Occupational Risk Factors and Asthma among Health Care Professionals

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Rationale: **Recent U.S. data suggest an increased risk of work-related asthma among health care workers, yet only a few specific determinants have been elucidated.**

Objectives: **To evaluate associations of asthma prevalence with occupational exposures in a cross-sectional survey of health care professionals.**

Methods: **A detailed questionnaire was mailed to a random sample (n = 5,600) of all Texas physicians, nurses, respiratory therapists, and occupational therapists with active licenses in 2003. Information on asthma symptoms and nonoccupational asthma risk factors obtained from the questionnaire was linked to occupational exposures derived through an industry-specific job-exposure matrix.**

Measurements: **There were two *a priori* defined outcomes: (*1*) physician-diagnosed asthma with onset after entry into health care ("reported asthma") and (*2*) "bronchial hyperresponsiveness–related symptoms," defined through an 8-item symptom-based predictor.**

Main Results: **Overall response rate was 66%. The final study population consisted of 862 physicians, 941 nurses, 968 occupational therapists, and 879 respiratory therapists (n = 3,650). Reported asthma was associated with medical instrument cleaning (odds ratio [OR], 2.22; 95% confidence interval [CI], 1.34–3.67), general cleaning (OR, 2.02; 95% CI, 1.20–3.40), use of powdered latex gloves between 1992 and 2000 (OR, 2.17; 95% CI, 1.27–3.73), and administration of aerosolized medications (OR, 1.72; 95% CI, 1.05–2.83). The risk associated with latex glove use was not apparent after 2000. Bronchial hyperresponsiveness–related symptoms were associated with general cleaning (OR, 1.63; 95% CI, 1.21–2.19), aerosolized medication administration (OR, 1.40; 95% CI, 1.06–1.84), use of adhesives on patients (OR, 1.65; 95% CI, 1.22–2.24), and exposure to a chemical spill (OR, 2.02; 95% CI, 1.28–3.21).**

Conclusions: **The contribution of occupational exposures to asthma in health care professionals is not trivial, meriting both implementation of appropriate controls and further study.**

Keywords: work-related asthma; health care workers

AT A GLANCE COMMENTARY

Scientific Knowledge on the Subject

Data suggest an increased risk of work-related asthma in U.S. health care workers, yet few specific determinants have been elucidated. Confirmation and estimation of risk in population-based studies has been inconsistent and more problematic.

What This Study Adds to the Field

Occupational exposures are important contributors to asthma in health care providers.

It is well established that certain occupational groups are at increased risk of developing asthma, including Western red cedar workers (1), isocyanate chemical workers (2), construction workers (3), and farmers (4). However, whereas the risk magnitude and etiologic agents are well characterized for many of these occupations, this has been less well studied in the case of health care workers (HCWs), where data largely derive from case series but relatively few population-based studies or surveillance systems.

In the 1990s, attention began focusing on respiratory hazards among HCWs, partly because of increasing concern over occupational latex allergy after passage of the 1992 Occupational Safety and Health Administration (OSHA) bloodborne pathogens standard, which resulted in a significant increase in the use of latex-containing personal protective equipment, such as powdered latex gloves. However, potential asthmagens in health care settings go beyond latex, and may include disinfectants and sterilants (e.g., glutaraldehyde, formaldehyde), pharmaceuticals (e.g., psyllium, antibiotics), sensitizing metals (e.g., in dental alloys), methacrylates, irritant aerosolized medications (e.g., pentamidine and ribavirin), and cleaning products (5, 6).

Previous studies from various countries have reported cases of work-related asthma among specific groups of HCWs, including physicians (7), respiratory therapists (8), workers in endoscopy units and radiology departments (9), nurses (10), and general HCWs (5). Confirmation and estimation of risk, however, in population-based studies has been more problematic. In a cross-sectional analysis of the European Community Respiratory Health Study (ECRHS), significant excesses of risk among HCWs were not consistently observed (4). In the United States, using data from the National Health and Nutrition Examination Survey III, conducted between 1988 and 1994, the odds for either work-related asthma or wheezing in health-related occupations were not significantly increased (11). Data from the 2001

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National Health Interview Survey did find significantly increased odds for physician-diagnosed asthma in the U.S. health care industry, but this excess was limited to white females (12). More recently, surveillance data from four U.S. states found that work-related asthma among HCWs represented 16% of total reported cases, exceeding their representation in the workforce (8%) (6). Interestingly, the U.S. National Institute for Occupational Safety and Health (NIOSH) reported that 5 of the top 11 industries and 9 of the 22 leading occupations associated with significantly increased asthma mortality were related to health care services (13).

Thus, results are inconsistent, and few studies have been conducted in HCW populations allowing a more detailed characterization of potential associations between asthma and various workplace exposures. Studies that address these remaining issues are particularly important considering that HCWs comprise approximately 8% of the U.S. workforce, and constitute one of the fastest growing sectors of the workforce (14). Using representative samples of selected HCW groups in Texas, the purpose of this study was to evaluate associations of asthma prevalence with occupational exposures in health care professionals, and to estimate their magnitude.

