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Respiratory morbidity in office workers in a water-damaged building.

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List of abbreviations:

BASE	Building Assessment Survey and Evaluation
BHR	Bronchial hyperresponsiveness
BRFSS	Behavioral risk factor surveillance system
EPA	Environmental Protection Agency
FEV_1	Forced expiratory volume in one second
FVC	Forced vital capacity
HP	Hypersensitivity pneumonitis
MCT	Methacholine challenge test
NHANES III	The third National Health and Nutrition Examination Survey
NIOSH	National Institute for Occupational Safety and Health

Abstract

We conducted a study on building-related respiratory disease and associated social impact in an office building with water incursions in the Northeastern United States. An initial questionnaire had 67% participation (888/1327). Compared with the U.S. adult population, prevalence ratios were 2.2 to 2.5 for wheezing, lifetime asthma and current asthma, 3.3 for adult-onset asthma, and 3.4 for symptoms improving away from work ($p < 0.05$). Two-thirds (66/103) of the adult-onset asthma arose after occupancy, with an incidence rate of 1.9/1,000 person-years before building occupancy and 14.5/1,000 person-years after building occupancy. We conducted a second survey on 140 respiratory cases, 63 subjects with fewer symptoms, and 44 comparison subjects. Health-related quality of life decreased with increasing severity of respiratory symptoms and in those with work-related symptoms. Symptom status was not associated with job satisfaction or how often jobs required hard work. Respiratory health problems accounted for one third of sick leave, and respiratory cases with work-related symptoms had more respiratory sick days than those without work-related symptoms, (9.4 vs. 2.4 days/year, $p < 0.01$). Abnormal lung function and/or breathing medication use was found in 67% of respiratory cases, 38% of participants with fewer symptoms and 11% of the comparison group ($p < 0.01$), with similar results in never-smokers. Post-occupancy onset asthma was associated with less atopy than pre-occupancy onset asthma. Occupancy of the water-damaged building was associated with onset and exacerbation of respiratory conditions, confirmed by objective medical tests. The morbidity and lost work-time burdened both employees and employers.

Introduction

As part of a program to study occupational respiratory disease in the nonindustrial environment, we investigated building-related respiratory health in the employees of a large 20 story office building in the Northeastern U.S. Since the mid 1990s, the building had incurred water intrusion through the roof, around windows, and through sliding doors of terraces. The upper floors had suffered the most water damage and mold contamination. During investigation of these problems, the building was found to be operating at a negative pressure with respect to the outdoors, which could lead to exacerbation of water incursion through the building envelope. Furthermore there had been plumbing leaks on many floors which had damaged interior walls. The first major construction activity related to water incursion began in 2000, with repair of roof copings and brick caulking. From 2000 to 2002, cubicle partitions and carpets were cleaned, wetted carpet and stained wallboard replaced, wallpaper and underlying mold removed from bathrooms, upgrades to the air handling system made, and windows caulked. In 2002, permanent repairs on the building exterior began to prevent water incursion, including roof replacement.

Building occupants had reported health conditions that they considered building-related. Symptom onset spanned several years with an increase in symptoms and frequency of complaints beginning in the fall of 2000. Sentinel cases of post-occupancy onset asthma, hypersensitivity pneumonitis (HP), and sarcoidosis had been diagnosed and relocated to another facility. HP is an immune-regulated granulomatous disease which has been associated with fungal contamination, and has been found to co-exist with asthma in damp office buildings

(Arnow et al. 1978; Kreiss 1989; Hoffman et al. 1993; Jarvis and Morey 2001). Sarcoidosis is an immune-regulated granulomatous disease of unknown etiology.

In this article we report evidence of excesses of respiratory symptoms and physician diagnosis of asthma in the occupants of the water-damaged building as well as verification of self-reported respiratory illness with objective testing. We also describe the burden of illness in terms of sick absences, breathing medication use, and health-related quality of life.

Methods and Materials

Study Design and population

September 2001 Questionnaire Survey. In September 2001, we offered a questionnaire to all 1327 employees working in the building. The questionnaire was administered to groups of approximately 50 employees at a time, using schedules prepared by management. During each group session, National Institute for Occupational Safety and Health (NIOSH) staff described the purpose of the survey and the consent process, and read the questions aloud from overhead transparencies as the participants completed them. By completing the questionnaire, the participants were indicating consent to take part in the survey. The questionnaire comprised sections on demographics; symptoms (upper and lower respiratory, systemic, headache and difficulty concentrating) in the last 4 weeks and 12 months, and in relation to being in the building; physician-diagnosis of asthma, HP and sarcoidosis, with dates of diagnosis; smoking history; and work history in the building. The completed questionnaires were electronically scanned into a data base with hand checking for quality control.

