Mold damage in homes and wheezing in infants

Seung-Hyun Cho, PhD*†; Tiina Reponen, PhD*; Grace LeMasters, PhD*; Linda Levin, PhD*; Jian Huang, MS*; Teija Meklin, PhD‡; Patrick Ryan, MS*; Manuel Villareal, MD§; and David Bernstein, MD§

Background: In most studies that investigate the association of mold or water damage and respiratory disorders in infants, the analysis is not adjusted for exposure to house dust mite (HDM), which is also a known cause of respiratory illnesses.

Objective: To investigate the relationship between visually observable mold or water damage and HDM (Der f 1) levels and the prevalence of lower respiratory tract symptoms and allergen sensitization in infants of atopic parents as part of a prospective birth cohort study.

Methods: On-site home visits (at the infants' age of 8 months) were performed to evaluate observable mold or water damage and HDM exposure. At a clinic visit near the infant's first birthday, medical histories, including parent-reported wheezing episodes, and a skin prick test to food and 15 common aeroallergens were conducted in 640 infants.

Results: More than half of the homes were found to have mold or water damage, and 5% had major mold or water damage with visible mold at 0.2 m^2 or more. Only 16% of homes had a HDM allergen (Der f 1) concentration of more than 2 μg/g. Major mold or water damage increased the risk of recurrent wheezing nearly 2 times in infants, 5 times in food or aeroallergen-sensitized infants, and 6 times in aeroallergen-sensitized infants. Neither visible mold or water damage nor HDM exposure was associated with sensitization to either mold or aeroallergens.

Conclusions: Visible mold was shown to be a significant risk factor for recurrent wheezing in infants at high risk of developing atopic disorders, whereas HDM exposure did not significantly increase the risk.

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INTRODUCTION

Fungi are ubiquitous organisms and can grow on almost any building material if there is sufficient moisture. Various studies in Europe, Canada, and the United States have found mold, mildew, or water damage in 15% to 36% of homes.[1–4] In a study conducted in Finland, evidence of current or previous moisture problems was found in 80% of randomly selected houses inspected by trained civil engineers.[5] Numerous epidemiologic studies have reported adverse health outcomes in adults and children associated with the presence of dampness and/or mold in indoor environments.[6–12] Reported wheezing has been associated with home dampness in various studies, and the risk of reported wheezing was increased up to 5-fold in homes with mold or water damage.[13–15]

Another important indoor air contaminant related to dampness is house dust mite (HDM) allergen. The prevalence of HDMs in relation to adverse health outcomes has also been widely explored.[16–25] Sporik et al[26] and Squillace et al[27] found a significant relationship between HDM exposure and asthma or wheezing in sensitized children. High relative humidity creates a favorable environment for HDM growth, and reduction in relative humidity has been reported to decrease the number of live HDMs.[28–30]

Although mold growth and HDM exposure have been associated with indoor dampness and each has been independently linked to adverse health effects, few studies have investigated mold or water damage in relation to respiratory symptoms and allergy in infants and young children while controlling for exposure to HDMs.[14,31–33] Furthermore, as indicated by Jaakkola et al,[34] most home dampness studies have been designed as cross-sectional or case-control studies, creating potential recall or reporting biases. We are currently conducting a longitudinal prospective birth cohort study (the Cincinnati Childhood Allergy and Air Pollution Study [CCAAPS]) aimed at investigating the role of aeroallergens and diesel exhaust particles in the development of atopy and atopic respiratory disorders.[35] As a part of the CCAAPS, this study represents a cross-sectional examination of data on the association of exposure to mold or water damage and HDM with the prevalence of recurrent wheezing and allergen sensitization in infants at the age of 1 year.

