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# The Relationship between Symptoms and IgG and IgE Antibodies in an Office Environment

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**Airborne fungi have been postulated as a cause of symptoms among office workers. Using the MAST chemiluminescent system, this study evaluated 36 IgG and 36 IgE antibody levels in 47 office workers from an area with elevated airborne fungal concentrations and 44 office workers from an otherwise similar area with lower airborne fungal exposure. No difference was found in IgG antibody to fungi between the lower and higher exposure areas, but high IgG antibody to one or more of the fungi studied was detected in 67% of all the workers tested. IgE antibody to one or more antigens was detected in 40% of the participants. Workers who reported atopic symptoms (sneezing, runny nose, and itchy eyes) or "sick building" symptoms (any three of the following temporally related to work: headache, fatigue, stuffy nose, irritated eyes, or sore throat) were more likely to have one positive IgE antibody test. Type I hypersensitivity to aeroallergens besides fungi may play a role in some symptoms reported by some participants in this office building.** 

***Key Words:*** **indoor environmental quality; fungi; antibodies; bioaerosols; allergy.**

## INTRODUCTION

The National Institute for Occupational Safety and Health (NIOSH) has, over the past few years, received an increasing number of requests for health hazard evaluations regarding symptoms that are believed to be associated with nonindustrial indoor environments (Crandall, 1996). Exposures to fungi in occupied office areas have been noted in some of these evaluations, yet neither the health impact of the fungal exposure at the levels commonly found in the office environment nor the level of exposure that is clinically significant is clear. In 1992 and 1993, NIOSH investigators evaluated a large office building because of symptoms felt, by employees, to be related to working in the building. These symptoms included cough, stuffy nose, fatigue, and sore throat. Indoor fungal reservoirs, particularly of airborne *Penicillium* species, were identified throughout the ventilation system of the building and dissemination of fungi from those reservoirs was found to be occurring (NIOSH, 1993). The environmental bioaerosol data documented a significantly greater airborne dissemination of *Penicillium* species from reservoirs in the fan coil units (FCU) to the area of the building where symptoms were originally reported than to other areas of the building. Mean airborne fungal levels in the higher exposed area were approximately 150 colony- forming units per cubic meter (CFU/m$^3$) in the 1992 survey and 140 CFU/m$^3$ in the 1993 survey. Mean airborne fungal levels in lower exposed areas were approximately 10 CFU/m$^3$ in the 1993 survey.

Results of a follow-up evaluation in September 1994 concurred with these earlier findings (Fig. 1) (NIOSH, 1994). Significant differences were found between samples collected in the higher exposed area and samples from the lower exposed area. In

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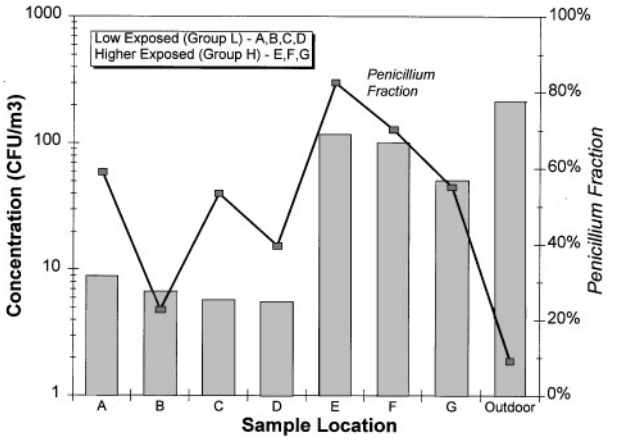


**FIG. 1.** Air sampling results for culturable fungi.

the higher exposed area, 55–83% of the culturable fungi identified were *Penicillium* species. Again, this is consistent with the results of the 1993 investigation. In contrast, the lower exposed area had 23–59% *Penicillium* species, and the outside samples, taken on the roof, were 9% *Penicillium* species. The variation in the rank order of predominant taxon between the outdoor and indoor environments indicates the presence of microbiologic reservoirs and dissemination of *Penicillium* species inside the building. Other fungal species were found including *Cladosporium*, *Alternaria*, and *Aspergillis*, although in lesser amounts than *Penicillium*.

