

Asthma and respiratory symptoms in hospital workers related to dampness and biological contaminants

Abstract The National Institute for Occupational Safety and Health investigated respiratory symptoms and asthma in relation to damp indoor environments in employees of two hospitals. A cluster of six work-related asthma cases from one hospital department, whose symptoms arose during a time of significant water incursions, led us to conduct a survey of respiratory health in 1171/1834 employees working in the sentinel cases hospital and a nearby hospital without known indoor environmental concerns. We carried out observational assessment of dampness, air, chair, and floor dust sampling for biological contaminants, and investigation of exposure-response associations for about 500 participants. Many participants with post-hire onset asthma reported diagnosis dates in a period of water incursions and renovations. Post-hire asthma and work-related lower respiratory symptoms were positively associated with the dampness score. Work-related lower respiratory symptoms showed monotonically increasing odds ratios with ergosterol, a marker of fungal biomass. Other fungal and bacterial indices, particle counts, cat allergen and latex allergen were associated with respiratory symptoms. Our data imply new-onset of asthma in relation to water damage, and indicate that work-related respiratory symptoms in hospital workers may be associated with diverse biological contaminants.

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Practical Implications

In healthcare facilities with indoor dampness and microbial contamination, possible associations between such conditions and respiratory health effects should be considered. Good building maintenance and housekeeping procedures should lead to improvements in employee respiratory health.

Introduction

A growing literature associates living and working in damp environments with adverse respiratory health effects including asthma. The 2004 Institute of Medicine (IOM) review (IOM, 2004) posed research questions about the contaminants causing health effects in damp indoor environments and about whether damp indoor environments cause asthma, as well as exacerbate it. Healthcare workers are at disproportionate risk for work-related asthma. Surveillance data from California, Massachusetts, Michigan, and New Jersey

from 1993 to 1997 indicated that 16% of reported work-related asthma cases occurred in healthcare workers who represented 8% of the workforce in the four states. The healthcare asthma cases reported cleaning products, latex, and indoor air pollution as the top three exposures associated with their symptoms. Mold was the exposure reported in 5% of the healthcare asthma cases (Pechter et al., 2005). A recent report from an international healthcare coalition (Health Care Without Harm, 2006) lists a number of biological and chemical agents related to asthma onset and exacerbation in healthcare settings. The report

surmises that excessive indoor dampness in hospitals could be a problem. There are no published reports of the prevalence of water incursions and dampness-related indoor environmental problems in US hospitals, but a recent study on hospitals in Finland indicated that 15% of the assessed areas in 10 hospitals had water-damage and mold contamination (Reijula, 2006). Investigations of asthma clusters in damp hospitals are limited, but studies in moisture-damaged hospitals in Finland have documented an outbreak of asthma, hypersensitivity pneumonitis, and rhinitis (Seuri et al., 2000) and a higher prevalence of asthma in moisture damaged sections of a hospital (Husman, 2004).

In early 2000, the occupational physician at two hospitals in the western US reported a temporal cluster of six asthma cases among the ~50 employees on the top floor of one of the two hospitals. Asthma symptoms in all case patients had arisen between 1997 and 1999, a time period in which significant roof and window leaks had occurred during heavy rains. In April, 2000, the National Institute for Occupational Safety and Health (NIOSH) was asked to assist in evaluating the situation. During an initial survey on the two top floors of the hospital with these six sentinel cases, we found fungal contamination in the walls and ceilings. During interviews in both hospitals, employees reported numerous instances of water leaks and damage over the past 5 years or more and that construction activities related to interior renovations had taken place in many departments. This paper describes the six work-related asthma cases and the cross-sectional study we conducted at the two hospitals on relationships among respiratory symptoms and reported doctor-diagnosed asthma and indoor environmental factors. This study thus addresses research questions posed in 2004 by the IOM review.

Methods

The NIOSH human subjects review board approved this research and all participants provided informed consent.

Work-related asthma cases

All the six work-related asthma cases from the 8th floor of the eight-storey hospital released their medical records to NIOSH, and we reviewed the records and abstracted and summarized lung function test data. After obtaining written informed consent from the six cases, we drew blood which was centrifuged and sent overnight on ice to the NIOSH immunology laboratory, where the serum was stored at -80°C until analyzed for latex-specific IgE and specific IgE for atopy assessment using the Pharmacia CAP system (Pharmacia and Upjohn, Kalamazoo, MI, USA). We

defined a negative latex-specific IgE as $<0.35 \text{ kU}_\text{A}/\text{l}$ (no detectable antibodies). We defined a negative IgE specific test for any of the common environmental allergens (house dust-mite mix, mold mix, weed mix, tree mix, grass mix, or epidermal [dog, cat, mouse, rat] mix) as $<0.7 \text{ kU}_\text{A}/\text{l}$.