METHODS

Study Population

Infants born in Cincinnati, OH, and Northern Kentucky between 2001 and 2003 were recruited using birth certificate data. The recruitment criteria have been previously explained in detail.[35] Eligibility for the study required that at least one parent was atopic, defined as having allergic symptoms and a positive reaction on a skin prick test (SPT) to at least 1 of 15

* Department of Environmental Health, University of Cincinnati, Cincinnati, Ohio.
† National Risk Management Research Laboratory, Office of Research and Development, US Environmental Protection Agency, Research Triangle Park, North Carolina.
‡ National Public Health Institute, Kuopio, Finland.
§ Department of Internal Medicine, University of Cincinnati, Cincinnati, Ohio.
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common aeroallergens (meadow fescue, timothy, white oak, maple, American elm, red cedar, short ragweed, *Alternaria* spp, *Aspergillus fumigatus, Penicillium* spp, *Cladosporium* spp, cat, dog, German cockroach, and HDM). The study was approved by the institutional review board of the University of Cincinnati.

On-Site Home Visit and Exposure Evaluation

On-site home visits in 777 homes were performed by several 2-person teams when the infants were 8 months old on average to investigate the prevalence of mold damage and to collect floor dust samples for exposure evaluation of HDM. Teams were trained to perform dust sampling and objectively identify mold or water damage and other home characteristics. The families were requested not to clean the floor for at least 1 day before the dust sampling. At the visit, a parent was asked to identify the room where the child spent most of his or her daytime, referred to as the child's primary activity room (PAR). Dust samples were collected from flooring materials in the PAR using a vacuum cleaner (Filter Queen Majestic, HMI Industries Inc, Seven Hills, OH) at a flow rate of 800 L/min. A custom-made cone-shaped high-efficiency particulate air filter trap (Midwest Filtration, Cincinnati, OH) was attached to the nozzle of vacuum cleaner to collect dust samples.

For carpeted floor, 2 separate samples were collected from the same area of 2 m^2 at a vacuuming rate of 2 min/m^2 (1 minute horizontally, 1 minute vertically). The 2 samples were combined to have a sufficient amount of fine dust, the fraction used for the allergen analysis. For noncarpeted floor (hard wood, linoleum, tile, or sheet floor), only 1 sample was collected from the entire room at a rate of 1 min/m^2. The home dust sample was sieved (355 μm sieve), and the fine dust was divided into subsamples and stored at -20°C before analyses.

Simultaneously with dust sampling, parents were interviewed using a questionnaire on home characteristics, which included history of water damage, existence of visible mold, and any repairs for water damage. Then, a visual observation of the house conditions was conducted inside the house. A checklist was used to standardize the results. Each room in the house, including the basement and the attic, was inspected for existence of any signs of visible mold or water damage. Location of damage, type of surface material, changes in the color and integrity of surface material, and the size of damaged surface were recorded on the checklist. Additionally, in the infant's PAR, the infant's bedroom, and the basement, the existence of moldy odor was recorded, and temperature and relative humidity were measured with a thermo-hygrometer (model 13306, Delta TRAK, Pleasanton, CA). Both questionnaire and visual observation were performed using a checklist. The checklist was developed with the existing questionnaires and home inspection protocols, which were used in previous studies,[14,36–38] and those published by professional organizations or governmental agencies.[39–42]

The training of teams included annual half-day classroom lectures and review of photograph gallery mold- or water-damaged field sites (Fungal Image Library, Field Investigation, CD, vol 1, Aerotech Laboratories Inc, Phoenix, AZ). In the beginning of the study, 10 supervised (by Dr Reponen) practice home inspections were performed in non-CCAAPS homes. Of 777 homes, 37 randomly selected homes (5%) had a subsequent home visit within 2 months for quality control purpose. The data from the subsequent visit were compared with the initial home visit to investigate the reliability of the home characteristics data.

