



ORIGINAL CONTRIBUTIONS

Symptoms of Wheeze and Persistent Cough in the First Year of Life: Associations with Indoor Allergens, Air Contaminants, and Maternal History of Asthma

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In a cohort of 849 infants with an asthmatic sibling, the authors examined the relations of exposure to allergens (dust mite, cockroach, cat, and dog), nitrogen dioxide, and mold with symptoms of wheeze and persistent cough in the first year of life (1998–2000). Among infants whose mothers had physician-diagnosed asthma, neither dust mite allergen nor dog allergen was associated with either symptom. Exposure to cockroach allergen (Bla g 1 at ≥ 2 U/g) modestly increased the risk for wheeze (odds ratio (OR) = 1.87, 95% confidence interval (CI): 0.94, 3.71), and exposure to cat allergen modestly decreased the risk (OR = 0.60, 95% CI: 0.35, 1.03). Among infants of mothers with no asthma history, exposure to gas stoves (OR = 1.50, 95% CI: 1.05, 2.15) and wood-burning stoves (OR = 2.09, 95% CI: 1.12, 3.91) increased the risk of persistent cough. Similarly, measured nitrogen dioxide concentration was associated with persistent cough (OR = 1.21, 95% CI: 1.05, 1.40). Persistent mold affected both infants of mothers with asthma (for wheeze, OR = 2.27, 95% CI: 1.27, 4.07; for cough, OR = 1.83, 95% CI: 1.04, 3.22) and infants of mothers without asthma (for cough, OR = 1.55, 95% CI: 1.04, 2.31). Reported exposure was confirmed by an association of measured fungi with wheeze (OR = 1.23, 95% CI: 1.01, 1.49). This appears to have been the first study to measure all of these home exposures (indoor allergens, nitrogen dioxide, fungi) and to prospectively measure the frequency of infant wheeze and persistent cough.

allergens; cockroaches; cough; dust; fungi; infant; nitrogen dioxide; respiratory sounds

Abbreviations: CI, confidence interval; OR, odds ratio.

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The prevalence and severity of asthma have increased dramatically in the past decade, especially among children

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(1). Genetic predisposition and exposure to various environmental agents, particularly during early childhood, seem to be important risk factors in sensitization to inhaled allergens and the development and exacerbation of asthma (2). Indoor allergens, endotoxin, and environmental tobacco smoke are environmental exposures identified as particularly important air contaminants during early childhood (2–7).

Exposures to cockroach, dust mite, and cat allergen, mold, and environmental tobacco smoke have been linked to sensitization and the development and exacerbation of asthma (2–6, 8–10). Several other air contaminants (nitrogen dioxide, sulfur dioxide, ozone, particulate matter, etc.) have been associated with reductions in lung function, asthma exacerbation, and respiratory symptoms in children but are generally not acknowledged to be significant risk factors for asthma development (11, 12). Previous studies have not simultaneously measured early childhood exposure to both indoor allergens and other air contaminants.

Among children whose mothers have asthma, increased risks of infant wheeze (13) and wheeze persisting until the child reaches school age (14, 15) have been reported. Additional research shows that parental history of asthma (16), specifically maternal asthma (17), increases the risk that a child will develop asthma. However, only one prior study has related allergen sensitization and asthma development to a maternal history of asthma (18). In this study, we examined the relations of exposure to dust mite, cockroach, cat, and dog allergen, gas stoves, wood-burning stoves, and mold with wheeze and persistent cough in early infancy. We considered these relations for infants of mothers with and without a history of physician-diagnosed asthma. Although these symptoms are common in infancy and many children who wheeze or cough will not develop asthma (19), these symptoms are significantly related to asthma development.

MATERIALS AND METHODS

Cohort

Between September 1996 and December 1998, 33,341 women delivering babies in four Connecticut hospitals and one south central Massachusetts hospital were screened for the study. Only mothers who already had a child under 11 years of age with a physician diagnosis of asthma participated. We enrolled a high-risk cohort to ensure that a sufficient number of index infants would develop asthma for subsequent analyses. Of 1,448 families identified as eligible, 1,002 (69.2 percent) enrolled, 334 declined, and 112 could not participate for technical reasons (e.g., they had no telephone or were moving out of the area). At enrollment, a research assistant visited the home and administered a questionnaire to each mother. The index child was 2–4 months old at the time of the home visit.

We obtained extensive information about home and family characteristics, including parents' education, ethnicity, asthma history, and family income. Mothers were asked about respiratory symptoms in each month of the child's life. Mothers were asked, "Since (infant's birth date) has (infant's name) had any of the following symptoms: wheeze, persistent cough?" If the mother responded "yes" to any symptom,

she was asked, "In the month of (each month reported), how many days did (infant's name) have (wheeze) (persistent cough)?" Mothers also answered questions about episodes of bronchitis, bronchiolitis, pneumonia, and croup. At the end of the interview, each mother was given a calendar and asked to record the days on which her child had had symptoms (wheeze, persistent cough).

Mothers were recontacted by telephone when the child was 6, 9, and 12 months old. Using the calendar as a reference, the symptom questions were repeated for each month since the prior interview. At age 12 months, the child's mother answered questions about household characteristics, including usual use of gas stoves, use of wood-burning stoves at least once per month, and the presence of persistent mold or mildew in the home living area, during the previous year. Only children whose mothers reported symptom information during the quarterly telephone interviews, whose mothers answered the 12-month household questionnaire, and who lived in homes where environmental samples were collected were analyzed ($n = 849$).

Collection and analysis of environmental samples

During the initial home interview, we collected dust samples in the index child's bed and in the main living area using a Eureka Mighty Mite portable vacuum cleaner (Eureka Company, Bloomington, Illinois) fitted with a Whatman cellulose extraction thimble (Whatman, Inc., Tewkesbury, Massachusetts). Dust sampling was conducted for 3 minutes over the exposed seat cushions, seat back, and arms of a couch or chair in the main living area and for 2 minutes over a 1.0-m² floor area. Samples were collected using standardized protocols described elsewhere (20). This analysis used dust samples collected in the main living area of the home, usually the site of the highest allergen levels. Samples were analyzed for the allergens of house dust mites (Der p 1 and Der f 1), cockroaches (Bla g 1), cats (Fel d 1), and dogs (Can f 1). Results are reported in micrograms per gram of fine dust for Der p 1, Der f 1, Fel d 1, and Can f 1 and in units per gram for Bla g 1. Fungal spores were collected by air sampling in both the main living area and the infant's bedroom using a Burkard portable air sampler (Burkard Manufacturing Company Ltd., Richmansworth, United Kingdom) for 1 minute, with an airflow rate of 20 liters per minute. Nitrogen dioxide was measured using a Palmes tube (21) placed in the main living area for 10–14 days.

