

Exposure to *Alternaria alternata* in US homes is associated with asthma symptoms

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Background: Exposure to the fungus *Alternaria alternata* is a risk factor for asthma. Few studies have examined *Alternaria* exposures in indoor environments.

Objective: We examined whether exposure to *A alternata* in US homes was associated with asthma-related outcomes.

Methods: The data for this study were collected as part of the National Survey of Lead and Allergens in Housing. This cross-sectional study surveyed a nationally representative sample of 831 housing units inhabited by 2456 individuals in 75 different locations throughout the United States.

An interviewer-administered questionnaire obtained information on demographics, household characteristics, and occupants' health status. Exposure to *A alternata* was assessed by measuring concentrations of *A alternata* antigens in vacuumed dust samples using a polyclonal anti-*A alternata* antibody assay. Dust samples were collected from a bed, a sofa, or a chair, and from bedroom, living room, and kitchen floors. Results: Lifetime prevalence of doctor-diagnosed asthma was 11.2%, and 6.9% of the study subjects reported active asthma symptoms in the past 12 months. The prevalence of current symptomatic asthma increased with increasing *Alternaria* concentrations in US homes; higher levels of *A alternata* antigens increased the odds of having asthma symptoms in the past year (relative to the lowest tertile, adjusted odds ratio was 1.52, 95% CI, 0.90-2.55 for the 2nd tertile; and 1.84, 95% CI, 1.18-2.85 for the 3rd tertile).

Conclusion: Exposure to *A alternata* in US homes is associated with active asthma symptoms.

Clinical implications: Measures that reduce indoor exposure to *A alternata* may help control asthma exacerbations. (J Allergy Clin Immunol 2006;118:892-8.)

Key words: *Alternaria alternata*, fungal allergen, antigen, indoor, exposure, asthma, allergy

Alternaria alternata is one of the most common fungi associated with asthma.^{1,2} Not only the presence of asthma but also persistence and severity of asthma have been

Abbreviations used

GSE: Geometric standard error of mean

NSLAH: National Survey of Lead and Allergens in Housing

OR: Odds ratio

strongly associated with sensitization and exposure to *A alternata*.³⁻⁸ Although exposure to *Alternaria* is an important risk factor for asthma, few studies have assessed exposure to this fungus in indoor environments.^{9,10}

A alternata, a cosmopolitan saprophyte commonly found in soil and plants, is usually considered an outdoor allergen.^{1,11,12} Although most intense exposure is likely to occur outdoors, *Alternaria* and other allergenic fungi are also found in indoor environments.^{1,13-15} Yet fungal allergen exposures in indoor environments have not been characterized as well as other indoor allergens (eg, house dust mite, cockroach, and pet allergens).

One of the major constraints in assessing exposure to fungal allergens has been the difficulty of accurately quantitating the exposure. Exposure to fungal allergens has been conventionally estimated by indirect methods using spore or fungal colony counts in air or dust samples as a proxy of exposure.^{15,16} Although spores are considered primary sources of fungal allergens,¹⁷ allergens and other biologically active molecules derived from fungi can be transported by means other than intact spores (eg, hyphael fragments, fragmented spores, and dust particles).^{1,18,19} For example, allergens can be released along the entire length of the hyphael tube in *A alternata*.¹⁸ Moreover, allergen content in spores may vary depending on environmental conditions.^{18,20} The complex nature of the exposure has hampered development of more sophisticated measuring techniques. Although several fungal allergens have been purified and cloned, availability of fungal immunoassays remains limited.^{15,21} Considerable progress, however, has been made in qualifying and quantifying *Alternaria* allergens.^{15,22}

The National Survey of Lead and Allergens in Housing (NSLAH) was the first population-based study that measured antigenic and allergenic components of *A alternata* in a nationally representative sample of US homes using a polyclonal anti-*A alternata* antibody assay. In this article, we examine the associations between indoor exposures to *A alternata* and asthma-related symptoms among the study population.

