Upper Respiratory Symptoms Associated With Aging of the Ventilation System in Artificially Ventilated Offices in São Paulo, Brazil*

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Background: The increase of work-related respiratory complaints in artificially ventilated buildings has multiple causes, and the role of allergen exposure and symptoms is still controversial. Study objectives: To analyze the risk factors and the association of work-related symptoms with allergen exposure and different conditions of the same air conditioning system in São Paulo, Brazil. Design: Workers were classified according to characteristics of the air conditioning system: the first group (group 1) with ventilation machinery and ducts with > 20 years of use, the second group (group 2) with ventilation machinery with > 20 years of use and ventilation ducts with < 2 years of use, and the third group (group 3) with ventilation machinery and ducts with < 2 years of use. Logistic regression was performed to check the associations between air conditioning groups, allergen exposure (fungi, mites, animal dander, and cockroach), and symptoms. Results: There was a higher prevalence of building-related worsening of respiratory symptoms (p = 0.004; odds ratio [OR], 8.53) and symptoms of rhinoconjunctivitis (p = 0.01; OR, 8.49) in group 1. There was a lower relative humidity (p = 0.05) and nonsignificant lower temperature in group 1, when compared to the other groups. The viable mold spores totals were higher outdoors than in the indoor samples (n = 45, p = 0.017). There were higher levels of Der p 1 in group 2 (p = 0.032). All allergen levels were considered low. Conclusion: There was a strong association of building-related upper-airway symptoms with places having ventilation systems with > 20 years of use.

Key words: air conditioning; air pollution, indoor; environmental exposure; occupational health

Abbreviations: CI = confidence interval; HVAC = heating, ventilation, and air conditioning; IAQ = indoor air quality; OR = odds ratio

The lifestyle of the urban population has been changing rapidly during the last decades. The increased amount of time spent indoors, even in tropical countries, makes indoor air quality (IAQ) a very important topic worldwide. IAQ problems have been consistently associated with artificial air conditioning systems, when compared to natural ventilation, in different countries.1 Problems associated with the indoor environment are the most common environmental health issues faced by clinicians,2 but the factors associated with the perceived IAQ are not fully understood, and include temperature, humidity; air-exchange rates, odors, air movement, ventilation, biological contaminants, volatile organic compounds, bacterial toxins, labor, and psychosocial factors.3 The role of allergy is still a matter of debate, since fungi,4,5 dust mites allergens,5 exposure to dust and carpeted surfaces,6,7 and animal dander exposure8,9 have been associated with respiratory symptoms in public places; and some host characteristics, such as atopy, are consistently involved as risk factors for IAQ-related symptoms developing.10–12 How-

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ever, no significant exposure to aerallergens is usually found. In many cases, previous epidemiologic studies have not used standardized and validated questionnaires for the diagnosis of allergic symptoms, so the use of specific methods of addressing the host susceptibility could add more information for this group of atopic individuals.

Geographic variations can lead to different IAQ perception. In São Paulo, Brazil, high temperatures (15°C to 35°C) and high relative humidity (60 to 94%) occur throughout the year, predisposing to dampness-related respiratory problems.

Aging and decaying of the ventilation system can lead to improper IAQ, due to biological contaminants, inadequate air exchange rates, poor filtration capacity, and loose control of the thermal parameters. Appropriate maintenance and cleaning of the air conditioning system are mandatory by health issues, but their effect on perception of IAQ is controversial. The aim of this study was to evaluate the association of work-related respiratory symptoms with artificial ventilation systems of different ages and with allergen exposure.

The objectives of this study were to determine the prevalence of respiratory symptoms among a group of office workers in São Paulo, and to analyze the risk factors and the associations of the symptoms with allergen exposure and different aging of the heating, ventilation, and air conditioning (HVAC) systems in the workplace.

### Materials and Methods

#### Office Buildings

Three different office buildings, located in the downtown area of São Paulo, in the same block and belonging to the same banking company, were studied. All had HVAC systems with a capacity of 10 tons of refrigeration, self-type (Hitachi; Tokyo, Japan). All offices had artificial illumination during daytime and were fully carpeted.

All of the selected places were not at the ground level, varying from the third to the 35th floor. Workers were classified according to the characteristics of the air conditioning system where they worked. The first group (group 1) had air conditioning machinery and ducts with >20 years of use; the second group (group 2) had a mixed ventilation system, with ducts with <2 years of use and machinery with >20 years of use. The third group (group 3) had an entire ventilation system with <2 years of use.