Statistical analysis

Der p 1 and Der f 1 were summed into one variable (Der 1, group 1 dust mite allergen). In the reported results, exposure to dust mite and cat and dog allergens was defined as exposure at ≥ 2 $\mu\text{g/g}$ and exposure to cockroach allergen was defined as exposure at ≥ 2 U/g. We examined exposures defined at lower allergen levels for Fel d 1 (1 $\mu\text{g/g}$) and Bla g 1 (1 U/g), as well as exposures defined at higher levels (10 $\mu\text{g/g}$ for Der 1 and Can f 1, 8 $\mu\text{g/g}$ for Fel d 1, and 8 U/g for Bla g 1); results were similar. The effect of nitrogen dioxide exposure is reported for

exposure greater than or equal to 10 parts per billion and nitrogen dioxide as a continuous variable.

Using the home interview and quarterly questionnaires, days of wheeze and persistent cough reported for each month were summed for 12 months, and the variables were analyzed as none, <30 days, or ≥ 30 days. This was done to distinguish children who had symptoms from those who did not and children with mild symptoms from those with severe symptoms. The choice of 30 days as the cutoff for severe symptoms was made a priori and was based on an asthma severity index developed in this cohort (22). Approximately 10 percent of children experienced 30 or more days of wheeze. Each allergen and environmental factor (gas stove, wood-burning stove, persistent mold or mildew) was compared with wheeze and persistent cough (none, <30 days, or ≥ 30 days).

We hypothesized that effects of allergens and other environmental factors on respiratory symptoms might differ between infants whose mothers had a history of physician-diagnosed asthma ($n = 256$) and children whose mothers did not ($n = 593$). We examined the simultaneous effects of all environmental risk factors on three levels of wheeze and persistent cough by maternal history. We used ordered logistic regression, which assumes that the odds ratio for some wheeze versus none is equal to the odds ratio for ≥ 30 days versus <30 days (SAS, version 6.12; SAS Institute, Inc., Cary, North Carolina). Goodness of fit was examined using the Score test (23); no significant lack of fit was detected for any model. Odds ratios and 95 percent confidence intervals for being in a higher category of the outcome variable were computed. In model 1, we considered the association of the allergens and environmental factors with symptoms of wheeze and persistent cough, independent of respiratory illness. In model 2, we considered this association while controlling for the effect of respiratory illness.

RESULTS

Table 1 shows the percentages of children who experienced wheeze or persistent cough in the first year of life in relation to personal and family characteristics. Boys, Hispanic children, children with a respiratory illness, and children whose mothers had physician-diagnosed asthma all experienced more wheeze and persistent cough. Having a father with asthma, smoking in the home, and smoke exposure in utero were not associated with these symptoms. Lower socioeconomic status, as measured by mother's education or family income, was associated with more respiratory symptoms.

Table 2 shows the relation of indoor allergens and other home exposures with wheeze and persistent cough. Dust mite allergen and dog allergen were not associated with either symptom. Infants exposed to cockroach allergen (≥ 2 U/g) had a tendency toward more symptoms, while infants exposed to cat allergen (≥ 2 μ g/g) were somewhat less likely to wheeze. A mother's report of persistent mold or mildew in the home was significantly associated with both wheeze and cough. Use of a wood stove was associated with persistent cough. Use of a gas stove was significantly associated with persistent cough, while nitrogen dioxide exposure of more

than 10 parts per billion was associated with wheeze; however, both exposures showed some indication of relations with either symptom.

Multivariate analysis (table 3, model 1) showed that among children whose mothers had a history of physician-diagnosed asthma, none of the indoor allergens (dust mite, cockroach, cat, or dog) was significantly related to increased risk of wheeze or persistent cough, although exposure to cockroach allergen modestly increased the odds for wheeze and cat allergen appeared to reduce it. A mother's report of persistent mold in the home was significantly associated with both wheeze and persistent cough, while use of a gas stove or wood-burning stove was not.

When the children of mothers who had never been diagnosed with asthma were analyzed (table 3), none of the allergens showed any association with increased wheeze or persistent cough. Use of a gas or wood stove and exposure to persistent mold were not associated with wheeze, but all were significant predictors of persistent cough.

Since respiratory illness is a frequent cause of wheeze and cough in infancy, we repeated the analysis while controlling for respiratory illness (one or more episodes of bronchitis, bronchiolitis, pneumonia, or croup) in the first year of life (table 3, model 2). The results differed for the children of mothers with diagnosed asthma and mothers without diagnosed asthma. With a maternal asthma history, mold was significantly related to increases in both wheeze and persistent cough, and cockroach allergen was modestly related to wheeze (odds ratio (OR) = 1.99, 95 percent confidence interval (CI): 0.97, 4.05). Among children of mothers without asthma, none of the allergens were associated with wheeze or persistent cough. Use of a gas stove and exposure to mold were significantly related to persistent cough.

Concentrations of air contaminants were measured in this study, and these were analyzed in the same models (table 4). When the total number of colonies of fungi was substituted for mother's report of persistent mold, there was increased risk of wheeze for children of mothers with asthma (OR = 1.23, 95 percent CI: 1.01, 1.49). When measured nitrogen dioxide concentration was substituted for reported gas stove use, there was increased risk of persistent cough (OR = 1.21, 95 percent CI: 1.05, 1.40) among children of mothers without asthma.

DISCUSSION

While many children who wheeze early in life do not develop asthma, early wheezing and persistent cough, particularly frequent episodes of wheeze, are important risk factors for development of asthma (8, 9). Smoking during pregnancy (24, 25), low birth weight (26), socioeconomic status and ethnicity (27, 28), and indoor allergens (29, 30) are additional factors related to wheeze. Indoor allergens associated with wheeze in young children include dust mite (29), cockroach (30), and cat (31) allergens. Exposure to environmental tobacco smoke (32), nitrogen dioxide (33), and mold (34) in the home have been associated with wheeze or persistent cough in some studies but not in others (35). Only recently has parental history of asthma been considered

TABLE 1. Wheeze and persistent cough in the first year of life in relation to personal and family characteristics, Connecticut and Massachusetts, 1998–2000

