We assessed the influence of current indoor levels of fungi, house dust mite allergen (Der p 1), and cat allergen (Fel d 1) on sensitization and asthma in adults. A total of 485 adults answered a questionnaire and had skin prick tests and lung function tests. Dust and air samples were collected from their bedrooms. The dust was analyzed for Der p 1, Fel d 1, and fungal biomass (ergosterol). Fungal propagules were measured in air samples. Current asthma was defined as having wheezed during the past 12 mo plus bronchial hyperreactivity (BHR) to methacholine. High exposure to total airborne fungi was associated with increased BHR, but perhaps paradoxically with a lower risk of being sensitized to fungi. Ergosterol levels in floor dust were a risk factor both for being sensitized to fungi and having wheezed within the last year. High Fel d 1 levels in floor dust were found to increase the risk of being sensitized to cats and in beds to increase the risk of current asthma. Although Der p 1 levels in homes were high, people exposed to high Der p 1 levels in floor dust were less likely to be sensitized to house dust mites or to have wheezed within the past year. Current indoor levels of fungi and Fel d 1, but not Der p 1, influenced sensitization and asthma in adults with high dust mite exposure.

Keywords: asthma; allergy; indoor environment; indoor allergens; house dust mites; fungi; ergosterol; cat

The importance of previous sensitization to various indoor allergens such as house dust mites (HDM) (1), cockroaches (2), fungi (3), and cats (4) as a risk factor for asthma has been increasingly recognized. However, the impact of current allergen levels on sensitization and clinical activity of asthma is controversial and has not been investigated adequately, particularly in adults. Although it is widely accepted that symptoms of asthma are directly related to the current environmental allergen levels, this has not been established.

Some studies have suggested that the current levels of HDM allergen (5), cockroach allergen (6), fungi (7), and cat allergen (8) are related to sensitization and clinical activity of asthma, whereas others have contradicted these findings (4, 9).

The literature suggests that indoor allergens may be interrelated. Fungi play an important role in the food chain of house dust mites as HDM flourish only on human dander that has been predigested by fungi (10). Concentrations of cat allergen were elevated in all houses with cats (11) and cat ownership was found to be associated with high levels of viable airborne fungi and ergosterol levels in floor dust (12). None of the studies that examined the association between allergen levels and asthma has accounted for the confounding effects of interrelated exposures, whereas only a few studies have accounted for other potential confounders such as medication use and parental asthma.

In the current study, we investigated the impact of common indoor allergens (i.e., HDM, fungi, and cat) on sensitization and clinical activity of asthma in a sample of 485 young adults in Melbourne, Australia, which has one of the highest prevalence rates of asthma in the world (13).

METHODS

Subjects

The subjects were participants in a follow-up study to the European Community Respiratory Health Survey (ECRHS), as undertaken by our center in Melbourne. The two-phase sampling procedure has been described elsewhere (14). Briefly, a questionnaire was mailed to a group of young adults randomly selected from the electoral roll during the first phase of the ECRHS in 1992. This comprised 4,500 subjects aged between 20 and 44 yr, of whom 3,210 (72%) responded. The prevalence of symptoms of asthma, that is, experience of nocturnal dyspnea, asthma within the past 12 mo, or being on medication for asthma, among the respondents was 17.6%. A random sample (n = 1,642) and a “symptomatic” sample (n = 433) of the respondents were invited to the laboratory for testing in the second stage of ECRHS, of whom 757 subjects attended between 1993 and 1994. This group was requested to participate in a follow-up study in 1996 and 485 complied. Among them, 349 were from the random sample and 136 from the symptomatic sample.

In the follow-up study, all the participants (n = 485) were visited once at home in random order during 1996. The respective numbers visited during summer, autumn, winter, and spring were 28, 146, 136, and 175. Air and dust samples were collected from their bedrooms, and a residential questionnaire was administered. Air samples were collected first and then the dust samples. The participants were requested to visit the laboratory to complete a detailed respiratory questionnaire and to undertake skin prick tests and lung function tests including methacholine inhalation challenge, and 480 complied.

Home-visit Questionnaire

A validated interviewer-administered questionnaire (15) was used to collect information about residential characteristics. Bedroom air temperature and relative humidity were recorded at the same visit using a digital thermohygrometer (Type THG-388, RS Components, China) and a standardized procedure (16). Absolute humidity for each house was calculated using the measurements of temperature and relative humidity.