The present study, conducted in November 1994, investigated whether specific IgG and IgE antibody levels among building occupants in the office environment were related to air concentrations of fungi. In addition, we evaluated whether specific IgG or IgE antibody levels to fungi, other allergens in the indoor environment, and other environmental allergens (including aero-allergens) were associated with the prevalence of symptoms, as determined by a questionnaire. We studied employees from two different areas within an office building; one area had greater airborne exposure to *Penicillium* than the other, as described above. Fungal exposure was remeasured at the same time as the blood draw for the antibody tests and these results were consistent with the September 1994 evaluation.

## METHODS

The study had four components: (1) air sampling for fungi; (2) a symptoms questionnaire; (3) determination of serum IgG levels to fungi, other antigens found in the indoor environment, and common foods (Table 1); and (4) determination of serum IgE levels to molds and other antigens found in the indoor and outdoor environment (Table 1). The study was approved by the NIOSH Human Subjects Review Board and all participants signed an approved consent form before questionnaire administration and blood draw.

### 1. Selection of Participants

Employees on two floors of an office building were selected for study. Based on previous measurements of airborne *Penicillium* sp., employees were dichotomized into a low fungal exposure group (L) and a higher fungal exposure group (H). Approximately 100 employees worked in each area and, because of available resources and logistic considerations, the target sample size for the study was approximately 50 persons from each area. Participants were selected based on the proximity of their workstation to the sampling pumps used for the environmental survey. Workers closest to the sampling pumps were selected first and the selection continued, in concentric circles from the pump location, until the required number of participants was achieved, or the number of available employees in the area was exhausted. All participants had worked in their present area for at least 6 months. The area was resampled for airborne fungi on the days of the blood draw to determine if there had been any changes in fungal species or growth in the month since the last environmental survey. Sixty-two employees were approached for participation in Group H and 44 enrolled (71%); 73 employees were approached for participation in Group L and 47 enrolled (64%).

### 2. Questionnaire

The participants received a self-administered questionnaire, based on one used by NIOSH in over 150 studies of nonindustrial workplaces (Malkin, 1996), that requested information concerning (1) symptoms occurring the last 4 weeks while at work, and whether the symptom improved when leaving work; (2) diagnoses of chronic respiratory disease and allergy; (3) perceived environmental comfort (including feeling too hot or cold, too dry or humid, or smelling any odors at work); and (4) medical conditions or therapy that might suppress the immune system. Only self-reported symptoms and diagnosed illnesses are reported in this paper; we did not attempt to verify the presence of a symptom or illness. Symptoms were considered to be present "while at work" if they were reported to have occurred once a week or more at work for the last 4 weeks; symptoms that occurred once a week or more for the

**TABLE 1**

IgG Antibodies Evaluated

| Fungi | Food | Aero-allergens |
|---|---|---|
| *Alternaria* | Corn | Bermuda grass |
| *Aspergillus* | Egg | Birch |
| Baker's yeast | Garlic | Cat |
| *Botrytis* | Milk | Cockroach |
| *Candida* | Peanut | Dog |
| *Cladosporium* | Soybean | *D. pteronyssinus* |
| *Epicoccum* | Tomato | *D. farinae* |
| *Fusarium* | Tuna | Grass |
| *Helminthosporium* | Wheat | House dust |
| *Penicillium* | | Oak |
| *Pullularia* | | Ragweed |
| *Rhizopus* | | *Thermoactinomyces* |
| Stemphylium | | |
| *Mucor* | | |

IgE Antibodies Evaluated

| Fungi | Plants | Grass and trees | Food | Animals | Others |
|---|---|---|---|---|---|
| *Alternaria* | Burningbush | Bahia grass | Almond | Cat | House dust |
| *Aspergillus* | Cocklebur | Beech | Cereal mix | Cockroach | |
| Baker's yeast | English plantain | Bermuda grass | Egg white | Dog | |
| *Candida* | Lamb's quarters | Birch (white) | Milk | *D. pteronyssinus*[a] | |
| *Penicillium* | Pigweed nettle | Box elder (maple) | Peanut | *D. farinae*[a] | |
| | Ragweed | Melaleuca | Shellfish | | |
| | Russian thistle | Nettle | Soybean | | |
| | | Oak (white) | | | |
| | | Perennial rye | | | |
| | | Sycamore (American) | | | |
| | | Timothy grass | | | |

[a]Dust mites

last 4 weeks and improved after the employee left the building were considered "building-related" (Malkin, 1996; Skov, 1987). The following symptom groupings were used for both symptoms reported "while at work" or being "building-related".