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METHODS

Study design and procedures

The data for this cross-sectional study were obtained from the NSLAH. The NSLAH surveyed 831 housing units, which were designed to represent the 96 million permanently occupied, non-institutional housing units that permit resident children. The surveyed housing units were inhabited by 2456 individuals, including 26.8% children. The survey was approved by the National Institute of Environmental Health Sciences Institutional Review Board in 1998. A detailed description of the study design and methodology has been published elsewhere.²³ Briefly, information on demographics, household characteristics, and occupant health status was collected by a questionnaire administered to an adult representative of the household. Environmental data were also acquired by sample collection and inspection of the housing units.

Assessment of health outcomes

The interview obtained information on doctor-diagnosed asthma and allergies, asthma symptoms in the past year, and current asthma medication use. In this survey, an adult respondent was asked whether anyone in the household had doctor-diagnosed asthma, including adults with childhood-onset asthma. If answered affirmative, an additional question ascertained whether the household members with doctor-diagnosed asthma had had asthma symptoms in the past year. Current asthma at the individual level, which was our primary outcome measure, was defined as symptomatic, doctor-diagnosed asthma. The respondent was also asked whether anyone in the household had doctor-diagnosed allergies (eg, hay fever, skin, or food allergies).

Exposure assessment

Single surface dust samples were collected from a bed, a sofa, or a chair, and from bedroom, living room, and kitchen floors as previously described.^{23,24} Each sampling site was vacuumed for 5 minutes using a Eureka Mighty-Might 7.0-ampere vacuum cleaner (Eureka Co, Bloomington, Ill) modified to collect dust into a 19 mm × 90 mm cellulose extraction thimble (Whatman International, Ltd, Maidstone, United Kingdom). Concentrations of *A alternata* antigens ($\mu\text{g/g}$) in dust were measured with a competitive inhibition ELISA using a commercially prepared polyclonal rabbit anti-*A alternata* antibody and *A alternata* antigen standard (Greer Laboratories, Inc, Lenoir, NC).²⁴ The assay detects major *A alternata* antigens, including the most common allergen, Alt a 1.²⁵

Statistical analyses

Alternaria alternata antigen concentrations were log-transformed for the statistical analysis. In addition to the site-specific concentrations, we calculated a house index (ie, the mean of all sampling location concentrations) to represent the average *Alternaria* concentration in the household. We maximized the number of samples in the analysis by assigning samples with concentrations less than the detection limit to $\frac{1}{2}$ the value of the detection limit.²⁴ If samples had insufficient amount of dust for the antigen analysis, they were considered missing. Assessing exposures with the average *Alternaria* concentration, 98.9% (N = 822) of the households were included in the analysis. In the site-specific analyses, the corresponding percentage varied from 76.1% to 85.4%, lowest for beds and highest for bedroom floors.

We calculated odds ratios (ORs) with 95% CIs for the asthma-related outcomes using logistic regression. Subjects with missing data on the exposures were excluded from the analyses. The following covariates were considered as potential confounders or modifying factors: age, sex, race and ethnicity, living area defined by the size of

population and census region, household income, education, family size, smoking in the household, presence of pets, presence of mold/moisture problems, main heating source, survey season, and personal history of atopy. Furthermore, we examined whether the effect estimates were influenced by dust weight and presence of other indoor allergens (Der f 1, Der p 1, Bla g 1, Fel d 1, Can f 1, mouse urinary protein) and bacterial lipopolysaccharide (endotoxin). The associations between *Alternaria* concentrations and asthma symptoms were not strongly confounded by the covariates; changes in ORs tended to be less than 10%. To maximize observations in the analysis and avoid multicollinearity, we chose to adjust our models for age, sex, race, education, smoking, and survey season. Because we did not have information on personal smoking, smoking exposure was assessed at the household level (indoor smoking in the home).

Logistic modeling was conducted using SUDAAN (Version 9.1; Research Triangle Institute, Research Triangle Park, NC), and Taylor series linearization methods were used to adjust SEs for the complex survey design. The SUDAAN software also took into account effects of clustering in the data including multiple occupants in the same household. Sample weights were applied to all estimates to account for housing selection probabilities, nonresponse, and poststratification. Details of statistical weighing for the NSLAH are described elsewhere.²³

To illustrate the associations between *A alternata* antigen concentrations and asthma symptoms graphically, we used smoothed plots to display trends in outcome prevalence across a range of concentrations. Nonparametric regression analyses were conducted using GAM function in S-Plus (v6; Insightful Corp, Seattle, Wash), and the fitted model relationships were graphed.