Collection of Dust Samples—Floor and Bed

A sample of dust was collected from the bedroom floor and bed of each subject using a standard protocol, with some modification (16).
The geometric mean weight of the total dust collected (n = 485) was 0.56 g (range: 0.06 to 4.57 g).

Measurement of Levels of HDM Allergens and Cat Allergens in Dust

Dust samples were analyzed for the major HDM allergen Der p 1 (17) and major cat allergen Fel d 1 (18) using standard enzyme-linked immunosorbent assays (ELISA) and a standardized procedure of which the details have already been published (16).

Der p 1 and Fel d 1 levels in bed dust were expressed as microgram/gram of fine dust only, whereas Der p 1 and Fel d 1 levels in floor dust were expressed as both microgram/gram of fine dust as well as microgram/square meter. The correlations for both floor Der p 1 and Fel d 1 between levels expressed as microgram/gram of fine dust and microgram/square meter were strong and statistically significant (r = 0.9 and r = 0.8, respectively; p < 0.001). Thus, further analyses were carried out on allergen levels expressed as microgram/gram of fine dust to ensure the comparability of the results with the available literature.

Measurement of Cumulative Fungal Levels in Floor Dust

The fungal membrane lipid ergosterol was used as an indicator of total fungal biomass (i.e., cumulative exposure to fungi) in dust samples, using a modification of the technique of Martin and coworkers (19). After aliquots of dust were taken for Der p 1 and Fel d 1 analysis, sufficient dust remained in only 447 of the original 485 samples for ergosterol analysis. Results were expressed as micrograms of ergosterol/gram of fine dust and micrograms/square meter of floor area and the correlation between these was 0.9 (p < 0.001). Hence, again we used only the ergosterol levels expressed as micrograms/gram of dust in further analyses.

Measurement of Total and Specific Fungal Levels in the Air

The identity and abundance of viable fungal propagules suspended in the air at the time of sampling were estimated using a two-stage Andersen sampler (Model 10-800; Graseby/Andersen, Atlanta, GA), potato dextrose agar plates, and a standardized procedure (12). Five genera, which have previously been identified as allergenic, Cladosporium, Alternaria, Epicoccum, Penicillium, and Aspergillus, were identified based on colony morphology. All the other colonies were aggregated into one group as “others.” Levels of airborne fungi were expressed as number of colony-forming units per cubic meter of air (CFU/m³).

ECRHS Questionnaire

An interviewer-administered questionnaire was used to collect information on sociodemographic details, respiratory symptoms during the preceding 12 mo, allergic symptoms, family history, home and work environment, and use of health care services and medications. The background and validity of this instrument have been presented previously (14).

Lung Function Testing and Methacholine Inhalation Challenge

Lung function was measured using a rolling seal spirometer (Sensor-Medics, Yorba Linda, CA). FEV₁ was recorded from the best of five blows, which met the American Thoracic Society criteria. Methacholine (MCh) (Methacholine Chloride, USP Methapharm Inc, Branford, ON, Canada) was delivered by a Mefar 3B dosimeter (Mefar, Bovezi, Italy) until FEV₁ fell by 20% from the initial value or up to a cumulative dose of 2 mg. The full protocol has been described elsewhere (14).

Skin Prick Tests

Skin prick testing (SPT) was performed on the volar surface of the forearm using lancets and a drop of allergen extract (Hollister-Stier, France). The allergen extracts used were Dermatophagoides pteronyssinus, Felis domesticus, Cladosporium herbarum, Aspergillus fumigatus, Alternaria tenuis, Epicoccum nigrum, and Penicillium with positive (histamine) and negative controls.

Definitions

A positive SPT was defined as a wheal diameter of 3 mm or more to an allergen with a positive reaction to histamine (i.e., 3 mm or more) and a negative reaction to saline. Atopy was defined as a positive SPT to at least one of the allergens in the panel. Sensitization to a given allergen was defined as having a positive SPT to the given allergen. Fungal sensitization was defined as having a positive SPT to at least one of the fungi in the panel.

Bronchial hyperreactivity (BHR) was defined as a PD₂₀ FEV₁ ≤ 2 mg MCh. Bronchial reactivity was also expressed as the dose–response slope (DRS) = (% change in FEV₁ + 3.5)/MCh dose (20).

