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Validated Asthma Questionnaire for Healthcare Workers

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LIST OF ABBREVIATIONS

BHR- bronchial hyperresponsiveness

HCW – healthcare workers

· NOES - National Occupational Exposure Survey

JEM - Job-Exposure Matrix

MSDS – Material Safety and Data Sheet

ECRHS – European Community Respiratory Health Study

ABSTRACT

Recent U.S. data suggest an increased risk of work-related asthma among healthcare workers. However, results have been inconsistent and lacking in detail. To assess the magnitude of asthma risk, evaluate associations with occupational exposures, and estimate the burden of work-related asthma in healthcare professionals, a new survey instrument for work-related asthma among health care workers was developed, validated and administered in a field study. The project was conducted in two separate and consecutive phases. In Phase I, the survey instrument was developed, validated and refined. In Phase II the validated questionnaire was administered to a population-based sample of selected groups of health care workers in Texas.

Phase I resulted in an eleven page questionnaire which required approximately 13 to 25 minutes to complete. Test-retest reliability of asthma and allergy items ranged from 75% to 94%, and internal consistency for these items was excellent (Cronbach's $\alpha \geq 0.86$). Against methacholine challenge, an 8-item combination of asthma symptom items had a sensitivity of 72% and specificity of 71%; against a physician diagnosis of asthma, this same combination showed a sensitivity of 89% and specificity of 98%.

In Phase II, using the questionnaire validated in Phase I, a cross-sectional statewide survey of 5600 Texas healthcare professionals (physicians, nurses, respiratory therapists and occupational therapists) was conducted. A simple random sample of 1400 persons was drawn from each of the four populations of professionals (physicians, nurses, respiratory therapists and occupational therapists) with active licenses in 2003. Information on asthma symptoms and nonoccupational asthma risk factors obtained from the survey was then linked to occupational exposures derived from an external asthma risk factor job-exposure matrix (also developed for this study). Overall response rate was 66%. The final study population consisted of 862 physicians, 941 nurses, 968 occupational therapists and 879 respiratory therapists (n=3650).

There were two *a priori* defined outcomes: a) physician-diagnosed asthma with onset after entry into healthcare ('reported asthma'), and b) 'bronchial hyperresponsiveness-related symptoms', defined through the 8-item symptom-based predictor.

Reported asthma was associated with medical instrument cleaning (OR, 2.22; 95% CI, 1.34-3.67), general cleaning (OR, 2.02; 95% CI, 1.20-3.40), use of powdered latex gloves between the years 1992 and 2000 (OR, 2.17; 95% CI, 1.27 to 3.73) and administration of aerosolized medications (OR, 1.72; 95% CI, 1.05 to 2.83). The risk associated with latex gloves disappeared 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). Occupational exposures contribute importantly to asthma in healthcare professionals, meriting both further study and implementation of appropriate controls.

HIGHLIGHTS/SIGNIFICANT FINDINGS

Phase II of this study found an approximate two-fold increased likelihood of asthma after entry into a healthcare 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. The association between powdered latex glove use and asthma disappeared with exposures occurring after the year 2000, suggesting that current workplace controls are having a positive effect. For previously described

associations confirmed in this study, the evidence is sufficiently strong to justify moving from descriptive studies to the implantation and evaluation of appropriate controls. For newly described findings, additional, more focused studies appear to be warranted.

Phase I of the study produced a new survey instrument for the study of asthma in healthcare worker groups

Phase II of the study produced a new asthma risk factor job-exposure matrix, specific to healthcare settings.

TRANSLATION OF FINDINGS

In Phase II, while causation could not be confirmed because of the cross-sectional nature of the study, the strong association between exposure to cleaning products and both reported asthma and BHR-related symptoms, taken together with the existing literature on asthma and cleaners, and the biological plausibility of such an association, lend support to the finding that there is an association of asthma in HCW exposed to cleaning activities. 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 provides an idea of the proportion of new asthma cases that might potentially be avoided through control of these exposures.

While powdered latex glove use is well established as a leading cause of occupational asthma in HCWs, this study adds important information to the body of literature. Because the time period of the two-fold increase in risk of reported asthma was restricted to 1992-2000, the findings from this study point to an encouraging reduction in risk after 2000, at least on a statewide level. This strengthens recent reports indicating the effectiveness of substitution of powdered latex gloves by low latex alternatives and other control measures.

A new association identified in this study concerns the increased risk of BHR-related symptoms and tasks involving application of adhesives, adhesive removers, solvents or similar products on patients. At present, evidence of a causal link should be considered speculative. However, given the high prevalence of exposure to these compounds (70%) and the strength of the associations, further research appears to be justified.

OUTCOMES/RELEVANCE/IMPACT

Healthcare-related occupations represent 50% of the top 30 fastest growing occupations in the U.S., and all four professional groups included in this study are expected to grow by more than 20% by 2012. Healthcare 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. Given the previous literature on established asthma risk factors (cleaning products, latex and aerosolized medications) and findings from Phase II, the estimated attributable fraction of preventable asthma or asthma symptoms in this worker population is estimated to range from could range from 7% to 33%.

SCIENTIFIC REPORT

Background

It is well established that certain occupational groups are at increased risk of developing asthma, including Western red cedar workers¹, isocyanate chemical workers², construction workers³, and farmers⁴. 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

healthcare 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, following 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 healthcare settings go beyond latex, and may include disinfectants and sterilants (e.g., glutaraldehyde, formaldehyde), pharmaceuticals (e.g., psyllium, antibiotics), sensitizing metals (e.g., dental alloys), methacrylates, irritant aerosolized medications (e.g., pentamidine and ribavirin) and cleaning products^{5,6}.

Previous reports from various countries have reported cases of work-related asthma among specific groups of HCWs, including physicians^{7,8}, pharmaceutical workers⁹, research animal handlers¹⁰, respiratory therapists^{11,12}, workers in endoscopy units and radiology departments¹³, Belgian nurses¹⁴, and general healthcare workers¹⁵. Confirmation and estimation of risk, however, in population-based studies has been more problematic. In the large European Community Respiratory Health Study (ECRHS), significant excesses among healthcare professionals were not consistently observed⁴. In the U.S. National Health and Examination Survey III, conducted between 1988 and 1994, the odds for either work-related asthma or wheezing in health-related industries and occupations were not significantly increased^{16,17}. Data from the 2001 National Health Interview Survey did find significantly increased odds for physician-diagnosed asthma in the U.S. healthcare industry, but this excess was limited to white females¹⁸. 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 healthcare services^{19,20}.

