Fungal Levels in the Home and Lower Respiratory Tract Illnesses in the First Year of Life

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The association between home dampness and lower respiratory symptoms in children has been well documented. Whether fungal exposures contribute to this association is uncertain. In a prospective birth cohort of 499 children of parents with asthma/allergies, we examined in-home fungal concentrations as predictors of lower respiratory illnesses (LRI) (croup, pneumonia, bronchitis, and bronchiolitis) in the first year. In multivariate analyses, we found a significant increased relative risk (RR) between LRI and high levels (more than the 90th percentile) of airborne *Penicillium* (RR = 1.73, 95% confidence interval [CI], 1.23, 2.43), dust-borne *Cladosporium* (RR = 1.52; CI, 1.02, 2.25), *Zygomycetes* (RR = 1.96; CI, 1.35, 2.83), and *Alternaria* (RR = 1.51; CI, 1.00, 2.28), after controlling for sex, presence of water damage or visible mold/mildew, born in winter, breastfeeding, and being exposed to other children through siblings. In a multivariate analysis, the RR of LRI was elevated in households with any fungal level at more than the 90th percentile (RR = 1.86; CI, 1.21, 2.88). Exposure to high fungal levels increased the risk of LRI in infancy, even for infants with nonwheezing LRI. Actual mechanisms remain unknown, but fungi and their components (glucans, mycotoxins, and proteins) may increase the risk of LRI by acting as irritants or through increasing susceptibility to infection.

Keywords: fungi; respiratory tract infections; infants; public health

There is abundant literature discussing the relationship between home dampness and lower respiratory symptoms in early life (1–5). However, it is unknown whether this association is partly related to exposure to fungi, which thrive in damp conditions.

Several studies have shown that the presence of visible mold growth is related to bronchitis, phlegm production, and chest illnesses (6–8). These studies relied on self-reported assessment of mold growth. There have been few attempts to quantify the relationship between fungal concentrations and the development of lower respiratory tract illnesses (LRIs) in the first year of life when children are in the process of developing immunocompetence.

Therefore, we have explored whether exposure to fungi and fungal products, and not just dampness, is associated with LRIs early in life. Determining risk factors for LRIs in infants and very young children is important because both wheezing and nonwheezing LRIs in early years have been shown to be associated with significant morbidity later in life (9–12).

(*Received in original form July 22, 2002; accepted in final form April 26, 2003*)

Supported by grant AI/EHS35786 from the National Institutes of Health and the Environmental Science and Engineering Program through unrestricted departmental funds and through the Yamaguchi Endowment (P.C.S.).

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Am J Respir Crit Care Med Vol 168. pp 232–237, 2003
Originally Published in Press as DOI: 10.1164/rccm.200207-730OC on April 30, 2003
Internet address: www.atsjournals.org

METHODS

Study Protocol

Participants were part of a metropolitan Boston prospective birth cohort designed to examine relationships between indoor allergens and the development of allergic sensitization and asthma. The screening and recruitment of families have been described elsewhere (13). In brief, with the approval of the Human Studies Committee at Brigham and Women's Hospital (Boston, MA), we enrolled 505 infants, or index children, from 499 families (six sets of twins) with a history of asthma or allergy in at least one parent. Consent was obtained to extract data (e.g., maternal age and child's birth weight) from the labor, delivery, and newborn nursery records.

Of the 1,405 families initially screened, 906 were excluded from the study before the first home visit. Reasons for exclusion were as follows: reluctance to participate in a longitudinal study (51% of those who refused), plans to move within 1 year (39%), early loss to follow-up (9%), and other (1%). Mothers gave consent for screening at the time of the first home visit when the index child was 2 or 3 months of age. During this first home visit, a trained technician visited the child's home to obtain household and socioecomonic characteristics and to conduct air and dust sampling. Every 2 months, beginning when the child was 2 months of age, a follow-up telephone questionnaire was administered to the child's primary caregiver. Information was recorded on respiratory symptoms and illnesses experienced by the index child since the previous telephone interview, daycare attendance, and selected home characteristics.