Factor	No.	Wheeze (%)			p value	Persistent cough (%)			χ^2 p value
		None	<30 days	≥30 days		None	<30 days	≥30 days	
All infants	849	55.1	34.0	10.8		48.4	34.5	17.1	
Gender									
Girl	430	59.3	32.6	8.1	0.01	52.8	30.5	16.7	0.02
Boy	419	50.8	35.6	13.6		43.9	38.7	17.4	
Ethnicity									
White	503	59.0	33.0	7.9	0.01	51.1	34.0	14.9	0.008
Black	117	53.0	33.3	13.7		54.7	29.9	15.4	
Hispanic	188	46.8	37.8	15.4		37.2	39.9	22.9	
Respiratory illness*									
No	592	64.9	27.5	7.6	0.001	57.1	30.4	12.5	0.001
Yes	249	32.9	48.6	18.5		28.5	43.4	28.1	
Mother has asthma									
No	593	59.0	31.7	9.3	0.002	52.4	32.7	14.8	0.001
Yes	256	46.1	39.4	14.4		39.1	38.7	22.3	
Mother has allergies									
No	357	58.0	32.5	9.5	0.31	51.5	31.4	17.1	0.22
Yes	492	53.0	35.2	11.8		46.1	36.8	17.1	
Father has asthma									
No	669	54.0	35.0	11.1	0.27	47.8	35.7	16.4	0.43
Yes	171	60.8	29.8	9.4		52.0	30.4	17.5	
Smoker in the home									
No	740	55.7	33.4	10.9	0.57	47.7	35.0	17.3	0.56
Yes	109	51.4	38.5	10.1		53.2	31.2	15.6	
Mother smoked while pregnant									
No	712	56.2	33.7	10.1	0.47	47.9	35.4	16.7	0.37
Yes	134	49.2	36.6	14.2		51.5	29.8	18.7	
Mother's education (years)									
<12	108	38.9	43.5	17.6	0.002	36.1	38.9	25.0	0.02
12–15	445	55.7	32.8	11.5		47.6	35.1	17.3	
≥16	295	60.0	32.5	7.5		53.9	32.2	13.9	
Annual family income									
<\$20,000	251	49.8	35.1	15.1	0.02	46.6	33.5	19.9	0.44
\$20,000–\$50,000	183	51.4	38.2	10.4		45.4	36.6	18.0	
>\$50,000	415	60.0	31.6	8.4		50.8	34.2	14.9	

* Includes one or more episodes of bronchitis, bronchiolitis, pneumonia, or croup in the first year of life.

in assessing the effect of environmental exposure on respiratory symptoms in infants (13).

Indoor allergens

Indoor allergens investigated in this study included house dust mite, cockroach, cat, and dog allergens. No allergen was significantly associated with increased wheeze or persistent cough in the first year of life. Cockroach allergen appeared

related to wheeze only among infants whose mothers had a history of asthma, even after adjustment for respiratory illnesses in the first year of life (OR = 1.99, 95 percent CI: 0.97, 4.05). This is a new observation, and it may indicate a genetic predisposition. All children in this cohort had a sibling with physician-diagnosed asthma; however, 30 percent of sibling pairs had the same mother but different fathers. Paternal history of asthma was not associated with increased risk of wheeze or persistent cough (table 2), and

TABLE 2. Prevalence of wheeze and persistent cough in the first year of life in relation to environmental risk factors, Connecticut and Massachusetts, 1998–2000

Factor	No.	Wheeze (%)			<i>p</i> value	Persistent cough (%)			χ^2 <i>p</i> value
		None	<30 days	≥30 days		None	<30 days	≥30 days	
Dust mite (Der 1)									
<2 µg/g	438	53.0	34.5	12.6	0.19	47.5	33.8	18.7	0.42
≥2 µg/g	411	57.4	33.6	9.0		49.4	35.3	15.3	
Cockroach (Bla g 1)									
<2 U/g	714	55.9	34.3	9.8	0.08	49.0	35.1	15.8	0.08
≥2 U/g	135	51.1	32.6	16.3		45.2	31.1	23.7	
Cat (Fel d 1)									
<2 µg/g	561	52.4	35.6	11.9	0.07	46.9	35.3	17.8	0.44
≥2 µg/g	288	60.4	30.9	8.7		51.4	33.0	15.6	
Dog (Can f 1)									
<2 µg/g	531	53.1	35.8	11.1	0.30	47.6	35.6	16.8	0.69
≥2 µg/g	318	58.5	31.1	10.4		49.7	32.7	17.6	
Mold/mildew									
No	656	57.5	32.6	9.9	0.05	51.5	32.5	16.0	0.006
Yes	176	47.2	39.8	13.1		38.1	40.9	21.0	
Wood stove use									
No	784	55.2	33.9	10.2	0.57	49.7	32.9	17.3	0.006
Yes	49	57.1	36.7	6.1		30.6	55.1	14.3	
Gas stove use									
No	547	57.9	32.5	9.5	0.08	51.7	31.4	16.8	0.03
Yes	285	50.2	37.2	12.6		42.5	39.6	17.9	
Nitrogen dioxide									
≤10 ppb*	459	59.9	29.4	10.7	0.005	51.8	33.1	15.0	0.06
>10 ppb	390	49.5	39.5	11.0		44.4	36.1	19.5	

* ppb, parts per billion.

children with a solely paternal history did not experience increased wheeze or persistent cough when exposed to cockroach allergen at ≥2 U/g.

This study was limited by the age of the participants. We could not distinguish which children had been sensitized to allergens. We did not perform skin-prick testing or allergen-specific immunoglobulin E testing, since sensitization to inhalant allergens in the first year of life is rarely detected (36, 37). Furthermore, we cannot distinguish at this early age which children will have persistent wheeze at age 6 years (19). Follow-up of this cohort is continuing.

Previous prospective studies have reported conflicting results for the relation between indoor allergens and respiratory symptoms. Two studies (29, 38) reported positive associations between dust mite levels measured in infancy and infant wheeze and/or cough (29) or wheeze at age 11 years (38). Each study had a sample size less than 100. Three additional studies (30, 39, 40) with sample sizes ranging from 453 to 885 failed to find any association between dust mite allergen or cat allergen (30, 39) and respiratory symptoms. Gold et al. (30) reported increased risk of wheeze for children exposed to cockroach allergen at ≥0.05 U/g. Our findings of some increased risk of wheeze among children

exposed to Bla g 1 at ≥2 U/g would appear to confirm these results. However, these results may also have been due to chance. Like us, Gold et al. found no increased risk of wheeze associated with exposure to house dust mite, cat, or dog allergen after controlling for major respiratory illness (bronchitis, bronchiolitis, pneumonia, and croup) (30). None of these studies stratified the data on maternal history of asthma. Van Strien et al. (29) stratified their data according to maternal atopy (physician-diagnosed or treated allergy to house dust or pets), and dust mite levels of ≥2 µg/g increased the risk of respiratory symptoms only among children whose mothers had allergies.