Questionnaire survey

In August, 2000, we invited 1834 current employees who worked in the two hospitals to complete a self-administered questionnaire, mailed to their home addresses 2 weeks before the NIOSH site visit to the hospitals. During the site visit, our staff was available to answer any questions on the survey and to collect completed questionnaires. We followed with two further mailings to non-respondents at monthly intervals. Lower respiratory symptoms were taken from two standard, validated questionnaires (Burney and Chinn, 1987; Venables et al., 1993). The upper respiratory symptom section included questions on throat, nasal, and sinus symptoms. We asked about asthma diagnosis date and symptoms onset dates and whether symptoms were no different, worsened or were better when away from work. We included questions on visible mold, mold odor, and water damage in the home during the last 12 months. We categorized an individual as having 'any nasal and sinus symptoms' if he/she reported having nasal (i.e. stuffy, blocked, itchy, or runny nose), and sinus (i.e. sinus headache, postnasal drip, or blowing thick mucus from nose) symptoms. We categorized an individual as having 'any chest symptoms' if he/she reported wheezing or whistling in the chest, shortness of breath, or chest tightness. We defined shortness of breath as an affirmative response to one of the following: attack of shortness of breath while not doing anything strenuous, attack of shortness of breath following strenuous activity, or awakened by shortness of breath. We defined chest tightness as an affirmative response to the question 'Have you woken up with a feeling of tightness in your chest at any time?' For lower respiratory symptoms that occurred in the last 4 weeks, we set a positive response as three or more affirmative responses to nine lower respiratory symptom questions taken from the Venables questionnaire. We categorized symptoms as work-related if an individual reported that the symptoms were 'better when away from work'. We categorized symptoms as non-work-related if an individual reported that the symptoms were 'the same or worse when away from work'.

Environmental assessment

Details of the environmental assessment are presented elsewhere (Rao et al., 2005). Briefly, during the August

2000 site survey, we took air, chair dust, and floor dust samples from 18 sites in the eight-storey hospital and eight sites in the five-storey hospital. The 8th floor (on which the six sentinel asthma cases worked) was closed for renovation and the department relocated to the 7th floor. Participants from this department were assigned the exposure values from the 7th floor sampling site.

Air samples were collected for endotoxin from 7 am to 7 pm over 4 days. We took five air samples over 3 days for fungi, bacteria and particle counts (size range of 0.02–1 μm here-after termed 'small particles'). We vacuumed chair and floor dusts for analyses of endotoxin, latex allergen, (1 $\rightarrow$ 3)- β -D-glucan, ergosterol, culturable fungi, culturable bacteria, extra-cellular polysaccharides specific for *Penicillium/Aspergillus* (EPS-Pen/Asp), and cat allergen. Participants in a department were assigned the same exposure values. More than one department was assigned the same exposure value based on proximity to sampling sites. For air sampling results, 567 participants in 38 departments were assigned 25 exposure values. For chair dust sampling results, 526 participants in 34 departments were assigned 23 exposure values. For floor dust sampling results, 499 participants in 33 departments were assigned 23 exposure values. The size of the exposure groups ranged from 3 to 42 with a median of 21 or 22. The participants assigned air, chair dust and floor dust exposure values represented approximately 68% of the total number of employees in the departments sampled.

We selected 50 areas which were assessed by research staff for observational indices of building dampness. The scores for the 50 areas were linked to 834 participants in 60 departments (62% of the total number of employees in those departments) based on proximity to the area scored.

Data analysis

We compared the prevalence of wheeze and lifetime physician-diagnosed asthma in the participants to the year 2000 data for the state from the Behavioral Risk Factor Surveillance System (BRFSS) (BRFSS, 2001) and to the US adult population data obtained from NHANES III (NHANES III, 1996). We used logistic regression analysis to examine associations between health outcomes and the observational dampness score, the reports of home dampness, mold odor, and visible mold, and the environmental sampling data used as continuous (and if significant, as categorical) variables. The continuous variables were natural log transformed as they tended to be right-skewed. [SAS version 9.1 software (SAS Institute, Cary, NC, USA)]. Models were adjusted for age, gender, smoking category, and self-reported signs of home dampness. Statistical significance was set at the $P \leq 0.05$ level, with a $P \leq 0.1$ to >0.05 considered marginally significant.

Results

Work-related asthma cases

The six work-related asthma cases were 26–58 year-old nurses or unit secretaries from a department with a total of 53 employees based on the top floor of the eight-storey hospital. All had onset of symptoms between 1997 and 1999, and reported improvement away from work. Five of the six cases had new onset asthma, and one of the cases reported childhood asthma in remission for about 20 years. Medical testing between 1998 and 2000 indicated that all cases were methacholine challenge-positive, with provocative doses causing a 20% drop in forced expiratory volume in one second (PC_{20}) from 0.23 to 3.58 mg/ml. Three met the American Thoracic Society guidelines for moderate to severe bronchial hyper-responsiveness ($\text{PC}_{20} < 1$ mg/ml) and a fourth case was at the level of 1 mg/ml (Crapo et al., 2000). None had abnormal latex allergen test results nor abnormal serological tests for house dust-mite mix, mold mix, weed mix, tree mix, grass mix, and epidermal mix in August 2000.

All six employees had kept peak flow diaries. For four of the cases, the medical records indicated that the peak flow results showed a work-related pattern with declines in peak flow during work days and improvement when off work. Two of these four cases had kept peak flow diaries after removal from the department, which showed a stabilization of peak flow variability. One of the remaining two cases showed a mixed response with drops in peak flow both at work and at home, although she did show some decline in peak flow over the work week. The other case did show some declines in peak flow on work days.