We used the September questionnaire to identify a group of employees who had worked in the building for at least one year and who met either an epidemiological case definition for lower respiratory illness or a comparison group definition. The respiratory case definition was: three or more of five lower respiratory symptoms (wheeze/whistling in the chest, chest tightness, shortness of breath, coughing, awakening by attack of breathing difficulty) occurring weekly over the past month; or at least two of three symptoms consistent with HP (shortness of breath when hurrying on level ground or walking up a slight hill, fever and chills, flu-like achiness or achy joints) occurring weekly over the past month; or current asthma with post-occupancy physician diagnosis, or physician-diagnosed HP or sarcoidosis. The comparison group definition was: none of the respiratory case lower respiratory or HP-like symptoms in the past year, and none of the respiratory case diagnoses.

June 2002 Medical Survey. We invited the 202 employees who met the case definition and the 154 employees who met the comparison group definition to participate in a questionnaire and medical testing survey in June 2002. During the site visit, an additional 15 employees requested to take part in the survey. All participants provided written informed consent (approved by the NIOSH Human Subjects Review Board). Results of the June questionnaire were used to reclassify participants into the respiratory case or comparison groups. Participants who reported lower respiratory or systemic symptoms but who did not meet the criteria of a respiratory case formed a third, "fewer symptoms" group.

Medical tests

Questionnaire. Participants completed an interviewer-administered computer-based questionnaire. The June 2002 questionnaire included sections on demographics, work history, health and symptom history, physician diagnoses, smoking, home environment, job stress and satisfaction as used in the U.S. Environmental Protection Agency (EPA) Building Assessment Survey and Evaluation (BASE) study (U.S. Environmental Protection Agency 1994), and health-related quality of life from the SF-12 (Medical Outcomes Study, Short Form) (Ware, Jr. et al. 1996). We included questions on the use of beta-agonist and corticosteroid inhalers, over-the-counter breathing medications, and other asthma medications in the previous four weeks, as well as oral corticosteroid use in the previous 12 months, adapted from an asthma severity score module (Blanc et al. 1996). To help with recall, participants were asked to bring to their testing session a list of the medications that they were taking for breathing problems.

Spirometry. Qualified technicians followed standard guidelines for spirometry (American Thoracic Society 1995). The test results were compared to expected values for a healthy, nonsmoking person of the same age, height, sex, and race using spirometry reference values and 95% normal confidence intervals generated from the third National Health and Nutrition Examination Survey (NHANES III) (Hankinson et al. 1999). Abnormal test results were categorized as having a pattern of obstruction, restriction, or a "mixed" pattern of both airways obstruction and a low forced vital capacity (FVC) (American Thoracic Society 1995). We defined airways obstruction as a low forced expiratory volume in one second (FEV_1) to FVC ratio (FEV_1/FVC %) with low FEV_1. We defined restriction as a low FVC and normal FEV_1/FVC%.

Methacholine Challenge Testing (MCT). To detect bronchial hyperresponsiveness (BHR), we performed MCT using standardized techniques (Crapo et al. 2000) with 0.125, 0.5, 2, 8, and 32 milligrams per milliliter (mg/mL) of methacholine. Five breaths of nebulized methacholine were administered for each dose, with FEV_1 measured 30 and 90 seconds later. If

FEV_1 dropped more than 20% of the baseline value, no further methacholine was given. We reported methacholine dose as PC_{20}, which is the provocative concentration of methacholine that causes an interpolated 20% decline in FEV_1 from the baseline. We defined BHR as a PC_{20} 4.0 mg/mL or less, and borderline BHR as a PC_{20} between 4.1 and 16.0 mg/mL (Crapo et al. 2000).

Bronchodilator Testing. In subjects with baseline FEV_1 less than 70% of the predicted value, MCT was not offered, but a bronchodilator test was offered to detect any reversible bronchoconstriction. Two puffs of a beta-agonist were administered via metered dose inhaler and were followed by spirometry. We defined reversibility as a 12% and 200 milliliter FEV_1 improvement after bronchodilator administration (American Thoracic Society 1991).

Allergen Skin Prick Testing. Extracts of seven common indoor and outdoor allergens and three mold mixes were applied using the GreerPIK system (Greer Laboratories, Lenoir, NC): dust mite mix (*D. farinae & D. pteronyssinus)*; German cockroach (*Blattella germanica*); cat hair; 7 grass mix; ragweed mix; common weed mix; Eastern 8 tree mix; *Dematiaceae* mix (outdoor molds: *Alternaria tenuis, Cladosporium herbarum, Helminthosporium sativum, Pullularia pullulans, Spondylocladium atrovirens, Curvularia spicifera*); *Aspergillus* mix; and *Penicillium* mix. The negative control was 50% glycerin in water, and histamine served as a positive control. For each wheal, the mean diameter (average of the length and width) at 15 minutes was calculated. A positive reaction was defined as an average diameter at least 3mm larger than the negative control and greater than 25% of the average diameter of the positive control. For the purposes of this study, atopy was defined as at least one positive skin test on allergy testing, using a total of seven common antigen extracts (excluding the mold mixes).