During the home visit, indoor air and dust samples were collected from the bedroom where the child usually slept. Indoor air samples were collected from each home using a Burkard culture plate sampler operated at 45 L/minute (calculated cutpoint = 2 μm) that collected particles onto Dichloran glycerol (DG18) agar in 90-mm petri dishes. Sequential duplicate air samples were collected in the bedroom 1–1.5 m above the area of the floor demarcated for dust collection. After air samples were collected, 2 m^2 of the floor surrounding the newborn's bed was vacuumed for 5 minutes using a Eureka Mighty-Mite canister vacuum cleaner (The Eureka Co., Bloomington, IN) modified to collect dust in a 19- $\times$ 90-cm cellulose extraction thimble (Whatman International, Ltd., Herefordshire, UK). In cases in which both a smooth floor and a rug were present, 2.5 minutes were devoted to sampling the rug, and 2.5 minutes were spent vacuuming the smooth floor surface (14, 15). After at least 10 days of incubation, fungal colonies were identified using standard mycologic criteria. The number of colonies recovered on the air sample plates was adjusted for multiple impactions (16). The calculated concentrations of dust-borne fungi were the number of cfu per gram of dust and those of airborne fungi were cfu/m^3 of air. The number of fungal colonies was determined only if sufficient dust was also available for allergen measurement. As a result, there are data on fungal levels from the child's bedroom floor for 419 homes. Analyses dealing only with dust-borne fungal levels are limited to these 419 children.

Definition of Fungal Predictors

Each fungal taxon was represented as a binary variable. The variable was coded as one if that home produced high levels of that fungus and as zero otherwise. We define "high" as greater than the 90th percentile. For a type of fungus to be included in the analysis, the 90th percentile has to be greater than 1 cfu per unit. We also created a binary variable to designate homes that had high levels of any of the fungal taxa. Homes were defined as having "high fungal levels" if they had levels of any airborne or dust-borne fungal taxa that were greater than the 90th percentile for that specific taxon, provided the 90th percentile was greater than 1 cfu per unit.

Definition of Other Predictors

In addition to the fungal data, we considered other potential predictors of LRI. First we explored host or familial factors, such as sex and race, to determine their effect on LRI. Then we considered prenatal and perinatal factors, such as whether the mother smoked during pregnancy and parental history of asthma. Finally, we examined socioeconomic and behavioral factors, such as exposure to other children through siblings or daycare or by sharing a bedroom. Additional detail on the variables considered is provided in the online supplement.

Definition of Outcome Variable

Every 2 months the primary caregiver was asked this: "Since we last spoke on (date given), has your child had a pneumonia, croup, bronchitis, or bronchiolitis diagnosed by a doctor?" The primary outcome variable was at least one report of LRI in the first year of life. Of the 505 children, 14 (2.8%) were missing their 12-month questionnaire. Eight of these children had previously reported experiencing a doctor-diagnosed LRI, and thus, they were included in the analysis. The other six children were excluded.

A child was considered to have a wheezing LRI if any self-report of wheezing occurred before or concurrent with the doctor-diagnosed LRI. If no report of wheezing occurred, the LRI was classified as non-wheezing.

Statistical Analysis

SAS statistical software (SAS Institute, Inc., Cary, NC) was used to evaluate associations between predictor variables and the outcome of at least one LRI in the first year of life. First, univariate associations between a categoric representation for each taxon and at least one reported LRI were examined with 2×2 contingency tables. Two-tailed p values from chi-squared tests were calculated. Then a multivariate regression model was created in SAS that included significant ($p \leqslant 0.05$) fungal taxa and significant independent predictors of LRI. Relative risks (RRs) were computed from PROC GENMOD using the log link and exponentiating the parameter estimates. Multivariate models were independently validated using the lasso approach for model shrinkage described by Tibshirani (17). This technique prevents the tendency to overfit a model by constraining the effect that the variables will have in the model. This is one approach used to combat the multiple comparisons hazards that arise when so many different taxa of fungi need to be considered.

RESULTS

Cohort Characteristics as Predictors of LRI

Of the remaining 499 children included in the analysis, 367 (74%) had no doctor-diagnosed LRI. One hundred seven (21%) had a report of LRI in one questionnaire. Twenty (4%) reported LRI in two questionnaires, and five (1%) reported LRI in three or more questionnaires.