Questionnaire

Participation in the questionnaire survey offered to current employees in the two hospitals was 64% (1171/1834). The questionnaire participants were predominantly female non-smokers with a mean tenure of 11 years (Table 1). The participants had a 17% prevalence of lifetime asthma (Table 2) which was elevated compared with the state adult population showing a

Table 1 Demographics of participants* in the questionnaire survey

	N (%)
Gender (Female)	929/1153 (80.6)
Age (Mean $\pm$ s.d. [†])	42.4 $\pm$ 11.1 ($n = 1098$)
Current smoker	154/1149 (13.4)
Former smoker	257/1149 (22.4)
Never smoker	738/1149 (64.2)
Tenure years (Mean $\pm$ s.d.)	11.1 $\pm$ 8.9 ($n = 1148$)

*There were 1171 participants, but denominators vary because of missing data.

[†]s.d., Standard deviation.

Table 2 Symptom and self-reported asthma prevalence* among participants in the questionnaire survey

Symptoms	N (%)
Chest symptoms in the past 12 months	388/1146 (33.9)
Proportion with work-related pattern	131/388 (33.8)
≥3 lower respiratory symptoms in the past 4 weeks	175/1142 (15.3)
Proportion with work-related pattern	64/175 (36.6)
Nasal and sinus symptoms in the past 12 months	724/1111 (65.2)
Proportion with work-related pattern	198/724 (27.3)
Nasal and sinus symptoms in the past 4 weeks	541/1107 (48.9)
Proportion with work-related pattern	168/541 (31.1)
Physician-diagnosed asthma	199/1160 (17.2)
Physician-diagnosed asthma with post-hire onset	79/1148 (6.9)

*There were 1171 participants, but denominators vary because of missing data.

prevalence ratio (PR) of 1.45 (95% CI, 1.27–1.67), and to the US adult population (PR 2.2, 95% CI 1.88–2.51). Overall 6.9% (79) of participants reported post-hire diagnosis of their asthma, and this accounts for 40% of the reported asthma cases. Among the 79 participants with post-hire asthma diagnosis, almost half (39) had a diagnosis in the 4-year period from 1997 to 2000, during a period when there were water incursions as well as renovations, while the other 40 participants had the diagnoses over an 18-year period from 1979 to 1996.

Wheezing in the last 12 months was elevated compared with the US population (PR 1.5, 95% CI 1.36–1.75). Thirty-four percent of the participants reported chest symptoms (wheezing or whistling in the chest, shortness of breath, or chest tightness) in the last 12 months, with a third of these symptomatic individuals reporting improvement in the symptoms when away from work. Similarly about a third of the 15% of participants having three-or-more lower respiratory symptoms in the last 4 weeks reported improvement in symptoms when away from work. The prevalence of physician-diagnosed asthma and chest symptoms in the last 12 months both overall and work-related showed

differences by floors of the two hospitals, with the participants working in the eight-storey hospital tending to report more work-related symptoms (Figure 1).

Health associations with reports of home leaks and mold

Overall, 267 of the 1164 (23%) participants reported having at least one of the following conditions in the home: leaks (12%), visible mold (12%) or mold odors (12%). For nominal polytomous logistic regression we created three categories for symptoms: no symptoms, symptoms with a non-work-related pattern, and symptoms with a work-related pattern. We set the reference group as those reporting no symptoms. Results indicated that reports of any of the home dampness indices were generally significantly associated with higher odds for non-work-related upper and lower respiratory symptoms after adjustment for age, gender and smoking category (Table 3). Looking at the participants reporting chest symptoms in the last 12 months, we found that of those reporting home dampness/mold, 74% reported symptoms which were no different away from work compared with 58% of the participants with no home dampness/mold.

Health associations with the observational assessment score

The observational assessment score of workplace dampness indices ranged from 0 to 20 with a median of 4. In models adjusted for age, gender, smoking status, reported mold or dampness at home, and which hospital worked in, reported physician-diagnosed post-hire onset asthma and work-related lower respiratory symptoms in the last 12 months and in the last 4 weeks were positively associated with the observational assessment score (Figure 2).

There were no significant associations found between the observational assessment score and work-related upper respiratory symptoms or the non-work-related

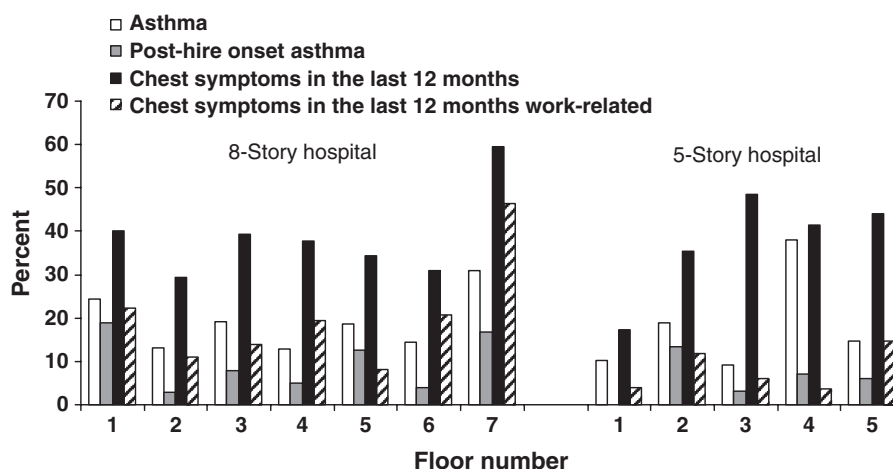
**Fig. 1** Prevalence of physician-diagnosed asthma and chest symptoms in the last 12 months stratified by floors within the two hospitals