METHODS

Survey Population

The following four groups of Texas health professionals with active professional licenses in 2003 were targeted for a cross-sectional confidential mail survey of asthma: physicians (n = 52,542), nurses (n = 161,557), respiratory therapists (n = 10,085), and occupational therapists (n = 7,207). On the basis of sample size calculations to ensure $\alpha = 0.05$ and $\beta = 0.20$, adjusted for an expected response rate of at least 50% and an expected proportion of eligible respondents of 90%, a random sample of 1,400 individuals in each of the four groups was generated (total = 5,600) (15). Given historically low response rates of physicians to mail surveys (16), limited *post hoc* oversampling of this group was performed to ensure a sufficient number of physicians for final analysis.

Survey Instrument and Conduct

Development and validation of the survey questionnaire were performed by a multidisciplinary team of industrial hygienists, occupational and pulmonary physicians, epidemiologists, and survey design experts as previously described (17). Asthma symptom items were originally derived from the International Union against Tuberculosis and Lung Diseases bronchial symptoms questionnaire (18), supplemented with questions on physician-diagnosed asthma and age at asthma diagnosis. The final validated survey instrument was formatted in two versions: a hard-copy booklet and an identical web-based version.

Based on the approach of Dillman (19), up to five contacts with potential study participants were planned. An initial "warm contact" letter was followed by a hard-copy questionnaire, an explanatory cover letter, a $1 token financial incentive, and a business reply envelope. Information on how to complete the survey online rather than by hard copy was included. Follow-up postcard reminders, a replacement questionnaire, and a final reminder letter were subsequently sent, if needed, over the next 5 weeks.

Ethical approval for the study was obtained from the University of Texas Committee for the Protection of Human Subjects before study initiation.

Asthma Risk Factor Job-Exposure Matrix

Occupational exposures were determined on the basis of an externally developed asthma risk factor job-exposure matrix (JEM), specifically designed for use in HCW populations. More commonly used for cancer studies, JEMs have recently been used successfully to study work-related asthma (20). Development of our JEM consisted of several steps. The initial information source for the development of the JEM was the NIOSH National Occupational Exposure Survey (NOES), conducted over 20 years ago (21). Advantages of the NOES database included its origin based on direct observations of a representative sample of U.S. workplaces, its public availability, the consideration of exposures that may no longer exist, and the use of common industry, occupation, and hazard codes. Next, additional sources of chemical lists developed after publication of the NOES were identified from the literature and reviewed. A subset of a generic JEM, developed with data from the NOES and limited to the health services industry (22), was combined with a list of 367 asthmagens, cross-referenced on NOES hazard codes (23), to produce an initial health services–specific matrix for known and suspected asthmagens. This matrix was then updated based on a series of hospital walk-through surveys conducted in 2002 in three Houston hospitals (a 350-bed pediatric hospital, a 450-bed cancer hospital, and a 1,200-bed tertiary referral and general hospital) by industrial hygienists and occupational physicians. All three hospitals were accredited by the Joint Commission on Accreditation of Healthcare Organizations (JCAHO). The final matrix structure featured two axes: (*1*) a job axis, subclassifying professional job titles (nurse, physician, etc.) by main practice setting (hospital, outpatient clinic, nursing home, etc.), and (*2*) an exposure axis, consisting of five main exposure classes (cleaning products, powdered latex gloves, aerosolized medications, adhesives/solvents/gases, and sensitizing metals). Cleaning products were subclassified by task into patient-centered cleaning/disinfection, instrument cleaning/disinfection, and cleaning/disinfection of building surfaces. Similarly, adhesives/solvents/gases were subdivided into patient centered, application to nonpatient surfaces, and a nonspecific miscellaneous category. Powdered latex glove use was subdivided according to time period of exposure, relative to the year of implementation of the OSHA bloodborne pathogens standard (24): pre-1992, 1992 to 2000, and post-2000.

Five experts (among the authors: one occupational physician, three academic industrial hygienists, and an industrial hygienist/safety specialist employed in a hospital) assigned codes to each matrix cell, based on probability that the majority of workers in that cell were occupationally exposed at least once per week to this class of agents. A code of "0" was assigned if there was a high probability of no exposure; a "1" or a "2" was assigned when the probability of exposure was either low or high, respectively. Disagreements among the experts were resolved by consensus. The coded matrix was then applied to each respondent's current and longest held job as an HCW, based on the job title and practice setting reported for that job.

Study Variables

Two dichotomous outcome variables were defined: (*1*) physician-diagnosed asthma with onset after entry into the health care profession ("reported asthma") and (*2*) bronchial hyperresponsiveness (BHR)–related symptoms. Reported asthma was calculated among persons with a history of physician-diagnosed asthma by comparing the age at which this diagnosis was made to the number of years employed as a health care professional. The presence of BHR-related symptoms was determined based on an 8-item, symptom-based predictor of PC_{20} (provocative concentration of methacholine causing a 20% fall in FEV_1) of 4 mg/ml for methacholine developed in the validation study (sensitivity, 61%; specificity, 85%) (17). The eight items related to trouble breathing, wheezing and/or attacks of shortness of breath in the previous 12 months, nocturnal cough and/or chest tightness in the previous 12 months, and current allergic symptoms when in the presence of animals, feathers, dust, trees, grasses, flowers, or pollen.