"Multiple atopic symptoms." All three of the following: sneezing, itchy eyes, runny nose.

"Multiple sick building syndrome symptoms." At least three of the following: headache, sore or dry throat, nasal congestion, unusual fatigue, irritated eyes. (These symptoms have been shown to have high prevalence rates in studies of the nonindustrial indoor environment by NIOSH and other researchers [NIOSH, 1992, 1994a; Malkin, 1996; Skov, 1987]).

"Multiple respiratory symptoms." At least three of the following symptoms: shortness of breath, cough, chest tightness, wheezing.

"Multiple neurologic symptoms." at least two of the following three symptoms: headache, concentration problems, dizziness.

### 3. Serum Antibody Testing

IgG and IgE antibody levels to the antigens listed in Table 1 were analyzed by the multiple allergen simultaneous testing (MAST) method (Brown, 1985) The MAST system is an automated chemiluminescent assay that measures multiple IgE and IgG antibody levels from small amounts of serum and is FDA approved for IgE determination. Antibody levels in the MAST system are reported in luminometer units (the amount of light emitted in the photoluminescent reaction), which are reported on a continuous scale from 0 to 300, or in MAST classification levels, which are based on luminometer readings. These classifications (and their corresponding luminometer scores) are reported as MAST levels 0 (0–11), 0/1 (12–26), 1 (27–65), 2 (66–142), 3 (143–242), and 4 (>242).

### 4. Data Analysis

All data were analyzed using SAS version 6.1 (SAS 1993). Missing responses on the symptoms part of

the questionnaire were considered negative responses as the author's previous experience with the questionnaire showed that respondents often only record a response for symptoms that they have experienced. Age was dichotomized as high (greater than or equal to the mean age of the entire group) or low (less than the mean age).

The antibody results were dichotomized differently for each type of antibody (IgE and IgG). For IgG, luminometer readings $\geq 143$ (MAST levels 3 and 4) were considered a "high" response and for IgE, luminometer readings $\geq 27$ (greater than or equal to MAST level 1) were considered as "positive." This difference in treatment of antibody levels was necessary because one would not expect to find any IgE antibody to a given antigen in an antibody test of an asymptomatic person. The IgE test is diagnostic, and according to the MAST company, physicians are instructed to consider a result $\geq 1$ to be a positive result on the test. The IgG test is not diagnostic and anyone might have some IgG antibody in response to a given exposure, so the test results were dichotomized into "high" ($\geq$ level 3) and "low" ($\leq$ level 2).

Calculation of whether differences existed in antibody levels between Groups L and H was done with the Student's *t* test, using the continuous luminometer score to compute group mean antibody levels. Because of the number of symptoms and antibodies evaluated, the relationship between antibody levels and symptoms was screened with a SAS macro using logistic regression; only a *P* value was generated from this screening. If a variable was found to have a statistically significant relationship ($P<0.05$), a full logistic regression was done for those variables and odds ratios (OR) and 95% confidence intervals (CI) were calculated.

Three variables were created to evaluate the relationship between the presence of multiple antibodies and the presence of symptoms. The first, which was designated "mold number," was the number of fungal antigens (maximum possible: 11) for which the MAST IgG antibody test was "high." The second was called "IgE number" and was the number of antigens (maximum possible: 36) for which the IgE test was positive. Logistic regression was used to determine the relationship between "mold number" and "IgE number" and the presence or absence of each symptom or symptoms group. The "IgE number" was further dichotomized to create a variable where having IgE antibody to any antigen was scored a "1" and having no IgE antibody was scored a "0." The relationship between this variable and each symptom or group was analyzed with $\chi^2$ tests. In addition, a variable called the "symptoms number" was developed; it was defined as the number of "building-related" symptoms present.