Table 3 Odds ratios and 95% confidence intervals* for non-work related lower and upper respiratory symptoms in relation to presence of home dampness/mold

Symptoms†	Home leaks OR (95% CI)	Home visible mold OR (95% CI)	Home mold odor OR (95% CI)
Non-work-related chest symptoms in the past 12 months	1.12 (0.72–1.75)	1.75 (1.15–2.66)	1.92 (1.25–2.95)
≥3 lower respiratory symptoms in the past 4 weeks, non-work-related	1.17 (0.63–2.18)	2.48 (1.47–4.19)	1.40 (0.76–2.58)
Non-work-related nasal and sinus symptoms in the past 12 months	1.83 (1.18–2.84)	3.45 (2.11–5.64)	2.64 (1.65–4.21)
Non-work-related nasal and sinus symptoms in the past 4 weeks	2.06 (1.38–3.08)	2.22 (1.47–3.35)	2.75 (1.81–4.18)

*Models adjusted for age, gender, and smoking status.

†Comparison group was the participants with no symptoms.

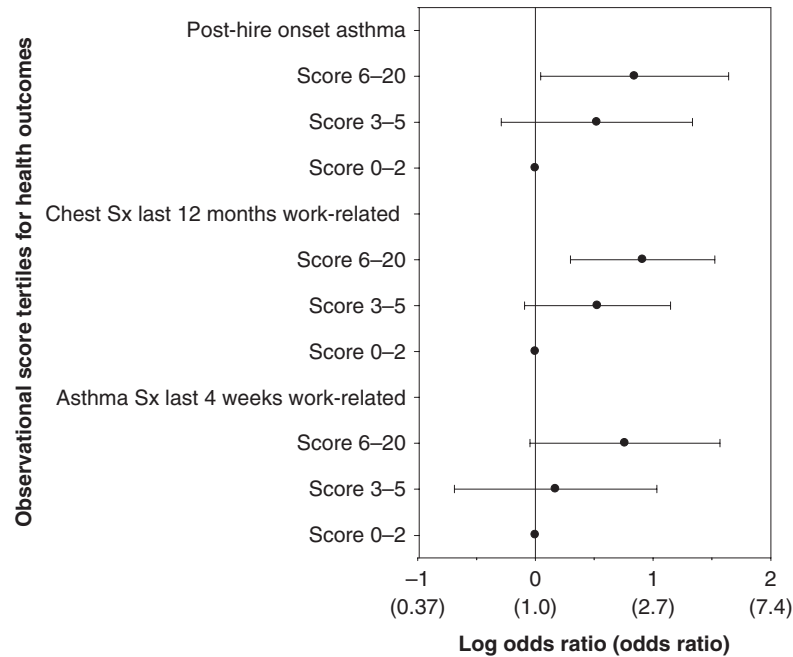


Fig. 2 Odds ratios and 95% confidence intervals* for post-hire onset asthma and work related lower and upper respiratory symptoms in relation to tertiles of the observational scores for dampness/mold. *Models adjusted for age, gender, smoking status, and reported mold or dampness at home

upper or lower respiratory symptoms, or pre-hire diagnosed asthma.

Health associations with analytes measured in air, chair and floor dust

The quartile values of the air, chair dust, and floor dust sampling results are shown in Table 4.

Post-hire onset asthma. Participants in the highest quartile of small particle exposure had 2.6 (95% CI 1.3–5.1) times the odds of having post-hire onset asthma compared with participants with lower exposures. When spore exposure categories based on quartile values were used, no significant associations were found, but participants with an exposure value of over 1000 spores/m³ (participants working on the 7th floor of the eight-storey hospital) had 3.1 (95% CI 1.1–8.6) times the odds of having post-hire onset asthma compared with participants with lower exposure values. No other associations were found for physi-

cian-diagnosed asthma with post-hire onset with measured contaminants in air, chair dust or floor dust.

Lower respiratory symptoms and air measures. All measured air contaminants (culturable fungi, culturable bacteria, fungal spores, small particle count, and endotoxin) were positively associated with work-related lower respiratory symptoms in the last 12 months and in the last 4 weeks, but they were not associated with non-work-related symptoms. The odds ratios for work-related lower respiratory symptoms comparing the highest quartile of exposure to lower exposures for the measured air contaminants ranged from 2.1 (95% CI 1.3–3.5) for endotoxin to 4.4 (95% CI 2.2–8.9) for small particles (data not shown).