#### Study Population

After due authorization of the managers and workers of the companies settled in the buildings, and the approval of the Ethics Committee of the University of São Paulo, a self-administered questionnaire regarding atopy, smoking status, respiratory symptoms, previous medical diagnosis of asthma and rhinitis, and work-related respiratory symptoms was distributed. The questionnaire was a combination of two previously standardized and raveled questionnaires: the ATS-DLD-78 and the International Study of Asthma and Allergies in Childhood. The main questions about asthma symptoms were as follows: did you have wheezing or whistling in your chest in the last 12 months when you did not have a flu, and have you ever had attacks of shortness of breath with wheezing? The core questions about nasal symptoms were as follows: in the past 6 months, have you had a problem with sneezing, or a runny or blocked nose when you did not have a flu, has this nose problem been accompanied by itchy-watery eyes in the past 6 months, and where are the above-mentioned symptoms more frequently evoked? The questionnaire was applied to 330 subjects with administrative positions and similar salaries, localized in three different buildings not previously known as “sick” buildings. The workers did not know the characteristics of their ventilation system or the specific objective of the study, which was conducted during an evaluation of the nonsmoking policy in the company.

#### Microbiological Assessment

Simultaneously with the population study, the presence of viable mold spores in the air of the buildings was determined using a six-stage Andersen sampler (Andersen Samplers; Atlanta, GA) with Sabouraud dextrose agar with 10 g/mL of chloramphenicol, for culture, identification, counting, and measuring the fungi spores dispersed in the air. Standard techniques with airflow of 28 L/min for 15 min were used. Dust sampling was collected in the three places during the three periods of the day: morning, afternoon, and evening between 30 nonconsecutive days. Every indoor sampling of the period was compared to an outdoor one, in a total of 72 sampling times. After growth, microscopic identification of colonies was performed at a magnification of ×400 or ×1,000.

Dust samples were collected with a high-power vacuum cleaner of 1,000 W, with an attached dust trap. Dust was collected from the carpets for 2 min in an area of 1 m² and designated to allergen content measures.

Dust was weighed and sieved (n = 12), and 100 mg was extracted in 2 mL of borate-buffered saline solution overnight at 4°C. After centrifugation, the supernatant was removed and assayed by two-site, monoclonal antibody-based enzyme-linked immunosorbent assay for dust mite (Der p 1, Der f 1, Der p 2, Der f 2), cat (Fel d 1), dog (Can f 1) allergens, expressed in micrograms per gram of dust, and cockroach allergens (Bl a 1 and Bla g 2) expressed in units per gram of dust as described elsewhere.

The temperature and humidity were measured using a psychrometer (Testo 601; Testo; Flanders, NJ). Measurements were done at every mold sampling (n = 72), during the morning, afternoon, and evening.

#### Statistical Analysis

The population characteristics, according to ventilation groups, were analyzed using one-way analysis of variance and \( \chi^2 \) tests. Univariate and multiple logistic regressions were used to analyze the variables associated with nasal and eye symptoms, recurrent wheezing, and worsening of the symptoms at work. The symptoms were the dependent variables, and the independent variables were gender, age, accumulated working time in the building, smoking habits, passive smoking, history of familiar atopy, previous medical diagnosis of asthma and rhinitis, and the ventilation system groups. Stepwise forward selection procedure was used, and the variables that remained at the final model were either significant (p < 0.05) or were confounding.
Results

Population Characteristics

The questionnaire response rate was 86.7%, totaling 286 of the available population of 330 subjects. Among the responders, 243 subjects identified themselves and 43 subjects decided to be anonymous. According to ventilation systems, there was no statistically significant difference in age, smoking habits, lower respiratory symptoms, previous diagnosis of asthma or rhinitis, familial atopy, and number of flu-like episodes (Table 1).