## RESULTS

### 1. Questionnaire Data

#### *A. Characteristics of Study Participants*

Eighty-nine of the 91 participants responded negatively to a question about preexisting immune dysfunction. Two participants did not answer this question, and they were excluded from further analysis, leaving 89 participants in the study, 43 in Group H and 46 in Group L. The mean age of these 89 employees was 44 years. The characteristics of the study population are given in Table 2. Group L participants had worked in their location longer and were more likely to be female and older than Group H participants. These differences were statistically significant. There was no difference between the two groups with regard to smoking status, dust allergy, or eczema. Six participants (7%), all from Group H reported a physician diagnosis of asthma. This finding was statistically significant (Fisher's exact test, two-tailed $P = 0.008$). No one reported a diagnosis of hypersensitivity pneumonitis and only three participants reported an allergy to mold (one from Group L and two From group H).

#### *B. Symptoms*

The questionnaire results for symptoms prevalences are shown in Table 3. The most common symptoms experienced "while at work" (and its prevalence rate) were fatigue (55%), irritated eyes (52%), stuffy nose or sinus congestion (49%), itchy

**TABLE 2**
**Characteristics of the Study Participants**

| | Group L[a] $n = 46$ | Group H[b] $n = 43$ | *P* value |
|---|---|---|---|
| Age greater than the mean | 80% | 33% | 0.001 |
| Percentage female | 89% | 70% | 0.02 |
| Current smokers | 29% | 35% | 0.70 |
| Dog ownership | 20% | 14% | 0.50 |
| Cat ownership | 22% | 7% | 0.05 |
| Hayfever | 29% | 40% | 0.30 |
| Eczema | 7% | 17% | 0.30 |
| Dust allergy | 10% | 19% | 0.26 |
| Mean no. of years at location in building | 4.8 | 2.9 | 0.006 |

[a] Low exposure group
[b] High exposure group

**TABLE 3**
**Symptoms Prevalence (%)**

| Symptoms of 89 workers | Frequently experienced last 4 weeks "while at work" $n = 89$ | Have frequent "building-related" symptoms | | |
|---|---|---|---|---|
| | | Total $n = 89$ | Group L $n = 46$ | Group H $n = 43$ |
| Unusual fatigue or drowsiness | 55 | 26 | 26 | 25 |
| Dry, or irritated eyes | 52 | 38 | 50 | 50 |
| Stuffy nose, or sinus congestion | 49 | 34 | 28 | 40 |
| Itchy eyes | 42 | 27 | 26 | 27 |
| Sneezing | 35 | 21 | 19 | 23 |
| Dry or itchy skin | 35 | 11 | 13 | 9 |
| Sore or dry throat | 33 | 18 | 17 | 19 |
| Headache | 32 | 21 | 26 | 17 |
| Cough | 29 | 18 | 15 | 21 |
| Runny nose | 28 | 17 | 20 | 14 |
| Muscle or joint pains | 24 | 8 | 9 | 7 |
| Difficulty with memory or concentration | 24 | 9 | 13 | |
| Dizziness | 20 | 13 | 13 | 14 |
| Shortness of breath | 16 | 9 | 9 | 9 |
| Wheezing | 15 | 10 | 55 | 44 |
| Chest tightness | 12 | 6 | 7 | 5 |
| Nausea | 9 | 6 | 8 | 2 |
| Sick building syndrome | 42 | 19 | 17 | 21 |
| Multiple neurologic | 23 | 10 | 11 | 9 |
| Atopic symptoms | 15 | 7 | 7 | 7 |
| Multiple respiratory | 10 | 4 | 4 | 4 |

eyes (42%), and sneezing (35%). The same five symptoms also had the highest prevalence rates for "building-related" symptoms. Overall, 58 (65%) respondents reported having one or more "building-related" symptoms. There was no statistically significant difference in symptoms prevalence between employees who worked on the high or low exposure floor for either any individual symptom or symptoms group. Age and sex were not related to symptoms or grouped symptoms prevalence.