Lower respiratory symptoms and floor dust measures. There were a number of positive associations between lower respiratory symptoms and markers of fungal biomass in the floor dust (EPS-Pen/Asp,

Table 4 Quartiles of analytes measured in air, chair dust and floor dust

Analyte	Upper quartile	Median	Lower quartile
Air measures			
Bacteria (CFU/m ³)	192	146	96
Particles 0.02–1 µm (count/cm ³)	3194	1768	1360
Fungal Spores (spores/m ³)	106	54	39
Culturable Fungi (CFU/m ³)	24	15	10
Endotoxin (EU/m ³)	1.70	1.24	1.07
Floor dust measures			
Culturable Fungi (CFU/m ²)	94,107	51,000	23,978
(1 → 3)-β-D-glucan (µg/m ²)	2650	1473	746
Ergosterol (pg/m ²)	237,521	145,610	53,247
EPS-Pen/Asp (units/m ²)	15,457	9161	3739
Bacteria (CFU/m ²)	1,544,857	490,431	48,475
Endotoxin (EU/m ²)	23,709	10,300	5676
Latex allergen (ng/m ²)	4764	2592	192
Cat allergen (fel d1) (µg/m ²)	3.42	0.95	0.34
Chair dust measures			
Culturable Fungi (CFU/chair)	133,720	93,555	65,550
(1 → 3)-β-D-glucan (µg/chair)	2525	1880	1193
Ergosterol (pg/chair)	227,230	165,079	94,057
EPS-Pen/Asp (units/chair)	14,880	10,780	7824
Bacteria (CFU/chair)	174,250	20,900	10,100
Endotoxin (EU/chair)	12,706	9193	5569
Latex allergen (ng/chair)	56,751	25,058	8027
Cat allergen (fel d1) (µg/chair)	46	24	13

(1 → 3)-β-D-glucan and ergosterol) (Table 5). Work-related lower respiratory symptoms showed a monotonically increasing odds ratio with ergosterol quartiles of exposure (Figure 3). Latex and cat allergen showed positive associations with symptoms.

Lower respiratory symptoms and chair dust measures. There were fewer significant associations between

lower respiratory symptoms and markers of fungal exposure in chair dust than in floor dust. EPS-Pen/Asp, endotoxin, and latex allergen in the chair dust showed positive associations with lower respiratory symptoms (Table 6).

Upper respiratory symptoms and air measures. All measured air contaminants were positively associated with work-related nasal and sinus symptoms in the last 12 months and in the last 4 weeks, but they were not associated with non-work-related symptoms. The odds ratios for work-related nasal and sinus symptoms comparing the highest quartile of exposure to lower exposures for the measured air contaminants ranged from 1.60 (95% CI 1.3–3.7) for endotoxin to 2.9 (95% CI 1.9–4.7) for small particles (data not shown).

Upper respiratory symptoms and dust measures. Nasal and sinus symptoms were in general not significantly associated with contaminants measured in the floor and chair dust. The exceptions were as follows. For participants exposed at the 75th percentile of ergosterol in floor dust vs. those exposed at the 25th percentile, odds ratios and 95% confidence intervals were 1.36 (0.97–1.91) for work-related symptoms in the last 12 months and 1.42 (1.01–2.01) for work-related symptoms in the last 4 weeks. There were increasing odds ratios with floor dust ergosterol quartiles of exposure for work-related nasal and sinus symptoms in the last 12 months and in the last 4 weeks (Figure 3). For participants exposed at the 75th percentile of

Table 5 Summary of associations between lower respiratory symptoms in the last 12 months and the last 4 weeks, classified as work-related, non-work-related or overall, and contaminants in floor dust as continuous variables*

Floor dust measures	Symptom time frame	Lower respiratory symptoms		
		Work-related	Non-work-related	Overall
Culturable Fungi	12 months	1.24 (0.88–1.75)	1.09 (0.82–1.44)	1.16 (0.91–1.47)
	4 weeks	1.22 (0.75–1.98)	0.92 (0.61–1.39)	1.06 (0.77–1.46)
(1 → 3)-β-D-glucan	12 months	1.17 (0.79–1.73)	1.15 (0.82–1.62)	1.15 (0.87–1.53)
	4 weeks	1.46 (0.89–2.39)	1.37 (0.83–2.35)	1.43 (0.99–2.07)^a
Ergosterol	12 months	1.65 (1.16–2.37)^b	0.84 (0.62–1.14)	1.12 (0.87–1.43)
	4 weeks	2.08 (1.31–3.32)^c	0.75 (0.47–1.21)	1.24 (0.89–1.73)
EPS-Pen/Asp	12 months	1.53 (0.99–2.38)^d	0.94 (0.65–1.34)	1.14 (0.84–1.55)
	4 weeks	1.90 (1.05–3.44)^e	1.14 (0.65–2.01)	1.50 (0.98–2.28)^f
Culturable Bacteria	12 months	0.92 (0.56–1.51)	0.47 (0.30–0.73)^g	0.63 (0.44–0.90)^h
	4 weeks	1.36 (0.70–2.61)	0.69 (0.35–1.36)	0.96 (0.60–1.56)
Endotoxin	12 months	0.95 (0.73–1.24)	1.00 (0.81–1.24)	0.97 (0.81–1.16)
	4 weeks	1.12 (0.82–1.52)	1.03 (0.74–1.44)	1.07 (0.85–1.36)
Latex allergen	12 months	0.98 (0.62–1.57)	1.63 (1.05–2.54)ⁱ	1.24 (0.88–1.76)
	4 weeks	0.92 (0.50–1.69)	1.48 (0.73–2.97)	1.14 (0.71–1.83)
Cat allergen	12 months	1.57 (1.01–2.45)^j	0.95 (0.67–1.35)	1.18 (0.87–1.59)
	4 weeks	1.64 (0.89–3.04)	0.73 (0.43–1.24)	1.07 (0.71–1.60)