Clinical activity of asthma was categorized into current asthma—having wheeze during the past 12 mo plus BHR; wheeze only during the past 12 mo; and BHR only. Subjects without any of these criteria were considered as the control group.

Occupation was classified according to the Australian Standard Classification for Occupations (ASCO). Managers, administrators (ASCO group 1), and professionals (ASCO group 2) were classified for the study as Class 1 and the remaining ASCO groups as Class 2.

Analysis

The Statistical Analytical System package (21) and STATA (22) were used to analyze the data. The distributions of airborne fungal levels, ergosterol levels, Der p 1 levels, Fel d 1 levels, and DRS were positively skewed. Logarithmic transformations normalized distributions of total fungal propagules, Cladosporium, ergosterol levels, Der p 1 levels, and DRS.

The two-phase sampling process oversampled symptomatic subjects. Therefore, a reweighting procedure (23) was applied to realign the sample to the symptomatic prevalence of 17.6% in the population aged 20–44 yr to assess the corresponding allergen levels and clinical outcomes. Applying these corrections using the Stata software (22) yielded negligible differences in allergen levels compared with unweighted analyses, principally because the symptomatic and asymptomatic subjects in the sample were comparable across all allergen levels. Therefore, only the unweighted results are presented. However, weighted analysis yielded important differences in clinical outcomes and the adjusted estimates along with unweighted estimates are presented. “Symptomatic status” as defined for sampling in ECRHS stage two was controlled in examining the associations between allergen levels and clinical outcomes.

The exposures under investigation (i.e., all allergen levels) were analyzed as continuous variables initially while including linear and quadratic terms in the regression models. In this analysis the significance of the quadratic term was examined first and the linear term was examined only when the quadratic term was not significant. Next allergen levels were categorized into quartiles to examine their influence on the outcomes of interest. Interquartile and median values are given in Table 1. Aspergillus, Epicoccum, and Alternaria were categorized as present or absent as the levels were too low to be categorized into quartiles. As results of both continuous and quartile analyses were similar, only the quartile analysis results are presented in the text and figures for simplicity.

In addition, Der p 1 and Fel d 1 levels were categorized by using the cut-off points that have been previously suggested as threshold levels for sensitization and symptoms of asthma, respectively, that is, 2 and 8 μg Fel d 1/g of dust and 2 and 10 μg Der p 1/g of dust (24).

There were eight comparisons per exposure variable on the levels of Der p 1 and Fel d 1 (i.e., Q1 versus Q2/Q3/Q4, Q1 versus Q2, Q1 versus Q3, Q1 versus Q4, Q2 versus Q3, Q2 versus Q4, Q3 versus Q4, and Q1 versus Q5).

<table>
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<tr>
<th>TABLE 1. INTERQUARTILE AND MEDIAN VALUES OF THE ALLERGEN LEVELS</th>
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<tr>
<td>Type of Allergen</td>
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<td>Ergosterol, μg/dust</td>
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<td>Total fungi, CFU/m³ of air</td>
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<td>Cladosporium, CFU/m³ of air</td>
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<td>Penicillium, CFU/m³ of air</td>
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Q3, Q1 vs Q4, dose–response linear + quadratic, and the two threshold levels. There were six comparisons per exposure variable on ergosterol and airborne fungal levels (i.e., Q1 versus Q2/Q3/Q4, Q1 versus Q2, Q1 versus Q3, Q1 versus Q4, dose–response linear + quadratic).

The outcomes of interest were sensitization to specific allergens, clinical activity of asthma (see above), and bronchial reactivity (dose–response slope).

Sociodemographic factors, current smoking, parental asthma/allergy, medication use, and the season during which the participant was investigated were considered as possible confounders. Factors that were associated with the relevant outcomes at the p < 0.2 level in the univariate analysis were controlled when examining the relevant associations.

The risk for sensitization to each allergen when exposure was in the top three quartiles (i.e., 26%–50% = second, 51%–75% = third, and 76%–100% = fourth) compared with the first quartile (0–25%) was examined in multiple logistic regression analysis, while adjusting for the potential confounders. Potential confounders were identified in the above analysis and symptomatic status as defined for sampling in ECRHS stage 2. In addition, Der p 1 and Fel d 1 levels in both bed and floor dust were adjusted simultaneously, while examining the influence of each allergen on the respective sensitization. Similarly, either ergosterol and total fungal allergens or fungal ergosterol and specific fungi were adjusted simultaneously, when examining the influence of these on fungal allergy.

