex glove use (2); 3) the frequency of glove use (9); 4) the number of hours worked in health care jobs (2); and 5) work in operating rooms and settings with frequent glove use versus work in areas with infrequent glove use (5). One study found an association between the prevalence of latex sensitivity and the number of surgical gloves used, but did not find any such association with the number of examination gloves used (4). Examination gloves commonly contain higher levels of protein allergens and generate higher exposures to aeroallergens (23). In contrast, another study found no difference in skin prick test conversion rates between users of powdered (high-protein) gloves and users of powder-free (low-protein) gloves followed prospectively for a year (21). Yet another study showed no relation between powdered glove use and latex-specific IgE antibodies (3). Other studies have failed to find evidence that latex glove use is associated with latex sensitization. In a prospective study of latex glove users, the incidence of latex sensitization (determined by skin prick test) was 1 percent per year among users of high-protein, powdered latex gloves and was 1 percent per year among users of low-protein, powder-free latex gloves (21). Similar findings were obtained in a recent cross-sectional study in which neither current nor past use of

latex gloves was associated with latex sensitization in hospital-based health care workers (34).

Postulated explanations for this lack of evidence of dose response include selection of sensitized workers out of latex-exposed jobs and avoidance of latex gloves by subjects after they have become sensitized. While both of these tendencies may exist, the absence of evidence of dose response remains an important argument against a conclusion that latex glove use is a cause of allergic sensitization. Other occupations in which there is an appreciable risk of IgE-mediated allergic sensitization (such as in workers exposed to laboratory animals, platinum salts, and grain dust) show unequivocal evidence of increasing risk with increasing duration, intensity, and frequency of exposure (39–47). Removal of sensitized workers and avoidance of exposure in these settings does not obscure the evidence that workers with heavier, longer, and more frequent exposure are at higher risk of sensitization (48).

Latex sensitization among patients is believed to be a result of intimate contact with latex-containing products during medical procedures, such as among patients with myelodysplasia (49), spina bifida (37, 50), meningocele (51), congenital genitourinary anomalies (36), and multiple surgeries (52), whereas the studies of latex glove use suggest that the relative risk of sensitization is low when there is only skin contact. Our findings are consistent with this interpretation. It is possible that immediate hypersensitivity reactions that are diagnosed after latex exposure in health care workers may reflect increased clinical surveillance rather than increased rates of sensitization.

The limitations of the NHANES III data include a lack of information about the specific job duties, specific types of gloves used, or subjects' handling of or exposure to other latex devices at work. As a result, the explanation for the association we observed between latex sensitization and current jobs in health care in which gloves were not used remains unclear and should be the subject of additional study. A further limitation of the NHANES III data is the lack of information on glove use in the longest-held occupations, which precluded any analyses of whether the risk of sensitization in longest-held jobs in health care work was related to glove use. It is possible that other sources of exposure to latex rubber in the general environment may be important determinants of sensitization. For example, exposure to latex antigens is common at low levels from sources such as vehicle tire dust and dusts deposited around freeways (53). It is possible that persons who held some specific occupations in our referent category (such as vehicle mechanics who repair tires, professional drivers, and rubber workers) were exposed to latex and that this may have increased the prevalence of sensitization in our referent group. However, it is likely that such an effect would be small because such persons made up a small proportion of the referent group. Moreover, this would not explain why health care workers who did not use gloves would be at substantially increased odds, while those who used gloves would not.

The estimates of latex antibody seroprevalence in this study are somewhat higher than those in other studies that

have also used the AlaSTAT method (5, 13, 15, 16). The reasons for this are not clear. The laboratory personnel who conducted the AlaSTAT assays at the CDC were blinded to the subjects' identities (27), making differential observation bias unlikely. Any systematic error in the AlaSTAT assays would likely have affected all of the NHANES III subjects and would be unlikely to account for the findings in any particular occupational group. Moreover, the pattern of associations with age, sex, and race found in this study agrees closely with findings from other studies that used the same methods, indicating that there was not random error adequate to obscure these associations.

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