We first identified potential independent predictors of LRI or potential confounders of the relationship between fungi and LRI. Tables 1–3 summarize familial and perinatal factors, parental and socioeconomic factors, and household and behavioral factors. In univariate analyses, males had an increased risk of LRI, whereas being born in the winter was inversely associated with LRI. Although we previously found low birth weight to be predictive of increased risk of wheezing (13), it was not associated with LRI. Breastfeeding was inversely associated with LRI. Factors such as maternal smoking during pregnancy, which we previously found to predict wheeze (18), and low income did not predict higher risk of LRI. Living in a single- or two-family home was marginally associated with an increased univariate risk of LRI. Exposure to other children, by the presence of siblings, was associated with an increased risk of LRI, as was water damage in the home or the presence of visible mold or mildew.

TABLE 1. FAMILIAL AND PERINATAL PREDICTORS OF LOWER RESPIRATORY ILLNESS IN THE FIRST YEAR OF LIFE

Factor	n	Percent with LRI	RR	95% CI
Sex				
Female	233	20.2		
Male	266	32.3	1.60	1.18, 2.18
Birth weight, kg				
3.79 to < 4.91	125	28.8		
3.46 to < 3.79	121	21.5	0.75	0.48, 1.16
3.18 to < 3.46	127	31.5	1.09	0.75, 1.59
1.84 to < 3.18	125	24.8	0.86	0.57, 1.30
Season of birth				
Winter, Dec–Feb	123	17.1		
Spring, Mar–May	144	26.4	1.55	0.96, 2.49
Summer, Jun–Aug	111	33.3	1.95	1.22, 3.12
Fall, Sep–Nov	121	30.6	1.79	1.12, 2.87
Race/ethnicity				
White	375	28.0		
Black	59	25.4	0.91	0.57, 1.45
Hispanic	30	23.3	0.83	0.43, 1.63
Asian	28	14.3	0.51	0.20, 1.28
Other	7	28.6	1.02	0.31, 3.33

Definition of abbreviations: CI = confidence interval; LRI = lower respiratory illness; RR = relative risk.

Description of Fungal Data

Table 4 illustrates the distributions of the fungal data considered in the analysis. For each taxon, we report the number of houses from which the taxon was cultured. In addition, the 10th and 90th concentration percentiles are given, as well as the mean and median amount cultured for each taxon. *Penicillium* was the most common taxon sampled from the air, but *Cladosporium* was the taxon that had the highest levels recovered from the air. From the dust samples, *Aspergillus* was most commonly recovered, but yeasts were found in the highest levels.

TABLE 2. PARENTAL SOCIOECONOMIC PREDICTORS OF LOWER RESPIRATORY ILLNESS IN THE FIRST YEAR OF LIFE

Factor	n	Percent with LRI	RR	95% CI
Maternal asthma				
No asthma	345	24.9		
Active	106	29.3	1.17	0.83, 1.66
Inactive	48	33.3	1.34	0.86, 2.08
Paternal asthma				
No asthma	376	26.5		
Active	78	28.2	1.05	0.71, 1.55
Inactive	36	25.0	0.93	0.52, 1.68
Maternal age, yr				
18 to < 30	124	25.0		
30 to < 33	125	26.4	1.06	0.69, 1.61
33 to < 36	125	28.0	1.12	0.74, 1.70
36 to < 46	125	27.2	1.09	0.72, 1.65
Maternal smoking in pregnancy				
No	467	27.0		
Yes	32	21.9	0.81	0.41, 1.59
Breastfeeding				
No	163	31.9		
Yes	336	24.1	0.76	0.56, 1.01
Family income, $1,000s				
50 and up	352	27.0		
30 to < 50	88	27.3	1.01	0.69, 1.48
Below 30	43	20.9	0.78	0.42, 1.42
Unknown	16	31.3	1.16	0.55, 2.44

Definition of abbreviations: CI = confidence interval; LRI = lower respiratory illness; RR = relative risk.