Clinical activity of asthma was analyzed as a nominal variable with four categories. Hence, the influence of allergen levels on clinical activity of asthma was examined by multinomial logistic regression while accounting for the potential confounders. Subjects without current asthma, BHR, or wheeze served as the control group in this analysis. Confounders included were those previously identified in the analysis, all the other allergen levels, and symptomatic status as defined for sampling in ECRHS stage 2. Multiple linear regression was used to assess the influence of allergen levels on log DRS while adjusting for the same variables as above. We also examined the influence of interactions between allergen levels on the clinical outcomes by including the relevant cross-product terms in the regression models.

Adjusted odds ratios (AOR), 95% confidence intervals (95% CI), and p values computed in both multiple logistic regression and multinomial logistic regression were examined to assess the strength and the significance of the associations. The adjusted regression coefficients, 95% CI, and p values for specific allergens were examined in the multiple linear regression. By convention p < 0.05 was considered significant.

Ethics
The study was approved by the Ethics Review Committee at The Alfred Hospital. Written informed consent was obtained from all participants.

RESULTS
Characteristics of the Study Sample
The age of the study participants ranged from 24 to 48 yr with a mean age of 37.5 yr. Sociodemographic characteristics and relevant clinical outcomes of the participants are described in Table 2. Sociodemographic characteristics were similar between the random and symptomatic samples, however, not surprisingly, all the relevant clinical outcomes (i.e., atopy, allergy to the specific allergens, dose–response slope, and clinical activity of asthma) were significantly higher in the symptomatic sample (p < 0.05). The estimates of clinical outcomes adjusted for oversampling of symptomatic subjects in ECRHS stage 2 are given in Table 2.

Sex, current employment status, occupational class, median age at completion of education, and current smoking were not associated with either atopy or asthma (p > 0.2). Participants with atopy and current asthma were on average 1 yr younger than control subjects (p = 0.1). Participants with current asthma were less likely to be Australian born (76%), whereas participants with wheeze only and BHR only were marginally more likely to be Australian born (83% and 93%, respectively) compared with the control group (80%) (p = 0.1).

Twenty-six percent of the participants investigated in winter and in autumn had current asthma compared with 18% in spring and 8% in summer (p = 0.07). Parental allergy/asthma and daily medication use for allergy/asthma were as expected, significantly associated with both atopy and asthma (p < 0.05). Participants with atopy were at a higher risk of having current asthma (OR = 5.5; 95% CI = 2.3–12.6; p < 0.001), BHR only (OR = 3.1; 95% CI = 1.4–6.4; p = 0.002), and wheeze only (OR = 2.3; 95% CI = 1.3–4.2; p = 0.007).

Thus, age and country of birth of the participant, parental allergy/asthma, daily medication use for allergy/asthma, and season were identified as confounders of the association between allergen levels and sensitization to allergens. In addition, atopy was also included as a confounder as well as an effect modifier in examining the association between allergen levels and asthma.

Levels of Der p 1, Fungi, Ergosterol, and Fel d 1
Very high levels of Der p 1 were observed almost uniformly in this sample of Melbourne homes and the results have been published (16). Briefly, the geometric mean Der p 1 level for beds was 20.3 (range: 0–361) µg/g of fine dust and for floors was 17.2 (range: 0–691) µg/g of fine dust. We observed Der p 1 levels of greater than 2 µg/g of dust in 90.3% of the bedroom floors and 96.9% of beds. Seventy-six percent of the floors and 77% of the beds had Der p 1 levels of greater than 10 µg/g of dust.

The levels of indoor fungi in this sample were also high and the results have been published (12). Briefly, ergosterol levels in 46 (10%) houses were below the detection limit. The median ergosterol level in bedroom floors was 3.8 (range: 0–61.5) µg/g of fine dust. Fifty-five percent of the houses (n = 485) had viable airborne fungal propagules exceeding 500 CFU/m³. The most commonly identified fungi were species of Cladosporium and Penicillium. Cladosporium was isolated in 90% of the houses and Penicillium in 76% of houses.

