The Work Environment and Workers' Health in Four Large Office Buildings

H. Jasmine Chao,[1] Joel Schwartz,[2] Donald K. Milton,[2] and Harriet A. Burge[2]

[1]Graduate Institute of Public Health, Taipei Medical University, Taipei, Taiwan; [2]Department of Environmental Health, Harvard School of Public Health, Boston, Massachusetts, USA

We conducted a 1-year epidemiologic study in Boston, Massachusetts, beginning May 1997, to examine the associations between environmental factors and office workers' health. We recruited 98 subjects (81 females and 17 males) in 21 offices in four office buildings. We conducted environmental sampling every 6 weeks and concurrently administered detailed questionnaires to collect information on work-related symptoms, psychosocial factors, and perceptions of the office environments. In multivariate analyses, eye irritation was positively correlated with floor dust [odds ratio (OR) = 1.46; 95% confidence intervals (CI), 1.14–1.86] and reported lack of office cleanliness (OR = 1.52; 95% CI, 1.11–2.08). Nonspecific symptoms were positively associated with unidentified chair fungi (OR = 1.87; 95% CI, 1.11–3.15) and several self-reported conditions, including a history of asthma (OR = 3.15; 95% CI, 1.26–7.87), more people in offices (OR = 1.71; 95% CI, 1.16–2.51), lack of office cleanliness (OR = 2.85; 95% CI, 1.72–4.73), and low job satisfaction (OR = 1.72; 95% CI, 1.06–2.81). Upper respiratory symptoms were positively associated with total fungal concentrations recovered from chair dust (OR = 1.35; 95% CI, 1.07–1.70) and the following self-reported conditions: more people in offices (OR = 1.45; 95% CI, 1.01–2.08), lack of office cleanliness (OR = 1.62; 95% CI, 1.15–2.30), and jobs frequently requiring hard work (OR = 1.43; 95% CI, 1.05–1.95). This study emphasizes the importance of maintaining a clean, uncrowded workspace and the importance of chair fungi as a correlate for health effects. *Key words:* **building-related symptoms, culturable fungi, indoor environmental quality, sick building syndrome.** *Environ Health Perspect* **111:1242–1248 (2003). doi:10.1289/ehp.5697 available via** *http://dx.doi.org/* **[Online 25 February 2003]**

Nonspecific building-related symptoms (BRS), sometimes called sick building syndrome, have emerged as an occupational and environmental health issue since the early 1980s (Burge et al. 1987; Mendell 1993). BRS refers to a group of symptoms (i.e., eye, nose, and throat irritation; fatigue; headache; or other discomfort). This group of symptoms cannot be assigned to a specific illness and usually does not have an identifiable cause, but it appears to be building related (American Conference of Governmental Industrial Hygienists 1999). Although not life threatening, this group of symptoms can be unpleasant and disruptive, causing lost work time and reduced productivity (Fisk and Rosenfeld 1997; Woods 1989).

Many cross-sectional epidemiologic and experimental studies have indicated that air contaminants [e.g., bioaerosols, volatile organic compounds (VOCs)], psychosocial factors (e.g., female sex, job satisfaction), and building characteristics (e.g., low ventilation rates) may be associated with BRS (Mendell 1993; Norback et al. 1990; Teeuw et al. 1994). However, a definitive causal relationship has not been established because of the lack of standardized investigating protocols, baseline data, and guidelines for interpretation. To address these issues, in 1994, the U.S. Environmental Protection Agency (EPA) conducted a cross-sectional epidemiologic study, the Building Assessment Survey and Evaluation (BASE) program (U.S. EPA 1994a). Using standardized protocols, the BASE program evaluated the indoor environment and occupant perceptions in randomly selected noncomplaint office buildings across the United States. Environmental data collected included observations of building characteristics; assessment of the heating, ventilating, and air-conditioning (HVAC) system; and measurements of temperature, relative humidity, VOCs, particulate matter, bioaerosols, among others. Occupants' perceptions of health and comfort were assessed by a comprehensive self-administered questionnaire (the BASE questionnaire). The goal was to establish a baseline database leading to guidelines for the indoor environment (U.S. EPA 1994b).

Despite the comprehensiveness of BASE, longitudinal variability and causal relationships could not be examined in the cross-sectional study design. Therefore, the U.S. EPA subsequently funded the present study to evaluate longitudinal relationships between several environmental variables and BRS. In this study, intensive sampling protocols were conducted every 6 weeks in four office buildings over a 1-year period. Detailed questionnaires were administered to subjects concurrently with each environmental sampling event to collect information on office workers' perceptions of health and comfort. In this article, we specifically examine the possible predictors of four symptom groups: upper respiratory, lower respiratory, eye irritation, and nonspecific symptoms.

Materials and Methods

Study design. We investigated 21 offices with open stations (low partitions) in four office buildings in Boston, Massachusetts, over 1 year beginning May 1997, and we recruited 98 occupants. Intensive environmental sampling was conducted every 6 weeks at workstations representing small groups of workers for airborne culturable fungi, dust-borne culturable fungi from floors and chairs, temperature, relative humidity, carbon dioxide concentrations, water activities of floor carpets, and surface dust levels on nontextile furniture. A total of 10 environmental measurement events were conducted at each sampling location over the year. Comprehensive questionnaires were administered to the participants concurrently with each environmental sampling event to collect information on participants' perceptions of their health and comfort and of the conditions of the work environments.