Respiratory Symptoms

Group 1 had an older population with a larger proportion of men than women. This population also had 68.4% of symptoms suggestive of rhinoconjunctivitis (nasal pruritus, blockage or water discharge concomitant with itchy-watery eyes), and 64.8% of the population who complained of respiratory symptoms stated that they worsened inside the building. The building-related worsening of all respiratory symptoms mainly consisted of upper respiratory symptoms: 96.6% of blocked, runny, or itching noses, and accompanied by itchy-watery eyes in 49.5% within this subgroup. When compared to the other ventilation groups, group 1 had a higher prevalence of building-related worsening of symptoms (p = 0.001). Cough and sinus symptoms (pain and purulent nasal discharge) were also more prevalent in group 1 (p = 0.002 and p = 0.042, respectively). No statistically significant differences were found concerning asthma symptoms (wheezing and breathlessness) or previous diagnosis of asthma and rhinitis (Table 1).

Logistic Regression

The univariate analysis of the risk factors of building-related worsening of the respiratory symptoms showed a strong association with the aging of the ventilation system (group 1), with an odds ratio (OR) of 5.23 (95% confidence interval [CI], 2.12 to 6.02). In the multivariate analysis, the factors associated with building-related worsening were working from 1.2 to 3 years in the building (OR, 2.12; 95% CI, 1.01 to 4.47), working > 3 years in the building (OR, 2.47; 95% CI, 1.16 to 5.26), and the aging of the ventilation system (OR, 8.53; 95% CI, 2.80 to 25.94).

In the univariate analysis, rhinoconjunctivitis was significantly associated with previous medical diagnosis of asthma (OR, 7.10; 95% CI, 2.88 to 17.50), previous diagnosis of allergic rhinitis (OR, 4.53; 95% CI, 2.67 to 7.69), familial atopy (OR, 1.83; 95% CI, 1.11 to 3.03), and the aging of the ventilation system (OR, 5.23; 95% CI, 1.91 to 14.36). The adjusted factors associated with rhinoconjunctivitis were working for > 3.2 years at the building (OR, 2.34; 95% CI, 1.14 to 4.82), and the aging of the ventilation system (OR, 8.49; 95% CI, 2.81 to 25.66).

Recurrent wheezing symptoms showed association with previous diagnosis of atopic diseases such as asthma (OR, 9.17; 95% CI, 3.90 to 21.54) and rhinitis (OR, 7.16; 95% CI, 3.40 to 15.06), as well as positive familial atopy background (OR, 2.14; 95% CI, 1.08 to 4.22), in the univariate analysis. The aging of the ventilation system showed no association with recurrent wheezing or breathlessness in the univariate or the multivariate models. All multivariate analysis

Table 1—Population Characteristics According to Ventilation Groups*

<table>
<thead>
<tr>
<th>Variables</th>
<th>Group 1 (n = 23)</th>
<th>Group 2 (n = 44)</th>
<th>Group 3 (n = 263)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participation</td>
<td>82.61</td>
<td>86.36</td>
<td>87.07</td>
<td>0.832³</td>
</tr>
<tr>
<td>Age, yr</td>
<td>35.6 (8.44)</td>
<td>31.49 (7.60)</td>
<td>30.33 (7.16)</td>
<td>0.017†</td>
</tr>
<tr>
<td>Working years</td>
<td>1.65 (1.08)</td>
<td>3.17 (2.92)</td>
<td>3.09 (2.86)</td>
<td>0.003†</td>
</tr>
<tr>
<td>Female gender</td>
<td>15.8</td>
<td>50</td>
<td>42.4</td>
<td>0.014†</td>
</tr>
<tr>
<td>Atopic background</td>
<td>36.8</td>
<td>52.6</td>
<td>43.7</td>
<td>0.528‡</td>
</tr>
<tr>
<td>Smoker</td>
<td>15.8</td>
<td>26.3</td>
<td>13.1</td>
<td>0.117‡</td>
</tr>
<tr>
<td>Passive smoker</td>
<td>15.8</td>
<td>7.9</td>
<td>20.5</td>
<td>0.789¶</td>
</tr>
<tr>
<td>Previous diagnosis of asthma</td>
<td>15.8</td>
<td>10.5</td>
<td>8.7</td>
<td>0.588‖</td>
</tr>
<tr>
<td>Previous diagnosis of rhinitis</td>
<td>31.6</td>
<td>44.7</td>
<td>33.2</td>
<td>0.384§</td>
</tr>
<tr>
<td>&gt; 3 flu-like episodes per year</td>
<td>21.1</td>
<td>23.7</td>
<td>24</td>
<td>0.980¶</td>
</tr>
<tr>
<td>Nasal symptoms</td>
<td>100</td>
<td>71.1</td>
<td>61.6</td>
<td>0.002¶</td>
</tr>
<tr>
<td>Nasal and ocular symptoms</td>
<td>68.4</td>
<td>39.5</td>
<td>29.3</td>
<td>0.002‡</td>
</tr>
<tr>
<td>Recurrent wheezing</td>
<td>26.3</td>
<td>23.7</td>
<td>12.2</td>
<td>0.053¶</td>
</tr>
<tr>
<td>Breathlessness</td>
<td>10.5</td>
<td>39.5</td>
<td>25.3</td>
<td>0.052¶</td>
</tr>
<tr>
<td>Building-related worsening</td>
<td>64.8</td>
<td>42.1</td>
<td>27.1</td>
<td>0.001†</td>
</tr>
<tr>
<td>Persistent cough</td>
<td>73.7</td>
<td>28.9</td>
<td>30.6</td>
<td>0.002¶</td>
</tr>
<tr>
<td>Sinus symptoms</td>
<td>55.2</td>
<td>28.9</td>
<td>35.5</td>
<td>0.042‡</td>
</tr>
</tbody>
</table>