After examining the coded JEM, it became apparent that the number of occupation–practice setting combinations assigned a code "1" (low probability) for exposure was very small for almost all considered exposures. As a result, this intermediate exposure group as such appeared to be too small for meaningful analyses. Therefore, occupational exposure variables were dichotomized by collapsing codes 1 and 2 from the JEM into a single "exposed" category, with code "0" reflecting the nonexposed groups. Sensitizing metals were excluded given the very small number of cells coded as exposed. JEM codes for longest held job were used because the majority ($\sim$ 60%) of respondents indicated that their current job was also their longest held job. For those with their longest held job outside the health care sector, JEM codes from the current job were used. In addition, from the questionnaire, a self-reported dichotomous occupational exposure variable, related to having ever been involved in a chemical spill or gas release at work, was included.

Covariates from the questionnaire were age, sex, race/ethnicity, professional group, years as a health professional ("seniority"), smoking, and obesity (body mass index [kg/m^2] $\geq$ 30). Atopy was defined based on a combination of history of allergies to dust and animals, developed in the validation study (sensitivity, 68%; specificity, 85%) (17).

Statistical Analysis

Post-stratification weighting was performed to obtain estimates of both counts and prevalences that were representative of the actual population sizes for each professional group. Regression analyses were performed on a subsample that excluded anyone with missing values for any variable. After evaluating collinearity, variables with a p value less than 0.25 in the univariate analyses were entered into unconditional multiple logistic regression models for each outcome. Interactions between atopy and occupational exposure were explored. Associations were expressed as the adjusted logistic odds ratio (OR) and 95% confidence interval (95% CI). Goodness-of-fit was assessed as recommended for survey sample data (25). Stata/SE version 9.2 (Stata Corporation, College Station, TX) was used for statistical analyses.

RESULTS

From the initial 5,600 mailed questionnaires, 213 participants were excluded due to death (7) and incorrect addresses (206), leaving a final eligible population of 5,387. Surveys were received from 3,529 participants (941 nurses, 968 occupational therapists, 741 physicians, and 879 respiratory therapists). Group response rates were highest for occupational therapists (73%) and nurses (70%), and lowest for physicians (54%) and respiratory therapists (65%), for an overall response rate of 66%. Physician oversampling resulted in an additional 121 surveys. The final number of returned completed surveys was 3,650.

The prevalence of reported asthma was 4.2% for physicians, 7.3% for nurses, 5.6% for respiratory therapists, and 4.5% for occupational therapists. BHR-related symptom prevalence varied by professional group: 18.0% in physicians, 29.2% in nurses, 30.3% in respiratory therapists, and 33.7% in occupational therapists. The overall weighted prevalences of reported asthma and BHR-related symptoms were 6.6 and 27.2%, respectively. Table 1 summarizes the descriptive statistics for the final analytic sample ($n = 2{,}738$), and the excluded sample ($n = 912$). As compared with the analytic sample, the excluded sample (i.e., those with incomplete questionnaires) was significantly older ($p < 0.001$), had a higher proportion of women ($p < 0.001$), a lower proportion of non-Hispanic whites ($p = 0.02$), had worked longer in health care ($p < 0.001$), and had a lower proportion of physicians ($p = 0.02$). There were no significant differences between the two groups with respect to prevalence of atopy, obesity, smoking status, or asthma outcomes. In addition, there were no significant differences between the two populations with respect to any of the JEM-derived occupational exposure variables: patient-centered cleaning ($p = 0.19$), instrument cleaning/disinfection ($p = 0.14$), cleaning of general surfaces ($p = 0.05$), powdered latex glove use before 1992 ($p = 0.64$), powdered latex glove use between 1992 and 2000 ($p = 0.41$), powdered latex glove use after 2000 ($p = 0.24$), administration of aerosolized medications ($p = 0.15$), use of adhesives on patients ($p = 0.36$), use of adhesives on nonpatient surfaces ($p = 0.76$), or miscellaneous use of adhesives ($p = 0.82$). Likewise, no significant difference between the analyzed and excluded populations was observed with ever having sustained an exposure to a chemical spill at work ($p = 0.58$).

Strong collinearity (correlation coefficients $\geq$ 0.70) was found between age and seniority, as well as between professional group and most of the occupational exposure variables (e.g., respiratory therapist and administration of aerosolized medications), raising an issue of quasi-complete case separation. Sex was strongly related with two of the professions (nursing and occupational therapy), with approximately 90% in each group being female. Some of the occupational exposures were also highly correlated (e.g., instrument cleaning and use of latex gloves, administration of aerosolized medications and use of latex gloves). For this reason, separate regression models were built for each class of occupational exposures.

In the univariate analyses (Table 2) for reported asthma, significantly elevated odds ratios were observed for age, sex, obesity, atopy, seniority, instrument cleaning, cleaning products used on building surfaces, use of powdered latex gloves between 1992 and 2000, administration of aerosolized medications, and application of adhesives/vapors/gases in patient care. Significant inverse associations were observed for use of adhesives on surfaces and miscellaneous use of adhesives/solvents/gases. BHR-related symptoms were significantly and positively associated with sex, obesity, atopy, exposure to a chemical spill at work, instrument cleaning, cleaning products used on building surfaces, use of powdered latex gloves in the 1992–2000 period, administration of aerosolized medications, and use of adhesives/solvents/gases in patient care. Age and miscellaneous use of adhesives/solvents/gases showed significant inverse associations. Smoking was not associated with either outcome.