Mold and water damage in homes were indexed by a mold or water damage classification with 3 degrees based on history of water damage, existence of visible mold, signs of mold or water damage and its size, and moldy odor. A class 0 home had no water damage history, visible mold or water damage, or moldy odor. A class 1 home had at least one of these signs, but the moldy area within one room was smaller than 0.2 m^2. A class 2 home had visible mold: either the moldy area within one room was greater than 0.2 m^2 or the combined area of mold and water damage on the same surface was greater than 0.2 m^2. These criteria were developed by Meklin et al[43] based on International Society of Indoor Air Quality and Climate guidelines for mold cleanup.[44]

Allergens were extracted from the sieved fine dust (50 mg) into 1 mL of 0.05% Tween 20 in phosphate-buffered saline (pH 7.4) by vortexing at high speed for 2 minutes with a vortex touch mixer. The extract was analyzed for HDM (*Dermatophagoides farinae* [Der f 1]) by enzyme-linked immunosorbent assay using monoclonal antibodies (Indoor Biotechnologies Inc, Charlottesville, VA). Results were given as micrograms of allergens per milliliter of extract and converted to micrograms of allergens per gram of sieved dust. The lower limit of detection was 0.1 μg/g.

Child SPTs and Medical Evaluation

During infants' first clinic visit at the average age of 13 months, infants underwent SPTs for food (milk and egg) and the aforementioned 15 aeroallergens. Infants who showed a positive reaction (3 mm greater than or equal to the negative control) to any of the food or aeroallergens were classified as sensitized. These criteria have a positive predictive value between 0.7 and 0.92 compared with food challenge in children younger than 2 years[45] and can be interpreted without difficulty in infants older than 3 months.[46] Meanwhile, medical evaluations for infants were directed at identification of wheezing symptoms. The parents were personally interviewed by a clinician regarding wheezing. The International Study of Asthma and Allergies in Childhood questionnaire for 6-year-old children was adapted to develop a wheezing question for our cohort.[47] At least 2 episodes of parent-reported wheezing without cold in the previous 12 months was defined as recurrent wheezing (regardless of SPT result). The recurrent wheezing in sensitized infants was divided into 2 subcategories: (1) recurrent wheezing combined with sen-

sitization to any allergen (either food or aeroallergen) and (2) recurrent wheezing combined with sensitization to at least one aeroallergen (positive SPT result to food alone was excluded). Infants with negative SPT reactions and no wheezing episodes were considered controls. Of 777 homes that had an on-site home visit for the exposure evaluation, at the time of this analysis, 640 families had brought their child for a SPT. Therefore, for the health outcome analysis, only these 640 infants were included with results from their homes.

Statistical Analyses

In statistical analyses, level of exposure to mold or water damage was classified as no damage, minor damage, and major damage (class 0, 1, and 2, respectively) and analyzed categorically. As a separate variable for mold or water damage, moldy odor was categorized into 2 groups: (1) moldy odor detected in the PAR, infant's bedroom, or basement or (2) no moldy odor in any of these rooms. Levels of HDM allergen were classified into 2 groups: 2 μg/g or less and more than 2 μg/g. Economic status as measured by annual income was divided into 2 groups with the cutoff at household income level of $20,000, which is close to the poverty threshold for a family of 4 (average number of residents in a home was 4) based on the data from the US Department of Commerce, Bureau of the Census.[48] Averaged relative humidity in homes was classified into 3 groups: less than 30%, 30% to 50%, and more than 50%.

In the final data analysis, relative risk (RR) estimates of overall recurrent wheezing, recurrent wheezing combined with sensitization to any allergen, recurrent wheezing combined with sensitization to aeroallergen, positive SPT result to mold, and positive SPT test result to aeroallergen were calculated by Poisson regression with robust error variance[49] using the SAS procedure PROC GENMOD (SAS Institute Inc, Cary, NC) in relation to mold or water damage with 3 classes adjusted for HDM and annual income.

RESULTS

We identified 862 families (881 infants) with at least 1 parent who tested positive on the SPT. Of this group, 777 families received a home visit evaluation and 640 of these infants (623 families) were enrolled in the study (ie, taken for their clinical evaluation). Of the 640 infants who had both a clinical and home evaluation vs the 137 who did not, some significant demographic differences were apparent ($P < .05$): 55.3% vs 45.3% were male, 81.1% vs 68.6% were white, and 14.8% vs 22.4% had incomes below $20,000. The prevalence of maternal and paternal asthma was not significantly different, however, between the 640 and 137 infants at 22.6% vs 19.9% and 10.7% vs 16.3%, respectively. Because race and income were highly correlated in our cohort,[35] the further analysis was controlled for income.