*Data are presented as mean (SD) or %.
†One-way analysis of variance.
‡χ².
models were adjusted by ventilation system, work time, gender, smoking habits, and atopic background.

**Microbiological Assessment**

The fungi allergens were counted as total viable mold spores in colony forming units per cubic meter. The means of the total viable mold spores were lower in the indoor than the outdoor samples \( (p = 0.017) \). The Cladosporium spp was the most prevalent airborne fungi found with 64.2%, and Aspergillus spp with 12.0% of the total viable mold spores. Aspergillus spp was the only fungi slightly more numerous in the indoor samples than the outdoors \( (n = 45, p = 0.2) \). Alternaria spp indoor counts were considered low \( (\text{mean}, 30.64 \text{ cfu/m}^3; \text{SD}, 51.72 \text{ cfu/m}^3) \). There was a significant difference of the total fungi levels between the sampling days, with counts nearly 10 times higher in the day 7 compared to the other sampling days \( (p < 0.001) \).

The index of indoor spore counts showed a marked difference within the ventilation groups with an impaired filtrating capacity of the group 1 system, allowing higher counts of particles > 5 μm and indoor spore counts higher than outdoor (Fig 1). The parameters of thermal comfort also showed differences between groups. Group 1 had lower relative humidity values \( (p < 0.05) \) and lower extreme temperatures \( (\text{not significant}) \) when compared to group 2 and outdoors (Fig 2). When included in the multivariate models as explanatory variables, the counts of fungal spores did not present significant associations with respiratory symptoms.

**Major Allergens and Ventilation Groups**

The mite allergens varied from undetectable to 1.9 μg/g of dust, and group 2 had higher mite allergen levels. The other allergens showed no differences between groups (Table 2).

**DISCUSSION**

All self-administered questionnaires can lead to bias. Workers experiencing more symptoms and perception of disease are more likely to complete the questionnaire. However, the high percentage of responders in our study \( (86.7\%) \) diminishes this selection bias. The inability to compare information from subjects in different ventilation categories is a potential source of information bias. The participants were informed about the general objective of studying the environmental health, launched together with the evaluation of the prohibition of smoking in the buildings 4 months earlier. The blinding of the study objective and the blinding of the division of the groups probably minimized the information bias. Job satisfaction and psychosocial factors or other unknown confounders could theoretically explain some of our observed relations, but the similarity of job positions and salaries probably homogenizes the group, in our case.
The symptom prevalence, in spite of being high, is similar to other studies in Brazil. In Canada, similar prevalence of building-related symptoms diminished with improved ventilation systems.

The dependent variables chosen for the logistic regression, besides the relation of the measurements in the buildings with the symptoms, were rhinoconjunctivitis and recurrent wheezing. Although we found differences concerning symptoms suggestive of cough and sinusitis, they are less specific and could be misleading.

The adjusted multivariate analysis model of the risk factors for worsening while in the building showed progressive odds as the ventilation system decays and the accumulated working time is longer. The adjusted risk factors for rhinoconjunctivitis showed association of nasal and ocular symptoms with accumulated work time at the building for >3.2 years, and with the aging of the ventilation system.