Final multivariable models for each class of occupational exposures were adjusted for seniority (quartiles), race/ethnicity, obesity, and atopy (Table 3). For reported asthma, statistically significant associations were observed for instrument cleaning (OR, 2.22; 95% CI, 1.34–3.67), cleaning products used on building surfaces (OR, 2.02; 95% CI, 1.20–3.40), powdered latex glove use in the 1992–2000 period (OR, 2.17; 95% CI, 1.27–3.73), and administration of aerosolized medications (OR, 1.72; 95% CI, 1.05–2.83). A significant inverse association was found for miscellaneous use of adhesives/solvents/gases (OR, 0.53; 95% CI, 0.32–0.88). For BHR-related symptoms, significant associations were found for cleaning products used on building surfaces (OR, 1.63; 95% CI, 1.21–2.19), administration of aerosolized medications (OR, 1.40; 95% CI, 1.06–1.84), use of adhesives/solvents/gases in patient care (OR, 1.65; 95% CI, 1.22–2.24), and exposure to a chemical spill at work (OR, 2.02; 95% CI, 1.28–3.21). None of the tested interactions was significant. Model fit was good for all of the models (F-adjusted mean residual test, $p > 0.05$).

DISCUSSION

This study found an approximately twofold increased likelihood of asthma after entry into a health care profession for tasks involving instrument cleaning and disinfection, general cleaning products used on indoor building surfaces, use of powdered latex gloves, and the administration of aerosolized medications. Significant associations were likewise found between BHR-related symptoms and use of surface cleaners, aerosolized medication administration, adhesives, or solvents as products in patient care, as well as with a history of sustaining an acute exposure to a chemical or gas at work. Study findings are consistent with previously reported associations between asthma and occupational exposures in health care settings, and identify new relationships warranting further evaluation. The associations observed with a history of acute exposures to chemical spills or gas releases at work and with tasks involving use of respiratory irritants provide further support for irritant-induced asthma in this population.

This study has several strengths. By drawing its sample from the actual populations of four groups of HCWs, it provides more accurate estimates of the magnitude of work-related asthma in

TABLE 1. COMPARISON OF BASELINE DESCRIPTIVE STATISTICS BETWEEN THE ANALYTIC SAMPLE (ALL MISSING VALUES EXCLUDED) AND THE EXCLUDED SAMPLE (ONLY THOSE WITH MISSING VALUES)

Variable	Analytic Sample (no missing values) (*n* = *2,738*)	Excluded Sample (missing values) (*n* = *912*)	p Value*
Age, yr (mean ± SEM)	46.7 ± 0.32	51.0 ± 0.57	< 0.001
Sex, n (%)			< 0.001
Male	935 (24.6)	218 (16.4)	
Female	1,803 (75.4)	634 (83.6)	
Race/ethnicity, n (%)			0.02
Non-Hispanic white	1,983 (75.0)	514 (65.7)	
Hispanic	381 (11.7)	114 (13.2)	
Non-Hispanic black	143 (4.9)	54 (7.5)	
Other	231 (8.4)	85 (13.5)	
Atopy	447 (15.4)	129 (15.7)	0.51
Obesity (BMI ⩾ 30 kg/m^2), n (%)	584 (23.7)	159 (20.4)	0.26
Smoking, n (%)			
Nonsmokers	1,816 (66.3)	568 (65.8)	
Current smokers	264 (9.6)	69 (8.0)	0.203
Former smokers	658 (24.0)	226 (26.2)	
Seniority (quartiles), n (%)			
0–9 yr	689 (25.2)	157 (18.3)	
10–16 yr	706 (25.8)	218 (25.4)	< 0.001
17–26 yr	675 (24.7)	225 (26.2)	
⩾ 27 yr	668 (24.4)	258 (30.1)	
Profession, n (%)			
Physicians	682 (24.9)	180 (19.7)	
Occupational therapists	717 (26.2)	251 (27.5)	0.02
Nurses	695 (25.4)	246 (27.0)	
Respiratory therapists	644 (23.5)	235 (25.8)	
Reported asthma†, n (%)	145 (6.6)	53 (6.4)	0.55
BHR-related symptoms‡, n (%)	761 (27.4)	75 (25.2)	0.58

Definition of abbreviations: BHR = bronchial hyperresponsiveness; BMI = body mass index.

Total study population = 3,650.

* Comparison of analytic and excluded samples, based on Student's *t* test for continuous variables and chi-square test for categorical variables for sample survey data.

† Asthma diagnosed by a physician after entry into the health care profession.