*Logistic models adjusted for age, gender, smoking status, and reported mold or dampness at home. Polytomous logistic regression used when modeling work-related and non-work-related symptoms, with participants with no symptoms as the comparison group. Odds Ratios and 95% confidence limits given for the inter-quartile range change in dust measures, thus the odds ratios are for presence of symptoms in subjects at the 75th percentile of exposure vs. subjects at the 25th percentile. When $P < 0.05$ or $P < 0.10$, results are bolded. Results for associations after omission of sentinel cases department are given as: ^a**1.45 (0.99–2.14)**, ^b**1.43 (0.97–2.10)**, ^c**1.92 (1.15–3.21)**, ^d1.42 (0.89–2.27), ^e**1.90 (0.96–3.75)**, ^f1.29 (0.95–1.76), ^g**0.46 (0.29–0.72)**, ^h**0.56 (0.39–0.81)**, ⁱ**1.58 (1.02–2.46)**, ^j1.26 (0.79–2.01).

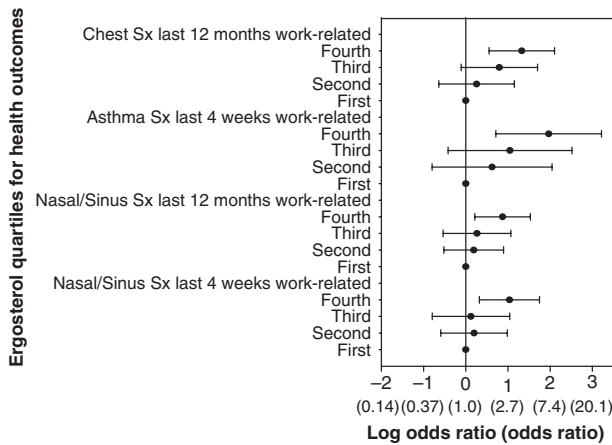


Fig. 3 Odds ratios and 95% confidence intervals* for work related lower and upper respiratory symptoms in relation to quartiles of ergosterol level in floor dust samples. *Models adjusted for age, gender, smoking status, and reported mold or dampness at home

EPS-*Pen/Asp* in chair dust vs. those exposed at the 25th percentile, the odds ratio and 95% confidence interval was 1.25 (1.01–1.54) for non-work-related symptoms in the last 12 months.

Discussion

The temporal and spatial cluster of asthma in six healthcare workers from one department was a sentinel for work-related respiratory illness in many hospital co-workers. These six sentinel cases accounted for only 8% of the 79 asthmatic participants with onset after hire at the hospitals. There were excesses of wheeze and

physician-diagnosed asthma in relation to state and national population data, and a third of participants with lower respiratory symptoms reported improvement of the symptoms when away from work.

Some portion of the work-related respiratory illness in these healthcare workers was no doubt associated with risk factors other than those related to dampness, as healthcare workers are at risk for asthma and respiratory symptoms from latex, disinfectants, cleaning agents, and aerosolized medications (Delclos et al., 2007; Gannon et al., 1995; Vandenplas et al., 1995). We found a positive association between lower respiratory symptoms and latex allergen in chair dust. The hospitals had over the year prior to our study begun phasing out the use of latex gloves which should reduce future risk of latex allergy in the workers. Hospital workers are also at risk for exposure to respiratory viruses including rhinoviruses (Bellei et al., 2007) and respiratory infections are a well documented cause of asthma exacerbation (Murray et al., 2004). Recent renovation and installation of new materials resulting in chemical emissions are associated with respiratory symptoms (Jaakkola et al., 2004; Mendell, 2007; Sieber et al., 1996; Wieslander et al., 1997). The study hospitals had ongoing and past renovations and remodeling on many floors of the buildings over the last few years. Not only could there have been chemical emissions from renovation activities, but hidden microbial contamination from past water damage could have been released during the renovation activities (Hameed et al., 2004; Horner, 2006). During an initial site visit to the facilities we saw fungal contamination of a hard plaster ceiling that was being torn down during

Table 6 Summary of associations between lower respiratory symptoms in the last 12 months and the last 4 weeks, classified as work-related, non-work-related or overall, and contaminants in chair dust as continuous variables*

Chair dust measures	Symptom time frame	Lower respiratory symptoms		
		Work-related	Non-work-related	Overall
Culturable fungi	12 months	0.89 (0.61–1.29)	1.41 (1.03–1.93)^a	1.16 (0.90–1.50)
	4 weeks	0.59 (0.35–1.02)^b	1.43 (0.89–2.30)	0.98 (0.69–1.40)
(1 → 3)- β -D-glucan	12 months	1.37 (0.90–2.09)	1.34 (0.92–1.97)	1.30 (0.96–1.77)
	4 weeks	1.03 (0.58–1.81)	1.29 (0.72–2.31)	1.17 (0.77–1.78)
Ergosterol	12 months	1.08 (0.72–1.62)	1.25 (0.87–1.79)	1.13 (0.85–1.51)
	4 weeks	0.92 (0.54–1.66)	0.96 (0.56–1.66)	0.95 (0.64–1.41)
EPS- <i>Pen/Asp</i>	12 months	1.06 (0.82–1.37)	1.33 (1.06–1.66)^c	1.20 (1.0–1.45)^e
	4 weeks	0.80 (0.55–1.15)	1.36 (0.97–1.91)^d	1.06 (0.82–1.36)
Culturable Bacteria	12 months	1.17 (0.76–1.83)	0.96 (0.64–1.43)	1.06 (0.77–1.46)
	4 weeks	1.16 (0.65–2.08)	0.75 (0.40–1.39)	0.96 (0.62–1.49)
Endotoxin	12 months	1.25 (0.93–1.68)	1.31 (1.00–1.73)^f	1.27 (1.02–1.58)^g
	4 weeks	1.02 (0.70–1.48)	1.30 (0.84–2.02)	1.15 (0.86–1.54)
Latex allergen	12 months	1.34 (0.88–2.04)	1.41 (0.97–2.05)^h	1.40 (1.03–1.92)ⁱ
	4 weeks	1.56 (0.87–2.78)	1.29 (0.71–2.32)	1.42 (0.93–2.17)
Cat allergen	12 months	1.07 (0.78–1.46)	1.22 (0.91–1.62)	1.11 (0.89–1.40)
	4 weeks	0.81 (0.53–1.23)	1.15 (0.75–1.77)	0.97 (0.71–1.32)