Evaluation of perceptions of health and work environments. Two types of questionnaires, the BASE questionnaire and 6-week questionnaires, were used to collect information on participants' psychosocial factors and to assess their perceptions of health, comfort, and the conditions of the work environments (National Institute for Occupational Safety and Health 1991).

The BASE questionnaires were distributed to the participants once at the beginning of the study. The 6-week questionnaire was a shorter form of the BASE questionnaire that followed changes in the office environment and participants' perceptions. This questionnaire was administered concurrently with environmental sampling every 6 weeks. The protocols were approved by the institutional review board for human studies, and informed written consent was obtained from each subject

BRS groups. The outcomes of interest in this study were BRS groups: eye irritation, nonspecific symptoms, upper respiratory symptoms, and lower respiratory symptoms.

Address correspondence to H.J. Chao, Graduate Institute of Public Health, Taipei Medical University, 250 Wu-Hsing St., Taipei, Taiwan 110. Telephone: 8862-2736-1661 ext. 6526. Fax: 8862-2738-4831. E-mail: hchao@tmu.edu.tw

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The first three symptom groups are commonly considered part of the BRS complex, although individual symptoms within each group may be associated with other well-defined diseases. Lower respiratory symptoms are usually considered as building-related illness and suggest the presence of asthma, hypersensitivity pneumonitis, or lower respiratory infection. Eye irritation included reported "dry/irritated eyes" and "tired eyes." The nonspecific symptom group included seven symptoms: "headache," "unusual tiredness," "tension," "difficulty concentrating/remembering things," "dizziness," "feeling depressed," and "nausea." Upper respiratory symptoms included "sore/dry throat," "sinus congestion," "cough," and "sneezing." Lower respiratory symptoms included "wheezing," "chest tightness," and "shortness of breath." The symptom groups were determined according to the categories commonly used in previous investigations (Eriksson et al. 1996; Redlich et al. 1997) and the clinical judgment of one coauthor.

A symptom was considered building related if a participant experienced the symptom at least one day per week during the past month and felt better when away from work (Sieber et al. 1996). A symptom group was then defined as present if a subject reported at least one BRS from the group, except that the nonspecific symptom group was defined as present if at least two of its components were reported. Symptom groups were used as outcome variables to correlate with predictor variables.

Predictor variables. Variables used for fungal exposures were total culturable airborne fungal concentrations [colony-forming units (CFU) per cubic meter of air], total culturable fungal concentrations in floor dust (CFU per square meter of floor), and total culturable fungal concentrations in chair dust (CFU/chair). In addition, we used factor scores of the fungal groups derived from principal component analysis (PCA) for airborne (four PCA factors), floor (six PCA factors), and chair fungi (six PCA factors). PCA is a variable reduction procedure that can identify important subsets (i.e., principal components) of the original set of variables (Cody and Smith 1997; Jongman et al. 1995; Kleinbaum et al. 1988). PCA factor scores were calculated using linear combinations of optimally weighted observed variables. The four subgroups (PCA factors) derived for airborne fungi were *a*) *Alternaria*, *Aspergillus*, *Cladosporium*, *Penicillium,* and unknown; *b*) yeast and nonsporulating fungi; *c*) *Aureobasidium*, *Coelomycetes*, and *Zygomycetes*; and *d*) *Paecilomyces* and *Wallemia*. The six subgroups for culturable fungi in floor dust were *a*) *Aureobasidium*, *Coelomycetes*, yeast, and nonsporulating fungi; *b*) *Alternaria*, *Cladosporium*, *Epicoccum*, *Fusarium*, and *Pithomyces*; *c*) *Curvularia*, *Paecilomyces*, and *Ulocladium; d*) *Aspergillus* and *Penicillium; e*) *Zygomycetes* and unknown; and *f*) *Botrytis* and *Drechslera*. The six subgroups for culturable fungi in chair dust were *a*) *Alternaria*, *Aureobasidium*, *Cladosporium*, *Epicoccum*, yeast, and nonsporulating fungi; *b*) *Aspergillus* and *Zygomycetes*; *c*) *Nigrospora*, *Pithomyces*, and *Trichoderma*; *d*) *Drechslera*, *Paecilomyces*, and unknown; *e*) *Botrytis*, *Penicillium*, and *Ulocladium*; and *f*) *Fusarium* and *Wallemia*.

Other environmental factors used as predictor variables in the data analysis included temperature, relative humidity, CO_2 levels, dust loads in floors and chairs (in grams), and surface dust levels (percentage of area covered by dust). Environmental data are presented elsewhere (Chao et al. 2002a, 2002b).

In addition to environmental variables, demographic factors, past medical history, and self-reported working conditions were examined for their effects on self-reported symptoms.