RESULTS

In the study population, 11.2% had been diagnosed with asthma sometime in their lifetime, whereas 6.9% reported current asthma. The prevalence of asthma was comparable to other national surveys.²⁶ The majority of the subjects with current asthma (71.2%) in this study used asthma medication. Subjects who reported doctor-diagnosed allergies were more likely to have diagnosed asthma (30.1% vs 5.6%; $P < .01$ for difference), especially with active symptoms (22.0% vs 2.6%; $P < .01$ for difference), than those who did not have diagnosed allergies. The lifetime prevalence of self-reported doctor-diagnosed hay fever was 16.2% among the participants, significantly higher among subjects with asthma than subjects without asthma (45.8% vs 12.0%; $P < .01$ for difference). The main characteristics of the study population are presented in Table I.

Exposure to *A alternata* antigens in US homes was common; 95% to 99% of the dust samples collected from 5 locations in the home had detectable levels of *A alternata* antigens. Of the sampled sites, living room floors had the highest concentrations (geometric mean, 5.73 $\mu\text{g/g}$; geometric standard error of mean [GSE], 0.20 $\mu\text{g/g}$), whereas bedroom beds had the lowest concentrations (geometric mean, 2.38 $\mu\text{g/g}$; GSE, 0.17 $\mu\text{g/g}$). The geometric mean for the average *Alternaria* concentration in the household was 4.88 $\mu\text{g/g}$ (GSE, 0.13 $\mu\text{g/g}$). Details of the exposure characteristics have been published previously in the Journal.²⁴

TABLE I. Characteristics of the study population from the NSLAH

| Characteristic | N | %* |
|-----------------------------|------|------|
| Age | | |
| <18 y | 762 | 26.8 |
| 18 y or older | 1643 | 73.2 |
| Sex | | |
| Male | 1189 | 48.2 |
| Female | 1256 | 51.8 |
| Race | | |
| White | 1788 | 79.9 |
| Black | 355 | 11.6 |
| Other | 262 | 8.5 |
| Living area | | |
| MSA, ≥1 million persons | 823 | 28.0 |
| MSA, <1 million persons | 1241 | 48.3 |
| Non-MSA | 392 | 23.7 |
| Census poverty† | | |
| At or below poverty level | 472 | 16.5 |
| Above poverty level | 1873 | 83.5 |
| Education‡ | | |
| High school level or lower | 758 | 29.7 |
| Above high school level | 1646 | 70.3 |
| Living with smoker(s) | | |
| Yes | 1124 | 46.0 |
| No | 1320 | 54.0 |
| Doctor-diagnosed asthma§ | | |
| Yes | 278 | 11.2 |
| No | 2162 | 88.8 |
| Current asthma | | |
| Yes | 174 | 6.9 |
| No | 2265 | 93.1 |
| Doctor-diagnosed hay fever§ | | |
| Yes | 309 | 16.2 |
| No | 1767 | 83.8 |

MSA, Metropolitan statistical area.

*Weighted for the multistage sampling design of the NSLAH.

†Poverty based on US Census Bureau poverty thresholds for 1996.

‡Highest education level attained in the household.

§Lifetime diagnosis.

Current asthma was positively associated with *A alternata* antigen levels in the home. Prevalence of current asthma increased significantly with higher antigen levels (Table II). Table III shows unadjusted and adjusted effect estimates for the association between current asthma and the average *Alternaria* concentration in the household (the house index). This association was not greatly influenced by dust weight, presence of other indoor allergens, or endotoxin (Table III; see this article's Table E1 in the Online Repository at www.jacionline.org). Consistent with the results, asthma medication use was associated with *A alternata* antigen levels in the home. Relative to the lowest tertile, the OR was 1.43, 95% CI, 0.74 to 2.79, for the 2nd tertile and 1.72, 95% CI, 1.02 to 2.90, for the 3rd tertile (ORs adjusted for age, sex, race, education, smoking, and sampling season). On the contrary, hay fever (Table III) and other diagnosed allergies were not associated with indoor levels of *A alternata* antigens. Although wheezing is often closely related to asthma,

