

Aeroallergens and work-related respiratory symptoms among office workers

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Objective: We sought to determine the association between office workers' respiratory tract symptoms and immediate skin test reactions with exposure to fungal and house dust mite aeroallergens at their work sites.

Methods: An initial prevalence survey was conducted among 1102 full-time workers in six mechanically ventilated, air-conditioned, nonindustrial buildings in downtown Montreal. Detailed environmental measures of 214 subjects' work sites were determined. Half of the workers reported frequent work-related respiratory tract symptoms on the initial survey. Participants simultaneously underwent allergy skin prick testing and completed a second self-administered questionnaire.

Results: Contaminant levels were low and not associated with symptoms in the great majority of workers. For approximately 17% of workers, symptoms were associated with exposure to total concentrations of house dust mite allergen greater than 1 µg/gm floor dust (odds ratio [OR], 5.0; 95% confidence interval [CI], 1.3, 19.5) or to detectable airborne *Alternaria* allergens in their offices (OR, 3.3; 95% CI, 1.2, 9.4) and in the ventilation system supplying their offices (OR, 3.9; 95% CI, 1.6, 9.6). Workers with positive skin test reactions to *Alternaria* extract were exposed at their work site to airborne *Alternaria* allergen (OR, 4.4; 95% CI, 1.4, 14.5) and cited significantly more respiratory symptoms on both questionnaires. Detection of airborne *Alternaria* allergen at work sites was significantly associated with detection in the ventilation system (OR, 4.0; 95% CI, 1.4, 10.9); this was in turn associated with lower efficiency filters.

Conclusions: Potentially avoidable exposure to aeroallergens accounted for symptoms in a small subgroup of office workers with frequent work-related respiratory tract symptoms. (J Allergy Clin Immunol 1998;101:38-44.)

Key words: Building-related illness, aeroallergens, respiratory symptoms, house dust mites, *Alternaria* spp.

There is considerable evidence to link respiratory health effects from exposure outdoors^{1,2} and in the home environment³⁻⁷ to aeroallergens of fungi and house dust mites. Cross-sectional surveys in nonindustrial buildings, selected without regard to the occupants'

Abbreviations used

CI:	Confidence interval
CFU:	Colony-forming unit
HVAC:	Heating, ventilation, and air-conditioning
OR:	Odds ratio
TVOC:	Total volatile organic compound

health status, have detected consistent associations of symptoms with markers of exposure to these allergens.⁸⁻¹³ A number of outbreaks of building-related illnesses have been linked to microbial exposures¹⁴⁻¹⁶ but at much higher concentrations than usually found in the nonindustrial environment.^{15,16} Epidemiologic (i.e., nonoutbreak) surveys of workers in nonindustrial buildings have not detected any consistent association between symptoms and actual measured concentrations of aeroallergens.^{17,18} This may be because of difficulty measuring exposure for all workers or finding causal relationships for all symptoms.

To test the hypothesis that office workers' respiratory tract symptoms and immediate skin test reactions were related to aeroallergen exposure, we measured these parameters directly at the work sites and performed allergy skin testing on workers with and without such symptoms.

METHODS

We conducted an initial prevalence survey of all occupants of six mechanically ventilated office buildings to identify workers with and without target respiratory symptoms. These subjects were selected for detailed environmental measures and allergy skin testing.

Environment

Six mechanically ventilated buildings with sealed windows located in downtown Montreal were selected. These represented all mechanically ventilated buildings belonging to a single owner who agreed to collaborate in the study. Major characteristics of these buildings and their heating, ventilation, and air-conditioning (HVAC) systems are shown in Table I.

Study population

In these six buildings, all permanent employees with a fixed identifiable work site who were present at least 2 full days per week were eligible. We excluded subjects who were on prolonged sabbatical or maternity leave during the study.