Thus, results are inconsistent, and few studies have been conducted in HCW populations that allow a better estimation of the prevalence and burden of work-related asthma in healthcare settings or a more detailed characterization of potential associations between asthma and various workplace exposures. Studies that address these remaining issues are particularly important when one considers that HCWs comprise approximately 8% of the U.S. workforce, and constitute one of the fastest growing sectors of the workforce²¹.

Study Objectives

The original specific aims were:

1. To develop, validate and conduct test-retest reliability of a new survey instrument of work-related asthma, for use in healthcare settings in a convenience sample of healthcare workers with and without asthma.
2. To adapt, refine, update and validate a previously developed National Occupational Exposure Survey (NOES)-based Job-Exposure Matrix (JEM) for use in the health services industry, to reflect exposures to known and suspected asthmagens.
3. To field test the new survey instrument in a population-based sample of four occupational groups of health care workers (HCWs): physicians, nurses, respiratory therapists and occupational therapists.
4. To estimate and compare the prevalence of work-related asthma in these four occupational groups.
5. To analyze associations between occupational and non-occupational exposures among health care workers with and without asthma in these four groups.

6. To estimate and compare the attributable risk of work-related asthma in these four occupational groups.

All study objectives were achieved for this project.

Procedures and Methods

The study was conducted in two separate and consecutive phases.

Phase I

Year One of the funding period was successfully initiated in October 2001. Project personnel, including a project coordinator, were hired immediately and project tasks began on schedule.

A subset of a generic job-exposure matrix developed with data from the NOES, limited to the health services industry, was combined with a list of 367 asthmagens, cross-referenced on NOES hazard codes²²⁻²⁴, to produce an initial health services-specific JEM for known and suspected asthmagens. This JEM was then updated, based on findings from a series of hospital walk-through surveys conducted in December 2001 by the industrial hygienists and occupational physicians on the research team in three Houston hospitals (a 350 bed, 3200 employee pediatric hospital; a 450 bed, 10000 employee cancer hospital and a 1200 bed, 4600 employee tertiary referral and general hospital). Potential chemical asthmagens identified through the walkthrough surveys and MSDS reviews were then compared to the health services-specific JEM, and newly identified agents were added to update that JEM. This information was combined and streamlined, leading to a final list of potential asthmagens that were incorporated into the questionnaire instrument, in order to assess self-reported exposures. In Phase II, final development and coding were completed for this JEM.

Development of the study instrument (questionnaire) began on schedule and was finalized in January 2002. In brief, the questionnaire was designed to be self-completed in under 30 minutes and consisted of 43 main questions grouped into four sections: a) asthma and asthma symptoms; b) occupational exposures and job history; c) non-occupational exposures and asthma risk factors; and d) demographics. The survey was developed by a multidisciplinary team that included industrial hygienists, occupational/pulmonary physicians, epidemiologists and survey design experts. Questionnaire items in the asthma section were originally derived from the International Union Against Tuberculosis and Lung Diseases (IUATLD) bronchial symptom questionnaire²⁵, and supplemented with questions on physician-diagnosed asthma, age or year of asthma diagnosis, and questions regarding work absences due to asthma or asthma symptoms. The occupational exposure section focused on self-reported job titles, current and longest jobs held, duration and frequency of exposure to a list of specific chemicals and a history of exposure to accidental chemical spills or gas releases. Two separate chemical lists were included: a) a list of 28 chemical agents, collapsed through factor analysis into 5 major groups ('cleaning agents', 'sterilizing agents', 'anesthetics/nebulized medications', 'strong odors' and 'miscellaneous') for which respondents were asked to indicate any exposure of at least one occasion per month for 6 months or longer, and b) a separate set of questions regarding frequency of exposure (never, at least once a month, at least once a week, every day or more than once a day) to six general classes of agents (disinfectant/sterilants, cleaning agents, latex products, aerosolized medications, adhesives/removers/glues, and gases/vapors). The nonoccupational asthma risk factors section of the questionnaire contained questions on common environmental allergies, family history of atopy and asthma, household pets, smoking habits, residential housing characteristics and recreational exposures.

Recruitment of study subjects for Phase I was initiated in January 2002. Each study subject participated in a testing session that consisted of completing the questionnaire, participating in an interview with an industrial hygienist, completion of a methacholine bronchial challenge and providing a sample of blood for allergy testing. Testing sessions began in February 2002 and were completed by August 2002. Data collection and entry were completed in August 2002, and analysis to validate and further refine the questionnaire began in preparation for Phase II of the project.

Phase II

Phase II was initiated in February 2004 by mailing 5600 survey booklets to four groups of health professionals in Texas: physicians, nurses, respiratory therapists and occupational therapists (1400 per group). The physician group was later oversampled, given previous evidence in the literature of low response rates to postal surveys in this professional group.; an additional 227 physicians were selected to receive survey booklets. Following the approaches of Dillman²⁶, Salant and Dillman²⁷ and Dillman²⁸ a total of five contacts were made to potential study participants. Approximately one week after mailing an initial “warm contact” letter, each participant received the questionnaire by mail, with a stamped returned envelope and a \$1 token incentive. Participants were given the choice of responding to the hard copy questionnaire or online via a web-based copy of the same questionnaire. One week later a follow-up post card was sent, thanking those who had returned the survey and politely requesting a response from nonresponders. Three weeks after the first questionnaire mailing, a new personalized letter along with a second copy of questionnaire and stamped returned envelope were sent to nonresponders. A final letter was sent approximately 5 weeks after the second questionnaire mailing. Data entry and cleaning were completed in August 2004 and analysis of the data began.