Fel d 1 levels in bedroom floor dust (n = 483) ranged from 0 to 7,805 µg/g of dust with a median of 1.2 µg/g of dust. Fel d 1 levels in bed dust (n = 481) ranged from 0 to 5,114 µg/g of dust with a median value of 1.8. Forty-seven percent of the floor dust samples and 53% of the bed dust samples had Fel d 1 levels of > 2 µg/g of dust. Thirty-two percent of the floor dust samples and 30% of the bed dust samples had Fel d 1 lev-
els of > 8 µg/g of dust. Median level of Fel d 1 in bedroom floor dust of houses with a cat was 88 µg/g of dust and without a cat was 0.8 µg/g of dust.

**Influence of Current Fungal and Allergen Levels on Sensitization**

Participants who slept in bedrooms with ergosterol levels in the upper three quartiles compared with the first quartile were at a higher risk of being sensitized to fungi (range of AOR = 2.4–2.7; p < 0.05) (Figure 1). Perhaps paradoxically, having total airborne fungal levels in the upper three quartiles compared with the lowest quartile was associated with almost 2-fold reduction in the risk of being sensitized to fungi (Figure 1). This apparent protective effect of total fungi on fungal allergy was specifically explained by the levels of Cladosporium and Penicillium, when the level of total fungi was replaced by the levels of specific fungi in the model. Thus, having either Cladosporium (range of AOR: 0.4–0.9) or Penicillium (range of AOR: 0.5–0.8) in the upper three quartiles was associated with a reduced risk of being sensitized to fungi. We did not observe any significant association between the levels of specific fungi and sensitization to the given genus.

Having floor Fel d 1 levels in the highest quartile (> 27.1 µg/g of dust) compared with the lowest quartile (< 0.8 µg/g of dust) was associated with a 3-fold increased risk of participants being sensitized to cats (Figure 1). We did not observe a significant association between levels above the proposed threshold of Fel d 1 for sensitization (24) and being sensitized to cats. There was no significant interaction among ergosterol levels, viable fungal spores, and Fel d 1 levels on sensitization to fungi.

Having current levels of Der p 1 in the floor dust in the upper three quartiles compared with the first quartile was associated with a reduced risk (range of AOR: 0.5–0.8) of being sensitized to house dust mites. There was no association between bed Der p 1 levels and sensitization to HDM (Figure 1). Similarly, no significant association was observed between levels above the proposed threshold of Der p 1 for sensitization (2 µg/g of dust) (24) and being sensitized to HDM.

**The Influence of Current Fungal and Allergen Levels on Clinical Activity of Asthma**

The influences of current allergen levels on current asthma, wheeze only, and BHR only are shown in Figures 2 to 4. We observed a significant increased risk of participants having “wheeze only” when the ergosterol levels were in the upper three quartiles compared with the first quartile (range of AOR: 3.6–4.7; p < 0.05) (Figure 3). We also observed a 3 to 4-fold increased risk of participants having “current asthma” when the ergosterol levels were in the upper three quartiles compared with the first quartile, although these associations were not significant (Figure 2).

DRS was found to be increased 1.6-fold when the total airborne propagules were in the highest quartile compared with the first quartile. The risk of having “BHR only” was increased 4.2-fold when the total fungal levels were in the highest quartile compared with the first quartile (Figure 4). Fungal levels in the highest quartile compared with the first quartile were associated with a 2.6-fold risk of having “current asthma” and a 2-fold risk of having wheeze only, but these associations were not significant (Figures 2 and 3).

The association between total fungal levels and BHR was specifically related to Cladosporium and Penicillium. Levels of Cladosporium and Penicillium in the highest quartile were, respectively, associated with 8.5-fold (95% CI: 1.6–44.3) and 3.9-fold (95% CI: 1.1–14.3) risks of participants having “BHR only.” Other fungi were not associated with asthmatic phenotypes.

Bed Fel d 1 levels in the highest quartile (> 14.7 µg/g of dust) compared with the first quartile (< 0.4 µg/g of dust) were strongly associated with current asthma (AOR = 6.29) (Figure 2). No significant association was observed between the levels above the proposed threshold of Fel d 1 for induction of asthma (8 µg/g of dust) (24) and clinical activity of asthma. There was no significant interaction between ergosterol levels, viable fungal spores, and Fel d 1 levels on asthmatic phenotypes.