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Table I. Characteristics of buildings

	Building no.					
	1	2	3	4	5	6
Year of construction	1963	1965	1970	1980	1960	1969
Height (No. of stories)	10	9	7	6	7	14
Total floor space (sq ft)	131,000	235,000	200,000	100,000	200,000	126,000
Type of ventilation system	CAV	CAV+VAV	CAV	CAV	CAV	CAV
Air-conditioning system	Yes	Yes	Yes	Yes	Yes	Yes
Humidification	No	Steam	No	No	No	No
HVAC filter efficiency	90%	90%	20%	90%	20%	20%

CAV, Constant air volume; VAV, variable air volume.

Participants selected from the initial prevalence survey included those who reported nasal symptoms (irritation, congestion, or discharge) or lower respiratory tract symptoms (cough or difficulty breathing) that occurred at work at least 2 days per week and improved away from work. These subjects were defined as having frequent work-related respiratory tract symptoms.

For contrast, an equal number of participants were selected from among all other participants in the same survey who did not report frequent work-related respiratory tract symptoms. These subjects were matched on the basis of gender, age within 5 years, and atopic status, which are recognized risk factors for respiratory symptoms and sick building syndrome.^{19, 20} Atopy was defined as present if participants reported a history of asthma, hay fever, allergies, or eczema and absent if participants reported none of these conditions. Participants consented to complete a questionnaire and allow environmental measures to be obtained at their work site. All subjects also signed a separate informed consent document to undergo allergy skin testing. This study was approved by an Ethics Committee of the Department of Epidemiology and Biostatistics at McGill University.

Data collection

An initial survey was conducted to determine prevalence of symptoms. Workers were asked to complete a self-administered questionnaire regarding personal characteristics, smoking, and medical history. They were also asked to record past occurrence of symptoms of headache; fatigue; difficulty concentrating; cough; and irritation of the eyes, nose, and throat.

At the time of this initial survey, temperature, humidity, CO₂, and fungal antigens were measured in the HVAC systems, as well as in a small sample of offices in each building. This was done to exclude major problems, such as building-wide contamination, which might have affected the entire population. These environmental results are not presented because no major problems were identified.

This initial survey was conducted from January 1991 to early April 1991. From May 1991 to October 1991, data from these questionnaires were entered into a database and analyzed to identify participants suitable for detailed environmental measures and allergy testing.

A detailed environmental study was conducted from December 1991 to early April 1992. For each participant, completion of a second questionnaire, allergy skin testing, and measure-

ment of environmental parameters in the office and HVAC system were all performed on the same day.

Participants in the second phase of the study completed a second self-administered questionnaire, which included items regarding: (1) respiratory symptoms of cough, phlegm, wheezing, and history of asthma or other respiratory illness taken verbatim from the American Thoracic Society questionnaire²¹; (2) indicators of dampness and mold in the home environment taken verbatim from a questionnaire developed and validated in a survey of over 17,000 Canadian homes⁵; (3) the office environment, including equipment, furnishings, and potential allergen exposure; and, (4) occurrence of symptoms at work over the past month.

The office was inspected by research personnel who completed a checklist for measures of light, noise, temperature, humidity, air movement, CO₂, CO, total volatile organic compounds (TVOCs), dust, and airborne fungi levels. After this, a sample of floor dust was collected for measurement of house dust mite antigens and fungal colony-forming units (CFUs).

On the same day as the measurement of each participant's office environment (those with symptoms and control subjects), temperature, relative humidity, and CO₂ concentrations were measured in outdoor, supply, and return air from the HVAC system supplying that office. Fungal parameters were also measured in the HVAC systems of each building on two occasions, one day in February and another in early June 1992. On each day, sampling for fungal spores and CFUs were performed in outdoor air and in the supply air systems "downstream" from the HVAC filters.

HVAC measures of temperature, humidity, CO₂, fungal spores, and CFUs were matched to each participant (subject with symptoms or control subject) according to the ventilation system design and location of the office on the floor plans provided by building management.