TABLE II. Prevalence of current asthma and diagnosed hay fever by average *A alternata* antigen level in the household (house index)

| Categorized <i>Alternaria</i> level* | Current asthma | | Diagnosed hay fever | |
|--------------------------------------|----------------|-----------------------|---------------------|----------------------|
| | N | Prevalence†‡ (95% CI) | N | Prevalence† (95% CI) |
| 1st tertile | 40 | 4.81 (3.32-6.92) | 93 | 16.44 (13.04-20.52) |
| 2nd tertile | 61 | 7.47 (5.18-10.64) | 122 | 17.14 (12.82-22.54) |
| 3rd tertile | 73 | 8.73 (6.70-11.30) | 93 | 15.21 (12.13-18.90) |

*1st tertile < 3.90 µg/g; 2nd tertile 3.90-6.27 µg/g; 3rd tertile ≥ 6.28 µg/g.

†Percentage (95% CI) weighted for the multistage sampling design of the NSLAH.

‡χ²; P < .05.

recent wheezing was not associated with indoor levels of *A alternata* (data not shown). In this population, wheezing was not restricted to asthma symptoms; more than half of those who reported wheezing in the past year (69.9%) did not report current asthma. It is well known that diseases other than asthma (eg, chronic obstructive pulmonary disease) may also contribute to wheezing, especially among adults.²⁷

We used nonparametric regression analysis to characterize further the relationship between current asthma and *A alternata* antigen levels in the home. The modeled relationships display estimated trends in current asthma prevalence across *Alternaria* concentrations. The smooth plots illustrating adjusted prevalence for the average and site-specific *Alternaria* concentrations are shown in Fig 1. The prevalence of current asthma tended to increase with increasing antigen concentrations across the sites. There was no clear indication of a threshold below which there was no increase in prevalence. Complementary to the smooth curves, Fig 2 presents adjusted ORs for the association between current asthma and *A alternata* antigen levels when the antigen concentration was modeled as a continuous variable in logistic models. The ORs correspond to a 2-fold increase in *A alternata* concentration (average and site-specific concentrations).

We also examined whether the effect of *Alternaria* exposure differed by age groups (children, adults) and by atopic status, which was based on reported doctor-diagnosed allergies. Neither of these differences reached statistical significance (Table IV).

DISCUSSION

This study demonstrates that exposure to *A alternata* in the home is positively associated with current asthma. Although fungal exposure levels in indoor environments are usually lower than outdoors,^{15,28} our results suggest that indoor exposure to *A alternata* contributes to asthma symptoms. Among the surveyed US population, the odds of having asthma symptoms in the past year increased significantly with higher indoor levels of *A alternata* antigens. This association

TABLE III. Current asthma and diagnosed hay fever in relation to average *A alternata* concentration in the household (house index)

| Logistic models* | Current asthma OR (95% CI) | Diagnosed hay fever OR (95% CI) |
|-------------------------------------------------------------------------------|----------------------------|---------------------------------|
| Unadjusted model | | |
| 1st tertile | 1.00 | 1.00 |
| 2nd tertile | 1.60 (0.93-2.77) | 1.06 (0.71-1.56) |
| 3rd tertile | 1.89 (1.21-2.93) | 0.91 (0.64-1.28) |
| Adjusted† model | | |
| 1st tertile | 1.00 | 1.00 |
| 2nd tertile | 1.52 (0.90-2.55) | 1.04 (0.71-1.51) |
| 3rd tertile | 1.84 (1.18-2.85) | 0.92 (0.65-1.31) |
| Adjusted‡ model including other indoor allergens | | |
| 1st tertile | 1.00 | 1.00 |
| 2nd tertile | 1.56 (0.96-2.53) | 1.04 (0.71-1.53) |
| 3rd tertile | 1.89 (1.25-2.85) | 0.91 (0.61-1.37) |
| Adjusted‡ model including other indoor allergens and dust weight | | |
| 1st tertile | 1.00 | 1.00 |
| 2nd tertile | 1.55 (0.96-2.52) | 1.03 (0.70-1.51) |
| 3rd tertile | 1.86 (1.22-2.84) | 0.89 (0.59-1.35) |
| Adjusted‡ model including other indoor allergens, dust weight, and endotoxin‡ | | |
| 1st tertile | 1.00 | 1.00 |
| 2nd tertile | 1.45 (0.88-2.39) | 1.07 (0.73-1.58) |
| 3rd tertile | 1.73 (1.08-2.77) | 0.98 (0.64-1.51) |