Mold

Reported mold was associated with wheeze (OR = 2.5, 95 percent CI: 1.4, 4.6) and persistent cough (OR = 1.9, 95 percent CI: 1.1, 3.4) among children whose mothers had asthma and with persistent cough only among children of mothers without asthma (OR = 1.5, 95 percent CI: 1.0, 2.3). Air sampling for fungi in the main living area confirmed these results. Measured fungi was associated with wheeze among children whose mothers had asthma (OR = 1.23, 95

TABLE 3. Environmental risk factors for wheeze and persistent cough in the first year of life, Connecticut and Massachusetts, 1998–2000

	Children whose mothers had asthma (<i>n</i> = 256)				Children whose mothers did not have asthma (<i>n</i> = 593)			
	Model 1*		Model 2†		Model 1*		Model 2†	
	OR‡,§	95% CI‡	OR§	95% CI	OR§	95% CI	OR§	95% CI
Wheeze¶								
Dust mite (Der 1)#	1.34	0.80, 2.26	1.04	0.60, 1.80	0.84	0.59, 1.19	0.78	0.55, 1.13
Cockroach (Bla g 1)	1.87	0.94, 3.71	1.99	0.97, 4.05	0.68	0.41, 1.15	0.68	0.41, 1.17
Cat (Fel d 1)	0.60	0.35, 1.03	0.64	0.36, 1.12	0.88	0.60, 1.28	0.84	0.57, 1.24
Dog (Can f 1)	0.79	0.46, 1.35	0.69	0.39, 1.21	0.86	0.60, 1.24	1.03	0.71, 1.49
Gas stove	0.98	0.57, 1.66	1.03	0.59, 1.79	1.31	0.91, 1.88	1.28	0.88, 1.86
Mold/mildew	2.27	1.27, 4.07	2.51	1.37, 4.62	1.29	0.85, 1.95	1.22	0.80, 1.88
Wood stove	NE‡		NE		1.03	0.53, 2.03	0.76	0.37, 1.55
Respiratory illness			5.56	3.09, 10.01			3.61	2.49, 5.24
Persistent cough**								
Dust mite (Der 1)#	1.48	0.90, 2.46	1.27	0.75, 2.15	0.81	0.58, 1.14	0.76	0.54, 1.07
Cockroach (Bla g 1)	1.30	0.66, 2.55	1.37	0.68, 2.76	1.01	0.61, 1.66	1.05	0.63, 1.75
Cat (Fel d 1)	1.06	0.63, 1.78	1.13	0.66, 1.94	0.84	0.58, 1.20	0.81	0.56, 1.17
Dog (Can f 1)	1.04	0.62, 1.75	0.91	0.53, 1.56	0.96	0.68, 1.36	1.11	0.78, 1.58
Gas stove	0.79	0.47, 1.32	0.79	0.46, 1.36	1.50	1.05, 2.15	1.52	1.06, 2.18
Mold/mildew	1.83	1.04, 3.22	1.91	1.07, 3.42	1.55	1.04, 2.31	1.53	1.01, 2.30
Wood stove	1.22	0.34, 4.37	1.04	0.27, 3.97	2.09	1.12, 3.91	1.68	0.89, 3.20
Respiratory illness			4.75	2.70, 8.36			3.04	2.12, 4.36

* Model 1 did not control for respiratory illness.

† Model 2 controlled for respiratory illness (one or more episodes of bronchitis, bronchiolitis, pneumonia, or croup).

‡ OR, odds ratio; CI, confidence interval; NE, not estimable (because of the small sample size).

§ Adjusted for all factors listed in the table as well as maternal education, ethnicity, the gender of the child, and smoking in the home.

¶ Categorized as none, <30 days, or ≥30 days in the first year of life.

Der 1 included Der p 1 and Der f 1 (group 1 mite allergen).

** Categorized as none, < 30 days, or ≥30 days in the first year of life.

percent CI: 1.01, 1.49) and less so among children of mothers without asthma.

Although it is difficult to eliminate publication bias from studies in this area, a recent literature review supports our

findings (34). Six studies were reviewed, and all of them reported positive associations between mold reported in the home and wheeze, with odds ratios ranging from 1.5 to 3.5. Five studies also examined the relation of mold and persis-

TABLE 4. Measured air contaminant exposures and their relation to wheeze and persistent cough in the first year of life, Connecticut and Massachusetts, 1998–2000

	Wheeze*		Persistent cough†	
	OR‡,§	95% CI‡	OR§	95% CI
Children whose mothers had asthma (<i>n</i> = 256)				
Measured fungi per 20 colonies	1.23	1.01, 1.49	1.04	0.87, 1.24
Measured nitrogen dioxide per 10-ppb‡ increase	1.10	0.87, 1.40	1.01	0.81, 1.26
Children whose mothers did not have asthma (<i>n</i> = 593)				
Measured fungi per 20 colonies	1.10	0.99, 1.23	0.99	0.89, 1.10
Measured nitrogen dioxide per 10-ppb increase	1.10	0.96, 1.25	1.21	1.05, 1.40

* Categorized as none, <30 days, or ≥30 days in the first year of life.

† Categorized as none, <30 days, or ≥30 days in the first year of life.

‡ OR, odds ratio; CI, confidence interval; ppb, parts per billion.

§ Adjusted for all factors listed in the table as well as for dust mite, cockroach, and cat and dog allergen, maternal education, ethnicity, the gender of the child, and smoking in the home.

tent cough, and four studies found positive associations. The association between reported mold and respiratory symptoms in children may result from biased reporting of either mold or respiratory symptoms (41). In all extant studies, the presence of mold or mildew was assessed by questionnaire and was not quantified by environmental monitoring. In our study, the association of reported mold and wheeze was confirmed by measured levels of fungi and wheeze, suggesting that reports of mold were not biased. Our study reports an exposure-response relation between measured residential mold and wheeze among infants of asthmatic mothers, with a 21 percent increase in wheeze per 20 colonies of mold. It is possible that mothers living in homes with obvious mold report respiratory symptoms differently than mothers who do not live in houses with mold; however, that seems unlikely. Mothers in this study were familiar with wheeze and persistent cough, since all index children had an older sibling with physician-diagnosed asthma.

Other air contaminants

Air contaminants from gas and wood-burning stoves were associated with respiratory symptoms only among children of mothers without a history of asthma. Use of a gas stove was associated with an increase in persistent cough (OR = 1.50, 95 percent CI: 1.05, 2.15). These risks were essentially unchanged after adjustment for respiratory illness and were similar to the effects of an increase in measured nitrogen dioxide concentration of 10 parts per billion.

Use of a wood-burning stove was associated with an increased risk of persistent cough (OR = 2.09, 95 percent CI: 1.12, 3.91) which declined after adjustment for respiratory illness (OR = 1.68, 95 percent CI: 0.89, 3.20). This suggests that exposure to wood stoves has an irritant effect that makes the child more susceptible to respiratory infection. Analysis of these relations was limited by the small number of wood stove users ($n = 49$).

Previous studies have reported associations between gas stove use or measured nitrogen dioxide concentration and respiratory illness among children aged 5–12 years. A meta-analysis (42) reported risk estimates for measured nitrogen dioxide (OR = 1.27, 95 percent CI: 1.09, 1.47) that were very similar to ours. Samet et al. (35) followed 1,100 infants from birth to age 18 months for daily respiratory symptoms. No increased risk of respiratory illness related to extensively monitored nitrogen dioxide concentrations in the infants' homes was observed. Our finding of an increase in persistent cough associated with nitrogen dioxide may be explained by our cohort's being more susceptible, since each infant had an asthmatic sibling.

Conclusions

In this study, different risk factors were associated with respiratory symptoms for children whose mothers had physician-diagnosed asthma and children whose mothers were not asthmatic. This may indicate underlying genetic differences in these children which make them more or less susceptible to specific environmental agents. Continued

research into specific gene-environment interactions might help to explain these differences.