Statistical analysis. We used SAS (version 6.12; SAS Institute Inc., Cary, NC, USA) to examine the relationships between symptoms and predictor variables. Generalized linear mixed models (Littell et al. 1996) were used to correlate self-reported symptoms with possible predictor variables, using a logistic link. To account for the correlation of repeated measurements of symptoms in both univariate and multivariable models, compound symmetry variance–covariance structure was assumed. Empirical (i.e., robust) standard errors were used to minimize effects of potential misspecification of the variance–covariance structure. Univariate associations between symptom groups and all the predictor variables were examined. The environmental, work-related, and job-perception variables with p-values ≤ 0.3 were selected for multivariate analysis. All of the demographic factors and variables for past medical history were tested in multivariate analyses to examine possible confounding

Table 1. Demographic characteristics of the subjects.

	Total	Female	Male
No. of subjects	98	81	17
Age distribution, years (%)			
< 30	29 (30)	25 (31)	4 (24)
30–39	31 (32)	24 (30)	7 (41)
40–49	24 (24)	18 (22)	6 (35)
≥ 50	11 (11)	11 (14)	0 (0)
Unknown	3 (3)	3 (4)	0 (0)
Job category distribution, no. (%)			
Managerial	11 (11)	8 (10)	3 (18)
Professional	25 (26)	20 (25)	5 (29)
Technical	4 (4)	3 (4)	1 (6)
Secretarial/clerical	57 (58)	49 (60)	8 (47)
Other	1 (1)	1 (1)	0 (0)
Education distribution, no. (%)			
High school graduate	20 (20)	19 (23)	1 (6)
Some college	23 (23)	22 (27)	1 (6)
College degree	41 (42)	31 (38)	10 (59)
Graduate degree	12 (12)	7 (9)	5 (29)
Unknown	2 (2)	2 (2)	0 (0)
Mean years working in the building ± SD	5.8 ± 5.6	6.0 ± 5.8	4.5 ± 4.3
Questionnaires completed per subject, no. (%)			
1–3	41 (42)	33 (41)	8 (47)
4–6	17 (17)	14 (17)	3 (18)
7–10	40 (41)	34 (42)	6 (35)

Table 2. Prevalence of health symptoms related to work environments.

Sampling set (date)	No. of sites	No. of questionnaires	Symptom prevalence (%) Total[a]	Eye irritation	Nonspecific	Upper respiratory	Lower respiratory
All sets	21[b]	529	48.0	28.4	10.1	16.0	2.4
1st (5/12/97)	20	87	62.1	42.9	17.4	27.7	5.1
2nd (6/23/97)	20	68	49.3	33.3	7.7	26.2	3.4
3rd (8/4/97)	20	56	42.6	28.3	5.6	9.6	0
4th (9/15/97)	20	49	42.6	19.2	14.9	11.1	2.2
5th (10/27/97)	21[b]	55	41.5	26.0	6.0	8.0	2.2
6th (12/8/97)	19	51	44.9	23.4	8.3	15.2	4.6
7th (1/19/98)	15	46	48.9	25.6	9.1	9.8	0
8th (3/2/98)	14	38	42.1	25.0	11.1	13.9	2.9
9th (4/13/98)	14	41	45.0	23.7	5.1	13.2	0
10th (5/25/98)	14	38	48.7	19.4	10.8	11.4	0

[a]At least 1 of 19 symptoms reported by subjects. [b]Twenty sampling sites were recruited in the beginning of the study, and one sampling site was recruited at the fifth sampling.

effects. Final models were developed for each symptom group, including all of the predictor variables with p values ≤ 0.05 and a few factors with p values ≥ 0.05 that were considered of special importance. Odds ratios (ORs) and 95% confidence intervals (95% CIs) are presented for the univariate and multivariate associations.

Results

Demographic characteristics of the participants are shown in Table 1. Approximately 80% of the participants were female. Most subjects had secretarial/clerical jobs and college degrees. Ten questionnaires (1 BASE and 9 six-week) were distributed over the year of study to each participant, and 10 environmental sampling events occurred. About 41% of the participants filled out the questionnaires consistently throughout the study.

Table 2 summarizes numbers of sampling sites, numbers of questionnaires, and symptom prevalence frequencies over the sampling year. A total of 20 sampling sites were recruited in the beginning of the study. One more site was recruited at the fifth environmental sampling. However, 7 sites were dropped before the end of the study because of low participant compliance. Symptom prevalence was defined as percentage of respondents who experienced the BRS on each occasion. Eye irritation, nonspecific, and upper respiratory symptoms had, on average, more than 10% overall prevalence. Lower respiratory symptom prevalence over time was very low (maximum, 5.1%), so this symptom group was excluded from modeling.

Univariate associations for all demographic factors and other categories of predictor variables with p values ≤ 0.3 are listed in Tables 3–5. Multivariate model results are shown in Tables 6–8. For environmental predictors, if a quadratic relationship was a better predictor than a linear one, both relationships are presented for univariate correlations. Because many environmental factors varied significantly with season, associations are controlled for sampling date (sampling dates were coded as 1–10 for the 10 equally spaced sampling events and were used as a continuous variable).

Eye irritation. Reports of eye irritation decreased over the course of the study. Therefore, the environmental variables in univariate and final models (Tables 5 and 6) were linearly adjusted for sampling date. Amount of dust in floors (grams per square meter of floor) was the only environmental measure positively related to eye irritation in the final models (Table 6). Univariately, total culturable fungal concentrations in floor dust and the fifth PCA factor for chair fungi (chair factor 5), including *Botrytis*, *Penicillium*, and *Ulocladium*, had nonlinear correlations with eye irritation (Table 5) after adjusting for sampling date. However the associations were not consistent after controlling for amount of floor dust.