*Models adjusted for age, gender, smoking status, and reported mold or dampness at home; polytomous logistic regression used when modeling work-related and non-work-related symptoms, with participants with no symptoms as the comparison group. Odds Ratios and 95% confidence limits given for the inter-quartile range change in dust measures, thus the odds ratios are for presence of symptoms in subjects at the 75th percentile of exposure vs. subjects at the 25th percentile. When $P < 0.05$ or $P < 0.10$, results are bolded. Results for associations after omission of sentinel cases department are given as: ^a**1.39 (1.02–1.91)**, ^b**0.49 (0.26–0.93)**, ^c**1.31 (1.05–1.64)**, ^d**1.35 (0.97–1.90)**, ^e**1.18 (0.98–1.42)**, ^f**1.29 (0.98–1.71)**, ^g**1.19 (0.96–1.48)**, ^h**1.38 (0.95–2.00)**, ⁱ**1.31 (0.95–1.80)**.

renovation activities and found evidence of fungal contamination in the wall cavities.

This study provides evidence to address the query posed by the IOM committee (IOM, 2004) about whether damp indoor environments can lead to development of asthma. A large portion of the asthma diagnosis dates were during a period when the hospitals had water incursions and were also undergoing renovations and remodeling. Post-hire onset asthma was associated with both our observational assessment of dampness indices and with fungal spore counts in the air. Since the IOM review, other investigations have indicated that exposure to damp indoor environments and mold can lead to the development of asthma (Cox-Ganser et al., 2005; Jaakkola et al., 2005; Pekkanen et al., 2007). Consistent with the IOM review conclusions regarding upper and lower respiratory symptoms and exposure to damp indoor environments, and also consistent with our findings from a study at a water-damaged community college (Park et al., 2004), we found positive associations between our observational assessment score for building dampness and work-related symptoms. We also found that participants who reported dampness or mold at home were more likely to report symptoms that were the same at work and home, as may be expected if they were potentially exposed to dampness-related agents both at work and home. Analysis of the large European Community Respiratory Health study found that reported mold exposure in homes in the last year was associated with current asthma, asthma symptoms, and bronchial responsiveness in adults, with odds ratios from 1.14 to 1.44. The authors concluded that the effects were consistent across different countries and that they were unlikely to have been caused by bias (Zock et al., 2002).

In our study, levels of fungal, bacterial and small particles in the air showed positive associations with work-related respiratory symptoms, even though the levels of fungi and bacteria in the air were modest. There were significant positive correlations among all these air contaminants (Rao et al., 2005) perhaps indicating a general difference in cleanliness and indoor air quality among the various departments and hospital areas. A recently published article concerning an early 1980s study of airborne fungi and bacteria levels in a Polish hospital ward for asthma patients found mean monthly levels of 257–436 CFU/m³ for bacteria and 10–96 CFU/m³ for fungi, which are of the same order of magnitude as the concentrations found here. Nine of the 24 asthma patients had decreases in lung function with increasing levels of airborne microorganisms (Augustowska and Dutkiewicz, 2006). A study on child respiratory health in Australia did not find associations between total airborne fungal spores in the home, but did find some significant associations between specific airborne fungal genera, and asthma and respiratory symptoms (Garrett et al., 1998).

Respiratory symptoms in workers in six office buildings were associated with indoor airborne endotoxin exposures, which were low, having geometric means from 0.5 to 3 EU/m³ in the six buildings (Reynolds et al., 2001). In a 2-year follow-up study on new-born children in Canada, airborne endotoxin levels were positively associated with episodes of respiratory illness. The airborne endotoxin levels found in the Canadian study were low (generally below 2 EU/m³), and the authors felt that the 5-day collection period used in their study led to a stable estimate of average endotoxin exposure (Dales et al., 2006). Little literature exists that links fine and ultrafine particle exposures and respiratory health effects in the indoor environment, but a recent review suggested that ultrafine particles may play an important role in triggering asthma symptoms (Weichenthal et al., 2007).