### 2. Antibody Data

*A. IgG*

Sixty-seven percent of the participants had "high" IgG antibody to at least one fungal genera and 19% had "high" IgG antibody to four or more fungal genera. Fifty-one percent of the participants had "high" levels of IgG antibody to *Penicillium*, the predominant organism found in the study areas. The prevalence of "high" levels of IgG antibodies to other fungi are given in Table 4. These range from 13% for *Aspergillis* to 42% for *Candida*. Despite the consistent difference in the levels of airborne *Penicillium* measured in the two areas, there was no statistically significant difference between areas with respect to IgG antibody levels to *Penicillium* (mean luminometer reading 158 in the group L and 152 in group H [$t = 0.35$, $P = 0.73$]). For no antigen, besides fungi, did more than two participants have "high" IgG antibody. No participant had "high" IgG antibody levels to dog, cat, dust, Bermuda grass, grass mix, ragweed, white birch, white oak, dust mites, or any food.

*B. IgE*

No participant had a "positive" IgE antibody test to *Penicillium*, *Candida*, *Aspergillus*, or any of the other fungi listed in Table 4. Three were "positive" for *Alternaria*; the highest prevalence of "positive" IgE antibody tests were to aero-allergens (Table 5). There was no difference between the two study groups with respect to prevalence of IgE to any of the tested antigens. Thirty-six (40%) of the participants had IgE antibodies to at least one of the studied antigens (range 1–19) and nine (10%) had antibodies to seven or more antigens. There was no statistically significant relationship between the "IgE number" and smoking status or sex, but age greater than the mean was negatively related to the presence of "positive" IgE antibody tests (OR = 0.2, 95% CI 0.09–0.6).

**TABLE 4**
**IgG Antibody Prevalence to Selected Antigens[a]**

| Antigen | "High" IgG antibody (both groups) | "High" IgG antibody Group L | "High" IgG antibody Group H | *P* value Group L vs Group H |
|---|---|---|---|---|
| *Aspergillis* | 13% | 17% | 9% | 0.26 |
| *Cladosporium* | 19% | 20% | 19% | 0.91 |
| *Candida* | 42% | 45% | 37% | 0.42 |
| *Fusarium* | 17% | 15% | 19% | 0.67 |
| *Pullalaria* | 20% | 20% | 21% | 0.87 |
| *Penicillium* | 51% | 54% | 47% | 0.46 |
| *Stemphyllium* | 16% | 13% | 18% | 0.47 |

[a] "High" responses ≥ MAST level 3.

### 3. Relationship between Symptoms and Antibodies

#### *A. IgG*

"High" IgG antibody to *Aspergillus* was associated with "building-related" atopic symptoms (OR 6.2, 95% CI 1.6–24) and runny nose (OR 4.8, 95% CI 1.3–18.0), and "high" antibody levels to *Cladosporium* were associated with "building-related" dizziness (OR 3.9, 95% CI 1.1–14.2). However, there were equally strong negative relationships. "High" IgG antibody to *Penicillium* was inversely associated with "building-related"cough (OR 0.26, 95% CI 0.08–0.9) and having "high" IgG antibody to *Candida* was negatively associated with "building-related" tiredness/fatigue (OR 0.30, 95% CI 0.10–0.90). No relationship was found between "mold number" and "building-related" symptoms groups (Table 6) or "mold number" and symptoms "while at work" (Table 7).

**TABLE 5**
**IgE Antibody Prevalence to Selected Antigens**

| Antigen | "Positive"[a] IgE antibody (both groups) | "Positive"[a] IgE antibody Group L | "Positive"[a] IgE antibody Group H | *P* value Group L vs Group H |
|---|---|---|---|---|
| Bahia grass[b] | 24% | 20% | 28% | 0.35 |
| Perennial rye grass[b] | 28% | 19% | 35% | 0.10 |
| Timothy grass[b] | 21% | 17% | 26% | 0.35 |
| Ragweed | 19% | 13% | 23% | 0.21 |
| Mite farinae | 21% | 20% | 21% | 0.87 |
| Mite-pteronysinus | 20% | 17% | 21% | 0.67 |
| Dog | 7% | 9% | 5% | 0.45 |
| Cat | 13% | 11% | 14% | 0.66 |
| Cockroach | 8% | 9% | 7% | 0.76 |
| IgE antibody to at least one antigen | 40% | 35% | 47% | 0.26 |

[a] "Positive" responses ≥ MAST level 1.
[b] These grasses are combined into a "grass mix" for IgG determination.