Data analysis

We compared the prevalence rates of respiratory symptoms and self-reported medical diagnoses observed in the building occupants during the September 2001 survey to the U.S. adult prevalence rates obtained from NHANES III (National Center for Health Statistics 1996), the 2001 data for the state from the Behavioral Risk Factor Surveillance System (BRFSS) (National Center for Chronic Disease Prevention and Health Promotion Behavioral Risk Factor Surveillance System 2001), and data for occupants of 41 office buildings with no known indoor environmental problems (Apte et al. 2000). For comparisons with NHANES III, we used indirect standardization for race (black, Hispanic, white), gender, age (17 to 39 years of age versus 40 to 69 years of age), and cigarette smoking status (current, former, or never smoker). For comparisons with BRFSS, we standardized for gender. We derived 95% confidence intervals (CI) using a method which assumes that the observed data are from a Poisson distribution (Kahn 1989).

To estimate incidence density rates of physician-diagnosed adult-onset asthma, for each participant we calculated person-time at risk for two time periods: from age 16 to building occupancy and from building occupancy to the September 2001 survey date. For subjects with physician-diagnosed adult onset asthma, time at risk ended on the date of diagnosis. Time at risk for each participant was summed to give person-years at risk. Participants with childhood asthma did not contribute any time at risk.

We used SAS (version 8.02; SAS Institute Inc. Cary, NC, USA) to analyze the data. Chi-square tests were used in statistical analysis of two-way classification tables. We used the Cochran-Mantel-Haenszel test in analysis of differences between proportions after adjustment for smoking, and the Cochran-Armitage test in analysis for linear trends in proportions. We used the GLM procedure to model number of days lost, and Duncan's multiple range test for multiple means comparisons.

Results of September 2001 survey

Participation. Participation was 67% (888/1327) in the cross-sectional questionnaire study. Participants were predominantly white, in their mid-forties, former or never smokers, who had been working in the building for about 6 years (Table 1). We had demographic and participation information on the 689 employees working for one of the two building tenant organizations. These employees had a mean age of 45 years, 74% were white, 19% were black, and 53% were female. There was 76% participation among these employees. Comparison between participants and non-participants showed no differences in mean age or race. There were proportionately more females among participants than non-participants (57% vs. 40% $p < 0.01$).

Excess respiratory symptoms and physician-diagnosed asthma. In comparisons with the U.S. adult population, prevalence ratios ranged from 2.2 to 2.5 for wheezing, lifetime asthma and current asthma ($p < 0.05$) (Table 2). Nasal and eye symptoms had a higher prevalence in the building occupants than lower respiratory symptoms, but had less of an elevation compared to U.S. adults (prevalence ratios 1.5 and 1.6, respectively $p < 0.05$). The building occupants reported wheeze, nasal, or eye symptoms improving when away from work at 3.4 times the rate of the U.S. population ($p < 0.05$). Compared to the state adult population, prevalence ratios were 1.4 (95% CI 1.2–1.6) for lifetime asthma, and 1.5 (95% CI 1.3–1.9) for current asthma. A majority (60% to 70%) of participants with wheeze, chest-tightness, shortness of breath or cough in the last 4 weeks reported an improvement in symptoms when away from the building.

Prevalence ratios for work-related lower respiratory symptoms compared to U.S. office workers were elevated and ranged from 2.7 to 4.7 ($p < 0.05$) (Table 3).

Adult onset asthma prevalence and incidence. The prevalence of adult-onset asthma was 12% (103/865). A comparison to the U.S. adult population gave a prevalence ratio of 3.3 (95% CI 2.7–4.0). Two-thirds (66/103) of the adult-onset asthma arose after occupancy of the study building. An analysis of adult onset asthma incidence density was conducted based on 19,173 person-years at risk before building occupancy and 4,564 person-years at risk after building occupancy. We found incidences of 1.9 per 1,000 person-years in the period before building occupancy and 14.5 per 1,000 person-years in the period after building occupancy. The incidence rate ratio was 7.5, indicating a large increase in asthma incidence in the period after building occupancy.

Asthma symptom severity and exacerbation. The participants with post-occupancy onset physician-diagnosed asthma had a higher mean value for the sum of cough, wheeze, chest tightness and shortness of breath occurring once or more per week in the last 4 weeks than any other participants ($p < 0.05$). There was also a significant trend ($p < 0.01$) in prevalence of lower respiratory symptoms that improved away from the building; from 52% of those with post-occupancy onset asthma, 41% of those with adult pre-occupancy onset asthma, 27% of those with childhood asthma to 23% of those with no physician-diagnosed asthma (Table 4).

HP and Sarcoidosis. Eight participants reported HP, 5 with post-occupancy onset and 1 with pre-occupancy onset (2 people did not give diagnosis dates). Sarcoidosis was reported by 6 participants, 3 with post-occupancy onset and 2 with pre-occupancy onset (1 person did not give a date of diagnosis). Fever and chills were reported as occurring once or more in the last 4 weeks by 9%, flu-like achiness or achy joints by 22% and excessive fatigue by 29% of participants. A work-related pattern was noted by 22% of those with fever and chills, by 30% of those with flu-like achiness or achy joints, and by 52% of those with excessive fatigue.