Separate from the mailings, work was also undertaken to complete development of the asthma risk factor-specific JEM for healthcare workers. The final matrix structure featured two axes: a) a job axis, subclassifying professional job titles (nurse, physician, etc.) by main practice setting (hospital, outpatient clinic, nursing home, etc.) and b) 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 non-patient 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 standard²⁹: pre-1992, 1992 to 2000 and post-2000. Five experts (one occupational physician, three 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 no exposure; a '1' or a '2' were 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 a HCW, based on the job title and practice setting reported for that job. 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 groups³⁰. Sensitizing metals were excluded because of a very small number of cells coded as exposed. JEM codes for longest held job were used since the majority (~60%) of respondents indicated that their current job was also their longest held job. An additional dichotomous occupational exposure variable, related to

having ever been involved in a chemical spill or gas release at work, was derived from the questionnaire.

Potential covariates from the questionnaire were age, gender, race/ethnicity, professional group, years as a health professional ('seniority'), smoking and obesity (BMI, or body mass index ≥ 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%).

Two separate dichotomous outcome variables were defined: a) physician-diagnosed asthma with onset after entry into the healthcare profession ('reported asthma'), and b) 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 healthcare professional (including years spent as a student in the field). The presence of BHR-related symptoms were determined based on the 8-item, symptom-based, predictor of $PC_{20} \leq 4$ mg/ml for methacholine developed in the validation study. 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.

Statistical Analysis (Phase II)

To account for the sampling design, poststratification weighting was performed to obtain estimates of both counts and prevalences that were representative of the actual population sizes for each of the four professional groups. After examining descriptive statistics, univariate logistic regression analyses were performed between independent variables and each of the two asthma outcomes. Regression analyses were performed on an analytic subsample that excluded

anyone with missing values for any of the independent or dependent variables. After evaluating collinearity, variables with a $p < 0.25$ in the univariate analysis were then entered into unconditional multiple logistic regression models for each outcome. Interactions between atopy and occupational exposure, based on clinical plausibility, were explored. Associations were expressed as the adjusted logistic odds ratio (OR) and 95% confidence interval (95% CI). Model goodness-of-fit was assessed as recommended by Archer and Lemeshow for survey sample data³¹. All statistical analyses were performed using STATA SE version 9 (Stata Corporation, College Station, TX).

Results

Phase I

The final study population (including an initial pilot phase of 16 persons) consisted of 118 nonsmoking subjects, who also underwent bronchial challenge testing, an interview with an industrial hygienist and measurement of specific IgE antibodies to common aeroallergens.

In the questionnaire validation study, we found that test-retest reliability ranged from 75% to 94%; internal consistency for items in the asthma and allergy sections was excellent (Cronbach's $\alpha \geq 0.86$). An 8-item combination of asthma symptoms had a sensitivity of 71% and specificity of 70% for prediction of bronchial hyperresponsiveness ($PC_{20} \leq 8 \text{ mg/ml}$) (61% and 85% for $PC_{20} \leq 4 \text{ mg/ml}$, respectively), and against a physician diagnosis of asthma, this same combination showed a sensitivity of 79% and specificity of 98%. Agreement between self-reported exposures and industrial hygienist review was moderate and similar to previous studies, with kappa scores for the final classes of agents, job titles and practice settings ranging from 0.41 to 0.67. For measurement of atopy, the best combinations of sensitivity (68%) and specificity (85%), when compared to specific serum IgE antibody titers to common aeroallergens, were

obtained for a history of allergies to dust, dust mite and animals. The results of this first phase were presented at the 2003 NORA Symposium in Arlington, Virginia; the manuscript was published in *Occupational and Environmental Medicine* March 2006. Another manuscript, entitled “A comparative study of three classification procedures: asthma among healthcare professionals in Texas” is under review with the *Journal of Applied Statistics*. A third manuscript, entitled “Mail versus Internet-based surveys of health professionals: a comparison of responder profiles” has also been drafted for submission to a journal on survey research. A copy of the final survey questionnaire is attached as Appendix A.

Phase II

From the initial 5600 mailed questionnaires, 213 participants were excluded due to death (7) and incorrect addresses (206), leaving a final eligible population of 5387. Surveys were received from 3529 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 3650.

Prevalence of reported asthma was 4.2% for physicians, 7.3% for nurses, 5.6% for respiratory therapists and 4.5% for occupational therapists. The prevalence of BHR-related symptoms varied by individual professional group: physicians–18.0%, nurses–29.2%, respiratory therapists–30.3% and occupational therapists–33.7%. 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 total study population (n=3650), the final analytic sample (n= 2738) and the excluded sample (n=912). As compared to the analytic

sample, the excluded sample 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, reported asthma or BHR-related symptoms.

Strong collinearity (correlation coefficients ≥ 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. Gender was strongly related with two of the professions (nursing and occupational therapy), with approximately 90% in each group being female. In addition, 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 analysis (Tables 2), for reported asthma, significantly elevated odds ratios were observed for age, gender, race/ethnicity, 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 female gender, race/ethnicity, 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. Significant inverse

associations were found for age and miscellaneous use of adhesives/solvents/gases. Smoking was not associated with either outcome.

Table 3 summarizes the final multivariate models for each class of occupational exposures, adjusted for seniority (quartiles), race/ethnicity, obesity and atopy. For reported asthma, statistically significant associations were observed for instrument cleaning (OR, 2.22; 95% CI, 1.34 to 3.67), cleaning products used on building surfaces (OR, 2.02; 95% CI, 1.20 to 3.40), use of powdered latex gloves in the 1992-2000 period (OR, 2.17; 95% CI, 1.27 to 3.73) and administration of aerosolized medications (OR, 1.72; 95% CI, 1.05 to 2.83). Although the odds for an association between reported asthma and use of adhesives/solvents/gases in patient care were elevated (OR, 1.68), the confidence interval included the null (95% CI, 0.99-2.86). 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 to 2.19), administration of aerosolized medications (OR, 1.40; 95% CI, 1.06 to 1.84), use of adhesives/solvents/gases in patient care (OR, 1.65; 95% CI, 1.22 to 2.24) and exposure to a chemical spill at work (OR, 2.02; 95% CI, 1.28 to 3.21). None of the first-order interaction terms were significantly associated with either of the two asthma outcome variables. Model fit was good for all of the models (F-adjusted mean residual test, $p > 0.05$).

A manuscript on the results of Phase II is being submitted to the *Journal of the American Medical Association*.