#### *B. IgE*

(*1) Individual symptoms and IgE antibodies.* Positive associations were found with IgE antibody to ragweed and "building-related" symptoms including runny nose (OR 4.3, 95% CI 1.2–14.6), itchy skin (OR 6.2, 95% CI 1.3–30.80), and cough (OR 3.8, 95% CI 1.1–12.7). Having IgE antibody to ragweed was related to both atopic symptoms present at work (OR = 5.7, 95% CI 1.3–24.5) and atopic symptoms that were "building-related" (OR 5.4, 95% CI 1.0–29.6). IgE antibody was found in 41% of the employees who reported any symptom, which is virtually identical to the prevalence of IgE antibody in the study population (40%). "IgE number" was not related to the "building- related" symptoms of runny nose (OR = 1.06, 95% CI = 0.94–1.19), itchy skin (OR = 1.09, 95% CI 0.94–1.2), or cough (OR = 1.06, 95% CI 0.92–1.20).

IgE antibody to *D. farinae* was significantly related to "building-related" fatigue (OR = 4.1, 95% CI 1.2–13.9), and IgE antibody to *D. pterynossinus* was also related to "building-related" fatigue although not as strongly (OR = 3.4, 95% CI 0.9–11.7). A similar relationship was seen for fatigue "while at work" (for *D. farinae*, OR = 3.6, 95% CI 1.0–16.28; for *D. pterynossinus*, OR = 3.2, 95% CI 0.88–14.82). IgE antibody to either species of dust mite was associated with itchy skin "while at work" (for *D. Farinae*, OR = 4.0. 95% CI 1.4–11.8; for *D. pteronys-sinus*, OR = 3.5, 95% CI 1.2–10.3).

Four of the six participants who reported a previous diagnosis of asthma had IgE antibody to at least one antigen. One had antibody to 3 antigens, one had antibody to 4 antigens, one had antibody to 7 antigens, and one had antibody to 13 antigens. The most common IgE antibodies among asthmatics were to perennial ryegrass and bahia grass (three persons each). IgE antibody to one or more of the antigens studied was found in 72% of people reporting an allergy to dust, 71% of the participants reporting hay fever, 67% of those reporting eczema, and 100% of the participants reporting allergy to mold.

(*2) Symptoms groups.* IgE antibody was found in 10 of the 13 (77%) participants reporting atopic symptoms "while at work" (OR = 6.4, 95% CI = 1.6–25.3) and in 5 of the 6 (83%) participants with "building-related" atopic symptoms (OR = 8.3, 95% CI = 0.9–75). No significant relationships were

**TABLE 6**
**Relationship between Antibody and "Building-Related" Symptoms, Odds Ratio (95% Confidence Interval)**

| Antibody | Atopic symptoms | Sick building symptoms | Neurological symptoms | Respiratory symptoms |
|---|---|---|---|---|
| Mold number (IgG) | 1.3 (0.91–1.91) | 1.0 (0.73–1.27) | 1.2 (0.8–1.55) | 0.9 (0.51–1.6) |
| IgE number | 1.1 (0.90–1.29) | 1.0 (0.92–1.19) | 0.9 (0.65–1.15) | 0.8 (0.54–1.34) |
| IgE antibody to any one antigen | 8.3 (0.9-75) | 3.5 (1.1-10.4) | 0.4 (0.08-2.0) | 0.5 (0.05-4.8) |

found between the presence of any IgE antibody and building-related multiple respiratory symptoms (OR 0.8, 95% CI 0.05–4.8) and multiple neurologic symptoms (OR 0.4, 95% CI 0.08–2.0). No relationships were found between increasing IgE number and any "building-related"grouped symptom (Table 6) and any grouped symptom experienced "while at work" (Table 7).