The temperature and relative humidity were measured with a Psychrometer (Cole and Palmer). Indoor and outdoor absolute water content were calculated as follows²²:

$$\text{Water Content (Kg H}_2\text{O/m}^3 \text{ dry air)} = \frac{[P/(RT_K)][H\%][(0.622)(6.112e^{[17.67TC]/[TC + 243.5]})]}{\div (p - 6.112e^{[17.67TC]/[TC + 243.5]})}$$

where P = ambient pressure (assumed to be 101.3 kilopascals), $R = 287\text{J/T}_K/\text{Kg}$, T_K = absolute temperature in degrees kelvin, $H\%$ = percent relative humidity, e = exponential, TC = temperature in degrees celsius, and p = total pressure (assumed to be 1000 millibars). The difference between the indoor and outdoor water content measured on the same day was termed

the *water content difference* and was considered indicative of local sources of water within the building.

Other environmental factors measured included: noise level, with the Simpson Sound Level Metre (Model 886); light, with the OPTIKON lux metre; CO₂, by direct reading of an infrared analyzer (ADC); CO, by direct reading of a photo-acoustic multi-gas monitor (Model 1302, Brüel and Kjær); and TVOCs, by direct reading of a photo-acoustic multi-gas monitor.

Total airborne particulates (dust) were collected over a 24-hour period with volumetric air samplers (SKC) at 2 L/min onto preweighed filters. Total dust was estimated from pre- and postfiltration dry weights. Airborne fungal spores were collected with Burkard personal volumetric air samplers at 10 L/min over 15 minutes onto gelatin-glycerine-coated slides and were counted and identified by microscopy ($\times 400$ and $\times 1000$ magnifications).

Fungal culturable units (CUs) were collected with Burkard personal volumetric samplers at 15 L/min over 15 minutes onto a Petri dish containing Sabouraud dextrose agar medium. Counting and identification were performed by the University of Montreal Aerobiological Research Group. The first stage consisted of incubating samples for 5 to 7 days in ambient conditions. At the end of the incubation period, the number of colonies was counted. This value was then used to determine the concentration of molds per cubic meter of air. Many of the spores or mycelian fragments impacting the medium fail to give rise to colonies; only viable spores or fragments generate colonies. The colonies were either analyzed immediately or reinoculated in new medium. Because the diagnostic keys are largely based on the appearance of the sporing body, only sporulated colonies could be identified. All other colonies, still in the vegetative phase, were reinoculated on malt agar. To accelerate sporulation, molds were exposed to UV light for 12 hours per day for approximately 1 week. Reinoculated spores that had not sporulated after 1 week were reinoculated again, this time on Czapek medium, a medium with a pH of approximately 7.3 and composed primarily of saccharose. If invasive molds such as *Mucorales* spp. were present, isolation of colonies was performed on mycobiotic medium, a Sabourau dextrose agar medium containing agents such as cycloheximide and chloramphenicol. The microscopic identification of molds was performed at a magnification of $\times 400$ or $\times 1000$. Several diagnostic keys were used, and cultures for which identification was equivocal or impossible were forwarded to the mold center at the federal Department of Agriculture's experimental farm.

Floor dust was collected by vacuuming the entire floor surface during a period of 100 seconds. The floor dust was collected in a polyester bag and transferred to a sterile container. Total dust was sieved and weighed. House dust mite antigen was measured by ELISA for Der p 1 and Der f 1 and expressed in micrograms per gram of dust.

The floor dust sample collected for the house dust mite assay was divided, and a portion was used to identify, but not to quantify, culturable fungi. The methods of culture used were the same as those used for collecting fungal culturable units (see above).

All participants were asked for consent for allergy skin testing, and those who agreed underwent skin prick testing administered by a registered nurse. Antigens used were *Dermatophagoides pteronyssinus*, *D. farinae*, ragweed, and mixed molds (prepared by Holister-Stier). Extracts of *Cladosporium herbarum*, *Alternaria alternata*, *Aspergillus fumigatus*, and *Penicillium* spp. were prepared and supplied by Dr. Hari Vijay of Health and Welfare Canada. Saline and histamine were used as

negative and positive controls. The diameter of the wheal was measured in millimeters after 10 or 15 minutes. The test result was considered positive if the maximal diameter of the wheal at 10 or 15 minutes was larger than that caused by the saline control and at least 3 mm.²³