Discussion

Phase I

It is well recognized that questionnaire-based definitions of asthma may not necessarily correspond to the clinical definition of asthma, and that there is no universally accepted “gold standard” definition of asthma for use in epidemiology studies³². Prior validation studies of asthma questionnaires have generally relied on comparison of questionnaire items on asthma and asthma-like symptoms to putative gold standards, including physiologic measures of nonspecific bronchial hyperresponsiveness, previously validated questionnaires or physician-diagnosed asthma³³⁻³⁵. Depending on the standard used, as well as on the nature of the questionnaire items, sensitivity and specificity have varied.

The Phase I validation study used an approach that compared the performance of the asthma section of the questionnaire to all three of these standards (PC20, MD asthma and the previously validated DFP). The sensitivity of 79% and specificity of 98% found with our 8-item predictor (94% of cases correctly classified), compares favorably with prior studies, supporting its suitability for use in future asthma epidemiology studies. The combination of several symptom-based questions to define asthma has been found to perform better, and is less conducive to misclassification, than reliance on a single question or questions that include the term “asthma”³².

Certain limitations of the Phase I study should be noted. An important limitation of many occupational asthma surveys is the inability to distinguish between pre-existing asthma and work-related asthma. Although not specifically validated in this study, this questionnaire also includes items regarding time of asthma onset (relative to entry into the healthcare profession), worsening of asthma and/or respiratory symptoms with work, amelioration when away from work and work absences due to asthma and/or respiratory symptoms. Combining these questions

with the validated asthma and bronchial hyperresponsiveness predictors should allow a better approximation to these asthma-workplace relationships. Although methacholine challenge testing was selected as the “gold standard” for asthma, it is well known that airway hyperresponsiveness is present in a certain proportion of asymptomatic persons without asthma, which could affect the specificity of certain questionnaire items³⁶⁻³⁷. In this regard, the 8-item predictor is more likely to represent bronchial hyperresponsiveness. Use of more than one “gold standard” for the definition of asthma in this study probably offset this effect, by providing a range of sensitivity and specificity values for the 8-item predictor that may allow a broader characterization of susceptible subgroups. A similar issue arises for the RAST antibody panel, where some asymptomatic persons may have significantly elevated titers of these antibodies³⁸. However, the good specificity (86%) shown by the questionnaire items for allergens known to be strongly related to asthma (dust mite and animals) suggests that this effect was small.

In summary, initial evaluation of the performance of this new questionnaire for the evaluation of asthma in healthcare workers indicated good validity and reliability for the detection of asthma and for the characterization of nonoccupational exposures and other asthma risk factors.

Phase II

The Phase II study found an approximate two-fold increased likelihood of asthma after entry into a healthcare 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 healthcare settings, and identify new relationships warranting further evaluation.

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 these workers. Use of an externally developed job-exposure matrix to assign exposures minimizes the chances of recall bias. 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.

There are also limitations to this study. It is possible that nonresponders may have differed from responders. Available descriptive information from the licensing boards was limited and varied across the four professional groups. As compared to physician nonresponders, physician responders were more likely to be female (25% versus 19%), older (52 versus 50 years of age), non-Hispanic white (73% versus 65%) and less engaged in direct patient care (81% versus 86%). For nurses, information was only available on general practice characteristics; there were no differences with respect to the proportion involved in direct patient care. Distribution of residence zip codes for both occupational and respiratory therapists showed no significant differences. There were also differences in sociodemographic and professional characteristics between the subsample used for the regression analyses and those excluded because of missing values, although not with respect to health-related variables. Since a response to all 8 questions was required in order to compute the BHR-related symptom, most of the missing values (n=657) were related to this variable. Because of this, it is possible that some of the risk estimates were biased. To examine this issue, we repeated the multivariate analyses using the full sample of 3650 respondents. For each significant association found using the

reduced analytic sample, with reported asthma as the outcome, the analysis with the full data set showed either no change or a slightly lower odds ratio, but all associations remained statistically significant. For BHR-related symptoms the odds ratios 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.

A recognized methodological limitation of many epidemiological studies and surveillance schemes is their inability to distinguish between occupational asthma (i.e., *de novo* asthma caused by a workplace exposure) and work-aggravated asthma (i.e., pre-existing asthma worsened by a workplace exposure)^{39,40}. However, the use of reported asthma (i.e., physician-diagnosed asthma with onset after entry into a healthcare profession) can be viewed as a surrogate for new-onset asthma, as has been done recently^{41,42}. In addition, inclusion of both a “sensitive” symptom-based definition for bronchial hyperresponsiveness, a cardinal feature of asthma, and a more “specific” asthma definition based on physician diagnosis, allows a broader assessment of the spectrum of asthma. The similar directionality of the point estimates for both asthma outcomes, with regard to the main associations found with cleaning tasks, use of powdered latex gloves, administration of aerosolized medications and adhesives or solvents used for patient care suggests that these associations are real. Furthermore, in all of these cases, the odds ratios tended to become stronger with reported asthma, i.e., the more specific outcome. As with any cross-sectional study, causal inferences cannot be made with certainty given the concomitant measurement of exposure and disease and the susceptibility of these studies to the healthy worker effect. However, these limitations were at least partially offset by use of a JEM, and its application to longest held, instead of current, job probably reduced the likelihood of

persons with respiratory symptoms self-selecting themselves out of the respondent pool. Finally, although findings from this study should be generalizable to other physicians, nurses, respiratory therapists and occupational therapists in the U.S., it is less clear whether this is the case for other U.S. healthcare professionals or for similar professionals in other countries. In many countries, respiratory therapy and/or occupational therapy are not officially recognized professional career tracks; 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.