Atopic status with previous medical diagnosis of asthma or allergic rhinitis increased the OR to have work-related symptoms in the three forms of ventilation as shown by other studies, but after adjustment, the atopic background lost its statistical significance. However, recurrent wheezing symptoms showed no statistically significant association with the HVAC system in the univariate or the adjusted model for familiar atopy, smoking habits, and gender.

Interestingly enough, building-related symptoms were not related to total viable spores, also in agreement with other studies. This negative finding should be carefully interpreted, since there was a high variation on mold counts during sampling time. In addition, mold allergenicity is complex and there is no widely accepted dose-response curve for mold allergens, and total viable mold spore counts may not reflect the actual allergenic exposure. The airborne fungi most frequently found in places with artificial ventilation were similar to those identified in other indoor and outdoor samples in São Paulo and other countries. There was also no evidence of significant exposure to Alternaria spp and Stachybotrys spp, which has been associated with respiratory symptoms in places with artificial ventilation. However, it is interesting to note that the group 1 system had a higher variation of the indoor/outdoor

<table>
<thead>
<tr>
<th>Allergens</th>
<th>Minimum/Maximum, µg/g</th>
<th>Mean (SD), µg/g</th>
<th>Differences Between Ventilation Groups, p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Der p 1</td>
<td>0.06/1.96</td>
<td>0.65 (0.51)</td>
<td>0.032 (group 2 &gt; group 1)</td>
</tr>
<tr>
<td>Der p 2</td>
<td>0.00/0.99</td>
<td>0.37 (0.28)</td>
<td>0.289</td>
</tr>
<tr>
<td>Der f 1</td>
<td>0.00/0.11</td>
<td>0.02 (0.04)</td>
<td>0.605</td>
</tr>
<tr>
<td>Can f 1</td>
<td>0.18/6.6</td>
<td>1.44 (1.92)</td>
<td>0.579</td>
</tr>
<tr>
<td>Fel d 1</td>
<td>0.1/0.71</td>
<td>0.25 (0.19)</td>
<td>0.108</td>
</tr>
<tr>
<td>Bla g 1</td>
<td>Undetectable</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bla g 2</td>
<td>Undetectable</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blo t 5</td>
<td>Undetectable</td>
<td></td>
<td></td>
</tr>
</tbody>
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index and a higher exposure to larger particles showing low filtering capacity (Fig 1).

The increased OR observed in individuals with previous medically diagnosed respiratory allergies, such as asthma or allergic rhinitis, to develop HVAC system-related symptoms suggests that previously overactive airways could produce a more pronounced response to the aging of the ventilation system and its consequences observed in the risk factors analysis. However, the fact that the effect of the ventilation system was maintained, even after adjustments for atopy in rhinoconjunctivitis and building-related symptoms, suggests that a nonallergic related problem, such as thermal comfort parameters, could be responsible for this finding.

There was a higher variation in temperature and relative humidity values in group 1 (Fig 2). These parameters were once considered to be comfort parameters, but there is increasing evidence that these parameters are important determinants of symptoms. The effect of cold and dry air is an irritant to the nasal mucosa and can induce mast cell degranulation, considering that subjects with rhinitis have an impaired capacity to warm and humidify the inhaled air, this could partially explain the higher prevalence of rhinoconjunctivitis complaints in the atopic individuals, related to the work place in group 1.

The Der p 1 levels were all < 2 μg/g of dust, indicating a low risk for mite allergen sensitization for predisposing individuals. Der p 1 levels were higher in group 2 when compared to group 1 (p = 0.032). This could be a consequence of the higher rates of relative humidity observed in group 2 (Fig 2). The exposures to mites and animal dander were low, all below threshold levels known to cause allergic symptoms in spite of the fact that detectable passive transport of pet allergens was observed independently of the ventilation system. Considering that pollen exposure in São Paulo is clinically irrelevant, the allergic exposure evaluation was considered very comprehensive.

The buildings studied were not previously known as sick ones, nor were there any outbreaks of respiratory symptoms or extraordinary exposure to any known sensitizing allergen. Instead, we studied buildings with sealed windows, and artificial ventilation systems with different ages. In spite of the relatively small number of workers in the study, the expanded time of exposure investigation may yield to a more accurate portrait of the variations of the airborne fungi allergen exposure. IAQ studies in Brazil are in early stages, and considering the potential impact of this issue, further studies to identify risk factors and intervention studies are necessary to develop strategies to achieve good IAQ in the tropics.

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