Results of June 2002 survey

Participation. There were 248 participants in the June 2002 survey. Participation was higher among the invited employees meeting the respiratory case definition in September 2001 (142/200, 71%) than among the comparison group invitees (91/154, 59%). Based on the June 2002 questionnaire results, there were 140 participants in the respiratory case group, 63 participants in the fewer symptoms group, and 44 participants in the comparison group. One participant had missing questionnaire information and could not be classified. A little over half of those asymptomatic in September 2001 reported symptoms 9 months later, with 17% achieving respiratory case status, and 38% falling into the fewer symptoms group. In contrast, a majority (81%) of those meeting the respiratory case definition in September 2001 still met this definition 9 months later, 17% fell into the intermediate group and 2% became asymptomatic. The demographics of the June 2002 participants stratified by respiratory status are given in Table 5. There were more females and more current smokers in the respiratory case group.

Lung function tests, breathing medication use and reported respiratory health. Respiratory cases had the highest proportions of abnormal breathing tests and breathing medication usage; the fewer symptoms group had the next highest; and the comparison group had the lowest proportions of these two outcomes (Tables 6 and 7). Test results indicated more obstruction than restriction, and the respiratory cases had a trend for a higher prevalence of obstruction than the other participants. BHR was higher in the two groups with symptoms than the comparison group, but this finding was not significantly different. We found very little breathing medication use reported by the comparison group as compared to almost half of the respiratory cases. Analyses on the never-smokers, showed very similar trends with a prevalence of abnormal lung function tests and medication use combined of 71% for respiratory cases, 30% for participants with fewer symptoms and 12% for the comparison group.

Quality of life. We compared responses to health-related quality of life questions among the three symptom status groups. We found statistically significant trends for increasing impairment in health-related quality of life with increasing severity of respiratory symptoms. The largest differences were seen for reported physical limitations (Figure 1). Within the respiratory case and the fewer symptoms groups we found statistically significant poorer health-related quality of life in relation to the presence of work-related symptoms, except for general health status (Figure 2). Similar results were found for health-related quality of life and post-occupancy symptom onset, except that statistical differences were seen for limitations in climbing stairs, physical health limiting accomplishments, and physical health limiting the kind of activities.

Job stress/dissatisfaction. There were no statistical differences among symptom status groups for responses on job satisfaction or how often work required a person to work hard. Being very or somewhat satisfied with their job was reported by 87% of respiratory cases, 90% of the group with fewer symptoms and 93% of the comparison group. Being required to work hard frequently or very often was reported by 51% of respiratory cases, 62% of the intermediate group, and 45% of the comparison group.

Work days lost. The number of days off work in the last 12 months due to respiratory problems was significantly associated with symptom status ($p < 0.01$). The respiratory cases had missed a mean of 6.9 days as compared to 1.7 days for the group with fewer symptoms and 2.0 days for the asymptomatic group. We found that 34% of respiratory cases had 6 or more days of respiratory sick leave, compared to 11% of the fewer symptoms group and 4.7% of the asymptomatic comparison group ($p < 0.01$). In contrast there was no statistically significant difference between the three groups for non-respiratory sick leave. The respiratory cases lost a mean of 4.5 days, the group with fewer symptoms lost 7.5 days and the asymptomatic group lost 4.1 days due to non-respiratory conditions.

The number of respiratory sick days was similar for symptomatic participants regardless of whether the onset had been pre- or post-occupancy. A large effect was seen for having respiratory symptoms that improved away from the building. Respiratory cases with work-related respiratory symptoms had more respiratory sick days than those with symptoms which did not improve away from the building, (9.4 vs. 2.4, $p < 0.01$). In the group with fewer symptoms, those with work-related respiratory symptoms had more respiratory sick leave than those with symptoms with no work-related pattern (3.7 vs. 1.1, $p < 0.05$).

We estimated sick days over the past year for respiratory conditions and total sick leave for building occupants by applying the mean work days missed for the three symptom groups to the number of participants in those categories from the September 2001 questionnaire (816 participants had adequate data). Respiratory health problems accounted for 34% of sick leave days (2490/7402). The respiratory case group represented 25% of the September 2001 participants but contributed 56% (1401/2490) of the respiratory sick leave days. Using the mean of 2 days of respiratory sick leave reported by the comparison group as a non-building related baseline for building occupants gives an estimated 858 days of excess respiratory sick leave

(2490 – 1632). Thus up to 12% (858/7402) of the preceding 12 months of employee sick leave days might have been attributable to building-related effects.

Breathing medication use. We looked at the prevalence of asthma controller medications (inhaled corticosteroids, cromolyn, nedocromil, oral antileukotrienes) and reliever medications (short-acting beta-agonists, and ipratropium bromide) use in the last 4 weeks in participants with physician-diagnosed asthma for comparison with a national sample of 1788 U.S. adults with current asthma (Adams et al. 2002) (Fuhlbrigge et al. 2002) using two-sample tests of proportions. Use of an asthma controller was reported by 39% of our study group vs. 21% of U.S. asthma cases overall ($p < 0.01$). The prevalence of 39% asthma controller use was marginally higher ($p = 0.07$) than the value of 29% reported for U.S. cases with severe persistent symptoms in the last 4 weeks. Reliever use was reported by 50% of our group vs. 63% of U.S. cases ($p < 0.05$).