‡ Eight-item predictor for BHR, PC_{20} ⩽ 4 mg/ml.

these workers. The use of an externally developed JEM to assign exposures reduces the chances of recall bias. In contrast, the use of self-reported exposures from questionnaires may lead to a differential bias (i.e., individuals with asthma and individuals without asthma may recall differently) (26, 27). When we compared our original JEM codings to self-reported exposures derived from the questionnaire in the full study population of 3,650 persons, individuals with asthma tended to show slightly greater agreement with the JEM than individuals without asthma for patient care–related cleaning, instrument cleaning, and administration of aerosolized medications; there was little difference with respect to latex glove use (data not shown). Our comparisons were not always on an identical category-by-category basis, however. For example, in the questionnaire, we asked about glutaraldehyde, but not about medical instrument cleaning as was the case for the JEM category.

The inventory of chemical products found in the hospital walk-throughs should be generalizable to other JCAHO-accredited hospitals in the United States, although it is less clear whether they can be extrapolated to hospitals outside the United States. JCAHO has uniform standards for infection control, including general cleaning/disinfection and instrument cleaning. Furthermore, we found that many of the chemical products overlapped, although the type of hospital was different. Although there could be some variation in the brand name products (e.g., for general cleaning and medical instrument cleaning) across the hospitals, the active ingredients used in these products were similar (e.g., quaternary ammonium compounds, bleach, citric-based cleaners, glutaraldehyde, paraffinic hydrocarbons). In recent years, JCAHO has also placed greater emphasis on employee protections, so policies and procedures such as those governing protective clothing, including gloves, tend to be similar across health care settings.

Among the study limitations, there were differences in sociodemographic and professional characteristics with the analytic sample, although none regarding any of the health-related or main occupational exposure variables. Because a response to all eight items was required to compute the BHR-related symptom, most of the missing values (n = 657, or 72%) were related to this variable. However, results using the full sample of 3,650 respondents (data not shown) remained essentially unchanged. Consequently, the magnitude of any bias is likely to have been small. On the other hand, restricting the analysis to a sample with no missing values allowed for the construction of more robust models as well as for better comparisons of the various associations found with the different models.

We were unable to distinguish between occupational asthma (i.e., *de novo* asthma caused by a workplace exposure) and work-aggravated asthma (i.e., preexisting asthma worsened by a workplace exposure) (5). However, the use of reported asthma (i.e., physician-diagnosed asthma with onset after entry into a health care profession) can be viewed as a surrogate for new-onset asthma, as has been done recently (8). Inclusion of both a "sensitive" symptom-based definition for BHR, a cardinal feature of asthma, and a more "specific" asthma definition based on physician diagnosis allowed a broader assessment of the spectrum of

TABLE 2. UNIVARIATE ANALYSIS BETWEEN INDEPENDENT VARIABLES, AS ASSESSED BY A JOB-EXPOSURE MATRIX, AND QUESTIONNAIRE FOR LONGEST HELD JOB AMONG TEXAS HEALTH CARE WORKERS, AND TWO ASTHMA OUTCOMES, WEIGHTED BY SURVEY SAMPLE SIZE IN THE ANALYTIC SAMPLE

	Reported Asthma*		BHR-related Symptoms†	
Variable	Odds Ratio (*95% CI*)	p Value	Odds Ratio (*95% CI*)	p Value
Sociodemographics				
Age (per 10-yr increments)	1.18 (1.00–1.38)	0.05	0.88 (0.79–0.98)	0.02
Sex (male)	1.00		1.00	
Female	2.31 (1.35–3.94)	0.002	2.28 (1.73–3.01)	< 0.001
Race/ethnicity (non-Hispanic white)	1.00	0.006‡	1.00	0.04‡
Hispanic	1.62 (0.86–3.04)		0.70 (0.46–1.07)	
Non-Hispanic black	0.20 (0.07–0.58)		1.23 (0.69–2.20)	
Other	1.13 (0.49–2.63)		0.56 (0.34–0.92)	
Obesity (BMI ⩾ 30 kg/m^2)	2.03 (1.23–3.34)	0.002	1.59 (1.18–2.13)	0.005
Smoking				
Nonsmokers	1.00		1.00	
Current smokers	1.16 (0.52–2.61)	0.75‡	0.95 (0.60–1.51)	0.86‡
Former smokers	1.22 (0.71–2.10)		1.08 (0.80–1.45)	
Atopy	3.31 (1.99–5.48)	< 0.001	8.80 (6.22–12.45)	< 0.001
Occupational exposures§				
Seniority (quartiles)				
0–9 yr	1.00	0.03‡	1.00	0.15‡
10–16 yr	2.08 (0.64–6.73)		0.67 (0.45–1.02)	
17–26 yr	3.37 (1.10–10.26)		0.78 (0.52–1.16)	
⩾ 27 yr	4.10 (1.39–12.11)		0.66 (0.45–0.96)	
Professional group (physicians)	1.00	0.02‡	1.00	< 0.001‡
Occupational therapists	1.06 (0.63–1.78)		2.32 (1.80–2.98)	
Nurses	1.89 (1.18–3.03)		1.95 (1.51–2.52)	
Respiratory therapists	1.30 (0.78–2.17)		2.01 (1.55–2.61)	
Spill at work	1.32 (0.58–2.99)	0.51	1.82 (1.16–2.85)	0.01
Cleaning agents				
Patient care	1.43 (0.19–10.81)	0.73	0.72 (0.29–1.75)	0.47
Instrument cleaning	2.07 (1.29–3.33)	0.003	1.40 (1.09–1.79)	0.01
Building surfaces	1.87 (1.14–3.05)	0.01	1.74 (1.34–2.26)	< 0.001
Latex gloves				
< 1992	1.84 (0.84–4.06)	0.13	1.02 (0.72–1.45)	0.91
1992–2000	1.94 (1.15–3.28)	0.01	1.36 (1.03–1.79)	0.03
> 2000	0.51 (0.16–1.65)	0.26	0.71 (0.42–1.21)	0.21
Aerosolized medications	1.66 (1.03–2.66)	0.04	1.57 (1.22–2.01)	< 0.001
Adhesives/solvents/gases				
Patient care	1.67 (1.01–2.77)	0.05	1.86 (1.42–2.44)	< 0.001
On surfaces	0.58 (0.36–0.93)	0.02	1.25 (0.98–1.59)	0.08
Miscellaneous/other	0.52 (0.32–0.84)	0.008	0.74 (0.57–0.95)	0.02