Since first described in the ECRHS, data linking asthma to general cleaning tasks has accumulated in both Europe and the U.S.⁴³⁻⁴⁵. Most of the reported increased risk, however, has been described in cleaners employed in industrial and, especially, private home settings⁴⁶⁻⁴⁸. Nevertheless, there is some limited evidence that cleaning in healthcare settings may pose a risk as well^{49,50}. These studies, however, primarily focused on professional cleaners. There has been less evidence of such an association when healthcare professionals themselves engage in general cleaning tasks. In the registry study conducted by Pechter and colleagues, 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 nurses⁵⁰. Among the products identified in their study were commonly used general cleaners (e.g., bleach, ammonia), as well as other compounds more specific to healthcare settings (e.g., quaternary ammonium compounds) that have been linked to occupational asthma⁵¹. These and several other commercial product ingredients, known to be potential respiratory sensitizers and/or irritants, were identified in the walkthroughs conducted as part of the development of the JEM in this study (Table 4). Although causation cannot be confirmed, the strong association between exposure to cleaning products and both reported asthma and BHR-related symptoms, taken together with the existing literature on

asthma and cleaners, and the biological plausibility of such an association, lends support to it. 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 provides an idea of the proportion of new asthma cases 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 risk of reported asthma. One of the most widely used cold liquid high-level disinfectants, glutaraldehyde, also identified in our hospital walkthroughs, has been linked to development of occupational asthma in several reports⁵²⁻⁵⁷, and its incidence may be increasing. In the United Kingdom, a doubling of the incidence rate of occupational asthma between the period 1989-1991 and 1992-1997 was accompanied by an increase in the number of cases attributed to glutaraldehyde and latex⁵⁷. Glutaraldehyde is especially useful for disinfecting heat-sensitive equipment, including fiberoptic endoscopes, dialysis instruments and surgical instruments; it may also be used as a tissue fixative in pathology laboratories or in developing radiographs. Dimich-Ward and colleagues found a prevalence of 6.9% for reported asthma among respiratory therapists (n=275) in British Columbia, slightly higher than in our population⁴². Sterilization of instruments with glutaraldehyde was associated with 2- and 3-fold increased odds of wheeze and reported asthma, respectively, in their study. Results from our study are consistent with these findings. More recently, controls have been recommended by NIOSH and OSHA out of concern for the toxicity of glutaraldehyde^{58,59}. In addition to enclosing the disinfection process and use of personal protective equipment, substitution of glutaraldehyde with alternative chemicals such as hydrogen peroxide-, peracetic acid-, and orthophthalaldehyde-based products is being encouraged. Orthophthalaldehyde may have similar respiratory irritative effects as glutaraldehyde, but has a lower vapor pressure and is

typically used in lower concentrations. 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 asthma⁶⁰. 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^{61,62}. In our walkthroughs, 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 have been reported in HCWs, this may warrant further research, given our findings.

Powdered latex glove use is well established as a leading cause of occupational asthma in HCWs^{14,15,54}. However, this study adds important information to the body of literature. In addition to the finding of a two-fold increase in risk of reported asthma, the time period of this risk was restricted to 1992-2000. 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 healthcare settings, including latex gloves⁶³. In 1997, in response to increasing reports of latex allergic reactions, NIOSH issued an alert calling for a reduction in undue use of latex gloves, to be balanced against their protective qualities⁶⁴. Findings from this study point to an encouraging reduction in risk after 2000, at least on a statewide level. 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^{65,66}. Based on our findings, we estimate that the fraction of reported asthma attributable to use of powdered latex gloves in the 1992 to 2000 period would be around 12%.

We also found an increased risk of both reported asthma and BHR-related symptoms associated with administration of aerosolized medications, consistent with previous studies, mainly conducted among respiratory therapists. Typically, the agents most often studied have been aerosolized pentamidine and ribavirin⁶⁷⁻⁶⁹. 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. In the study by Dimich-Ward, administration of aerosolized ribavirin was associated with a greater than 2-fold risk of both having an asthma attack and of reported asthma⁴². Administration of aerosolized medications via a tent or hood was also a risk factor for both of these asthma outcomes. Although our study, conducted in a larger sample, did not gather specific information on methods of aerosol delivery or types of medications administered, its results are consistent with these findings. 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 identified in this study concerns the increased risk of BHR-related symptoms and tasks involving application of adhesives, adhesive removers, solvents or similar products on patients. The odds ratio was elevated to a similar degree for reported asthma, but was marginally not significant. These compounds are commonly used for application and/or removal of dressings, adhesive bandages or in stoma care. The walkthroughs 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 the 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) with their asthma⁵⁰. At present, evidence of a causal link should be considered speculative. However, given the high prevalence of exposure to these compounds (70%) and the strength of the associations, further research appears to be justified. Finally, an inverse association was found between reported asthma and the miscellaneous category of adhesives/gases/solvents, which we were unable to explain. A review of the chemical compounds identified in the walkthrough that were subsequently classified into this category included only mercury and methanol, which under normal use conditions are not notable respiratory irritants or sensitizers. It is, therefore, possible that this was a spurious association.

Although most occupational asthma is felt to be allergic in origin², evidence is accumulating that irritant-induced asthma may be more common than previously thought. Thus, the European literature on asthma in cleaners suggests that a large proportion of cases are related to exposure to chemical irritants⁷⁰. Among physician reports of work-related asthma in California, over 50% of cases were associated with agents not known to be allergens⁴⁷. Typically, irritant-induced asthma is characterized by exposure 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 exposure is typically a single, one-time intense exposure, such as a chemical spill or gas release^{71,72}. This has also been described in HCWs, following an acute overexposure to glacial acetic acid⁷³. An alternative presentation is a series of short-term overexposures to respiratory irritants occurring over days to a few weeks⁷⁴. It is less clear whether chronic low-level exposure to irritants can lead to asthma², although it is well established that airborne irritants can trigger asthma exacerbations⁷⁵. 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 months) asthma symptoms, it is not possible to distinguish causation from aggravation, although the finding is certainly suggestive of an irritant mechanism underlying the symptoms. 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.

Healthcare 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 in 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 studies appear to be warranted.

Conclusions

Phase I

Previous studies in various countries have described an increased occurrence of asthma among specific groups of health care workers. Although some questionnaires exist for the evaluation of asthma and exposures in the workplace, to our knowledge none have undergone formal validation in a healthcare worker population. Evaluation of the performance of this new questionnaire for the study of asthma in healthcare workers indicates good validity and reliability for the detection of asthma and for the characterization of nonoccupational exposures and other asthma risk factors. The validity and reliability of assessment of occupational exposures was similar to previous studies based on self-report. Although the instrument was specifically

designed for use in the healthcare sector, this methodology could also be adapted for studies of other worker populations.