Statistical analysis

Differences found were tested for significance with the chi-square test for responses on questionnaires and presence or absence of items on visual inspection; *t* tests for mean values of normally distributed environmental measures; and nonparametric tests for nonnormally distributed continuous environmental parameters.²⁴ The population attributable risk percent was calculated for aeroallergen exposures significantly associated with symptom status.²⁵ Logistic regression was used to obtain adjusted estimates for factors found to be significant by univariate analysis.²⁶ Matched analysis was conducted with paired *t* tests and McNemar tests in univariate analysis for continuous and categorical variables, respectively, and conditional logistic regression for multivariate analysis.²⁶

RESULTS

Of 1415 eligible workers identified, 1102 (78%) participated in the initial prevalence survey. Of these, 121 (11%) were identified as having frequent work-related respiratory tract symptoms, and 113 of those participated in the study. One hundred twenty-one workers without these symptoms were also identified as potential control subjects, and 107 of these agreed to participate. This resulted in 107 matched pairs of participants with symptoms and control subjects, or 214 persons whose results were analyzed and are presented here. The 214 participants' mean age was 42 years, they had worked for 10 years at their present jobs, and 60% were female. Twenty percent of the subjects worked in secretarial, 19% in management, and 43% in professional positions; and more than half worked in single-occupant offices. None of these characteristics differed significantly between those with and without the target symptoms. Current cigarette smoking was reported by 17% of workers with respiratory symptoms compared with 8% of workers without such symptoms ($p = 0.064$).

Workers with respiratory tract symptoms were significantly less likely to report a number of potential sources of allergens in their homes, including forced-air heating systems, wall-to-wall carpeting, or older carpeting. Other home characteristics (i.e., type or age of dwelling; hobbies; activities; and the presence of pets, other smokers, air conditioners, humidifiers, or dehumidifiers) were not different, nor were reports of dampness or damp or moldy odors at home (data not shown).

In univariate analysis, the environment of workers with symptoms differed only in that airborne *Alternaria* allergen was detected more frequently in their offices and in the HVAC systems supplying their offices (Table II). Workers with symptoms who were current smokers were less likely to have detectable airborne *Alternaria* allergen levels or total house dust mite levels greater than 1 mg/gm of floor dust in their office compared with nonsmoking workers with symptoms (data not shown).

Table II. Results of direct measures of aeroallergens in offices of participants

	Workers with symptoms (n = 107)		Workers without symptoms (n = 107)		OR*	95% CI
	No.	(%)	No.	(%)		
Fungi detected in office air						
<i>Alternaria</i> spp.	15	(14)	5	(5)	3.3	(1.2, 9.4)
<i>Aspergillus</i> spp.	85	(79)	89	(83)	0.8	(0.4, 1.5)
<i>Cladosporium</i> spp.	65	(61)	65	(61)	1.0	(0.6, 1.7)
<i>Penicillium</i> spp.	55	(51)	62	(58)	0.8	(0.5, 1.3)
Fungi detected in HVAC supply air						
<i>Alternaria</i> spp.	24	(22)	7	(7)	3.9	(1.6, 9.6)
Dust mites in floor dust						
Mite DP + DF ≥ 1 $\mu\text{g/gm}$	17	(16)	10	(9)	1.8	(0.8, 4.2)

DP, *D. pteronyssinus*; DF, *D. farinae*.

*Odds ratio that workers with symptoms had exposure compared with workers without symptoms.

Table III. Adjusted odds that workers with respiratory symptoms had exposures in office environment (from conditional logistic regression)

Exposure	Comparison	OR*	95% CI
<i>Alternaria</i> spp. in office air	Detectable vs absent	4.2	(1.1, 16.2)
Total house dust mite (DP + DF)	≥ 1 $\mu\text{g/gm}$ vs <1 $\mu\text{g/gm}$	5.0	(1.3, 19.5)
Water content difference†	Per change of 1 SD*	1.4	(1.0, 1.9)
Current smoker	Yes vs no	4.1	(1.0, 17.2)

DP, *D. pteronyssinus*; DF, *D. farinae*.