Definition of abbreviations: BHR = bronchial hyperresponsiveness; BMI = body mass index; CI = confidence interval.
Total n = 2,738 in the analytic sample.
* Self-reported history of physician-diagnosed asthma, with onset after entry into the health care profession.
† Eight-item predictor for BHR, PC_{20} ⩽ 4 mg/ml.
‡ Based on *F*-test for categorical variables for sample survey data.
§ All exposures as assessed by external job-exposure matrix (low or high probability of exposure), except seniority and spill at work, which were self-reported through questionnaire. Except where indicated, reference category for all exposure variables is the absence of such exposure.

asthma. The similar directionality of the point estimates for both asthma outcomes, with regard to the main associations found, suggests that these associations are real. Moreover, the associations tended to become stronger with reported asthma (i.e., the more specific outcome). Greater specificity might have been gained by applying the JEM to a period of time around which a participant was diagnosed with asthma. The cross-sectional study design, however, made this difficult to do. We did not obtain full lifetime job histories for all participants; instead, information was collected only on current and longest held jobs. Data on time period for these jobs were limited to start and end dates; in many cases, this encompassed several years, making it difficult to define a sufficiently narrow window of time around the date of diagnosis of asthma.

Among persons who had ever had a physician diagnosis of asthma, 70% also responded positively to BHR-related symptoms. In addition to the possibility of false negatives, the 30% of persons with asthma who did not report BHR-related symptoms could also represent persons with asthma who were either asymptomatic or under good medical control. The latter is particularly possible because many of the BHR-related symptom items referred to a more recent time frame of the previous 12 months. Among persons without a physician's diagnosis of asthma, 80% did not respond positively to BHR-related symptoms. In addition to false positives, the remaining 20% who had BHR-related symptoms could also represent individuals with respiratory symptoms not due to asthma, atopic persons, or as yet undiagnosed individuals with asthma.

A dose–response relationship was found between reported asthma and increasing seniority in the univariate analysis. This is not unexpected, because the chances of being diagnosed with asthma increase with both age and longer at-risk periods.

TABLE 3. ASSOCIATIONS BETWEEN OCCUPATIONAL EXPOSURES AND ASTHMA AMONG TEXAS HEALTH CARE WORKERS: FINAL MULTIVARIABLE LOGISTIC REGRESSION MODELS*

		Odds Ratio (*95% CI*)†	
Occupational Exposure	n (%)	Reported Asthma‡	BHR-related Symptoms§
Cleaning agents			
Used in patient care	2,705 (98.8)	1.60 (0.18–14.16)	0.79 (0.35–1.78)
Instrument cleaning	1,257 (45.9)	**2.22 (1.34–3.67)**	1.26 (0.95–1.67)
Surface cleaners	1,943 (71.0)	**2.02 (1.20–3.40)**	**1.63 (1.21–2.19)**
Latex			
Pre-1992	1,907 (69.7)	2.04 (0.87–4.75)	1.04 (0.72–1.51)
1992–2000	1,556 (56.8)	**2.17 (1.27–3.73)**	1.26 (0.93–1.72)
After 2000	88 (3.2)	0.42 (0.13–1.29)	0.61 (0.34–1.11)
Aerosolized medications	1,255 (45.8)	**1.72 (1.05–2.83)**	**1.40 (1.06–1.84)**
Adhesives/solvents/gases			
Used in patient care	1,921 (70.2)	1.68 (0.99–2.86)	**1.65 (1.22–2.24)**
On surfaces	581 (21.2)	0.59 (0.26–1.33)	0.98 (0.64–1.51)
Miscellaneous	869 (31.7)	**0.53 (0.32–0.88)**	0.78 (0.60–1.01)
Spill at work	163 (6.0)	1.23 (0.53–2.87)	**2.02 (1.28–3.21)**

Definition of abbreviations: BHR = bronchial hyperresponsiveness; CI = confidence interval.

Total n = 2,738 in the analytic sample. Values shown in boldface are statistically significant.

* Adjusted for seniority (quartiles), race/ethnicity, body mass index, and atopy; weighted survey samples.

† Goodness-of-fit, assessed through *F*-adjusted mean residual test for sample survey data, $p > 0.05$ for all models. Reference category for all exposure variables is the absence of such exposure.