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ORIGINAL CONTRIBUTIONS

Symptoms of Wheeze and Persistent Cough in the First Year of Life: Associations with Indoor Allergens, Air Contaminants, and Maternal History of Asthma

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In a cohort of 849 infants with an asthmatic sibling, the authors examined the relations of exposure to allergens (dust mite, cockroach, cat, and dog), nitrogen dioxide, and mold with symptoms of wheeze and persistent cough in the first year of life (1998–2000). Among infants whose mothers had physician-diagnosed asthma, neither dust mite allergen nor dog allergen was associated with either symptom. Exposure to cockroach allergen (Bla g 1 at ≥ 2 U/g) modestly increased the risk for wheeze (odds ratio (OR) = 1.87, 95% confidence interval (CI): 0.94, 3.71), and exposure to cat allergen modestly decreased the risk (OR = 0.60, 95% CI: 0.35, 1.03). Among infants of mothers with no asthma history, exposure to gas stoves (OR = 1.50, 95% CI: 1.05, 2.15) and wood-burning stoves (OR = 2.09, 95% CI: 1.12, 3.91) increased the risk of persistent cough. Similarly, measured nitrogen dioxide concentration was associated with persistent cough (OR = 1.21, 95% CI: 1.05, 1.40). Persistent mold affected both infants of mothers with asthma (for wheeze, OR = 2.27, 95% CI: 1.27, 4.07; for cough, OR = 1.83, 95% CI: 1.04, 3.22) and infants of mothers without asthma (for cough, OR = 1.55, 95% CI: 1.04, 2.31). Reported exposure was confirmed by an association of measured fungi with wheeze (OR = 1.23, 95% CI: 1.01, 1.49). This appears to have been the first study to measure all of these home exposures (indoor allergens, nitrogen dioxide, fungi) and to prospectively measure the frequency of infant wheeze and persistent cough.

allergens; cockroaches; cough; dust; fungi; infant; nitrogen dioxide; respiratory sounds

Abbreviations: CI, confidence interval; OR, odds ratio.

Editor's note: An invited commentary on this article appears on page 203.

The prevalence and severity of asthma have increased dramatically in the past decade, especially among children

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(1). Genetic predisposition and exposure to various environmental agents, particularly during early childhood, seem to be important risk factors in sensitization to inhaled allergens and the development and exacerbation of asthma (2). Indoor allergens, endotoxin, and environmental tobacco smoke are environmental exposures identified as particularly important air contaminants during early childhood (2–7).

Exposures to cockroach, dust mite, and cat allergen, mold, and environmental tobacco smoke have been linked to sensitization and the development and exacerbation of asthma (2–6, 8–10). Several other air contaminants (nitrogen dioxide, sulfur dioxide, ozone, particulate matter, etc.) have been associated with reductions in lung function, asthma exacerbation, and respiratory symptoms in children but are generally not acknowledged to be significant risk factors for asthma development (11, 12). Previous studies have not simultaneously measured early childhood exposure to both indoor allergens and other air contaminants.

Among children whose mothers have asthma, increased risks of infant wheeze (13) and wheeze persisting until the child reaches school age (14, 15) have been reported. Additional research shows that parental history of asthma (16), specifically maternal asthma (17), increases the risk that a child will develop asthma. However, only one prior study has related allergen sensitization and asthma development to a maternal history of asthma (18). In this study, we examined the relations of exposure to dust mite, cockroach, cat, and dog allergen, gas stoves, wood-burning stoves, and mold with wheeze and persistent cough in early infancy. We considered these relations for infants of mothers with and without a history of physician-diagnosed asthma. Although these symptoms are common in infancy and many children who wheeze or cough will not develop asthma (19), these symptoms are significantly related to asthma development.

MATERIALS AND METHODS

Cohort

Between September 1996 and December 1998, 33,341 women delivering babies in four Connecticut hospitals and one south central Massachusetts hospital were screened for the study. Only mothers who already had a child under 11 years of age with a physician diagnosis of asthma participated. We enrolled a high-risk cohort to ensure that a sufficient number of index infants would develop asthma for subsequent analyses. Of 1,448 families identified as eligible, 1,002 (69.2 percent) enrolled, 334 declined, and 112 could not participate for technical reasons (e.g., they had no telephone or were moving out of the area). At enrollment, a research assistant visited the home and administered a questionnaire to each mother. The index child was 2–4 months old at the time of the home visit.

We obtained extensive information about home and family characteristics, including parents' education, ethnicity, asthma history, and family income. Mothers were asked about respiratory symptoms in each month of the child's life. Mothers were asked, "Since (infant's birth date) has (infant's name) had any of the following symptoms: wheeze, persistent cough?" If the mother responded "yes" to any symptom,

she was asked, "In the month of (each month reported), how many days did (infant's name) have (wheeze) (persistent cough)?" Mothers also answered questions about episodes of bronchitis, bronchiolitis, pneumonia, and croup. At the end of the interview, each mother was given a calendar and asked to record the days on which her child had had symptoms (wheeze, persistent cough).

Mothers were recontacted by telephone when the child was 6, 9, and 12 months old. Using the calendar as a reference, the symptom questions were repeated for each month since the prior interview. At age 12 months, the child's mother answered questions about household characteristics, including usual use of gas stoves, use of wood-burning stoves at least once per month, and the presence of persistent mold or mildew in the home living area, during the previous year. Only children whose mothers reported symptom information during the quarterly telephone interviews, whose mothers answered the 12-month household questionnaire, and who lived in homes where environmental samples were collected were analyzed ($n = 849$).

Collection and analysis of environmental samples

During the initial home interview, we collected dust samples in the index child's bed and in the main living area using a Eureka Mighty Mite portable vacuum cleaner (Eureka Company, Bloomington, Illinois) fitted with a Whatman cellulose extraction thimble (Whatman, Inc., Tewkesbury, Massachusetts). Dust sampling was conducted for 3 minutes over the exposed seat cushions, seat back, and arms of a couch or chair in the main living area and for 2 minutes over a 1.0-m² floor area. Samples were collected using standardized protocols described elsewhere (20). This analysis used dust samples collected in the main living area of the home, usually the site of the highest allergen levels. Samples were analyzed for the allergens of house dust mites (Der p 1 and Der f 1), cockroaches (Bla g 1), cats (Fel d 1), and dogs (Can f 1). Results are reported in micrograms per gram of fine dust for Der p 1, Der f 1, Fel d 1, and Can f 1 and in units per gram for Bla g 1. Fungal spores were collected by air sampling in both the main living area and the infant's bedroom using a Burkard portable air sampler (Burkard Manufacturing Company Ltd., Richmansworth, United Kingdom) for 1 minute, with an airflow rate of 20 liters per minute. Nitrogen dioxide was measured using a Palmes tube (21) placed in the main living area for 10–14 days.