TABLE 3. HOUSEHOLD AND BEHAVIORAL PREDICTORS OF LOWER RESPIRATORY ILLNESS IN THE FIRST YEAR OF LIFE

Factor	n	Percent with LRI	RR	95% CI
Child shares room at night				
No	189	25.9		
Yes	310	27.1	1.05	0.77, 1.41
Number of children in home				
1	230	19.6		
2	174	31.6	1.62	1.15, 2.27
3	70	32.9	1.68	1.10, 2.57
4+	25	40.0	2.04	1.18, 3.53
Child attends daycare				
No	261	24.1		
Yes	238	29.0	1.20	0.90, 1.61
Child attends daycare or has siblings				
No	108	13.9		
Yes	391	29.9	2.15	1.32, 3.53
Water damage in home				
No	323	24.2		
Yes	169	31.4	1.30	0.97, 1.75
Mold/Mildew inside home				
No	304	23.7		
Yes	188	31.4	1.33	0.99, 1.77
Water damage or mold/mildew in home				
No	203	22.2		
Yes	295	29.2	1.32	0.96, 1.80
Live in building with three or more units				
No	384	28.7		
Yes	114	20.2	0.70	0.47, 1.05

Definition of abbreviations: CI = confidence interval; LRI = lower respiratory illness; RR = relative risk.

Having high levels of one fungus did not necessarily imply that the household would have high levels of another fungus (Table 5). For example, there were 44 homes with high levels of dust-borne *Alternaria*, but only 14 of those homes also had high levels of dust-borne *Cladosporium*.

Fungal Exposure as Predictor of LRI

Table 6 illustrates the relationship between LRI and the specific airborne and dust-borne fungal concentrations in the house. In adjusted analyses, the fungi that remained significantly associated with LRI, even after controlling for other factors associated with doctor-diagnosed LRIs, were airborne *Penicillium* (RR = 1.73; 95% confidence interval [CI], 1.23, 2.43), dust-borne *Cladosporium* (RR = 1.52; CI, 1.02, 2.25), dust-borne *Zygomycetes* (RR = 1.96; CI, 1.35, 2.83), and dust-borne *Alternaria* (RR = 1.51; CI, 1.00, 2.28). The factors adjusted for included male sex, born in winter, breastfeeding, having siblings, and presence of water damage or visible mold/mildew in the home. The results for *Alternaria* and *Zygomycetes* were stronger for LRI with wheezing than for LRI without wheezing, but the results for *Penicillium* were stronger for nonwheezing LRIs.

TABLE 4. DESCRIPTON OF FUNGI ELIGIBLE TO CONTRIBUTE TO INDEX*

Fungi	n > 0	10th Percentile	Median	Mean	90th Percentile
Airborne, cfu/m^3					
Aspergillus	311	0	11	37	100
Cladosporium	384	0	44	177	411
Penicillium	422	0	33	131	189
Yeasts	172	0	0	18	33
Dust-borne, cfu/g					
Alternaria	236	0	435	3,789	8,333
Aspergillus	373	0	4,762	73,965	33,195
Aureobasidium	328	0	2,727	9,103	24,000
Cladosporium	322	0	3,650	19,694	31,579
Coelomyces	95	0	0	1,906	2,632
Fusarium	50	0	0	503	400
Penicillium	367	0	3,802	18,257	26,087
Ulocladium	60	0	0	317	435
Wallemia	61	0	0	2,481	1,053
Yeasts	367	0	8,261	35,731	58,000
Zygomycetes	57	0	0	1,877	870

* Must have been sampled from the indoor environment and have a 90th percentile of greater than 1 cfu.

In Table 7, we see the effect of being in an environment where high fungal levels exist on the prevalence of at least one LRI in the first year. There were 324 homes that had high levels of at least one type of fungi. Children in environments with more than the 90th percentile for one or more taxa had an 86% increased risk of developing an LRI in the first year (RR = 1.86; CI, 1.21, 2.88). In addition, the effect of high household fungal levels was larger and stronger when focusing on nonwheezing LRIs compared with wheezing LRI (RR = 3.88; CI, 1.43, 10.52 versus RR = 1.58; CI, 0.95, 2.64).