‡ Self-reported history of physician-diagnosed asthma, with onset after entry into the health care profession.

§ Eight-item predictor for BHR, $PC_{20} \leq 4$ mg/ml.

However, this pattern was not observed with BHR-related symptoms. In fact, the highest quartile of seniority showed a significant inverse relationship between seniority and BHR-related symptoms. Seniority represented the total number of years devoted to a health care profession. This self-reported variable was therefore, to a certain extent, independent of the exposure classification by the JEM. It is possible that persons with a long seniority and reported asthma were no longer in a job that triggered their asthma symptoms and/or were under good therapeutic control.

Although cross-sectional studies are limited with regard to causal inference, this limitation was partly offset by use of the longest held, instead of current, job, which probably reduced the likelihood of persons with respiratory symptoms self-selecting themselves out of the respondent pool.

It is also unclear whether the results would be generalizable to other HCWs, in the United States or abroad. In many countries, respiratory and/or occupational therapy are not officially recognized professions; hence, their tasks are fulfilled by other HCWs. In this regard, the emphasis that this study placed on tasks rather than professional credentials should serve to make the findings more generalizable and relevant.

Since first described in the ECRHS, data linking asthma to general cleaning tasks have accumulated in both Europe and the United States (4, 11). Most of the reported increased risk, however, has been described in cleaners employed in non–health care industrial and private home settings (28, 29). Nevertheless, there is some limited evidence that cleaning in health care settings may pose a risk as well (29, 30), although these studies primarily focused on professional cleaners. There has been less evidence of such an association when HCWs themselves engage in general cleaning tasks. In a recent registry study, the most commonly reported exposure linked to asthma among HCWs were cleaning products, which accounted for 24% of all cases, including 21% of the cases reported among nurses (6). Both general (e.g., bleach, ammonia) and more specific (e.g., quaternary ammonium compounds) cleaning products have been linked to occupational asthma (31). These and other commercial product ingredients, known to be potential respiratory sensitizers and/or irritants, were identified in the walk-throughs conducted for the development of our JEM (Table 4). The associations between exposure to cleaning products and both reported asthma and BHR-related symptoms in this study, taken together with the existing literature on asthma and cleaners, and the biological plausibility of such an association, provide sufficiently strong evidence to warrant consideration of interventions. The high prevalence of exposure to general cleaning products in this population (71%) and the strength of the associations observed produce an estimated attributable fraction of 33%, which suggests the proportion of reported asthma that might potentially be avoided through control of these exposures.

Tasks associated with cleaning and/or disinfection of medical instruments were also associated with an increased prevalence of reported asthma. Glutaraldehyde, also identified in our walk-throughs, has been linked to occupational asthma in several reports (9, 32, 33), and its incidence may be increasing (34). Glutaraldehyde is especially useful for disinfecting heat-sensitive equipment, including fiberscopes, dialysis instruments, and surgical instruments; it is also used as a tissue fixative in pathology laboratories or for developing radiographs. Dimich-Ward and colleagues found a prevalence of 6.9% for reported asthma among respiratory therapists in British Columbia (8). Sterilization of instruments with glutaraldehyde was associated with increased odds of wheeze and reported asthma, findings consistent with ours. Because of concerns with glutaraldehyde, the NIOSH and OSHA recently recommended implementation of controls, including substitution with less toxic alternatives (35, 36). Subtilisins are bacterially derived enzymes used in detergents for their ability to remove stains and deposits. In the 1960s, exposure to subtilisins derived from *Bacillus subtilis* among detergent-manufacturing workers was found to cause sensitization and occupational asthma (37). However, subsequent product reformulations aimed at reducing subtilisin-containing aerosols, coupled with stringent recommended exposure levels, have generally been successful at controlling further cases of asthma, especially among detergent end-users (38). In our walk-throughs, we identified subtilisins as a component of some products used in medical instrument cleaning (Table 4). Although, to our knowledge, no cases of occupational asthma linked to these compounds

TABLE 4. PARTIAL LISTING OF PRODUCTS AND CHEMICALS USED FOR INSTRUMENT CLEANING, BUILDING SURFACE CLEANERS, AND ADHESIVES OR SOLVENTS USED FOR PATIENT CARE, IDENTIFIED THROUGH A SERIES OF HOUSTON AREA HOSPITAL WALK-THROUGHS IN 2002–2003

Instrument Cleaning/Disinfection	Building Surface Cleaners	Adhesives Used in Patient Care
Glutaraldehyde	Acetic acid/acetic acid anhydride	Adhesive removers
Isopropanol	Ammonia/ammonium hydroxide	Acetone
Orthophthaldehyde	Bleach	Dipropylene glycol methyl ether
Sodium sesquicarbonate	Butyl paraben, ethyl paraben, methyl paraben	Ethanol
Subtilisins (enzymatic cleaners)	Diethanolamine	Isoparaffinic hydrocarbons
	Diethylene-glycol n-butyl ether	Isopropanol
	Hydrochloric acid	Stoma care products
	Isoparaffinic hydrocarbons	Carboxymethyl ether
	Phosphoric acid	Hexane-based skin bond
	Quaternary ammonium compounds	Methylbenzene
	Sodium sulfate	Other
	Sulfuric acid	Methylene chloride
		Trichloroethane

have been reported in HCWs, this finding may warrant further research.