Floor Der p 1 levels in the upper three quartiles were associated with a reduced risk of having “wheeze only” (range of AOR: 0.3–0.4) (Figure 3). There was no demonstrable association between the levels above proposed threshold of Der p 1 for induction of asthma (10 µg/g of dust) (24) and clinical activity of asthma.

**DISCUSSION**

Almost all participants in this Melbourne sample were exposed to Der p 1 levels above the proposed threshold level for sensiti-
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zation to house dust mite allergens of 2 μg/g of dust (24) and three-quarters of the sample were exposed to Der p 1 levels above the proposed level for inducing attacks of asthma of 10 μg/g of dust (24). Perhaps because of these high levels, there was no consistent association between Der p 1 levels and the outcomes that we studied, that is, sensitization to Der p 1, wheeze, BHR, or current asthma. Over half of the Melbourne homes in this sample had hazardous levels of indoor airborne fungi, defined as >500 CFU/m³ according to World Health Organization guidelines (25). Total fungal levels in the air were associated with increased bronchial reactivity. High ergosterol levels as an estimate of fungal biomass were found to increase the risk of being sensitized to fungi and also having wheeze within the past 12 mo. About half of the sample was exposed to Fel d 1 levels of above the proposed threshold for sensitization to cat allergens of 2 μg/g of dust (24). One-third of the sample was exposed to levels above the proposed threshold for induction of asthma symptoms of 8 μg/g of dust (24). High floor Fel d 1 levels were found to increase the risk of cat sensitization and high levels of bed Fel d 1 were associated with current asthma.

Similar to our results, high levels of Der p 1 and indoor fungi have been observed previously in homes in the Latrobe Valley, 150 km southeast of Melbourne (26). However, prevalence of cat allergen levels in Australia has not been previously reported.

The finding of the significant impact of current Fel d 1 levels on sensitization and current asthma has major implications for cat owners. In previous studies, allergy to cat was also observed to be a risk factor for asthma (27) and furthermore cat allergen levels have been shown to be associated with asthma severity in adults with asthma (8). However, current cat allergen levels were related neither to sensitization (28) nor to asthma (28) in community samples. Failure to control for confounding effects may explain the negative findings in these studies. The current study is the first to show that the level of exposure to Fel d 1 is important in sensitization and asthma at a community level. This highlights the importance of reducing cat ownership in the population, as we do not yet have adequate evidence of effectiveness of the interventions such as air cleaners (29) and washing of cats (30) in reducing cat allergens.

Figure 2. Risk of having current asthma when the allergen levels are in the upper three quartiles compared with the lowest quartile—AOR and 95% CI adjusted for potential confounders.

Figure 3. Risk of having wheeze only when the allergen levels are in the upper three quartiles compared with the lowest quartile—AOR and 95% CI adjusted for potential confounders.
Seven of the nine studies that quantified the fungal exposure identified positive associations between one or more indices of fungal exposure and symptoms of respiratory disease (31). In our study, markers of fungal exposure were related to some features of the asthma phenotypes. Self-reported visible mold in homes, which is a predictor of fungal exposure, has been found to be associated with asthma (32).

We observed a clear deleterious effect of high airborne fungal propagule levels in the bedroom air on bronchial reactivity, and high ergosterol levels in bedroom floor dust on wheezing within the past 12 mo. Levels of fungi in the bedroom air, which are a better indication of the current fungal exposure than ergosterol, were measured shortly before the laboratory visit during which the bronchial reactivity was measured. In contrast, ergosterol in the dust is an indication of cumulative exposure to fungi (19), which may explain its significant impact on wheezing over the past 12 mo. The effect of ergosterol and total fungi on current asthma defined as a combination of wheezing and BHR was consistent and seemed clinically relevant but was not significant. Similarly, dampness and mold have previously been associated with respiratory symptoms, but not with current asthma, which was defined as physician-diagnosed asthma with current symptoms in children aged 8–12 yr (32). This may indicate that high fungal exposure is an important risk factor along the natural history pathway of asthma, but becomes less relevant toward the severe end of the spectrum of disease.

In the present study, the effect of total fungal levels on BHR was mainly related to the levels of Cladosporium and Penicillium. Levels of indoor Cladosporium (33) and Penicillium (7, 33) have been previously associated with doctor-diagnosed asthma in children. In addition, respiratory symptoms have been observed to be more common with high indoor exposure to Cladosporium (33).