On average, the infants spent 92% of their weekly time at home, and 52.5% of infants spent all their time at home. For those children who did not spend all their time at home (47.5%), the average percentage of their weekly time spent outside the home was only 18% (range, 1% to 71%). When at home most infants spent their daytime in either the living room (56%) or family room (36%) as their PAR. More than half of the homes had some visible mold or water damage: class 0 (no damage), 44%; class 1 (minor damage), 51%; and class 2 (major damage), 5%. Mold or water damage data from the subsequent home visit in 37 homes agreed well (Wilcoxon signed rank test: $P = .56$) with initial home visit data, which were collected 2 months earlier, demonstrating good reproducibility of home visit data. The level of HDM (Der f 1) allergen was below the lower detection limit in 60% of the homes, and 16% of homes were exposed to a concentration of more than 2 μg/g, which is a level considered to increase the risk of sensitization.[50] Among mite-sensitized infants, 95% were exposed to mite allergen level below 2 μg/g. The average mite allergen concentration in homes of mite-sensitized infants was 0.5 μg/g.

In a preliminary analysis, prevalence of recurrent wheezing was significantly different between homes of 3-level categorical mold or water damage. However, when using 2-level mold or water damage (no damage vs any damage), the prevalence of recurrent wheezing was not significantly related to mold damage. The association of moldy odor and recurrent wheezing was also examined, but only a borderline positive relationship was found ($P = .06$). The average relative humidity in homes was not significantly associated with mold class and HDM allergen and, thus, was not included in the final analysis. An attempt was made to investigate the interactive effect between mold or water damage and HDM exposure on health outcomes. The number of homes with high HDM allergen level, however, was not sufficient for this interaction to be included in the final statistical analysis. Income level was significantly associated with recurrent wheezing ($P = .004$).

Table 1 gives the final analysis on the prevalence of health outcomes in 640 infants by mold class, HDM allergen level, and annual income. Higher prevalence of recurrent wheezing was observed in infants who live in mold class 2 homes compared with mold class 0 or 1 homes. Table 2 gives the RRs of the health outcomes in association with mold class (3 levels), HDM allergen level, and annual income. In the Poisson regression analysis adjusting for HDM and annual income, the RR of recurrent wheezing was significantly increased with the exposure to major mold or water damage (class 2). Furthermore, exposure to major mold or water damage increased the RR of recurrent wheezing nearly 5 times when it was combined with sensitization to any allergen and 6 times when combined with sensitization to aeroallergen. Mold or water damage was not a significant risk factor, however, for sensitization to either mold or aeroallergens. There was no significant association between HDM exposure and any of the aforementioned health outcomes.

Fourteen percent of the homes in our study belonged to an income group of $20,000 or less. Recurrent wheezing was reported in 31% of this low-income group compared with 17% of the income group greater than $20,000 (Table 1).

Table 1. Prevalence of Health Outcomes in 640 Infants by Mold Class, House Dust Mite Allergen (Der f 1), and Annual Income

Health outcomes	Total No.	No. (%) of infants				
		RW	RW combined with positive SPT result to any allergen	RW combined with positive SPT result to aeroallergen	Positive SPT result to mold	Positive SPT result to aeroallergens
Mold class						
0	280	47 (17)	14 (8)	10 (6)	16 (6)	54 (19)
1	330	66 (20)	24 (11)	15 (7)	30 (9)	55 (17)
2	30	12 (40)	6 (35)	5 (31)	1 (3)	9 (30)
House dust mites						
≤2 μg/g	527	101 (19)	34 (10)	23 (7)	42 (8)	96 (18)
>2 μg/g	110	23 (21)	10 (13)	7 (10)	5 (5)	22 (20)
Annual income						
≤$20,000	91	28 (31)	6 (12)	5 (10)	7 (8)	17 (19)
>$20,000	549	97 (18)	38 (10)	25 (7)	40 (7)	101 (18)

Abbreviations: RW, recurrent wheezing; SPT, skin prick test.