**Alternaria* concentration categorized into tertiles.

†Adjusted for age, sex, race, education, smoking, and sampling season.

‡The model adjusted for endotoxin includes fewer observations than the other adjusted models (current asthma/no current asthma [n/N] = 170/2145 for the adjusted models, 168/2061 for the endotoxin adjusted model; hay fever/no hay fever = 300/1683 for the adjusted models, 290/1623 for the endotoxin adjusted model).

remained consistent after adjusting for other potential risk factors, including exposures to other indoor allergens and endotoxin.

Indoor exposures are of great importance in relation to asthma because people spend most of their time in indoor environments, especially at home.²⁹ In addition to the major indoor allergens, generated from arthropods and animals, exposure to fungal allergens has been associated with asthma.^{2,15} In particular, *Alternaria* sensitivity and increased *Alternaria* spore counts in the atmosphere have been repeatedly associated with asthma-related outcomes.^{1,2,4-8,12} However, few studies have assessed exposure to *Alternaria* in indoor environments^{9,10}; exposure to *Alternaria* has been generally thought to arise primarily from outdoor environments.

In this study, higher levels of *A alternata* antigens in the home increased the odds of having asthma symptoms in

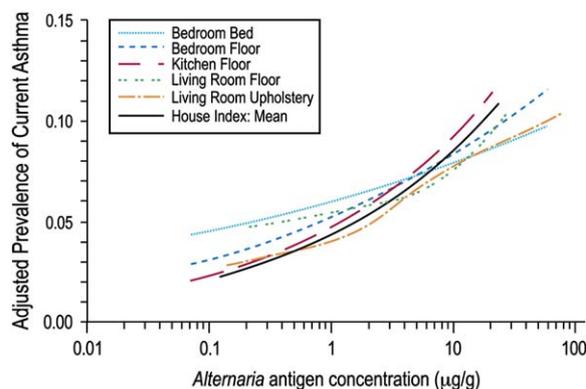


FIG 1. Smoothed plots showing adjusted prevalence of current asthma by *A alternata* antigen concentration for the house index and each sampling location. The estimated prevalence is adjusted for age, sex, race, education, smoking, and survey season.

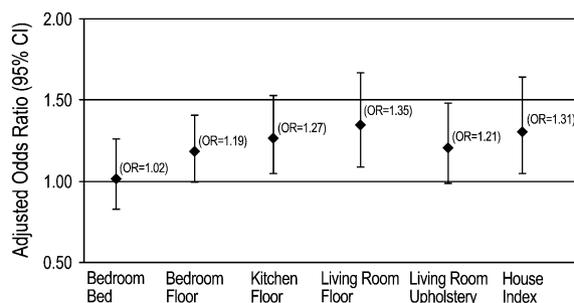


FIG 2. Adjusted ORs and 95% CIs for the association between current asthma and *A alternata* antigen concentration in the household (continuous variable). The house index (the mean of the site-specific concentrations) and site-specific ORs correspond to a 2-fold increase in *Alternaria* concentration adjusting for age, sex, race, education, smoking, and survey season.

the past year. The relationship is likely exposure-dependent because the prevalence of current symptomatic asthma increased with increasing *Alternaria* concentrations. All sampling sites showed an increasing trend, although the association was weaker for bedroom beds. Despite fairly uniform distributions across the sites, *Alternaria* concentrations were lowest in beds.²⁴ Although *Alternaria* levels were correlated to some extent with the levels of dust mite allergens, mouse urinary protein, and endotoxin (data not shown), indoor exposure to *Alternaria* contributed independently to asthma symptoms. After adjusting for potential confounders, including the presence of other indoor allergens, endotoxin, or dust weight, the ORs did not change appreciably, and the magnitude of the effect remained the same (Table III; see this article's Table E1 in the Online Repository at www.jacionline.org).