*Odds ratios for continuous variables calculated as odds for mean vs (mean – 1 SD).

†Difference between indoor water content and outdoor water content (see Methods for calculation).

After adjusting for smoking in multivariate analysis (Table III), *Alternaria* allergen in the office air, higher total dust mite concentration, and greater indoor humidity were all significantly associated with respiratory symptoms. On the basis of these results, the population-attributable risk for work-related respiratory tract symptoms was 9.5% for *Alternaria* allergen and 7.7% for house dust mites.

This result meant that symptoms of less than 20% of workers were explained by the environmental parameters measured because there were no other significant differences in measured environmental parameters such as temperature, humidity, sound, light, carbon monoxide, carbon dioxide, total dust and TVOCs. There were also no differences in observer-recorded work site characteristics such as size of office, presence of carpets, plants, curtains, water damage, or photocopiers. Despite these findings, workers with symptoms reported that their office environment was significantly more stuffy and that airborne and surface dust were significantly worse compared with workers without symptoms (data not shown).

Mean levels of *Alternaria* allergen were low. In offices or HVAC supply systems where *Alternaria* allergen was detected, mean levels were 7 and 6 CFU/m³, respectively (near the detectable limit of 4 CFU/m³). Airborne *Alternaria* allergen was detected at 20 work sites and was

significantly associated with its presence in HVAC air (odds ratio [OR], 4.0; 95% confidence interval [CI], 1.4, 10.9) but was not associated with its presence in floor dust. It was also not associated with temperature; humidity; chemical contaminants; presence of carpets, potted plants, or equipment; or office location (interior/perimeter) and orientation (north, south, east, west). *Alternaria* allergen was not detected in any of the six samples of outdoor air taken in February but was present in two of three outdoor air samples taken in June of the same year. *Alternaria* allergen levels were detected in five of 14 (36%) samples taken in HVAC supply air downstream from 20% to 30% efficiency filters, compared with zero of 12 samples taken downstream from intact 85% to 90% efficiency bag filters ($p = 0.04$, two-tailed Fisher's exact test). The presence of detectable levels of house dust mite allergen was associated with the presence of carpets at the work site (OR, 7.0; 95% CI, 2.8, 17.5), but total house dust mite levels greater than 1 $\mu\text{g/gm}$ floor dust were not associated with carpets or humidity and only associated with lower light intensity (541 lux vs 725 lux, $p < 0.01$) (data not shown).

Of the 214 participants, 169 consented to allergy skin testing. In this subgroup there were no substantial or significant differences in age, gender, history of atopic illness, or smoking among the 83 with and the 86 without respiratory tract symptoms. There were also no impor-

Table IV. Results of allergy skin testing: number and percent with positive reaction

	Workers with symptoms (n = 83)		Workers without symptoms (n = 86)		OR*	95% CI
	No.	(%)	No.	(%)		
Skin-test antigen						
Histamine	81	(98)	85	(99)	1.0	(0.1, 5.4)
Any test positive†	44	(53)	46	(53)	1.0	(0.5, 1.8)
Mite						
<i>D. farinae</i>	26	(31)	30	(35)	0.9	(0.5, 1.6)
<i>D. pteronyssinus</i>	25	(30)	27	(31)	1.0	(0.5, 1.8)
Ragweed	29	(35)	31	(36)	1.0	(0.5, 1.8)
Fungal						
Mixed mold	9	(11)	5	(6)	2.0	(0.6, 6.2)
<i>Aspergillus</i> spp.	6	(7)	3	(3)	2.2	(0.5, 8.9)
<i>Alternaria</i> spp.	15	(18)	3	(3)	6.1	(1.7, 22.0)
<i>Cladosporium</i> spp.	8	(10)	6	(7)	1.4	(0.5, 4.3)
<i>Penicillium</i> spp.	3	(4)	5	(6)	0.6	(0.1, 2.6)

*Odds that workers with symptoms had skin test reactions compared with workers without symptoms.