High ergosterol levels were a risk factor for sensitization to fungi and specifically to Cladosporium, but paradoxically high levels of total airborne fungi appeared to be a protective factor for sensitization to fungi. The protective effect of total fungi was specifically related to the effect of high levels of Cladosporium and Penicillium. It is likely that any fungal avoidance measures taken by allergic subjects in the recent past had an immediate impact on the airborne fungal levels but did not affect ergosterol levels, which represent the long-term cumulative exposure. Greater exposure to Cladosporium and Penicillium in winter has been found to increase allergy to fungi in children (7), but we did not observe season to modify this effect in our data. This may be related to the cross-sectional nature of our study design, which did not allow for examination of the seasonal effects as precisely as in a longitudinal study.

The apparent protective effect of Der p 1 levels in floor dust on sensitization and asthma seems counterintuitive, but it may well indicate that ongoing exposure to high Der p 1 levels is not as important as previously presumed, in either sensitization or ongoing disease activity among young adults. This is in fact consistent with findings by many other researchers who have examined this association in children living in areas with high HDM exposures (1, 9). Although Peat and coworkers observed current Der p 1 levels to be associated with prevalence of asthma and sensitization in children aged 8–11 yr living in areas with high HDM exposure in an ecological analysis, at the individual level current Der p 1 levels were associated only with airway hyperresponsiveness and even this was very modest (34).

It has been argued that the HDM allergen levels in reservoir dust do not represent the actual amount of allergen entering the lungs. However, the association observed between dust Der p 1 levels and asthma severity in adults with asthma (5, 8) suggests that this index of exposure is reliable. Current Der p 1 levels were found to significantly influence PD_{20}, log dose–response slope, and peak expiratory flow variability in HDM-sensitive methacholine reactors (5) and to be significantly higher in the bedrooms floor of sensitized patients with severe asthma compared with sensitized patients with mild asthma (8). However, these samples were recruited from asthma clinics and represented the severe end of the spectrum of disease in contrast to our community-based sample. Furthermore, these clinic patients lived in areas with quite high HDM exposure, but not nearly as high as in the studies that have not observed a clinical relationship with HDM exposure, including the current one. Hence these findings may indicate that the severity of the disease modifies the association between current Der p 1 levels and asthma. Current exposure to Der p 1 may be important in clinical activity of asthma among patients with severe asthma, but not at the community level, especially in areas with high HDM exposure. Alternatively, this almost uniform exposure to Der p 1 at very high levels as in our study may be sufficient to maintain maximum asthma symptoms in all susceptible patients with asthma, so that the dose–response relation between levels and asthma activity is lost. Even in the studies that showed an association between ambient Der p 1

![Figure 4. Risk of having BHR only when the allergen levels are in the upper three quartiles compared with the lowest quartile—AOR and 95% CI adjusted for potential confounders.](image-url)
levels and asthma. Der p 1 levels were not related to sensitization. Again, this lack of association between current allergen exposure and sensitization in adults as observed in this study and older children (1, 9) in contrast to younger children (35), may be due to levels of HDM being sufficient to sensitize all the potential atopics during childhood.

In conclusion, our results suggest a significant influence of fungal and cat allergen exposure on clinical activity of asthma and sensitization in young adults in Melbourne. However, current HDM allergen exposure may not be relevant in adult asthma at the general community level. Our findings on the influence of ergosterol on sensitization to fungal and clinical activity of asthma are novel. We recommend the use of this marker of indoor fungal exposure in future research. There is a need for further studies, especially of interventions to reduce the mold and cat allergen exposures. From a public health perspective, we would encourage measures to reduce the exposures to fungi and cat allergen in the community. Frequent airing, regular use of kitchen exhaust fans and bedroom ceiling fans, removal of old wall-to-wall carpets, exclusion of pets, frequent vacuuming, and cleaning visible mold patches are identified as potentially effective measures to reduce mold exposure (12). However, controlling cat allergen levels is much more difficult as no determinants of Fel d 1 have been identified apart from pet ownership itself. People who do not currently own cats should be warned of the risk associated with cat ownership and current owners should be advised to reduce their exposure by keeping the pets outdoors (15) or preferably getting rid of them.

Acknowledgment: The authors acknowledge the assistance in data collection from Tina Colgan and John Elliot.

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