Exposure and sensitization to *Alternaria* have been shown to be important risk factors for asthma, particularly among children.^{5,6,8,12} In our population, active asthma

TABLE IV. Current asthma in relation to a 2-fold increase in average *Alternaria* concentration in the household (house index) stratified by age groups and atopic status

| Stratification by | Current asthma OR (95% CI)* | P value for interaction |
|----------------------|-----------------------------|-------------------------|
| Age† | | .62 |
| All | 1.31 (1.05-1.64) | |
| Children | 1.47 (0.83-2.62) | |
| Adults | 1.25 (0.99-1.58) | |
| Diagnosed allergies‡ | | .97 |
| All | 1.28 (1.04-1.57) | |
| No | 1.27 (0.89-1.82) | |
| Yes | 1.28 (0.98-1.67) | |

*Adjusted model, *Alternaria* concentration modeled as a continuous variable.

†Children (<18 years old), adults (18 years or older).

‡The model has fewer observations because of missing values (current asthma/no current asthma [n/N] = 170/2145 for the age-stratified model, 167/1857 for the atopy-stratified model).

symptoms were slightly more prevalent among children than among adults (8.4% vs 6.5%; $P = .12$ for difference), but the observed effect was not modified by age. Although the point estimate for the association was higher among children than among adults, there was no evidence of significant interaction. We did not have detailed information on asthma severity among the study participants, but indoor exposure to *A alternata* appeared to contribute to active asthma symptoms irrespective of whether subjects used asthma medication.

Although sensitization to *Alternaria* has also been associated with allergic rhinitis,^{30,31} indoor exposure to *A alternata* antigens was not associated with doctor-diagnosed hay fever in this population. The lack of association was not necessarily unexpected because we had no information on whether individuals with diagnosed hay fever manifested any active symptoms. Prevalence of symptomatic hay fever usually tends to decline with advancing age, after reaching its peak during adolescence.^{32,33} Correspondingly, skin test response rates to common allergens, including *Alternaria*, have been shown to decline with older age.³⁴ Because the prevalence of doctor-diagnosed hay fever was higher among adults than among children (18.2% vs 12.0%; $P < .01$ for difference), many of the individuals with hay fever diagnosis may have been symptom-free because of declined reactivity to allergens.

The effects of fungal exposure are generally greater among individuals who have skin prick test sensitivity to fungal allergens.^{3-5,8,15} Sensitization to *Alternaria* has been found to be significantly higher among subjects with asthma than among subjects without asthma.³⁵ We were unable to ascertain *Alternaria* sensitivity among the study participants because we lacked detailed information on their sensitization status. Although the odds of having asthma diagnosis were significantly higher among those who reported doctor-diagnosed allergies, the observed association between current asthma and indoor exposure to

A alternata was not modified by atopy. Although fungal allergens are known to induce IgE-mediated hypersensitivity, exposure to fungi can induce non-IgE-mediated inflammatory and immunological processes; particulates derived from fungi contain a variety of biologically active molecules, not only allergens.^{2,36} It has been suggested that fungal exposure may promote adjuvant effects on allergic immune responses.³⁷ Fungal proteases may also interact directly with airway epithelium. For example, a recent study showed that proteases present in *A alternata* extracts induced morphological changes, cell desquamation, and production of proinflammatory cytokines.³⁸