Skin prick allergy tests. Over half of the participants met the definition for atopy. There was no statistical difference in the prevalence of atopy between the respiratory case group, the group with fewer symptoms and the comparison group. However, pre-occupancy onset asthma was associated with a higher prevalence of atopy ($p < 0.05$). The results of individual skin prick allergen tests showed that pre-occupancy onset asthma cases had a higher prevalence of positive reactions to cat, dust mites and weed mix ($p < 0.01$) as well as to cockroach ($p < 0.05$). We found that the post-occupancy onset asthma cases had the lowest reaction to the mold mixes ($p = 0.05$) (Figure 3).

Discussion

Physician-diagnosed asthma and respiratory symptoms occurred in excess among our study participants and was confirmed by an excessive rate of airway obstruction and BHR. Studies of building occupants with known health concerns are subject to reporting bias. In our study, in addition to reported symptoms and physician diagnoses, we examined measures of respiratory disease, including medication usage and medical tests. Two-thirds of those classified as respiratory cases based on symptoms or physician-diagnoses, had either objective pulmonary function abnormalities or prescription medications for breathing difficulties (given with the goal of normalizing lung function). The higher rate of lung function abnormalities and breathing medication use in the participants reporting respiratory symptoms validates the symptom reports.

The majority (60 to 70%) of participants with respiratory symptoms reported a work-related pattern, implying a building-related exposure. The 7% overall prevalence of work-related wheeze was higher than the 2% to 4% in studies of non-problem buildings (Apte et al. 2000) and the 2% to 6% found in studies of problem buildings (Malkin et al. 1996). In the 9-month interval between the building-wide questionnaire survey and the nested case control survey, more than half (55%) of the comparison group chosen because they had no lower respiratory or systemic symptoms in September 2001 had become symptomatic, including 17% who were classified as respiratory cases. Improvement was rare in September 2001 cases (17%), suggesting a continued effect of building occupancy on respiratory health. Some of this response pattern may be attributable to over-reporting due to general concern about water incursions and sentinel cases with health effects, but such concerns had been present since before the September 2001 survey.

The estimated incidence of physician-diagnosed adult onset asthma among the study participants (1.9 per 1000 person-years) before building occupancy was within the range of other estimates for adults, e.g. 2.1 per 1000 person-years (McWhorter et al. 1989), 3.8 per 1000 person-years (Sama et al. 2003) and about 1 per 1,000 person-years (Reed 1999). In contrast, after building occupancy, incidence rose 7.5 times to 14.5 per 1000 person-years, consistent with the symptoms which developed in the previously asymptomatic comparison group.

The burden of respiratory problems in this population was reflected in substantial respiratory sick leave attributable to building occupancy (estimated at 12% of total). The presence of work-related respiratory symptoms was positively associated with respiratory sick leave but time of symptom onset was not, suggesting that having a work-related pattern to respiratory symptoms was a larger determinant of respiratory sick leave than whether the symptoms arose before or after building occupancy.

The proportion of our study respiratory cases with 6 or more days of respiratory sick leave was 34%. In comparison, a population study of 1,788 adults with asthma in the U.S. found that 11% of participants had 6 or more days of sick leave in the past year, related to their asthma (Fuhlbrigge et al. 2002). In our study, respiratory cases had a mean of 6.9 respiratory sick days in comparison to 4.4 annual work absences because of breathing problems among Canadian asthmatics (Ungar and Coyte 2000). In the Canadian study more productivity was lost due to a decrease in level of functioning at work on days when breathing problems were worse than usual than due to days off work. Although we have no estimate of productivity loss due to a decrease in functioning at work for our study participants, the high prevalence of work-related symptom exacerbation suggests a substantial amount might have occurred. High respiratory morbidity was also indicated by the high use of asthma controller medication and decreased prevalence of quick-relief medications. This pattern of medication use is consistent with persistent asthma associated with daily work-related exacerbation.

We found strong associations between respiratory symptom status and lower health-related quality of life, confirming the social burden of respiratory morbidity in building occupants. In contrast, we found no relation between job stress, job satisfaction, or perceived work burdens with symptom status; this is consistent with the findings of another investigation of building-related respiratory disease (Jarvis and Morey 2001) and reduces the likelihood that disgruntled employees in a problem building exaggerate their symptoms.

The specific etiology and mechanisms of the respiratory disease in this building remain undefined. The skin prick test results for immediate hypersensitivity responses to common aeroallergens were unexpected. Pre-occupancy onset asthma was associated with atopy, as anticipated (National Asthma Education and Prevention Program (NAEPP) 1997; Peden 2000). However, post-occupancy onset asthma cases had much lower prevalence of IgE-mediated allergen skin-test positivity (atopy). Perhaps the airway inflammation was not driven by an IgE mechanism. It is possible that non-biological irritant exposures were present, and furthermore, although molds have allergenic properties (Lander et al. 2001), the development of asthma in damp/moldy conditions may not be IgE-mediated (Savilahti et al. 2001; Douwes et al. 2003).