Statistical analysis

Der p 1 and Der f 1 were summed into one variable (Der 1, group 1 dust mite allergen). In the reported results, exposure to dust mite and cat and dog allergens was defined as exposure at ≥ 2 $\mu\text{g/g}$ and exposure to cockroach allergen was defined as exposure at ≥ 2 U/g. We examined exposures defined at lower allergen levels for Fel d 1 (1 $\mu\text{g/g}$) and Bla g 1 (1 U/g), as well as exposures defined at higher levels (10 $\mu\text{g/g}$ for Der 1 and Can f 1, 8 $\mu\text{g/g}$ for Fel d 1, and 8 U/g for Bla g 1); results were similar. The effect of nitrogen dioxide exposure is reported for

exposure greater than or equal to 10 parts per billion and nitrogen dioxide as a continuous variable.

Using the home interview and quarterly questionnaires, days of wheeze and persistent cough reported for each month were summed for 12 months, and the variables were analyzed as none, <30 days, or ≥ 30 days. This was done to distinguish children who had symptoms from those who did not and children with mild symptoms from those with severe symptoms. The choice of 30 days as the cutoff for severe symptoms was made a priori and was based on an asthma severity index developed in this cohort (22). Approximately 10 percent of children experienced 30 or more days of wheeze. Each allergen and environmental factor (gas stove, wood-burning stove, persistent mold or mildew) was compared with wheeze and persistent cough (none, <30 days, or ≥ 30 days).

We hypothesized that effects of allergens and other environmental factors on respiratory symptoms might differ between infants whose mothers had a history of physician-diagnosed asthma ($n = 256$) and children whose mothers did not ($n = 593$). We examined the simultaneous effects of all environmental risk factors on three levels of wheeze and persistent cough by maternal history. We used ordered logistic regression, which assumes that the odds ratio for some wheeze versus none is equal to the odds ratio for ≥ 30 days versus <30 days (SAS, version 6.12; SAS Institute, Inc., Cary, North Carolina). Goodness of fit was examined using the Score test (23); no significant lack of fit was detected for any model. Odds ratios and 95 percent confidence intervals for being in a higher category of the outcome variable were computed. In model 1, we considered the association of the allergens and environmental factors with symptoms of wheeze and persistent cough, independent of respiratory illness. In model 2, we considered this association while controlling for the effect of respiratory illness.

RESULTS

Table 1 shows the percentages of children who experienced wheeze or persistent cough in the first year of life in relation to personal and family characteristics. Boys, Hispanic children, children with a respiratory illness, and children whose mothers had physician-diagnosed asthma all experienced more wheeze and persistent cough. Having a father with asthma, smoking in the home, and smoke exposure in utero were not associated with these symptoms. Lower socioeconomic status, as measured by mother's education or family income, was associated with more respiratory symptoms.

Table 2 shows the relation of indoor allergens and other home exposures with wheeze and persistent cough. Dust mite allergen and dog allergen were not associated with either symptom. Infants exposed to cockroach allergen (≥ 2 U/g) had a tendency toward more symptoms, while infants exposed to cat allergen (≥ 2 μ g/g) were somewhat less likely to wheeze. A mother's report of persistent mold or mildew in the home was significantly associated with both wheeze and cough. Use of a wood stove was associated with persistent cough. Use of a gas stove was significantly associated with persistent cough, while nitrogen dioxide exposure of more

than 10 parts per billion was associated with wheeze; however, both exposures showed some indication of relations with either symptom.

Multivariate analysis (table 3, model 1) showed that among children whose mothers had a history of physician-diagnosed asthma, none of the indoor allergens (dust mite, cockroach, cat, or dog) was significantly related to increased risk of wheeze or persistent cough, although exposure to cockroach allergen modestly increased the odds for wheeze and cat allergen appeared to reduce it. A mother's report of persistent mold in the home was significantly associated with both wheeze and persistent cough, while use of a gas stove or wood-burning stove was not.

When the children of mothers who had never been diagnosed with asthma were analyzed (table 3), none of the allergens showed any association with increased wheeze or persistent cough. Use of a gas or wood stove and exposure to persistent mold were not associated with wheeze, but all were significant predictors of persistent cough.

Since respiratory illness is a frequent cause of wheeze and cough in infancy, we repeated the analysis while controlling for respiratory illness (one or more episodes of bronchitis, bronchiolitis, pneumonia, or croup) in the first year of life (table 3, model 2). The results differed for the children of mothers with diagnosed asthma and mothers without diagnosed asthma. With a maternal asthma history, mold was significantly related to increases in both wheeze and persistent cough, and cockroach allergen was modestly related to wheeze (odds ratio (OR) = 1.99, 95 percent confidence interval (CI): 0.97, 4.05). Among children of mothers without asthma, none of the allergens were associated with wheeze or persistent cough. Use of a gas stove and exposure to mold were significantly related to persistent cough.

Concentrations of air contaminants were measured in this study, and these were analyzed in the same models (table 4). When the total number of colonies of fungi was substituted for mother's report of persistent mold, there was increased risk of wheeze for children of mothers with asthma (OR = 1.23, 95 percent CI: 1.01, 1.49). When measured nitrogen dioxide concentration was substituted for reported gas stove use, there was increased risk of persistent cough (OR = 1.21, 95 percent CI: 1.05, 1.40) among children of mothers without asthma.

DISCUSSION

While many children who wheeze early in life do not develop asthma, early wheezing and persistent cough, particularly frequent episodes of wheeze, are important risk factors for development of asthma (8, 9). Smoking during pregnancy (24, 25), low birth weight (26), socioeconomic status and ethnicity (27, 28), and indoor allergens (29, 30) are additional factors related to wheeze. Indoor allergens associated with wheeze in young children include dust mite (29), cockroach (30), and cat (31) allergens. Exposure to environmental tobacco smoke (32), nitrogen dioxide (33), and mold (34) in the home have been associated with wheeze or persistent cough in some studies but not in others (35). Only recently has parental history of asthma been considered

TABLE 1. Wheeze and persistent cough in the first year of life in relation to personal and family characteristics, Connecticut and Massachusetts, 1998–2000