High fungal levels and the presence of mold, mildew, or water damage were independent predictors of LRI in the first year of life. High fungal levels were highly statistically significant, whereas the variable representing the presence of mold, mildew, or water damage exhibited a strong trend ($p = 0.06$). The two variables, however, were virtually uncorrelated ($R = 0.08$). Of the houses with water damage or visible mold or mildew, 75.4% had high fungal levels; of the houses without water damage or visible mold or mildew, 67.9% had high fungal levels.

DISCUSSION

Fungal Exposure and Related Health Effects

Fungal exposure, even to one type of fungus, is complex. Exposure often includes allergens, irritants, toxins, and sometimes even potentially infectious organisms (19). People are routinely exposed to more than 200 different species of fungi. Exposure occurs universally and is impossible to avoid completely. Often there are no adverse effects from these exposures, but at times, exposure to fungi can directly and indirectly influence an individual's health. Recently, there has been a significant focus on health effects associated with fungal exposure. Several studies have shown that the presence of visible mold growth is related to bronchitis, phlegm production, and chest illnesses (6–8). These studies relied on self-reported assessment of mold growth. Relationships between exposure to fungi, such as *Alternaria*, *Aspergillus, Penicillium,* and *Trichoderma,* and asthma exacerbation and allergic rhinitis in children (20, 21) have been suggested. In addition, the mycotoxins produced by the fungus *Stachybotrys chartarum* have been shown to produce bronchiolar inflammation and hemorrhage in laboratory mice (22). *Stachybotrys* was recovered very rarely in our homes, both because it is rare in homes without water damage and because the culture media used (DG18) does not support its growth well.

Household Fungal Levels as a Predictor of LRI

We have demonstrated a strong relationship between high household fungal levels and an increased incidence of doctor-diagnosed LRI in the first year of life. This relationship holds even after controlling for the significant independent predictors of LRI discussed previously here. The independent effects of visible mold or mildew suggest that dampness-related factors other than exposure to the common culturable fungi are important. Previously we have presented in more detail the weak relation-

TABLE 5. NUMBER OF HOMES WITH HIGH FUNGAL LEVELS FOR EACH TAXON

		Airborne								*Dust-borne*						
High Fungal Level	n	*Aspergillus*	*Cladosporium*	*Penicillium*	Yeasts	*Alternaria*	*Aspergillus*	*Aereobasidium*	*Cladosporium*	*Coelomyces*	*Fusarium*	*Penicillium*	*Ulocladium*	*Wallemia*	*Yeasts*	*Zygomycetes*
Airborne, cfu/m^3																
Aspergillus	44		3	10	8	3	12	2	2	5	3	6	4	8	3	3
Cladosporium	50			6	2	8	5	10	12	3	3	5	3	2	7	3
Penicillium	49				4	4	6	2	6	6	3	3	2	5	4	1
Yeasts	56					1	7	2	2	4	5	3	9	4	7	3
Dust-borne, cfu/g																
Alternaria	44						7	17	14	7	2	8	0	8	5	4
Aspergillus	42							3	8	4	5	9	2	10	8	6
Aureobasidium	40								7	6	3	6	1	4	9	6
Cladosporium	41									3	3	11	4	7	6	5
Coelomyces	41										3	5	5	7	4	4
Fusarium	41											2	8	2	9	10
Penicillium	39												1	3	7	12
Ulocladium	45													3	1	7
Wallemia	41														5	4
Yeasts	41															8
Zygomycetes	42															

The value for n represents the number of homes with high levels of that fungi. Reading across the rows, the numbers correspond to the number of those homes with high levels of the other fungi. For example, there are 44 homes with high levels of airborne *Aspergillus*. Of those 44 homes, 3 have high levels of airborne *Cladosporium.*

ship between home dampness and measurable fungi (23). *Penicillium*, *Cladosporium*, *Zygomycetes*, and *Alternaria* appear to be the most closely related to LRI. *Penicillium* and *Cladosporium* are fungi that are usually part of fungal growth populations in indoor environments. Su and colleagues used factor analysis to determine that *Cladosporium* and *Alternaria* tend to occur in tandem (24). Dharmage and coauthors found that total indoor fungal levels (comprised mostly of *Cladosporium*) were associated with an increased risk of asthma in adults (25). *Zygomycetes* and *Alternaria* were associated with LRI with wheeze, and this relationship may represent an early allergic response. *Alternaria* is the fungal taxon most commonly implicated in allergy.