Table 2. Adjusted Relative Risks of Health Outcomes in 640 Infants by Mold Class, House Dust Mite Allergen (Der f 1), and Annual Income

Health outcomes	RW		RW combined with any allergen		RW combined with aeroallergen		Positive SPT result to mold		Positive SPT result to aeroallergens	
	n*	RR (95% CI)†	n*	RR (95% CI)†	n*	RR (95% CI)†	n*	RR (95% CI)†	n*	RR (95% CI)†
Mold class										
0	280		168		164		280		280	
1	330	1.2 (0.9–1.7)	203	1.4 (0.7–2.6)	194	1.2 (0.6–2.7)	330	1.6 (0.9–3.0)	330	0.9 (0.6–1.2)
2	30	2.1 (1.2–3.6)	16	4.7 (2.1–10.5)	15	6.0 (2.2–14.2)	30	0.6 (0.1–4.0)	30	1.6 (0.9–3.0)
House dust mites										
≤2μg/g	527		340		329		527		527	
>2 μg/g	110	1.1 (0.8–1.7)	75	1.4 (0.7–2.8)	72	1.6 (0.7–3.5)	110	0.5 (0.2–1.4)	110	1.1 (0.8–1.7)
Annual income										
≤$20,000	91		52		51		91		91	
>$20,000	549	0.6 (0.4–0.8)	365	1.0 (0.4–2.2)	352	0.8 (0.3–2.0)	549	0.9 (0.4–1.9)	549	1.0 (0.7–1.7)

Abbreviations: CI, confidence interval; RR, adjusted relative risk; RW, recurrent wheezing; SPT, skin prick test.
* Number of infants included in the regression analysis in each category of health outcomes.
† Adjusted for all independent variables in the model, mold class, house dust mite, and income.

Table 2 indicates that infants in the high-income group had a significantly lower risk of recurrent wheezing than those in the low-income group. Prevalence of recurrent wheezing combined with sensitization to any allergen or sensitization to aeroallergen, positive SPT result to mold, and positive SPT result to aeroallergens were not significantly different between groups.

DISCUSSION

Two well-known risk factors for respiratory illnesses, indoor mold or water damage and HDMs, were investigated in this cohort study. With our study design, we were able to show the temporal relation between early exposure and health outcome, reducing potential information or recall bias. The information bias was minimized in the exposure evaluation, because mold or water damage was inspected by home visit teams instead of using parental reports and before the infant was evaluated for wheeze. Objective measurements on types of damage and size of damaged area in our study improved the exposure evaluation compared with qualitative measurement or parental report, as shown by Nafstad et al.[31] Children were seen at the age of 1 year, so there also was minimal time for recall.

Since infants spend most of their time at home,[51] as was also shown in our study, exposure to indoor contaminants can be a critical factor for developing illnesses. Our results suggest that infants living in homes with major mold or water damage (class 2) are at 2 times greater risk of developing recurrent wheezing compared with infants in nondamaged homes after controlling for dust mite exposure. This estimate was comparable to or somewhat higher than other studies that also showed significant associations between respiratory symptoms and mold, such as the studies by Belanger et al[14] (subgroup of cohort: infants of mothers with asthma: odds

ratio [OR], 2.3; 95% confidence interval [CI], 1.3–4.0), Waegemaekers et al[15] (children: OR, 2.8; 95% CI, 1.2–6.6), Dekker et al[7] (children: OR, 1.6; 95% CI, 1.4–1.9), Dales et al[8] (children: OR, 1.6; 95% CI, 1.4–1.8), and Wickman et al[52] (toddlers: OR, 1.3; 95% CI, 1.0–1.8). Mold exposures in these studies were reported by parents or children as the presence of mold or water damage. Our study is unique because SPTs were performed in the entire cohort to establish infants' atopic phenotype. As a result, we found that infants sensitized to any allergens (either food or aeroallergens) are at a nearly 5-fold risk of developing recurrent wheezing in association with major mold damage (class 2) compared with nonsensitized infants who were not exposed to mold or water damage (class 0). The respective risk in infants sensitized to at least one aeroallergen was 6-fold. However, mold or water damage did not significantly increase the risk of sensitization. This implicates that wheezing is not only an allergic response but also a reaction to airway irritation as shown in other studies,[53] and it seems that this reaction is more prominent in sensitized infants in this study population.