The rarity of clusters of HP in the general population points to a work-related etiology for the cluster in the building occupants. The recent Institute of Medicine report on damp indoor spaces and health found sufficient evidence for an association between mold or other agents in damp indoor environments and upper respiratory tract symptoms, cough, wheeze, asthma symptoms in sensitized persons, and HP in susceptible persons (Institute of Medicine 2004). The cluster of sarcoidosis raises concern that this granulomatous lung disease was misdiagnosed HP (Forst and Abraham 1993) or has overlapping environmental causes (Kucera et al. 2003).

The major limitation of this study is the possible influence of participation bias. We had a 67% participation in our September 2001 survey, and differences in health status of participants and non-participants could have led to overestimation of symptom and asthma prevalence, particularly since women were more likely to be participants. Using the most conservative approach, we compared minimum possible prevalences among the entire building population to the external reference populations. We still found excesses of asthma and symptoms in comparison to the U.S. population and to office workers in buildings not known to have indoor environmental problems (data not shown), but no differences in asthma prevalence in comparison to the state population. Counterbalancing possible response bias among those occupants who participated in our study is our finding of gradients of non-subjective tests and reported medication use in relation to symptom intensity.

In conclusion, this study contributes to the growing literature that water-damaged built environments can be associated with work-related respiratory disease. This investigation documents the considerable respiratory illness, adverse effects on quality of life, and absenteeism that have placed personal, social, and economic burdens on many employees and their employers. Building-related respiratory disease warrants increased public health, medical research, and policy attention.

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Table 1. Demographics of 888 participants in the September 2001 questionnaire survey.

Characteristic	Proportion or Measure
Women	59%
Age in years (mean, ± SD)	46 ± 9
White	74%
Black	19%
Hispanic	6%
Building occupancy in years (mean, ± SD)	6 ± 2
Current smoker	14%
Never smoker	62%

Table 2. Comparison of health outcomes prevalences with NHANES III [a].

Standardized Questions	Building Prevalence	Prevalence Ratio	95% Confidence Interval
Asthma ever	17.7% (143/810)	2.2	1.9–2.6
Asthma current	12.8% (103/804)	2.4	2.0–3.0
Wheezing or whistling in your chest in the last 12 months	35.9% (291/811)	2.5	2.2–2.8
Stuffy, itchy or runny nose in the last 12 months [b]	79.3% (643/811)	1.5	1.4–1.6
Watery, itchy eyes in the last 12 months	63.4% (510/804)	1.6	1.4–1.7
Wheezing, nose, or eye symptoms better on days off work	72.1% (468/649)	3.4	3.1–3.7

[a] The prevalence ratios were adjusted for age, gender, race, and smoking category. Missing information on these characteristics led to comparisons based on fewer than the total 888 participants. [b] Our question included 'sneezing'.

Table 3. The prevalence of work-related lower respiratory symptoms which occurred frequently in the previous 4 weeks, compared to U.S. office workers.

	Prevalence	Prevalence Ratio [a]	95% C.I.
Wheezing	6.9%	2.9	(2.2–3.7)
Coughing attacks	14.8%	2.7	(2.3–3.2)
Chest tightness	11.3%	4.7	(3.8–5.7)
Shortness of breath	9.6%	4.6	(3.7–5.7)

[a] The prevalence of the 888 study participants compared with results from 41 non-problem buildings (Apte, et al. 2000)

Table 4. Mean number of lower respiratory symptoms [a] and prevalence of work-related symptoms in the last 4 weeks by asthma status and onset period.

	Post-occupancy onset asthma	Pre-occupancy adult-onset asthma	Childhood-onset asthma	No reported asthma
Number of lower respiratory symptoms (mean ± SD) [b]	1.7 ± 1.6 [A]	1.1 ± 1.3 [B]	0.7 ± 1.3 [CB]	0.5 ± 0.9 [C]
Work-related lower respiratory symptoms	34/66 (52%) **	15/37 (41%)	8/30 (27%)	169/731 (23%)

[a] Sum of wheeze, cough, chest tightness and shortness of breath. [b] Means in the row with the same letter are not significantly different at alpha = 0.05, using Duncan's multiple range test
** Cochran-Armitage trend test $p < 0.0001$

Table 5. Demographics of June 2002 participants by respiratory symptom status.

	Respiratory case group n = 140	Fewer symptoms group n = 63	Comparison group n = 44
Women **	73%	44%	59%
Age in years (mean, ± SD)	47 ± 8	46 ± 9	46 ± 8
Occupancy duration (mean years, ± SD)	7 ± 2	7 ± 2	7 ± 2
Current smoker	17%	6%	9%
Never smoker	56%	70%	70%

** Chi-square test on gender, $p = 0.0004$
Due to missing values, age and duration of occupancy in respiratory case group are based on 137 participants. For age, the fewer symptoms group = 62 and the comparison group = 42.

Table 6. Breathing test results for participants, stratified by symptom status in June 2002.