The results for *Alternaria* and *Zygomycetes* were stronger for LRI with wheezing than for LRI without wheezing, but the results for *Penicillium* and the composite were stronger for nonwheezing LRIs. Although children who have repeated wheeze in early infancy have a greater risk of allergic asthma in later childhood than those without wheeze, for many children, early wheeze in infancy may represent nonallergic inflammation in small airways.

TABLE 6. RELATIONSHIP BETWEEN LOWER RESPIRATORY ILLNESS AND FUNGAL EXPOSURE

	Any LRI*		LRI without Wheeze†		LRI with Wheeze*	
High Fungal Level	RR	95% CI	RR	95% CI	RR	95% CI
Airborne, cfu/m^3						
Aspergillus	0.99	0.58, 1.68	0.80	0.26, 2.44	1.05	0.55, 2.01
Cladosporium	1.17	0.77, 1.77	1.33	0.61, 2.91	1.13	0.64, 2.00
Penicillium	1.73	1.23, 2.43	3.32	1.83, 6.04	1.56	0.92, 2.65
Yeasts	0.80	0.47, 1.38	0.73	0.28, 1.91	0.78	0.38, 1.60
Dust-borne, cfu/g						
Alternaria	1.51	1.00, 2.28	1.12	0.44, 2.88	1.82	1.08, 3.08
Aspergillus	0.94	0.54, 1.65	1.80	0.86, 3.76	0.47	0.16, 1.41
Aureobasidium	1.21	0.76, 1.93	0.85	0.28, 2.56	1.42	0.80, 2.50
Cladosporium	1.52	1.02, 2.25	1.68	0.78, 3.60	1.57	0.91, 2.69
Coelomyces	1.09	0.66, 1.79	‡		0.82	0.36, 1.88
Fusarium	1.28	0.79, 2.09	1.13	0.44, 2.90	1.35	0.71, 2.57
Penicillium	1.07	0.61, 1.86	0.62	0.16, 2.43	1.28	0.67, 2.47
Ulocladium	1.24	0.83, 1.85	‡		1.33	0.76, 2.35
Wallemia	0.92	0.54, 1.57	‡		0.46	0.15, 1.36
Yeasts	0.93	0.55, 1.57	1.77	0.85, 3.71	0.53	0.21, 1.35
Zygomycetes	1.96	1.35, 2.83	1.19	0.47, 3.00	2.60	1.63, 4.16

Definition of abbreviations: CI = confidence interval; RR = relative risk.

* Controlling for male, water damage or mold/mildew, siblings, born in winter, and breastfed ever.

† Controlling for male, siblings, born in winter, and breastfed ever.

‡ Models did not converge.

TABLE 7. FINAL MULTIVARIATE MODELS

	Any LRI		LRI without Wheeze[1]		LRI with Wheeze	
Factor	RR	95% CI	RR	95% CI	RR	95% CI
Male child	1.64	1.21, 2.22	2.32	1.27, 4.26	1.54	1.04, 2.29
Water damage or mold/mildew	1.34	0.99, 1.82	–	–	1.35	0.90, 2.04
Born in winter	0.65	0.44, 0.97	0.84	0.44, 1.60	0.50	0.28, 0.91
Breastfed ever	0.74	0.55, 0.98	0.54	0.31, 0.93	0.82	0.55, 1.21
Siblings	1.56	1.14, 2.15	1.51	0.85, 2.67	1.82	1.18, 2.79
High fungal levels	1.86	1.21, 2.88	3.88	1.43, 10.52	1.58	0.95, 2.64

Definition of abbreviations: CI = confidence interval; RR = relative risk.

Water damage or mold/mildew was not included in this model. It was not significant in a univariate model ($p = 0.15$), and the model with all six variables will not converge because of so few events.