Older age and history of asthma increased the chance of reported eye irritation (Table 6, Models 2 and 3). In univariate analyses, a history of hay fever and allergy to mold were better predictors (with smaller p-values) than was history of asthma (Table 3). However, after adjusting for age, asthma remained significantly correlated with eye irritation, but the relationships for hay fever and allergy to mold were no longer significant. Perceptions of workstation cleanliness were positively correlated with eye irritation symptoms in the final model (Table 6, Model 3). Conversational privacy and freedom from distracting noise also had marginal univariate correlations with symptom reports (Table 4), but the relationships did not persist after adjusting for other predictors.

Nonspecific symptoms. The relationships between nonspecific symptoms and predictor variables are shown in Tables 3–5 and 7. Because this symptom group had a nonlinear relationship with sampling date, the environmental variables were adjusted for a quadratic term of sampling date (date + date^2)

Table 3. Univariate predictors for symptoms: demographic and past medical history.

Predictors	Eye irritation OR (95% CI)	Nonspecific OR (95% CI)	Upper respiratory OR (95% CI)
Demographic			
Sex (male)[a]	0.63 (0.25–1.59)	0.07 (0.01–0.48)	1.38 (0.52–3.70)
Age			
< 30	1.24 (0.92–1.67)[b]	1.41 (0.38–5.23)	1.77 (0.44–7.02)
30–39		2.58 (0.67–9.94)	0.99 (0.24–4.10)
40–49		2.50 (0.73–8.49)	1.48 (0.37–5.98)
≥ 50		1.00	1.00
Education			
High school graduate	0.69 (0.23–2.06)	8.85 (1.96–39.98)	1.81 (0.31–10.44)
Some college	0.61 (0.23–1.62)	5.99 (1.36–26.47)	4.94 (0.95–25.70)
College degree	0.57 (0.23–1.41)	2.74 (0.65–11.48)	2.89 (0.59–14.07)
Graduate degree	1.00	1.00	1.00
Job categories			
Managerial	2.06 (0.81–5.25)	0.71 (0.13–3.90)	0.50 (0.10–2.60)
Professional	1.38 (0.67–2.83)	0.60 (0.17–2.11)	1.43 (0.63–3.26)
Technical	0.58 (0.30–1.15)	2.06 (0.35–12.06)	4.09 (0.74–22.68)
Secretarial/clerical	1.00	1.00	1.00
Working year (no. of years)[c]	1.32 (0.88–1.97)	1.72 (1.08–2.74)	1.25 (0.79–2.00)
Past medical history			
Asthma[d]	1.86 (0.75–4.63)	4.42 (1.68–11.60)	2.61 (0.99–6.88)
Hay fever[d]	1.97 (0.89–4.37)	—	—
Allergic to mold[d]	2.39 (1.13–5.05)	—	2.00 (0.71–5.67)
Migraine[d]	—	—	1.84 (0.67–5.07)
Smoking			
Never	—	—	0.51 (0.19–1.36)
Former			0.28 (0.08–0.92)
Current			1.00

[a]Female was used as the reference group. [b]Age was treated as a four-level linear variable for predicting eye irritation because it was more statistically significant than if it was treated as a categorical variable; ORs and 95% CI were calculated using one unit of change. [c]ORs and 95% CI were calculated using interquartile range change (7 years). [d]Individuals without the disease were used as the reference group.

Table 4. Univariate predictors for symptoms: self-reported working conditions.

Predictors	Eye irritation OR (95% CI)	Nonspecific OR (95% CI)	Upper respiratory OR (95% CI)
No. of people in office[a]	—	1.66 (1.16–2.35)	1.55 (1.06–2.27)
Station cleanliness[b]	1.49 (1.10–2.02)	2.81 (1.74–4.54)	1.85 (1.28–2.69)
Work station			
One person private office	—	0.27 (0.07–1.06)	—
Shared private office		0.59 (0.07–5.12)	
Open space with partitions		0.89 (0.35–2.27)	
Open space without partitions		1.00	
Table comfort[c]	—	1.76 (1.17–2.65)	—
Conversational privacy[d]	1.20 (0.98–1.48)	1.34 (0.98–1.84)	1.28 (0.95–1.71)
Freedom from distracting noise[d]	1.24 (1.00–1.55)	1.37 (0.91–2.05)	—
Job satisfaction[d]	1.24 (0.88–1.74)	2.12 (1.31–3.44)	1.38 (0.93–2.04)
Job requires to work very fast[e]	—	—	1.19 (0.94–1.50)

ORs and 95% CI for four-level or five-level linear variables were calculated using one unit of change.
[a]Four levels are 1) 1 person, 2) 2–3 persons, 3) 4–7 persons, and 4) ≥ 8 persons. [b]Four levels are 1) very clean, 2) reasonably clean, 3) somewhat dirty, and 4) very dirty. [c]Four levels are 1) very comfortable, 2) reasonably comfortable, 3) somewhat uncomfortable, and 4) very uncomfortable. [d]Four levels are 1) very satisfied, 2) somewhat satisfied, 3) not too satisfied, and 4) not at all satisfied. [e]Five levels are 1) rarely, 2) occasionally, 3) sometimes, 4) fairly often, and 5) very often.

for univariate and multivariate analyses (Tables 5 and 7).