†Reaction to antigen exceeding reaction to saline control and wheal at least 3 mm in diameter.²³**Table V.** Relationship of positive *alternaria* extract skin test responses to symptoms and environmental measurements

Frequent work-related respiratory tract symptoms	<i>Alternaria</i> (+) (n = 18)		<i>Alternaria</i> (-) (n = 151)		p Value*
	N	(%)	N	(%)	
(Original questionnaire)	15	(83)	68	(45)	<0.01
Recent symptoms at work (Second questionnaire in winter)					
Cough	12	(65)	54	(36)	<0.05
Wheeze	6	(35)	15	(10)	<0.1
Chest tightness	5	(29)	21	(14)	NS
Dyspnea	7	(41)	29	(19)	<0.05
Sneezing	15	(82)	72	(48)	<0.05
Watery itchy eyes	15	(82)	80	(53)	<0.05
Detectable airborne <i>Alternaria</i> allergen at worksite	5	(28)	12	(8)	<0.01
Work environment					
Temperature (Celsius)	22.4	(1.3)†	22.2	(1.4)†	NS
Relative humidity (%)	26%	(8)	21%	(7)	<0.01
Water content difference (kg H ₂ O/m ³)	0.23	(0.16)	0.17	(0.16)	NS
TVOC μg/m ³	2170	(600)	1850	(870)	<0.01
CO ₂ (ppm)	639	(134)	630	(126)	NS

NS, Not significant.

*p value from chi-square test (categorical variables) or t test (continuous environmental data) with unmatched analysis.

†Values are mean (SD).

tant differences in these characteristics among the 118 participants in the 59 originally matched pairs and the 51 subjects who underwent skin testing but whose matched pairs did not. Therefore to take advantage of information from all 169 subjects who underwent skin testing, unmatched analysis was conducted. Reactions to mites and ragweed were virtually identical in the two groups, whereas reactions to mold extracts were more frequent

in the group with symptoms (Table IV). As shown in Table V, subjects with positive reactions to *Alternaria* extract were more likely to have frequent work-related respiratory tract symptoms and to have detectable *Alternaria* levels (OR, 4.4; 95% CI, 1.4, 14.5), as well as higher TVOC levels and humidity, levels in their work environment. Among those with positive skin test responses to *Alternaria* extract, workers with symptoms

had higher mean levels of *Alternaria* allergen in their offices (with symptoms, 1.7 CFU vs without symptoms, 0 CFU). For those with negative skin test responses to *Alternaria* extract, mean levels were lower and there was less difference in mean levels between workers with and without symptoms (0.7 CFU/m³ vs 0.4 CFU/m³, respectively).

DISCUSSION

The two major findings of this study were the association of work-related respiratory tract symptoms with low-level aeroallergen exposures in some of the workers and the failure to identify any environmental cause for more than 80% of workers with symptoms. The findings of this study should be strengthened by comparison of workers with relatively homogeneous symptoms with nonaffected workers selected from the same population and the extensive environmental measurements taken directly at each subject's workstation. We questioned whether these results were valid, biologically plausible, and generalizable. We also considered what implications they may have.

In addressing the problem of sick building syndrome, we did not study "sick buildings" (a poorly defined term²⁰) or buildings with known outbreaks of respiratory illness. Instead, we selected buildings with sealed windows, mechanical ventilation, and air conditioning—building characteristics previously identified as risk factors for frequent occurrence of symptoms.⁸⁻¹¹ Given the large study population, these findings should be reasonably generalizable to other office workers. However, because five of the six buildings studied were constructed in the mid-to-late 1960s, it is possible that findings would be different in buildings of different age or design.