Factor	No.	Wheeze (%)			<i>p</i> value	Persistent cough (%)			χ^2 <i>p</i> value
		None	<30 days	≥30 days		None	<30 days	≥30 days	
All infants	849	55.1	34.0	10.8		48.4	34.5	17.1	
Gender									
Girl	430	59.3	32.6	8.1	0.01	52.8	30.5	16.7	0.02
Boy	419	50.8	35.6	13.6		43.9	38.7	17.4	
Ethnicity									
White	503	59.0	33.0	7.9	0.01	51.1	34.0	14.9	0.008
Black	117	53.0	33.3	13.7		54.7	29.9	15.4	
Hispanic	188	46.8	37.8	15.4		37.2	39.9	22.9	
Respiratory illness*									
No	592	64.9	27.5	7.6	0.001	57.1	30.4	12.5	0.001
Yes	249	32.9	48.6	18.5		28.5	43.4	28.1	
Mother has asthma									
No	593	59.0	31.7	9.3	0.002	52.4	32.7	14.8	0.001
Yes	256	46.1	39.4	14.4		39.1	38.7	22.3	
Mother has allergies									
No	357	58.0	32.5	9.5	0.31	51.5	31.4	17.1	0.22
Yes	492	53.0	35.2	11.8		46.1	36.8	17.1	
Father has asthma									
No	669	54.0	35.0	11.1	0.27	47.8	35.7	16.4	0.43
Yes	171	60.8	29.8	9.4		52.0	30.4	17.5	
Smoker in the home									
No	740	55.7	33.4	10.9	0.57	47.7	35.0	17.3	0.56
Yes	109	51.4	38.5	10.1		53.2	31.2	15.6	
Mother smoked while pregnant									
No	712	56.2	33.7	10.1	0.47	47.9	35.4	16.7	0.37
Yes	134	49.2	36.6	14.2		51.5	29.8	18.7	
Mother's education (years)									
<12	108	38.9	43.5	17.6	0.002	36.1	38.9	25.0	0.02
12–15	445	55.7	32.8	11.5		47.6	35.1	17.3	
≥16	295	60.0	32.5	7.5		53.9	32.2	13.9	
Annual family income									
<\$20,000	251	49.8	35.1	15.1	0.02	46.6	33.5	19.9	0.44
\$20,000–\$50,000	183	51.4	38.2	10.4		45.4	36.6	18.0	
>\$50,000	415	60.0	31.6	8.4		50.8	34.2	14.9	

* Includes one or more episodes of bronchitis, bronchiolitis, pneumonia, or croup in the first year of life.

in assessing the effect of environmental exposure on respiratory symptoms in infants (13).

Indoor allergens

Indoor allergens investigated in this study included house dust mite, cockroach, cat, and dog allergens. No allergen was significantly associated with increased wheeze or persistent cough in the first year of life. Cockroach allergen appeared

related to wheeze only among infants whose mothers had a history of asthma, even after adjustment for respiratory illnesses in the first year of life (OR = 1.99, 95 percent CI: 0.97, 4.05). This is a new observation, and it may indicate a genetic predisposition. All children in this cohort had a sibling with physician-diagnosed asthma; however, 30 percent of sibling pairs had the same mother but different fathers. Paternal history of asthma was not associated with increased risk of wheeze or persistent cough (table 2), and

TABLE 2. Prevalence of wheeze and persistent cough in the first year of life in relation to environmental risk factors, Connecticut and Massachusetts, 1998–2000

Factor	No.	Wheeze (%)			<i>p</i> value	Persistent cough (%)			χ^2 <i>p</i> value
		None	<30 days	≥30 days		None	<30 days	≥30 days	
Dust mite (Der 1)									
<2 µg/g	438	53.0	34.5	12.6	0.19	47.5	33.8	18.7	0.42
≥2 µg/g	411	57.4	33.6	9.0		49.4	35.3	15.3	
Cockroach (Bla g 1)									
<2 U/g	714	55.9	34.3	9.8	0.08	49.0	35.1	15.8	0.08
≥2 U/g	135	51.1	32.6	16.3		45.2	31.1	23.7	
Cat (Fel d 1)									
<2 µg/g	561	52.4	35.6	11.9	0.07	46.9	35.3	17.8	0.44
≥2 µg/g	288	60.4	30.9	8.7		51.4	33.0	15.6	
Dog (Can f 1)									
<2 µg/g	531	53.1	35.8	11.1	0.30	47.6	35.6	16.8	0.69
≥2 µg/g	318	58.5	31.1	10.4		49.7	32.7	17.6	
Mold/mildew									
No	656	57.5	32.6	9.9	0.05	51.5	32.5	16.0	0.006
Yes	176	47.2	39.8	13.1		38.1	40.9	21.0	
Wood stove use									
No	784	55.2	33.9	10.2	0.57	49.7	32.9	17.3	0.006
Yes	49	57.1	36.7	6.1		30.6	55.1	14.3	
Gas stove use									
No	547	57.9	32.5	9.5	0.08	51.7	31.4	16.8	0.03
Yes	285	50.2	37.2	12.6		42.5	39.6	17.9	
Nitrogen dioxide									
≤10 ppb*	459	59.9	29.4	10.7	0.005	51.8	33.1	15.0	0.06
>10 ppb	390	49.5	39.5	11.0		44.4	36.1	19.5	

* ppb, parts per billion.

children with a solely paternal history did not experience increased wheeze or persistent cough when exposed to cockroach allergen at ≥2 U/g.

This study was limited by the age of the participants. We could not distinguish which children had been sensitized to allergens. We did not perform skin-prick testing or allergen-specific immunoglobulin E testing, since sensitization to inhalant allergens in the first year of life is rarely detected (36, 37). Furthermore, we cannot distinguish at this early age which children will have persistent wheeze at age 6 years (19). Follow-up of this cohort is continuing.

Previous prospective studies have reported conflicting results for the relation between indoor allergens and respiratory symptoms. Two studies (29, 38) reported positive associations between dust mite levels measured in infancy and infant wheeze and/or cough (29) or wheeze at age 11 years (38). Each study had a sample size less than 100. Three additional studies (30, 39, 40) with sample sizes ranging from 453 to 885 failed to find any association between dust mite allergen or cat allergen (30, 39) and respiratory symptoms. Gold et al. (30) reported increased risk of wheeze for children exposed to cockroach allergen at ≥0.05 U/g. Our findings of some increased risk of wheeze among children

exposed to Bla g 1 at ≥2 U/g would appear to confirm these results. However, these results may also have been due to chance. Like us, Gold et al. found no increased risk of wheeze associated with exposure to house dust mite, cat, or dog allergen after controlling for major respiratory illness (bronchitis, bronchiolitis, pneumonia, and croup) (30). None of these studies stratified the data on maternal history of asthma. Van Strien et al. (29) stratified their data according to maternal atopy (physician-diagnosed or treated allergy to house dust or pets), and dust mite levels of ≥2 µg/g increased the risk of respiratory symptoms only among children whose mothers had allergies.