The fourth PCA factor for chair fungi (chair factor 4) was positively correlated with nonspecific symptoms in final multivariate models (Table 7). The major component of chair factor 4 is "unknown." This category includes fungi that cannot be identified or are overgrown by other colonies. Total culturable fungal concentrations in floor dust had a nonlinear univariate relationship with nonspecific symptoms (Table 5). However, the relationship was not significant when controlled for other predictors.

Sex, education, and number of years working in the building had statistically significant correlations with nonspecific symptoms in univariate models (Table 3). The associations for sex and years working in the building remained significant after controlling for environmental variables and medical histories (Table 7, Model 2). However, after additional adjustment for self-reported working condition (Table 7, Model 3), sex and year of work were not significant. The lack of sex significance might be in part because of its correlation with station cleanliness (Mantel-Haenszel chi-square = 56.62, $p = 0.001$), which was a significant predictor of nonspecific symptoms in the multivariate model. Females more frequently reported lack of station cleanliness. A history of asthma was associated with more frequently reported symptoms in both univariate and multivariate models. Remaining medical history variables were not associated with nonspecific symptoms.

Many of the self-reported working conditions had univariate correlations with nonspecific symptoms, including number of persons in the office, workstation cleanliness, table comfort, and job satisfaction. Except for table comfort, all these variables were also significant in the final multivariate model (Table 7, Model 3).

Upper respiratory symptoms. Tables 3–5 and 8 show the correlations between upper respiratory symptoms and predictor variables. The univariate model for environmental measurements (Table 5) and the final models (Table 8) were adjusted for quadratic sampling date (date + date^2) to account for seasonal effects.

After adjusting for sampling date, upper respiratory symptoms had significant relationships with CO_2 concentrations, total airborne fungal concentrations, total fungal concentrations in chair dust, and the second PCA factor for chair fungi (chair factor 2), which included *Aspergillus* and *Zygomycetes* (Table 5). In the multivariate model for environmental measurements (Table 8, Model 1), CO_2 concentrations and total chair fungal concentrations remained significant predictors of upper respiratory symptoms. Although total airborne fungal concentrations had a marginally significant quadratic relationship with the symptoms, they were not included in the final model. The smoothing plot of the correlation suggested that this quadratic relationship might have resulted from a threshold effect of airborne fungi on upper respiratory symptoms. Thus, categorical variables and a threshold effect of airborne fungi were examined. However, neither of these methods produced a significant association. Because of the difficulty in interpreting the effect of airborne fungi on

Table 5. Univariate predictors for symptoms controlling for sampling date: environmental measurements.

Predictors	Level	Eye irritation OR (95% CI)	Nonspecific OR (95% CI)	Upper respiratory OR (95% CI)
Temperature	Linear[a]	0.90 (0.67–1.21)	—	—
Relative humidity	Linear	0.81 (0.60–1.10)	—	—
	Quadratic[b]	0.89 [$p = 0.27$, 0.16]	—	—
CO_2	Linear	0.95 (0.72–1.26)	1.24 (0.86–1.78)	1.49 (1.09–2.03)
	Quadratic	0.26 [$p = 0.08$, 0.02]	—	—
Log_{10} (floor dust)	Linear	1.34 (1.04–1.71)	—	—
Log_{10} (chair dust)	Linear	1.05 (0.86–1.27)	—	1.26 (0.95–1.69)
Log_{10} (air fungi)[c]	Linear	0.86 (0.62–1.18)	—	0.77 (0.48–1.24)
	Quadratic	—	—	0.76 [$p = 0.005$, 0.02]
Air factor 2[d]	Linear	1.16 (0.89–1.52)	—	0.86 (0.64–1.16)
Log_{10} (floor fungi)[c]	Linear	1.06 (0.89–1.26)	0.88 (0.58–1.32)	—
	Quadratic	1.05 [$p = 0.05$, 0.05]	0.87 [$p = 0.02$, 0.02]	—
Floor factor 2	Linear	1.11 (0.90–1.38)	—	—
Floor factor 3	Linear	1.15 (0.97–1.37)	—	—
Floor factor 6	Linear	1.06 (0.96–1.17)	—	1.05 (0.90–1.23)
Log_{10} (chair fungi)[c]	Linear	—	1.08 (0.74–1.60)	1.42 (1.13–1.78)
	Quadratic	—	1.05 [$p = 0.16$, 0.16]	—
Chair factor 2	Linear	—	—	1.42 (1.10–1.82)
Chair factor 4	Linear	—	1.85 (1.16–2.95)	—
Chair factor 5	Linear	1.13 (0.94–1.36)	—	1.07 (0.85–1.34)
	Quadratic	1.34 [$p = 0.03$, 0.02]	—	—

[a]ORs and 95% CIs for all linear variables were calculated using interquartile range change. [b]A quadratic variable included both linear and quadratic terms of the variable, for example, relative humidity and relative humidity squared; because 95% CIs could not be derived using the statistical software, ORs [*p*-values for linear and quadratic terms, respectively] were presented instead for these variables. [c]Log_{10} (air fungi), log_{10} (floor fungi), and log_{10} (chair fungi) were base-10 logarithm of total culturable fungal concentrations in air, floors, and chairs, respectively. [d]Air factor 2 was the second PCA factor (subgroup) for airborne fungi; similar expressions were used for PCA factors of floor and chair fungi.