The number of workers with respiratory symptoms was 11%. This is relatively low because a more stringent definition was used compared with other surveys.⁸ The prevalence of symptoms also may have been low relative to the general population because of the "healthy worker effect." However, this should not have biased comparison of those with and without symptoms because they were drawn from the same working population. Selection bias should have been minimized by the high participation rates in the initial and follow-up surveys. However, because 78% of eligible workers participated in the initial survey, this may have resulted in some selection bias. In past surveys nonparticipants had personal and work characteristics associated with reduced symptom reporting.²⁷ Nevertheless, this should not have biased comparison of those with or without symptoms among the participants in this initial survey. Potential bias introduced by selection of control subjects should have been minimized by the study design in which both participants with symptoms and control subjects were drawn from the same population.

We also attempted to determine whether the purportedly work-related symptoms were actually caused by exposures in other environments. Outdoor exposures to aeroallergens were unlikely because the study was con-

ducted in winter, when outdoor allergen levels are generally low. Exposures at home were less likely to have been responsible for symptoms because the group with symptoms reported significantly fewer markers of microbial and dust exposure in their homes, possibly reflecting changes already made in their home environment to reduce potential allergen exposures.

In the majority of past surveys of workers in large office buildings, exposure has been estimated from environmental measures taken at a sample of work sites. Because of the expense and complexity of these environmental measures, the sample was usually only one to seven sites per building.^{17, 28-30} The significant spatial variability in the concentration of many environmental parameters in large office buildings^{18, 27, 31} means that these "area" measurements fail to accurately estimate individual exposures, resulting in failure to detect exposure-response relationships.^{17, 28-30} In this survey, to enhance the accuracy of exposure estimation, all environmental parameters were measured directly at the workstations of participants who were selected on the basis of symptom status. However, the accuracy of these person-specific exposure estimates may have been limited by failure to account for temporal variation of these parameters.^{18, 32}

In previous surveys of workers in nonindustrial buildings, symptoms have been consistently associated with surface dust,^{12, 13} carpets,^{12, 13} or air-conditioning systems,⁸⁻¹¹ possibly because these are markers for long-term exposure to aeroallergens.^{8, 33, 34} In addition, culturable fungal particles have been demonstrated in humidification systems,^{14, 16, 35} on air-conditioning cooling coils,³⁶ in HVAC filters,³⁷ and in ventilation ducts.^{38, 39} Fungal particles may be retained and later released into the indoor environment,³⁵ or they may release mycotoxins.³⁸

Despite this, epidemiologic or nonoutbreak surveys of office workers have failed to detect any relationship between symptoms and total fungal spores or viable (culturable) fungi.^{17, 18, 40} This is because the total fungus level is a very crude measure of exposure, given the diversity and complexity of fungi present in this environment. In this study symptoms and skin test results were not associated with total fungal levels but only with exposure to a single species, *Alternaria*.

There is increasing evidence that species of *Alternaria* are potent allergens^{1, 7} and may be important in the pathogenesis of asthma.^{1, 4, 6, 7} Nevertheless, the airborne levels measured in the offices and HVAC systems of workers with symptoms were very low, raising the question of biologic plausibility. In this study the workers with skin test reactivity to *Alternaria* extract represented 18% of the workers with frequent respiratory symptoms, who in turn represented 11% of the total population surveyed. Therefore those with respiratory symptoms and positive skin test responses to *Alternaria* extract represented only 2% of the total population. Such a small subgroup of the total population could have represented those most susceptible

to *Alternaria* allergen who might respond to very low levels of exposure.

In this study respiratory symptoms were linked to exposure to *Alternaria* allergens detected in the HVAC system downstream from the filters in winter (when no *Alternaria* allergens were detectable outdoors). This suggests that the source was the ventilation system, and exposure may have been preventable through use of higher efficiency bag filters. More efficient filters could also reduce other airborne microbes, their associated endotoxins and mycotoxins, and other allergens and dust levels, potentially resulting in greater health benefits than would be predicted from our results alone.

We thank the owners, operators, and particularly the occupants of the six buildings studied for their help and collaboration and Dr. H. Vijay (Health Canada) for supplying the *Alternaria*, *Aspergillus*, *Cladosporium*, and *Penicillium* extracts used in this study.

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