Our on-site home visit included only observable mold or water damage. Often microbial colonization exists in enclosed building cavities within walls and ceilings and is not always visually observable. However, our semiquantitative evaluation of mold or water damage was able to identify a higher environmental risk group, showing a significant increase of wheezing in class 2 homes. The cutoff size of visible mold of 0.2 m^2 or higher for class 2 seems to be appropriate to identify substantial mold damage in homes. In a separate data analysis, the existence of mold or water problems in class 1 plus 2 homes (combination of class 1 and 2 homes) or the presence of moldy odor alone was not associated with wheezing in infants.

Exposure to HDMs was not a significant risk factor for wheezing or sensitization to aeroallergens in our study. Only 3% of infants were sensitized to HDMs, and the average concentration of HDM allergen among the sensitized infants was 0.5 μg/g. Similar results were also reported by Lau et al[17] and Wahn et al,[18] demonstrating a low prevalence of HDM sensitization in infants with low levels of HDM exposure (median concentration of 0.2 μg/g). Lau et al[17] found a higher prevalence of wheezing in HDM-sensitized children only after the age of 2 years. Similarly, other studies found dose-dependent prevalence of sensitization or increasing risks of wheezing and other asthmatic symptoms in HDM-sensitized children ages 9 to 16 years.[16,26,27]

The power of the study to detect a 2-fold increase in the high vs low HDM exposure groups (1-tailed $\alpha = .05$) was 72% for wheezing combined with sensitization to any allergen, 55% for wheezing combined with sensitization to aeroallergen, and 99% for any persistent wheezing. Note that the RR estimates for the 2 first wheezing outcomes were higher, 1.4 and 1.6, respectively, than for any persistent wheezing (RR = 1.1). However, the number of patients for the latter outcome was larger (Table 2).

Because of the lack of studies that investigated exposure and health outcomes in early infancy and differences in target populations and methods of measuring health outcomes, it is difficult to compare this study with others. Most studies did not report sensitization patterns to identify allergies to aeroallergens in infants, but only after the children were older.[22,23,24] Testing for sensitization in the beginning and during the follow-up is needed to identify clear exposure-sensitization relationship for future longitudinal studies. We have recently determined that in our CCAAPS cohort, the prevalence of SPT positivity at the age of 1 year was 28.4%, with 18.0% of these positive to 1 or more aeroallergens. In addition, by the age of 2 years, the prevalence increased to 40.7%, with 36.7% positive to at least 1 aeroallergen.[54] Hence, infants in this study have a high prevalence of SPT positivity at the age of 1 year, which is expected to continue to increase in successive years. In this study, the future annual SPTs and medical examinations will provide important information on incidence and the evolution of allergen sensitization in children in relation to their exposures. Other types of aeroallergens have also been measured and will be used in future analyses to investigate combined health effects of multiple exposures.

In conclusion, visible mold was shown to be a significant risk factor for recurrent wheezing in high-risk infants with at least 1 parent who was aeroallergen sensitized. The allergen level of HDM, however, was not associated with any of the investigated health outcomes. It remains to be determined how environmental exposure affects the development of sensitization and wheezing and what relationship exists between the early onset of wheezing and the development of asthma in these infants as they age.

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Requests for reprints should be addressed to:
Tiina Reponen, PhD
Department of Environmental Health
University of Cincinnati
PO Box 670056
3223 Eden Ave
Cincinnati, OH 45267-0056
E-mail: Tiina.Reponen@uc.edu