Table 6. Multivariate regression models for eye irritation, controlling for sampling date.

Predictors	Level	Model 1[a] OR (95% CI)	Model 2[b] OR (95% CI)	Model 3[c] OR (95% CI)
Environmental				
Log_{10} (floor dust)	Linear	1.35 (1.04–1.74)[d]	1.42 (1.11–1.82)[d]	1.46 (1.14–1.86)[d]
Demographic and past medical history				
Age	Linear	—	1.48 (1.06–2.06)[e]	1.40 (0.98–1.99)[e]
Asthma	Yes	—	2.85 (1.09–7.46)	2.43 (0.95–6.22)
	No		1.00	1.00
Self-reported working conditions				
Station cleanliness	Linear	—	—	1.52 (1.11–2.08)[e]

[a]Environmental variables. [b]Model 1 + demographic + medical history. [c]All variables. [d]For interquartile range change. [e]For one unit of change.

Table 7. Multivariate regression models for nonspecific symptoms, controlling for sampling date.

Predictors	Level	Model 1[a] OR (95% CI)	Model 2[b] OR (95% CI)	Model 3[c] OR (95% CI)
Environmental				
Chair factor 4	Linear	1.85 (1.16–2.95)[d]	1.95 (1.16–3.30)[d]	1.87 (1.11–3.15)[d]
Demographic and medical history				
Sex	Male	—	0.11 (0.02–0.85)	—
	Female		1.00	
Working year	Linear	—	1.64 (1.09–2.47)[d]	—
Asthma	Yes	—	4.34 (1.95–9.66)	3.15 (1.26–7.87)
	No		1.00	1.00
Self-reported working conditions				
No. of people in office	Linear	—	—	1.71 (1.16–2.51)[e]
Station cleanliness	Linear	—	—	2.85 (1.72–4.73)[e]
Job satisfaction	Linear	—	—	1.72 (1.06–2.81)[e]

[a]Environmental variables. [b]Model 1 + demographic + medical history. [c]All variables. [d]For interquartile range change. [e]For one unit of change.

symptoms, we did not include airborne fungal concentrations in our final models. Chair factor 2 was positively related to upper respiratory symptoms in the univariate analysis. Yet, after controlling for total fungal concentrations in chair dust, Chair factor 2 was not significant.

History of asthma had a marginally significant positive correlation with upper respiratory symptoms in the univariate model (Table 3) and in the multivariate model (Table 8, model 2). However, the relationship became insignificant ($p = 0.18$) after adjusting for self-reported working conditions. This might have occurred because having a history of asthma was correlated with reported office cleanliness (Mantel-Haenszel chi-square = 7.334, $p = 0.007$) (i.e., asthmatics tended to perceive their office environments as less clean). In addition to station cleanliness, number of people in the office, and "job requires to work very hard" were significant predictors of upper respiratory symptoms in both univariate and multivariate models. The relationship between CO_2 concentrations and symptoms was not significant after adjusting for number of people in the office (Table 8, Models 2 and 3).

Discussion

Health effects of environmental conditions in indoor environments have become the focus of many cross-sectional epidemiologic studies in recent years (Li et al. 1997; Mendell 1993). A number of factors have been consistently identified that related to BRS, including air conditioning, carpets, crowding, and low ventilation rates (Mendell 1993; Mendell and Smith 1990). Other factors such as total VOCs and bioaerosols have shown only inconsistent relationships (Harrison et al. 1992; Hodgson et al. 1991; Li et al. 1997; Tenbrinke et al. 1998). The main goal of this study was to perform a longitudinal evaluation of some of these environmental factors as predictors for BRS.

Longitudinal study design. In our study, repeated measurements allowed us to explore seasonal variation of environmental factors (Chao et al. 2002a, 2002b) and to control for the temporal pattern of symptoms, resulting in more precise estimates of the relationships of interest. The highest symptom prevalence (Table 2) was observed at the beginning of the study. If people are more enthusiastic and tend to report more symptoms in the beginning of a study, the validity of symptom reporting might be questionable in a cross-sectional design. We controlled for sampling date in all symptom models, which not only controlled for temporal variation but also partially controlled for other time-varying factors not measured. Another important characteristic of longitudinal study design is that only consistent patterns across subjects will be detected, which increases the precision of inferences (Diggle et al. 1995). Therefore, in order for a variable to be significant, it has to consistently predict symptoms. Important predictors that are rarely present could be missed because of the relatively small population size in our study. However, these relationships may also be missed in a cross-sectional study if the predictor is absent during the study.

Environmental measurements. Total fungal concentrations recovered from chair dust and the fourth PCA factor for chair fungi (chair factor 4) were positively associated with upper respiratory symptoms and nonspecific symptoms, respectively. The major component of chair factor 4 is "unknown," which includes primarily unidentified species and fungi lost to overgrowth. Although a more likely source of fungal exposure than floor dust, chair dust has seldom been considered as an exposure indicator and is not usually a focus for remediation. More studies are needed to further examine the relationship between BRS and exposure to fungi in chair dust. However, use of impermeable chair covering or frequent cleaning might be effective interventions.