Use of this validated questionnaire in epidemiological studies of healthcare workers should improve the quality of asthma research in this large sector of the employed workforce. The rigorous methodological approach to questionnaire validation employed in this study may serve as a model for epidemiological studies of other occupational groups.

Phase II

Healthcare-related occupations represent 50% of the top 30 fastest growing occupations in the U.S., and all four professional groups included in this study are expected to grow by more than 20% by 2012. Healthcare 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. Given the previous literature on established asthma risk factors (cleaning products, latex and aerosolized medications) and findings from Phase II, the estimated attributable fraction of preventable asthma or asthma symptoms in this worker population is estimated to range from would range from 7% to 33%.

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PUBLICATIONS

To date, the following publications have resulted from this study:

1. Delclos GL, Arif AA, Aday L, Carson A, Lai D, Lusk C, Stock T, Symanski E, Whitehead LW, Benavides FG, Anto JM. Validation of an asthma questionnaire for use in healthcare workers. *Occup. Environ. Med.* 2006; 63; 173-179.
2. Delclos, G.L., Arif A., Aday LA, Bartholomew K, Carson AI, Lai D, Lusk C, Stock T, Symanski E, Whitehead LW. Reliability and validity of an asthma questionnaire for healthcare workers. NORA 2003 Symposium: Working Partnerships Research to Practice Conference, Washington DC, June 23-24, 2003.

INCLUSION OF GENDER AND MINORITY STUDY SUBJECTS

Phase 1 - Inclusion Enrollment Report Table

This report format should NOT be used for data collection from study participants.

Study Title: A Validated Asthama Questionnaire for Health Care Workers – Phase I

Total Enrollment: 102

Protocol Number: HSC-SPH-99-067

Grant Number: 5 R01 OH03945-01A1

PART A. TOTAL ENROLLMENT REPORT: Number of Subjects Enrolled to Date (Cumulative) by Ethnicity and Race				
Ethnic Category	Sex/Gender			Total
	Females	Males	Unknown or Not Reported	
Hispanic or Latino	17	4	0	21 **
Not Hispanic or Latino	59	22	0	81
Unknown (Individuals not reporting ethnicity)	0	0	0	0
Ethnic Category: Total of All Subjects*	76	26	0	102 *
Racial Categories				
American Indian/Alaska Native	1	0	0	1
Asian	8	3	0	11
Native Hawaiian or Other Pacific Islander	0	0	0	0
Black or African American	22	7	0	29
White	40	14	0	54
More than one race	0	0	0	0
Unknown or not reported	5	2	0	7
Racial Categories: Total of All Subjects*	76	26	0	102 *
PART B. HISPANIC ENROLLMENT REPORT: Number of Hispanics or Latinos Enrolled to Date (Cumulative)				
Racial Categories	Females	Males	Unknown or Not Reported	Total
American Indian or Alaska Native	0	0	0	0
Asian	0	1	0	1
Native Hawaiian or Other Pacific Islander	0	0	0	0
Black or African American	1	0	0	1
White	11	3	0	14
More Than One Race	0	0	0	0
Unknown or not reported	5	0	0	5
Racial Categories: Total of Hispanics or Latinos**	17	4	0	21 **

* These totals must agree.

** These totals must agree.

Phase 2 - Inclusion Enrollment Report Table

This report format should NOT be used for data collection from study participants.

Study Title: A Validated Asthama Questionnaire for Health Care Workers – Phase 2

Total Enrollment: 102

Protocol Number: HSC-SPH-99-067

Grant Number: 5 R01 OH03945-01A1

PART A. TOTAL ENROLLMENT REPORT: Number of Subjects Enrolled to Date (Cumulative) by Ethnicity and Race				
Ethnic Category	Sex/Gender			
	Females	Males	Unknown or Not Reported	Total
Hispanic or Latino	294	200	1	495 **
Not Hispanic or Latino	2075	926	9	3010
Unknown (Individuals not reporting ethnicity)	68	27	50	145
Ethnic Category: Total of All Subjects*	2437	1153	60	3650 *
Racial Categories				
American Indian/Alaska Native	20	8	0	28
Asian	169	124	0	293
Native Hawaiian or Other Pacific Islander	0	0	0	0
Black or African American	168	59	1	228
White	1932	867	10	2809
More than one race	0	0	0	0
Unknown, Other or not reported	1483	95	49	292
Racial Categories: Total of All Subjects*	2437	1153	60	3650 *
PART B. HISPANIC ENROLLMENT REPORT: Number of Hispanics or Latinos Enrolled to Date (Cumulative)				
Racial Categories	Females	Males	Unknown or Not Reported	Total
American Indian or Alaska Native	2	0	0	2
Asian	14	7	0	21
Native Hawaiian or Other Pacific Islander	0	0	0	0
Black or African American	4	3	0	7
White	150	114	1	264
More Than One Race	0	0	0	0
Unknown, Other or not reported	124	76	0	200
Racial Categories: Total of Hispanics or Latinos**	294	200	0	495 **

* These totals must agree.

** These totals must agree.

INCLUSION OF CHILDREN

The study population included only adults licensed health care professionals and did not involve children.

MATERIALS AVAILABLE FOR OTHER INVESTIGATORS

Copies of the validated questionnaire and Job Exposure Matrix (included as Appendix A and B) are available through the Principal Investigator at the following address:

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Appendix A

Survey Questionnaire

Appendix B

Job Exposure Matrix

Appendix C

Tables

Table 1. Comparison of baseline descriptive statistics between full study sample, the analytic sample (with all missing values excluded) and the excluded sample (only those with missing values).