Powdered latex glove use is a well-established cause of occupational asthma in HCWs (10, 34, 39). However, this study adds important information to the body of literature. In addition to the finding of a twofold increase in risk of reported asthma, the time period of this statistically significant elevated risk was restricted to 1992–2000. Although the magnitude in the odds ratios for the pre-1992 and 1992–2000 periods were similar, the former had wide confidence intervals and was not statistically significant. This is consistent with events in the 1990s that resulted in an initial increase, and subsequent decrease, in the use of powdered latex gloves. Passage of the 1992 OSHA bloodborne pathogens standard mandated the implementation of universal precautions when handling hazardous body fluids. This was promptly followed by a marked increase in use of personal protective equipment in health care settings, including latex gloves (40). In 1997, in response to increasing reports of latex allergic reactions, NIOSH issued an alert calling for a reduction in undue use of powdered latex gloves (41). Subsequently, although overall sales in the United States have continued to increase, the total protein and powder content in gloves has decreased markedly (40). Findings from this study point to an encouraging reduction in risk after 2000. They also strengthen recent, generally single-site, reports indicating the effectiveness of substitution of powdered latex gloves by low-latex alternatives and other control measures (42, 43). For the remaining JEM exposure categories, use of similar classification by calendar periods was not possible. In contrast to powdered latex gloves, which represent a "single" product, the other categories (cleaning agents, aerosolized medications, and adhesives) included a number of different compounds, not all of which may have changed over time.

We also found an increased risk of both reported asthma and BHR-related symptoms associated with administration of aerosolized medications, consistent with previous studies conducted mostly among respiratory therapists. The most commonly cited agents have been aerosolized pentamidine and ribavirin (8, 44, 45). However, administration of aerosolized medications is not limited to respiratory therapists, as this task may also be performed by nurses and, less often, by physicians. This is particularly true in countries where the profession of respiratory therapist does not exist, and these duties are assumed by other workers. Given the previous literature and findings from this study, the estimated attributable fraction of preventable asthma or asthma symptoms in this worker population would range from 7 to 14%.

A new association was found between BHR-related symptoms and tasks involving application of adhesives, adhesive removers, and solvents or similar products on patients. The odds ratio was elevated to a similar degree for reported asthma, but was marginally not significant. Such compounds are commonly used for application and/or removal of dressings and adhesive bandages or in stoma care. The walk-throughs identified several potential respiratory irritants among the compounds used for these purposes (Table 4). Many have noticeably strong odors; some are solvents and may be linked more to transient respiratory symptoms than actual asthma. In a study by Pechter and colleagues, exposure to solvents accounted for 7% of reported work-related asthma; 29% of "aides/therapists" with asthma identified miscellaneous chemicals (including glues and solvents) associated with their asthma (6). At present, though, evidence of a causal link should be considered speculative. A single, statistically significant inverse association was also observed between reported asthma and exposure to a miscellaneous category of adhesives, adhesive removers, solvents, or gases/vapors. Compounds in this category were few, generally unrelated, and with relatively little detail to allow further examination. The reason for this association, therefore, is unclear pending further confirmation, and may well be spurious.

Although most occupational asthma is believed to be allergic in origin (5), evidence is accumulating that irritant-induced asthma may be more common than previously thought. The European literature on asthma in cleaners suggests that a large proportion of cases are related to exposure to chemical irritants (46). Among physician reports of work-related asthma in California, over 50% of cases were associated with agents not known to be allergens (28). Typically, irritant-induced asthma is characterized by overexposure to an established respiratory irritant, with no latency between exposure and development of asthma symptoms. In its best-known presentation, reactive airways dysfunction syndrome (RADS), the inciting event is a single, one-time intense exposure, such as a chemical spill or gas release (47). This has also been described in HCWs, after an acute overexposure to glacial acetic acid (48). An alternative presentation is a series of short-term overexposures to respiratory irritants occurring over days to a few weeks (49). It is less clear whether chronic low-level exposure to irritants can lead to asthma (5), although it is well established that airborne irritants can trigger asthma exacerbations (50). In this study, we found an increased association between having sustained an acute exposure to a chemical spill or gas release at work and BHR-related symptoms, but not with reported asthma. Because the 8-item predictor for BHR-related symptoms emphasized recent (i.e., current and/or within past 12 mo) asthma symptoms, it is not possible to distinguish causation from aggravation or nonspecific triggering of symptoms, although the finding is certainly suggestive of an underlying irritant mechanism. Future studies should explore in greater detail both the nature of these acute exposures as well as their relationship to onset of asthma in HCWs.

Health care–related occupations represent 50% of the top 30 fastest growing occupations in the United States, and all four professional groups included in this study are expected to grow by more than 20% by 2012 (14). Health care settings present an opportunity for exposure to several respiratory irritants and sensitizers, and our findings indicate that the contribution of occupational exposures to asthma in HCWs is not trivial. For previously described associations confirmed by this study, the evidence is sufficiently strong to justify moving from descriptive studies to the implementation and evaluation of appropriate controls. For newly described findings, additional, more focused confirmatory studies appear to be warranted.

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