Absence of standardized measurement techniques for evaluation of fungal allergen exposures has been a major constraint in risk assessment. Because interpretation of fungal exposure data is both complex and contentious, no exposure thresholds exist. Although mAb-based assays are more sensitive and specific for a single allergenic protein (eg, Alt a 1), allergenic fungi express great variability in allergen profiles depending on the environmental conditions under which they grow.^{17,25} Some previous studies have had difficulties in detecting *Alternaria* allergens in environmental samples with mAb-based assays, even among populations in which *Alternaria* sensitivity and exposure to *Alternaria* spores are known to be common.^{22,39,40} We measured concentrations of *A alternata* antigens in dust with a polyclonal anti-*A alternata* antibody assay, which was the best available assay at the time of the survey. Because the polyclonal rabbit anti-*A alternata* antibodies (Greer Laboratories, Inc) were raised against the cellular antigens derived from whole mycelial extracts of *A alternata*, they bind to a variety of antigenic components, including, but not limited to, known allergens. Although the possibility of cross-reactivity cannot be excluded in the current study, monoclonal fungal antibodies can also have widespread cross-reactivity.⁴¹ It is also worth noting that the diagnosis of *Alternaria*-induced allergy and asthma has largely relied on the use of crude filtrate and mycelial extracts of *A alternata*, which are variable and lack standardization.

Although the most intense exposure to *Alternaria* occurs outdoors during summer and fall months when the atmospheric spore counts peak,¹ our findings suggest that indoor exposure may contribute to perennial asthma symptoms independently. It is unlikely that the indoor level of *Alternaria* is a surrogate for outdoor levels because the indoor levels of *Alternaria* did not reflect the seasonal patterns that are typical of outdoor levels (see this article's Table E2 in the Online Repository at www.jacionline.org). In agreement with previous studies,^{28,42-44} we have recently shown that regional factors, housing characteristics, and occupants' behavior can significantly affect indoor fungal levels.²⁴

A key difficulty in all epidemiological studies that examine asthma prevalence has been the problem of validation, because there is no gold standard for asthma. In this study, asthma-related outcomes were based on self-reported symptoms, diagnosis, and medication use, which may introduce bias. However, prevalence of asthma

in the study population did not significantly differ from that in other national prevalence estimates (eg, ever-diagnosed and current asthma).²⁶

We acknowledge that the cross-sectional nature of the study is a limitation. We focused primarily on active asthma symptoms in the past 12 months, because the temporal relationship between outcomes and exposures can be difficult to determine in cross-sectional studies. We lacked detailed sensitization data (eg, skin prick test, specific IgE), but on the other hand, the association between current asthma and *Alternaria* levels was not modified by atopic status. To characterize the exposure in detail, we assessed exposure levels across multiple household sites. Although we were not able to assess seasonal variability in *Alternaria* levels in individual homes, sampling in the survey was conducted throughout summer, fall, and winter months in each geographic region to capture seasonal variation in the data. Settled dust samples are often thought to be less influenced by temporal and spatial variability, are reproducible, and represent long-term exposure better than short-term air sampling, although there is no clear agreement how to assess fungal exposure over time.^{21,45} For other common indoor allergens, however, measurement of allergen concentration in reservoir dust has generally been used as the standard index of exposure.

One of the main strengths of this study is that the survey sample is nationally representative. The weighted characteristics of the survey sample, including distributions of housing characteristics, socioeconomic, and demographic factors, were very similar to characteristics obtained from other national surveys.²³ The NSLAH is the first population-based study that not only measured antigenic and allergenic components of *A alternata* but also simultaneously estimated levels of other common indoor allergens and endotoxin in the US housing stock.

This study provides new information on *Alternaria* exposures in relation to asthma, suggesting that indoor exposure to *A alternata* antigens is associated with active asthma symptoms. To determine clinically relevant exposure levels in indoor environments, further research is warranted, because immunoassays that are used to assess fungal allergen exposures have not achieved the same reliability as have similar assays for other allergens.¹ However, avoidance of asthma triggers has been a fundamental part of treatment of patients with asthma.^{46,47} Although it is essential to restrict outdoor exposure to *Alternaria* when atmospheric concentrations of spores are high, measures that reduce indoor exposure to *Alternaria* may also help control asthma exacerbations, especially among *Alternaria*-sensitive individuals. Indoor levels of *A alternata* antigens are influenced by both regional and residential factors, of which some are modifiable.²⁴ Subjects with asthma are likely to benefit from preventing mold and moisture-related problems and having their homes cleaned on a regular basis, because these measures may not only reduce *Alternaria* antigen levels but also lower levels of other potential asthma triggers in the home.

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