Culturable fungi recovered from floor dust is frequently assessed as a potential source of airborne fungi and a possible surrogate for long-term fungal exposures (Gyntelberg et al. 1994; Verhoeff and Burge 1997). However, we did not find any correlations between floor fungi and symptoms. This is similar to findings in some cross-sectional office building studies (Gyntelberg et al. 1994; Skov et al. 1990). Fungal populations recovered from floor dust have likely settled from air or are tracked in from outdoors, subsequently forming an independent ecosystem. Many of the fungi in floor dust are not dominant in air (e.g., *Aureobasidium*, *Coelomycetes*), and routes of exposure in office buildings are not obvious. Chair fungi, on the other hand, represent a population more like that found in air, and exposure could be related to the bellows effect that occurs with the action of sitting down or getting up. The lack of strong correlation between culturable floor fungi and reported symptoms may also be because our buildings were relatively dry, with no reported major flooding during the study. In buildings where such events have occurred, culturable floor fungi may better predict symptoms.

Airborne culturable fungal concentration is the most frequently used fungal exposure measurement (Hunter et al. 1988; Li and Kendrick 1994). We found a significant quadratic relationship between total airborne fungal concentrations and upper respiratory symptoms. A threshold effect of total airborne fungal concentrations or the effects of specific fungal species could have caused reported symptoms, although we could not prove these hypotheses in this study. We did not find strong linear correlations between any of several airborne fungal measures and BRS. Our airborne fungal concentrations (mean = 42 CFU/m^3, median = 22 CFU/m^3) were much lower than those reported in homes and other work environments (Chew 1997; Li et al. 1997) but were similar to those previously reported in large office buildings studies (Harrison et al. 1992; Skov et al. 1990). Harrison et al. (1992) found a positive correlation between BRS and total airborne fungal levels (median = 26 CFU/m^3 and 36 CFU/m^3 in air-conditioned and mechanically ventilated buildings, respectively). The Danish Town Hall study (Skov et al. 1990) reported slightly lower airborne fungal concentrations (mean = 32 CFU/m^3) compared with ours, and there was no association with BRS. In these studies, as in ours, airborne fungal levels were low by comparison with current standards/guidelines (Rao et al. 1996). Both of these studies had much larger study populations (> 1,000 subjects) than our study. Therefore, either these low exposures or, less likely, lack of statistical power may have prevented detection of linear associations. Our longitudinal study should have had the power to detect effects of time varying fungal concentrations. Future studies should examine not only linear relationships with BRS but also the possible threshold effects of airborne fungal concentrations.

Another problem is the representativeness of cultural grab samples as measures of exposure. We collected air samples in the

Table 8. Multivariate regression models for upper respiratory symptoms, controlling for sampling date.

Predictors	Level	Model 1[a] OR (95% CI)	Model 2[b] OR (95% CI)	Model 3[c] OR (95% CI)
Environmental				
CO_2	Linear	1.45 (1.01–2.08)[d]	1.41 (0.98–2.03)[d]	—
Log_{10} (chair fungi)	Linear	1.39 (1.09–1.76)[d]	1.36 (1.07–1.73)[d]	1.35 (1.07–1.70)[d]
Demographic and medical history				
Asthma	Yes	—	2.52 (1.01–6.27)	—
	No		1.00	
Self-reported working conditions				
No. of people in office	Linear	—	—	1.45 (1.01–2.08)[e]
Station cleanliness	Linear	—	—	1.62 (1.15–2.30)[e]
Job requires to work very hard	Linear	—	—	1.43 (1.05–1.95)[e]

[a]Environmental variables. [b]Model 1 + demographic + medical history. [c]All variables. [d]For interquartile range change. [e]For one unit of change.

mornings and afternoons on Tuesdays and Thursdays during each week of sampling resulting in a total of sixteen 2-min culture plate samples for each site during each sampling week. Even though this protocol is relatively intensive, it is still possible that airborne fungal variations were not fully captured and, therefore, that the effects of exposure were not detected. Because total culturable fungal concentrations in air and in chair dust were possible predictors of BRS, β-(1→3)-D-glucans (components of the fungal cell wall) and ergosterol (a membrane sterol unique to fungi) might be good predictors as well. In recent years, β-(1→3)-D-glucans and ergosterol have been used to estimate total fungal biomass in many studies (Dales et al. 1999; Gehring et al. 2001). In addition to a marker of total fungi, β-(1→3)-D-glucans, which are potent proinflammatory agents, have also been suggested as causative agents for BRS (Rylander et al. 1992). More epidemiologic studies are needed to examine the significance of β-(1→3)-D-glucans and ergosterol as biomarkers of total fungi and/or as causal agents of BRS.

CO_2 is usually used as an indicator for adequate outdoor air supply or a surrogate for odor-producing bioeffluents (Federspiel et al. 2000; Hill et al. 1992). In our study, CO_2 concentrations in the studied buildings (mean = 689 ppm) were within the range of typical office levels and below recommended standards (Nagda and Rector 2000). CO_2 concentrations were associated with upper respiratory symptoms before adjustment for self-reported working conditions. CO_2 concentrations in offices are determined by the number of people in the offices, their level of activity, and amount of fresh air intake (Burgess et al. 1989). CO_2 concentration is likely to be an indicator for "number of people in the office" in its relationship with upper respiratory symptoms. However, when we controlled for number of people in the office, the relationship with CO_2 was no longer significant.