IgE antibody to at least one antigen was found in 11 of the 17 individuals (65%) with "building-related" sick building syndrome symptoms (OR 3.45, 95% CI 1.1–10.4). This relationship was not seen for employees reporting sick building syndrome symptoms "while at work"; IgE antibody to any one antigen was found in 17 of the 36 employees (47%) who reported sick building syndrome symptoms "while at work" (OR 1.5, 95% CI 0.6–3.5). Since many of the symptoms of sick building syndrome are similar to those of the atopic group (stuffy nose, runny nose; irritated eyes, itchy eyes), we felt it possible that the symptoms of sick building syndrome were merely reflecting the atopic status of the participants. Six different individuals reported both atopic group symptoms and "building-related" sick building syndrome symptoms. When these participants were removed from the atopic symptoms group, IgE antibody was found in 7 of the 11 (64%) remaining participants who had "building-related" sick building syndrome symptoms (OR 4.2, 95% CI 1.1–16.2).

## DISCUSSION/CONCLUSIONS

This study identified IgG antibody to *Penicillium* and other molds in two-thirds of the study participants but did not find a relationship between IgG or IgE antibody and exposure to airborne *Penicillium*. A relationship was found between having IgE antibody (to any antigen) and "building-related" atopic symptoms and "building-related" sick building syndrome symptoms even when atopics were removed from the latter group. The role that "IgE-positive" individuals, who may truly be reacting to something in their environment, play in the development of widespread symptoms in an office setting is unknown. Although the percentage of respondents with any "building-related" symptom who also had IgE antibody (41%) was similar to the percentage of all participants with IgE antibody to any one antigen (40%), the finding that 41% of employees have IgE antibody and a "building-related" symptom may indicate that certain symptoms are manifestations, for some people, of allergy. The presence of these employees in an office building may also serve as a catalyst for reporting of symptoms by others, with resulting attribution of these symptoms to the office environment. This hypothesis warrants further investigation.

The symptoms prevalence rates found in this study were similar to those found in a previous NIOSH study of 80 "problem" office buildings, except for wheezing and cough, which were higher in this study. In the previous NIOSH study, the most commonly reported "building-related" symptoms (that were also reported in the present study) were irritated eyes (30%), fatigue (25%), headache (25%), and sneezing (18%). (Malkin, 1996). That study included neither antibody testing nor air measurements for fungi. Many prevalence rates in both the earlier NIOSH study and this study were similar; the etiology of some of the symptoms in the earlier

**TABLE 7**
**Relationship between Antibody and Symptoms "While at Work," Odds Ratio (95% Confidence Interval)**

| Antibody | Atopic symptoms | Sick building symptoms | Neurological symptoms | Respiratory symptoms |
|---|---|---|---|---|
| Mold number (IgG) | 1.3 (0.98–1.71) | 1.1 (0.91–1.40) | 1.2 (0.93–1.51) | 1.0 (0.69–1.41) |
| IgE number | 1.1 (0.95–1.24) | 1.1 (0.90–1.12) | 0.9 (0.79–1.08) | 0.9 (0.67–1.16) |
| IgE antibody to any one antigen | 6.4 (1.6–25.34) | 1.5 (0.62–3.48) | 0.7 (0.24–1.88) | 0.4 (0.76–1.98) |

study might have been related to allergy, as was found in this study or, in both studies, to unstudied factors.

A limitation of the IgE analysis is the lack of a total serum IgE determination from the MAST test. The decision to use the MAST system was based on the large number of specific antibodies that could be assessed. Using this methodology, we found that having IgE antibody to one or more antigens on the panel was strongly related to atopic symptoms and that there was no relation between increased number of IgE specific antibodies to different antigens and atopic symptoms. It is not known if a similar relationship would be found using total IgE antibody; symptoms might have been related to other proteins, allergens, or irritants for which no tests were run.