Variable	Respiratory cases group	Fewer symptoms group	Comparison group
Spirometry testing [a]			
Abnormal	24% (31/131) [b]	13% (8/62)	7% (3/42)
Obstructed or mixed	15% (20/131)	6% (4/62)	7% (3/42)
Restriction (low FVC)	8% (11/131)	6% (4/62)	0% (0/42)
% Predicted FEV1 (Mean ± SD)	92% ± 16 [c]	96% ± 17	103% ± 12
% Predicted FVC (Mean ± SD)	94% ± 14 [d]	97% ± 16	103% ± 11
Methacholine challenge testing			
Abnormal (< 16 mg/ml)	19% (19/99)	20% (10/51)	6% (2/36)
< 4 mg/ml (BHR)	6% (6/99)	8% (4/51)	0% (0/36)
> 4 and < 16 mg/ml (borderline BHR)	13% (13/99)	12% (6/51)	6% (2/36)
Bronchodilator testing positive	18% (2/11)	None done	None done
Abnormal methacholine challenge or bronchodilator tests	19% (21/110)	20% (10/51)	6% (2/36)
Any abnormal lung function test [e]	39% (44/114) [f]	29% (16/55)	11% (4/37)

[a] Two invalid tests by the symptomatic participants were not included. [b] Across the row there was a significant Cochran-Armitage trend test ($p < 0.01$). The significant differences by symptom status remained after adjusting for smoking category (Cochran-Mantel-Haenszel test ($p < 0.05$)). [c] In a linear regression model adjusting for smoking category, there was a significant effect of symptom status ($p < 0.01$). The group meeting the respiratory case definition had a lower mean percent predicted FEV1 than either of the other two groups. [d] In a linear regression model adjusting for smoking category, there was a significant effect of symptom status ($p < 0.01$). The group which met the respiratory case definition had a lower mean percent predicted FVC than the asymptomatic group. [e] Participants who had either a negative spirometry, or a negative methacholine/bronchodilator test, and who had not done the other tests were excluded. [f] Across the row there was a significant Cochran-Armitage trend test ($p < 0.01$). The significant differences by symptom status remained after adjusting for smoking category (Cochran-Mantel-Haenszel test ($p < 0.01$)).

Table 7. Medication usage and combined medication usage and abnormal lung function stratified by symptom status in June 2002.

	Respiratory cases group [a]	Fewer symptoms group	Comparison group
Any medication for breathing problems	46% (65/140)	13% (8/63)	2% (1/44)
Oral steroids	21% (29/140)	8% (5/63)	2% (1/44)
Inhaled steroids	19% (27/140)	2% (1/63)	0% (0/44)
Beta-agonists	28% (39/140)	2% (1/63)	0% (0/44)
Positive for any medication for breathing problems or an abnormal lung function test	67% (83/124)	38% (21/55)	11% (4/37)

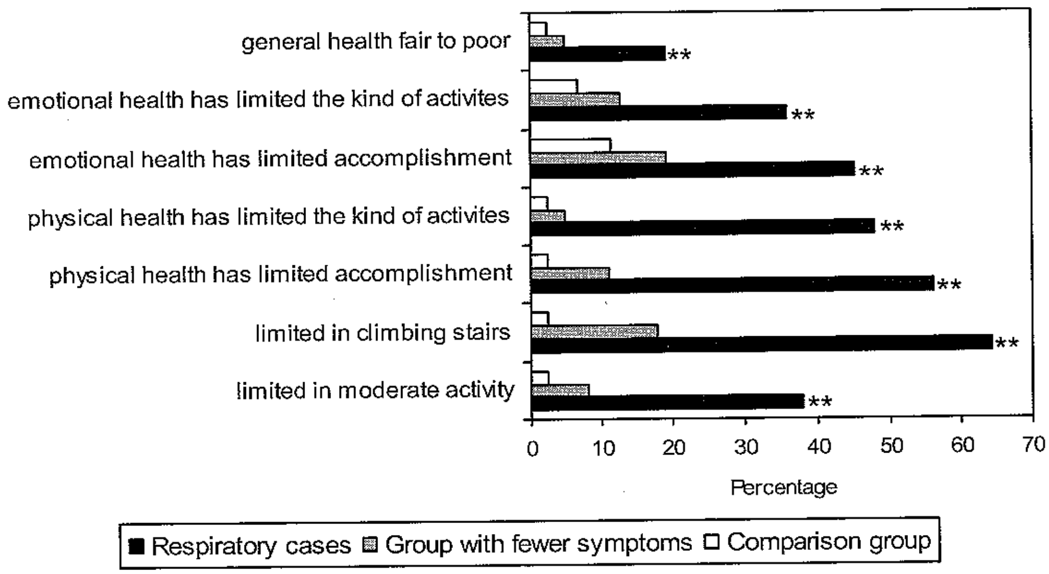
[a] Across all rows there were significant Cochran-Armitage trend tests ($p < 0.01$). The significant differences by symptom status remained after adjusting for smoking category (Cochran-Mantel-Haenszel tests ($p < 0.01$)).

Figure 1. Quality of life, comparisons among symptom groups.

Figure 2. Quality of life in the respiratory case and the fewer symptoms groups, stratified by work-relatedness of symptoms.