Variable	Full sample (n=3650)	Analytic sample (no missing values) (n=2738)	Excluded sample (missing values) (n=912)	p value*
Age in years (mean ± S.E.M.)	47.7 ± 0.28	46.7 ± 0.32	51.0 ± 0.57	<.001
Gender (%) :				
Male	1153 (22.6)	935 (24.6)	218 (16.4)	
Female	2437 (77.4)	1803 (75.4)	634 (83.6)	<.001
Race/ethnicity (%) :				
Non-Hispanic white	2497 (73.0)	1983 (75.0)	514 (65.7)	
Hispanic	495 (12.0)	381 (11.7)	114 (13.2)	
Non-Hispanic black	197 (5.5)	143 (4.9)	54 (7.5)	0.02
Other	316 (9.5)	231 (8.4)	85 (13.5)	
Atopy	576 (15.5)	447 (15.4)	129 (15.7)	0.51
Obesity (BMI ≥ 30)	743 (23.0)	584 (23.7)	159 (20.4)	0.26
Ever smokers (%)	1213 (33.9)	920 (33.8)	293 (34.2)	0.83
Seniority in years (mean ± S.E.M.)	21.8 ± 0.29	21.0 ± 0.33	24.3 ± 0.61	.001
Profession (%) :				
Physicians	862 (23.6)	682 (24.9)	180 (19.7)	
Occupational therapists	968 (26.5)	717 (26.2)	251 (27.5)	
Nurses	941 (25.8)	695 (25.4)	246 (27.0)	0.02
Respiratory therapists	879 (24.1)	644 (23.5)	235 (25.8)	
Reported asthma † (%)	198 (6.6)	145 (6.6)	53 (6.4)	0.55
BHR-related symptoms ‡ (%)	836 (27.2)	761 (27.4)	75 (25.2)	0.58

* Comparison of analytic and excluded samples, based on student's t-test for continuous variables and chi-square for categorical variables for sample survey data. † Asthma diagnosed by a physician after entry into the healthcare profession. ‡ 8-item predictor for bronchial hyperresponsiveness (BHR), PC₂₀ ≤ 4 mg/ml.

Table 2. Univariate analysis between independent variables, as assessed by a job-exposure matrix (JEM) and questionnaire for longest held job among Texas healthcare workers, and two asthma outcomes, weighted by survey sample size in the analytic sample (n=2738).

Variable	Reported asthma*		BHR-related symptoms†	
	Odds Ratio (95% CI)	p value	Odds Ratio (95% CI)	p value
Sociodemographics				
Age	1.02 (1.00-1.03)	0.05	0.99 (0.98-1.00)	0.02
Gender				
Male	-		-	
Female	2.31 (1.35-3.94)	0.002	2.28 (1.73-3.01)	<0.001
Race/ethnicity				
Non-Hispanic White	-		-	
Hispanic	1.62 (0.86-3.04)		0.70 (0.46-1.07)	
Non-Hispanic Black	0.20 (0.07-0.58)	0.006‡	1.23 (0.69-2.20)	0.04‡
Other	1.13 (0.49-2.63)		0.56 (0.34-0.92)	
Obesity (BMI ≥ 30.0)	2.03 (1.23-3.34)	0.002	1.59 (1.18-2.13)	0.005
Ever smoker	1.21 (0.74-1.97)	0.44	1.05 (0.80-1.37)	0.74
Atopy	3.31 (1.99-5.48)	<0.001	8.80 (6.22-12.45)	<0.001
Occupational Exposures§				
Seniority				
First quartile	-		-	
Second quartile	2.08 (0.64- 6.73)		0.67 (0.45-1.02)	
Third quartile	3.37 (1.10-10.26)	0.03 ‡	0.78 (0.52-1.16)	0.15 ‡
Fourth quartile	4.10 (1.39-12.11)		0.66 (0.45-0.96)	
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

*Self-reported history of physician-diagnosed asthma, with onset after entry into the healthcare profession. † 8-item predictor for bronchial hyperresponsiveness (BHR), PC₂₀≤4 mg/ml. ‡ Based on F-test for categorical variables for sample survey data. § All exposures as assessed by external JEM (low or high probability of exposure), except seniority and spill at work which were self-reported through questionnaire.

Table 3. Associations between occupational exposures and asthma among Texas healthcare workers: final multivariable logistic regression models* (n=2738).

Occupational exposure	Reported asthma [†]	BHR-related symptoms [‡]
	Odds Ratio (95% CI) [§]	Odds Ratio (95% CI) [§]
Cleaning agents		
Used in patient care	1.60 (0.18-14.16)	0.79 (0.35-1.78)
Instrument cleaning	2.22 (1.34-3.67)	1.26 (0.95-1.67)
Surface cleaners	2.02 (1.20-3.40)	1.63 (1.21-2.19)
Latex		
Pre-1992	2.04 (0.87-4.75)	1.04 (0.72-1.51)
1992-2000	2.17 (1.27-3.73)	1.26 (0.93-1.72)
After 2000	0.42 (0.13-1.29)	0.61 (0.34-1.11)
Aerosolized medications	1.72 (1.05-2.83)	1.40 (1.06-1.84)
Adhesives/solvents/gases		
Used in patient care	1.68 (0.99-2.86)	1.65 (1.22-2.24)
On surfaces	0.59 (0.26-1.33)	0.98 (0.64-1.51)
Miscellaneous	0.53 (0.32-0.88)	0.78 (0.60-1.01)
Spill at work	1.23 (0.53-2.87)	2.02 (1.28-3.21)

* Adjusted for seniority (quartiles), race/ethnicity, body mass index, and atopy; weighted survey samples. [†] Self-reported history of physician-diagnosed asthma, with onset after entry into the healthcare profession. [‡] 8-item predictor for bronchial hyperresponsiveness (BHR), PC₂₀ ≤ 4 mg/ml. [§] Goodness-of-fit, assessed through F-adjusted mean residual test for sample survey data, p > 0.05 for all models.

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 walkthroughs in 2002-2003.

Instrument cleaning/disinfection	Building surface cleaners	Adhesives used in patient care
Glutaraldehyde	Acetic acid/acetic acid anhydride	<i>Adhesive removers:</i>
Isopropanol	Ammonia/ammonium hydroxide	Acetone
Orthophthalaldehyde	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	<i>Stoma care products</i>
	Isoparaffinic hydrocarbons	Carboxymethyl ether
	Phosphoric acid	Hexane-based skin bond
	Quaternary ammonium compounds	Methylbenzene
	Sodium sulfate	<i>Other:</i>
	Sulfuric acid	Methylene chloride
		Trichloroethane



DATE: June 8, 2007

TO: William D. Bennett
Data Systems Team, Information Resources Branch, EID, NIOSH, P03/C18

THRU: W. Allen Robison, Ph.D., Acting Program Lead *W. Allen Robison*
Office of Extramural Coordination and Special Projects, NIOSH, E74

FROM: Jim Newhall, Ph.D., Scientific Program Administrator *Allen Robison for Jim Newhall*
Office of Extramural Coordination and Special Projects, NIOSH, E74

SUBJECT: Final Report Submitted for Entry into NTIS, Grant Number: 5R01OH003945-03

The attached final report has been received from the principal investigator on the subject NIOSH grant. When the document is forwarded to the National Technical Information Service, please inform us of the document number. This will allow us to respond to inquiries received about the final report. Publications are highlighted on the attached final report summary.