It was not possible for us to develop an antigen for the MAST panel that was specific for the species of *Penicillium* found in the building. According to the manufacturer, the *Penicillium* antigen used on the MAST panel uses a very broad epitope, to allow the antibody from various species to be detected. We did not have additional samples of the *Penicillium* found in the building to enable us to determine whether there were shared epitopes with the MAST antigen. However, the IgG antibody response to *Penicillium* among employees was greater than would be expected from a population with no known exposure using the MAST analysis. According to the manufacturer, the serum is diluted 300:1 to increase the selectivity of the test and to allow for only an approximately 10% positive response to most antigens in a randomly selected population. Of the approximately 10% positive, only 3% would have antibody >MAST classification 1. In a study of blood bank donors, company researchers reported that 18% had "high" IgG antibodies to similar molds examined in this study (Eldridge, 1988). In our study, 51% of the participants had "high" *Penicillium* IgG levels, which may indicate an ongoing exposure affecting most of the employees in the study either inside or out of the building. The MAST titrations are based on randomly collected sera in California and it is not known whether the higher levels found in our study are typical for the East Coast city where the study was conducted or specific to the building. Although the validity and correlation of the MAST IgE assay with other techniques (RAST, skin prick) have been reported previously (Ogino, 1993; Wang, 1992), it is not identical to these other testing techniques, and data derived from other tests may not be comparable to the MAST results. One study reported differences in assays, particularly in the low range, with the MAST test being more sensitive at lower levels (Mosbech, 1992).

The lack of a relationship between IgG antibody levels to either *Penicillium* or other molds and either exposure levels or individual symptoms may be due to the relatively lower exposures found at the building. The air concentration of *Penicillium* at the building was two orders of magnitude less than that reported in studies of highly exposed occupations, where a dose-response relationship between antibody and exposure has been shown. For example, Hedenstierna *et al.* noted greater IgG antibody levels to the mold *Rhizopus* among workers exposed to 50,000 CFU/$m^3$ than among workers exposed to 2000 CFU/$m^3$ (Hedenstierna, 1986). In this study, the highest measured airborne exposure to *Penicillium* was 200 CFU/$m^3$. The lack of a comparison group from outside the building limits our ability to explain these findings as antibody levels may be a reflection of the exposure in the local environment. Since none of the antigens are specific to the study building, without environmental data from other sites, such as participants' homes, it was impossible to determine where the exposure to *Penicillium* or other molds may have occurred.

Only three people had "positive" IgE antibody tests to any fungus (all to *Alternaria*), and none had IgE antibody to *Penicillium*. IgE antibodies to *Penicillium* and other molds were not detected, possibly due to the blocking effect on IgE antibody of the high levels of IgG antibody found in this study, or possibly because there truly were none. In either case, this finding may indicate that Type 1 reactions to mold are not a factor in the reporting of symptoms in the building, but that Type 1 reactions to other antigens may be related to some of the reported symptoms. Most positive IgE antibody tests were to common aero-allergens such as ragweed, grasses, and trees. The percentage of individuals with IgE antibody among participants in this study was greater than that reported in the general population and may reflect the urban environment in which the building was located or the testing methodology used (skin prick test vs. MAST). For example, skin testing was done as part of the National Health and Nutrition Examination Survey (NHANES II) to the antigens dust, cat, dog, *Alternaria*, ragweed, perennial ryegrass, and Bermuda grass. The results of that survey found that 20% of the participants reacted to at least one of those antigens, and that living in urban areas was related to greater skin test reactivity (Gergen, 1987). In contrast, this study found that 35% of participants had positive IgE tests to similar antigens and that 40% of participants had IgE

antibody to at least any one antigen, irrespective of symptoms.

In conclusion, the presence of IgE antibody was related to the reporting of some symptoms, but we were unable to find any IgE antibody to fungi in this population, in which airborne fungi were documented in the work environment. We were also unable to detect a relationship between the relatively low levels of fungal exposure and symptoms prevalence or IgG antibody levels. The lack of a difference in the level of IgG antibody between the two study groups may mean either that the environmental fungal levels are lower than required to show a dose-response relationship or that in this study, the antibody response to exposures outside the building overwhelmed the response due to exposures inside the building.

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