Of note were our findings of positive associations between work-related respiratory symptoms and ergosterol in floor dust. The literature on ergosterol and health outcomes is sparse and the results are mixed. Currently it is not known whether ergosterol can directly induce respiratory health effects or if it is only a surrogate measure of fungal exposure. In a recent NIOSH study of a water-damaged office building, the risk of being a respiratory case was positively associated with the level of ergosterol in floor dust (Park et al., 2008). A study of young adults who were part of the European Community Respiratory Health Survey, found a significant association of ergosterol levels in bedroom dust with sensitization to fungi and having wheezed in the last year (Dharmage et al., 2001). Conversely, Canadian researchers did not find associations between airborne ergosterol levels in bedrooms and respiratory symptoms or nocturnal cough among elementary school children (Dales et al., 1999).

The six sentinel asthma cases were all negative on skin prick testing using common aeroallergens. This finding is consistent with results of a study of occupants of a water-damaged office building (Cox-Ganser et al., 2005). In the office study, post-occupancy asthma cases had lower prevalence of IgE-mediated allergen skin-test positivity than did pre-occupancy cases. Although mechanisms of respiratory effects of damp indoor environments are not fully understood, it is possible that the development of asthma in damp/moldy conditions may not be only IgE-mediated (Douwes et al., 2003; Savilahti et al., 2001; Zock et al., 2002).

Our exposure assessment had limitations. We sampled only a limited number of sites and thus all employees in departments in proximity to the sampling sites were assigned the same exposure values. We sampled at one time-point and exposures may have varied over the time period asked about in the questionnaire.

Cross-sectional studies are prone to healthy worker effects, in which affected employees either leave employment or relocate away from areas where the onset of health problems occurred, but this effect would tend to lessen the chance of finding positive exposure-response relations. Although we had a fairly good participation rate of 64%, self-selection into the questionnaire survey may have led to biases in estimation of prevalence of respiratory problems. There was a correlation of 0.39 ($P < 0.05$) between participation within departments and the observational score, thus employees who worked in department with dampness problems were somewhat more likely to take part in the survey. Although higher participation should give more accurate prevalence of symptoms or physician-diagnosed asthma, it is possible that some over-reporting occurred. Since the sentinel occupational asthma cases had come from the eight-storey building and it was possible that employees in that hospital were more aware of concerns with mold, we adjusted for which hospital the subjects worked in for the regression models of asthma and respiratory symptoms in relation to the observational assessment score, but the odds ratios for the observational assessment scores remained similar. We repeated the models omitting the 42 participants from the department in which the sentinel asthma cases worked. The odds ratio for post-hire onset asthma for participants in the highest exposure tertile of the observational assessment score changed from 2.44 ($P = 0.03$) to 2.12 ($P = 0.07$); for work-related lower respiratory symptoms in the last 12 months it lowered from 2.57 ($P = 0.003$) to 1.80 ($P = 0.08$); and for work-related lower respiratory symptoms in the last 4 weeks it lowered from 2.20 ($P = 0.06$) to 1.50 ($P = 0.37$).

When participants from the sentinel cases' department were omitted from the analyses on air measures and lower respiratory symptoms culturable fungi and endotoxin were no longer significant. Odds ratios for associations with culturable bacteria, fungal spores and small particles count were lower but remained significant or marginally significant. For example, the odds ratio for the association of lower respiratory symptoms in the last 4 weeks with airborne fungal spores changed from 4.0 (95% CI 2.0–8.2) to 2.8 (95% CI 1.2–6.4); while for small particles the odds ratio changed from 4.4 (95% CI 2.2–8.9) to 3.3 (95% CI 1.5–7.4). For models of upper respiratory symptoms associations with airborne culturable fungi, culturable bacteria, fungal spores and endotoxin were no longer significant. Associations with small particles remained similar with the odds ratio for work-related upper respiratory symptoms in the last 12 months; changing from 2.9 (95% CI 1.9–4.7) to 2.4 (95% CI 1.4–4.0). The department in which the sentinel cases worked was one of the highest in many environmental measures, thus omitting this department also attenuated the

range of exposures. Most associations between respiratory symptoms and dust measures remained significant or marginally significant as indicated in the results.

The results of these sensitivity analyses indicate that participants from the sentinel cases' department did not drive all the significant associations found between respiratory outcomes and measures of exposure in air and dusts.

We did not use medical records or medical testing to validate the participants' reporting of physician-diagnosed asthma, except for the six sentinel asthma cases. In epidemiologic studies of causes of asthma, definitions with high specificity are preferred. The question based on physician-diagnosed asthma is among those with the highest specificity (Torén et al., 1993). Our survey may have underestimated the prevalence of asthma because asthma definitions based on a doctors' diagnosis increase the fraction of false negatives as they have lower sensitivity. Participants with mild asthma are probably more likely not to report their asthma diagnosis (Nathell et al., 2001).

Strengths of our study include our objective measures of biological contaminants that are not subject to reporting bias. Our observational assessments of dampness indices were significantly correlated with endotoxin levels in air and (1 → 3)- β -D-glucan in floor dust (Rao et al., 2005).

In conclusion, this study reinforces the importance of following up sentinel cases of building-related asthma to identify risk to co-workers. Our data imply new-onset of building-related asthma in relation to water damage. Furthermore, our results indicate work-related respiratory symptoms in hospital employees were associated with diverse biological exposures including fungi, bacteria, cat allergen, and latex allergen. The implication for healthcare settings is that good building maintenance and housekeeping procedures should lead to improvements in employee respiratory health.

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Disclaimer

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