Attachments:

Final Report Summary

cc: Sherri Diana, EID, P03/C18

Title: A Validated Asthma Questionnaire for Healthcare Workers

Investigator: George Delclos

Affiliation: University of Texas Health Science Center Houston

State: TX

Telephone: (713) 500-9459

Award Number: 5R01OH003945-03

Start & End Dates: 9/30/2001-9/29/2005

Program Area: Respiratory Diseases

NIOSH Scientific Administrator: Bridgette Garrett, Ph.D.

Final Report Abstract:

Recent U.S. data suggest an increased risk of work-related asthma among healthcare workers. However, results have been inconsistent and lacking in detail. To assess the magnitude of asthma risk, evaluate associations with occupational exposures, and estimate the burden of work-related asthma in healthcare professionals, a new survey instrument for work-related asthma among health care workers was developed, validated and administered in a field study. The project was conducted in two separate and consecutive phases. In Phase I, the survey instrument was developed, validated and refined. In Phase II the validated questionnaire was administered to a population-based sample of selected groups of health care workers in Texas.

Phase I resulted in an eleven page questionnaire which required approximately 13 to 25 minutes to complete. Test-retest reliability of asthma and allergy items ranged from 75% to 94%, and internal consistency for these items was excellent (Cronbach's $\alpha \geq 0.86$). Against methacholine challenge, an 8-item combination of asthma symptom items had a sensitivity of 72% and specificity of 71%; against a physician diagnosis of asthma, this same combination showed a sensitivity of 89% and specificity of 98%.

In Phase II, using the questionnaire validated in Phase I, a cross-sectional statewide survey of 5600 Texas healthcare professionals (physicians, nurses, respiratory therapists and occupational therapists) was conducted. A simple random sample of 1400 persons was drawn from each of the four populations of professionals (physicians, nurses, respiratory therapists and occupational therapists) with active licenses in 2003. Information on asthma symptoms and nonoccupational asthma risk factors obtained from the survey was then linked to occupational exposures derived from an external asthma risk factor job-exposure matrix (also developed for this study). Overall response rate was 66%. The final study population consisted of 862 physicians, 941 nurses, 968 occupational therapists and 879 respiratory therapists (n=3650). There were two a priori defined outcomes: a) physician-diagnosed asthma with onset after entry into healthcare ('reported asthma'), and b) 'bronchial hyperresponsiveness-related symptoms', defined through the 8-item symptom-based predictor.

Reported asthma was associated with medical instrument cleaning (OR, 2.22; 95% CI, 1.34-3.67), general cleaning (OR, 2.02; 95% CI, 1.20-3.40), use of powdered latex gloves between the years 1992 and 2000 (OR, 2.17; 95% CI, 1.27 to 3.73) and administration of aerosolized medications (OR, 1.72; 95% CI, 1.05 to 2.83). The risk associated with latex gloves disappeared 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). Occupational exposures contribute importantly to asthma in healthcare professionals, meriting both further study and implementation of appropriate controls.

Impact of the Project:

Phase II of this study found an approximate two-fold increased likelihood of asthma after entry into a healthcare 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. The association between powdered latex glove use and asthma disappeared with exposures occurring after the year 2000, suggesting that current workplace controls are having a positive effect. For previously described associations confirmed in this study, the evidence is sufficiently strong to justify moving from descriptive studies to the implantation and evaluation of appropriate controls. For newly described findings, additional, more focused studies appear to be warranted.

Phase I of the study produced a new survey instrument for the study of asthma in healthcare worker groups.

Phase II of the study produced a new asthma risk factor job-exposure matrix, specific to healthcare settings.

Translation Of Findings

In Phase II, while causation could not be confirmed because of the cross-sectional nature of the study, the strong association between exposure to cleaning products and both reported asthma and BHR-related symptoms, taken together with the existing literature on asthma and cleaners, and the biological plausibility of such an association, lend support to the finding that there is an association of asthma in HCW exposed to cleaning activities. 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 provides an idea of the proportion of new asthma cases that might potentially be avoided through control of these exposures.

While powdered latex glove use is well established as a leading cause of occupational asthma in HCWs, this study adds important information to the body of literature. Because the time period of the two-fold increase in risk of reported asthma was restricted to 1992-2000, the findings from this study point to an encouraging reduction in risk after 2000, at least on a statewide level. This strengthens recent reports indicating the effectiveness of substitution of powdered latex gloves by low latex alternatives and other control measures.

A new association identified in this study concerns the increased risk of BHR-related symptoms and tasks involving application of adhesives, adhesive removers, solvents or similar products on patients. At present, evidence of a causal link should be considered speculative. However, given the high prevalence of exposure to these compounds (70%) and the strength of the associations, further research appears to be justified.

Outcomes/Relevance/Impact

Healthcare-related occupations represent 50% of the top 30 fastest growing occupations in the U.S., and all four professional groups included in this study are expected to grow by more than 20% by 2012. Healthcare 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. Given the previous literature on established asthma risk factors (cleaning products, latex and aerosolized medications) and findings from Phase II, the estimated attributable fraction of preventable asthma or asthma symptoms in this worker population is estimated to range from could range from 7% to 33%.

Publications:

Delclos, G.L., Arif A., Aday LA, Bartholomew K, Carson AI, Lai D, Lusk C, Stock T, Symanski E, Whitehead LW. Reliability and validity of an asthma questionnaire for healthcare workers. NORA 2003 Symposium: Working Partnerships Research to Practice Conference, Washington DC, June 23-24, 2003.

Delclos GL, Arif AA, Aday L, Carson A, Lai D, Lusk C, Stock T, Symanski E, Whitehead LW, Benavides FG, Anto JM. Validation of an asthma questionnaire for use in healthcare workers. *Occup. Environ. Med.* 2006; 63; 173-179.