Sensitivity to inhaled allergens, including mold, as measured by skin testing or by radioallergosorbent test, is uncommon in infancy. Although children who repeatedly wheeze with LRI in infancy are more likely to develop allergic asthma, many wheezing LRIs are related to nonallergic inflammatory responses in small airways. In infancy, nonwheezing LRIs are even less likely than wheezy LRIs to be allergy related. The strong association of higher household fungal levels with nonwheezing LRIs suggests that for many children the mechanism leading to this association in infancy is likely to be nonallergic.

Exposure to Fungal Components

Most fungal spores are known to contain, or with germination to produce, allergens (26). However, as mentioned previously here, it is unlikely that allergy is the dominant mechanism through which fungal spores influence the risk of LRI in infancy. Instead, the effects are likely due to other fungal spore components or to metabolites released from actively growing fungi. It has been demonstrated that a component of the fungal cell wall, (1 → 3)-β-D-glucan, induces inflammation. In addition, it appears that (1 → 3)-β-D-glucan and other fungal products may have more drastic effects in atopic children (27).

Mycotoxins are by-products of fungal metabolic processes. They accumulate in fungal spores, mycelia, and growth substrates (28), and inhalation exposure occurs in particulate form. It is well established that the ingestion of mycotoxins can cause deleterious health effects. However, much less is known about the effect of inhalation. Many mycotoxins have been shown to interfere with macrophage functioning, which is an important part of the defense system of the lung (29, 30). It may be the case that mycotoxins in the low concentrations likely to be present indoors can have some irritant effect in infants, such as inflammation, that would increase the likelihood of contracting a symptomatic LRI in the first year of life.

To digest foods, fungi excrete enzymes into the environment to break down complex carbon compounds. These enzymes are some of the major fungal allergens (19). It may be that these enzymes, which can elicit an allergic response in susceptible individuals with fully developed immune systems, can cause a physiologic response in infants that will make them more susceptible to contracting a LRI. *Alternaria alternata* extracts have been shown to induce cell shrinking and cell desquamation in adults (31).

Potential Study Limitations

We have no skin test or specific IgE data on allergy to *Alternaria* in these infants. However, allergy to this inhaled allergen is rarely measured in infants, even those who eventually develop measurable allergy in later childhood. Our study had additional limitations as well. First, the air and dust samples were taken once, for a brief period of time. Therefore, it is not clear how representative the samples were of the true household fungal levels. When measuring indoor fungal concentrations, it is very difficult to determine whether the source of the fungi collected was originally the indoor environment or the outdoor environment, although it is likely that the indoor air fungal measurements represent a larger contribution from the outdoors than the dust fungal measurements, particularly during seasons when windows were open. We used only a culture-based analysis to determine fungal concentrations, which underestimated actual fungal spore exposures and did not account for other fungal agents. Also, the culture media used for the air samples, DG18, had high solute concentration, which limited the amount of available water. Thus, xerophilic or xerotolerant fungi may have been over-represented. Also, the children were selected based on a family history of asthma or allergy, and thus, the results may not be generalizable to children without a family history of allergy or asthma. Finally, all relationships discussed in this article were related to exposures that occurred in the first home in which the child lived and did not account for conditions in any future homes.

Conclusion

Several studies have suggested that there is no need for fungal sampling in the home. The fungi to which the residents are exposed, the studies argue, are the result of visible mold growth. Others support the claim that fungal exposures explain the association between home dampness and LRIs. However, we demonstrate here that the relationship between fungal exposure and LRI (pneumonia, croup, bronchitis, or bronchiolitis) is independent of parent-reported visible mold/mildew. Others have demonstrated that the fungi that are aerosolized and/or present in floor dust are not necessarily the same fungi that are visible on walls. These data suggest that the measurement of fungi and the report of water damage or visible mold provide independently useful exposure data associated with respiratory disease outcomes.

Finally, our study suggests that exposure to high fungal levels can increase the risk of nonwheezing as well as wheezing LRI during infancy. The mechanisms for these associations may be, in great part, nonallergic.

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