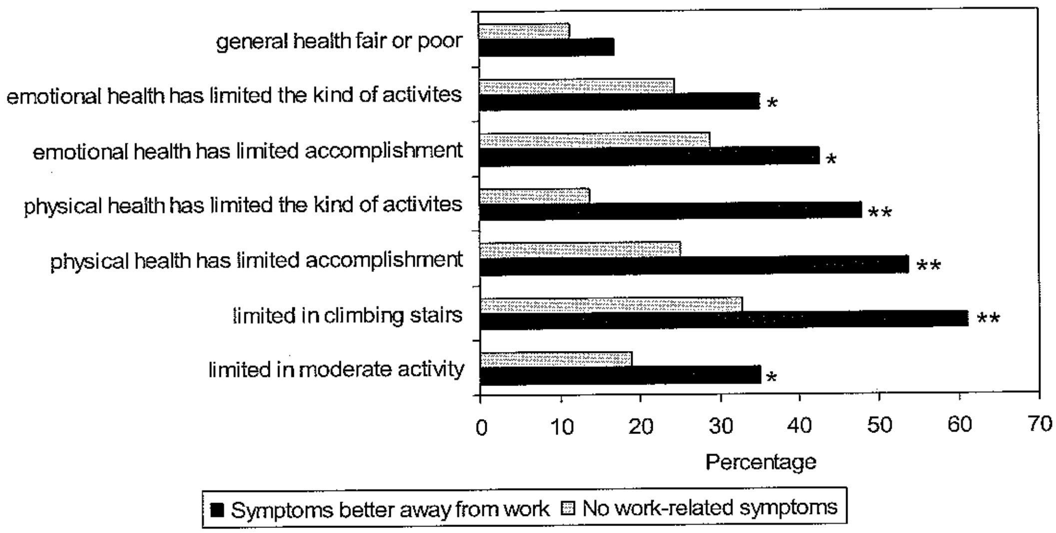
Figure 3. Allergy skin test results by asthma diagnosis.

Figure 1.



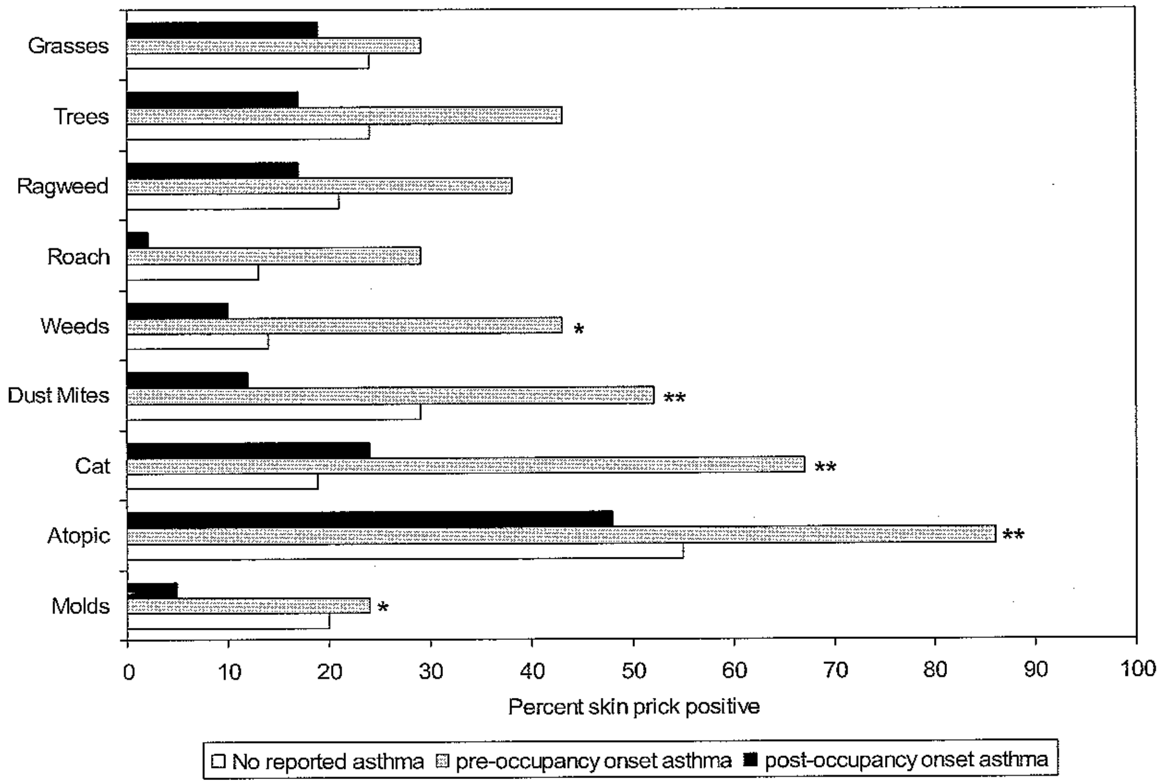
** Cochran-Armitage trend test $p < 0.01$

Figure 2.



** Chi-square test p < 0.01, * Chi-square test p < 0.05

Figure 3.



** Chi-square test $p < 0.01$, * Chi-square test $p < 0.05$