Mold

Reported mold was associated with wheeze (OR = 2.5, 95 percent CI: 1.4, 4.6) and persistent cough (OR = 1.9, 95 percent CI: 1.1, 3.4) among children whose mothers had asthma and with persistent cough only among children of mothers without asthma (OR = 1.5, 95 percent CI: 1.0, 2.3). Air sampling for fungi in the main living area confirmed these results. Measured fungi was associated with wheeze among children whose mothers had asthma (OR = 1.23, 95

TABLE 3. Environmental risk factors for wheeze and persistent cough in the first year of life, Connecticut and Massachusetts, 1998–2000

	Children whose mothers had asthma (<i>n</i> = 256)				Children whose mothers did not have asthma (<i>n</i> = 593)			
	Model 1*		Model 2†		Model 1*		Model 2†	
	OR‡,§	95% CI‡	OR§	95% CI	OR§	95% CI	OR§	95% CI
Wheeze¶								
Dust mite (Der 1)#	1.34	0.80, 2.26	1.04	0.60, 1.80	0.84	0.59, 1.19	0.78	0.55, 1.13
Cockroach (Bla g 1)	1.87	0.94, 3.71	1.99	0.97, 4.05	0.68	0.41, 1.15	0.68	0.41, 1.17
Cat (Fel d 1)	0.60	0.35, 1.03	0.64	0.36, 1.12	0.88	0.60, 1.28	0.84	0.57, 1.24
Dog (Can f 1)	0.79	0.46, 1.35	0.69	0.39, 1.21	0.86	0.60, 1.24	1.03	0.71, 1.49
Gas stove	0.98	0.57, 1.66	1.03	0.59, 1.79	1.31	0.91, 1.88	1.28	0.88, 1.86
Mold/mildew	2.27	1.27, 4.07	2.51	1.37, 4.62	1.29	0.85, 1.95	1.22	0.80, 1.88
Wood stove	NE‡		NE		1.03	0.53, 2.03	0.76	0.37, 1.55
Respiratory illness			5.56	3.09, 10.01			3.61	2.49, 5.24
Persistent cough**								
Dust mite (Der 1)#	1.48	0.90, 2.46	1.27	0.75, 2.15	0.81	0.58, 1.14	0.76	0.54, 1.07
Cockroach (Bla g 1)	1.30	0.66, 2.55	1.37	0.68, 2.76	1.01	0.61, 1.66	1.05	0.63, 1.75
Cat (Fel d 1)	1.06	0.63, 1.78	1.13	0.66, 1.94	0.84	0.58, 1.20	0.81	0.56, 1.17
Dog (Can f 1)	1.04	0.62, 1.75	0.91	0.53, 1.56	0.96	0.68, 1.36	1.11	0.78, 1.58
Gas stove	0.79	0.47, 1.32	0.79	0.46, 1.36	1.50	1.05, 2.15	1.52	1.06, 2.18
Mold/mildew	1.83	1.04, 3.22	1.91	1.07, 3.42	1.55	1.04, 2.31	1.53	1.01, 2.30
Wood stove	1.22	0.34, 4.37	1.04	0.27, 3.97	2.09	1.12, 3.91	1.68	0.89, 3.20
Respiratory illness			4.75	2.70, 8.36			3.04	2.12, 4.36

* Model 1 did not control for respiratory illness.

† Model 2 controlled for respiratory illness (one or more episodes of bronchitis, bronchiolitis, pneumonia, or croup).

‡ OR, odds ratio; CI, confidence interval; NE, not estimable (because of the small sample size).

§ Adjusted for all factors listed in the table as well as maternal education, ethnicity, the gender of the child, and smoking in the home.

¶ Categorized as none, <30 days, or ≥30 days in the first year of life.

Der 1 included Der p 1 and Der f 1 (group 1 mite allergen).

** Categorized as none, < 30 days, or ≥30 days in the first year of life.

percent CI: 1.01, 1.49) and less so among children of mothers without asthma.

Although it is difficult to eliminate publication bias from studies in this area, a recent literature review supports our

findings (34). Six studies were reviewed, and all of them reported positive associations between mold reported in the home and wheeze, with odds ratios ranging from 1.5 to 3.5. Five studies also examined the relation of mold and persis-

TABLE 4. Measured air contaminant exposures and their relation to wheeze and persistent cough in the first year of life, Connecticut and Massachusetts, 1998–2000

	Wheeze*		Persistent cough†	
	OR‡,§	95% CI‡	OR§	95% CI
Children whose mothers had asthma (<i>n</i> = 256)				
Measured fungi per 20 colonies	1.23	1.01, 1.49	1.04	0.87, 1.24
Measured nitrogen dioxide per 10-ppb‡ increase	1.10	0.87, 1.40	1.01	0.81, 1.26
Children whose mothers did not have asthma (<i>n</i> = 593)				
Measured fungi per 20 colonies	1.10	0.99, 1.23	0.99	0.89, 1.10
Measured nitrogen dioxide per 10-ppb increase	1.10	0.96, 1.25	1.21	1.05, 1.40

* Categorized as none, <30 days, or ≥30 days in the first year of life.

† Categorized as none, <30 days, or ≥30 days in the first year of life.

‡ OR, odds ratio; CI, confidence interval; ppb, parts per billion.

§ Adjusted for all factors listed in the table as well as for dust mite, cockroach, and cat and dog allergen, maternal education, ethnicity, the gender of the child, and smoking in the home.

tent cough, and four studies found positive associations. The association between reported mold and respiratory symptoms in children may result from biased reporting of either mold or respiratory symptoms (41). In all extant studies, the presence of mold or mildew was assessed by questionnaire and was not quantified by environmental monitoring. In our study, the association of reported mold and wheeze was confirmed by measured levels of fungi and wheeze, suggesting that reports of mold were not biased. Our study reports an exposure-response relation between measured residential mold and wheeze among infants of asthmatic mothers, with a 21 percent increase in wheeze per 20 colonies of mold. It is possible that mothers living in homes with obvious mold report respiratory symptoms differently than mothers who do not live in houses with mold; however, that seems unlikely. Mothers in this study were familiar with wheeze and persistent cough, since all index children had an older sibling with physician-diagnosed asthma.

Other air contaminants

Air contaminants from gas and wood-burning stoves were associated with respiratory symptoms only among children of mothers without a history of asthma. Use of a gas stove was associated with an increase in persistent cough (OR = 1.50, 95 percent CI: 1.05, 2.15). These risks were essentially unchanged after adjustment for respiratory illness and were similar to the effects of an increase in measured nitrogen dioxide concentration of 10 parts per billion.

Use of a wood-burning stove was associated with an increased risk of persistent cough (OR = 2.09, 95 percent CI: 1.12, 3.91) which declined after adjustment for respiratory illness (OR = 1.68, 95 percent CI: 0.89, 3.20). This suggests that exposure to wood stoves has an irritant effect that makes the child more susceptible to respiratory infection. Analysis of these relations was limited by the small number of wood stove users ($n = 49$).

Previous studies have reported associations between gas stove use or measured nitrogen dioxide concentration and respiratory illness among children aged 5–12 years. A meta-analysis (42) reported risk estimates for measured nitrogen dioxide (OR = 1.27, 95 percent CI: 1.09, 1.47) that were very similar to ours. Samet et al. (35) followed 1,100 infants from birth to age 18 months for daily respiratory symptoms. No increased risk of respiratory illness related to extensively monitored nitrogen dioxide concentrations in the infants' homes was observed. Our finding of an increase in persistent cough associated with nitrogen dioxide may be explained by our cohort's being more susceptible, since each infant had an asthmatic sibling.

Conclusions

In this study, different risk factors were associated with respiratory symptoms for children whose mothers had physician-diagnosed asthma and children whose mothers were not asthmatic. This may indicate underlying genetic differences in these children which make them more or less susceptible to specific environmental agents. Continued

research into specific gene-environment interactions might help to explain these differences.

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