The amount of floor dust was a significant predictor of eye irritation. Amount of floor dust might be associated with BRS as a physical agent or because of its components [e.g., β-(1→3)-D-glucans or fungal allergens]. A few experimental studies have demonstrated a relationship between eye irritation and dust exposure, and BRS reports were reduced by floor cleaning (Kildeso and Schneider 2000). β-(1→3)-D-Glucan concentrations in dust have been associated with the amount of floor dust and could play a role in BRS reports (Gehring et al. 2001). Dust-borne fungal allergens and dust-borne Gram-negative bacteria have also been associated with BRS (Gyntelberg et al. 1994; Vincent et al. 1997). More studies are needed to examine the effect of the amount of floor dust on indoor environmental health and to address whether the amount of floor dust alone can be a good predictor of BRS (Gehring et al. 2001).

Past medical histories and demographic parameters. A history of asthma was positively associated with eye irritation and nonspecific symptoms, and marginally correlated with upper respiratory symptoms. Apparently, asthmatic office occupants were more sensitive to building environments and experienced more BRS. We also found that asthmatics more frequently reported lack of office cleanliness, but not other self-reported working conditions. Thus, the two predictor variables, a history of asthma and office station cleanliness, are likely to confound each other in their relationships with BRS. It is possible that both factors would have been stronger predictors for symptoms if the other variable had not been included in modeling. With the rising incidence of asthma, control of factors (i.e., office cleanliness, chair fungal levels) associated with BRS is essential.

Female sex has been positively related to BRS in many studies (Bachmann and Myers 1995; Jaakkola et al. 1991). However, in our study, sex was not significantly associated with BRS. The lack of association might be due to the small proportion of male participants (17%) in our study leading to a lack of statistical power to detect a small effect. Also, failure of sex to predict nonspecific symptoms in multivariate models might arise because female sex was associated with reported lack of station cleanliness, which was a strong predictor of symptoms. Although a statistically significant association was not found between sex and BRS in this study, the importance of sex could not be neglected.

Older age was associated with reported eye irritation. Age is one of the most studied demographic factors in relation to BRS, but outcomes have been inconsistent. In contrast to our findings, Vincent et al. (1997) and Hill et al. (1992) found that age less than 40 years and age less than 45 years, respectively, were associated with more eye symptom reports. Yet some studies have shown that dry eyes increase with age, especially in women (Hikichi et al. 1995; McCarty et al. 1998). The inconsistency is in part due to different definitions and scaling of eye symptoms, arbitrary aggregation of symptom scores (Kjaergaard 2000), and different study populations and study designs. Standardized protocols are needed in future studies to examine the effects of factors associated with building-related eye symptoms, including age.

Self-reported working conditions. Perceptions of work environments and work stress have been correlated with BRS in many epidemiologic studies that have used questionnaires to collect information on occupants (Eriksson et al. 1996; Hedge et al. 1996). We also found that some self-reported working conditions were associated with health symptoms. Perception of office cleanliness was positively related to all of the three symptom groups, similar to findings in other studies (Hedge et al. 1996; Wargocki et al. 2002). More health symptoms were reported if the office environments were considered less clean. Perception of office cleanliness might represent the satisfaction level of the occupants about their office environments, and it might also reflect the real cleanliness of the physical environment. Therefore, office cleanliness might have been associated with symptoms both physically and psychologically.

Number of people in the office had positive relationships with nonspecific and upper respiratory symptoms, consistent with previous findings (Hodgson et al. 1991; Zweers et al. 1992). Number of people in the office was a more objective self-reported measurement than other perceptions of working conditions. More people in the office may indicate a greater chance of infectious disease transmission, possibly resulting in a higher symptom report.

Job stress/dissatisfaction have been consistently associated with BRS in many epidemiologic studies (Eriksson et al. 1996; Hedge et al. 1996). We also found "job requiring to work very hard" and "job dissatisfaction" had positive relationships with upper respiratory symptoms and nonspecific symptoms, respectively. These stress factors might influence occupants' perceptions of health psychologically or increase the susceptibility to environmental exposures physically. More studies are needed to examine the complex effects of psychosocial factors on BRS.

We used a longitudinal study to examine the possible effects of environmental exposures on BRS, using extensive environmental sampling protocols. Airborne culturable fungal concentrations and culturable fungal concentrations in chair dust were quadratically and linearly related to BRS, respectively, indicating the value of these measures as important exposure metrics. We also found that perceptions of office cleanliness and history of asthma were consistent predictors of BRS, which should be examined and controlled for in future studies. We further confirmed that, longitudinally, BRS is associated with multiple factors, including environmental contaminants, personal characteristics, perceptions of physical work environments, and job-related stress. Although we had a relatively strong study design (longitudinal) compared with other large building studies (cross-sectional), fewer participants (98 subjects) and relatively clean environments might limit the generalizability of our results. In perspective, large-scale longitudinal studies are recommended to further examine the health effects of environmental exposures and psychosocial factors.

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