House dust mite and cockroach exposure are strong risk factors for positive allergy skin test responses in the Childhood Asthma Management Program*

Karen Huss, RN, DNSc,[a] N. Franklin Adkinson, Jr, MD,[a] Peyton A. Eggleston, MD,[a] Christopher Dawson,[b] Mark L. Van Natta, MHS,[b] and Robert G. Hamilton, PhD[c]

Baltimore, Md

Background: Children with asthma have a high prevalence of environmental allergies, especially to indoor allergens. The relationships of exposure to indoor allergens (dust mites, cat, dog, cockroach, and molds) and other host factors to allergy sensitization have not been evaluated simultaneously in a large cohort.

Objectives: We studied 1041 children aged 5 to 12 years with mild-to-moderate asthma to determine risk factors associated with having positive allergy skin test responses to indoor allergens. Also, we described, compared, and contrasted 6 allergens in the home environments of these children from 8 North American cities.

Methods: Data were used from baseline visits of the Childhood Asthma Management Program. Patients' sensitivities to house dust mites (*Dermatophagoides farinae* and *Dermatophagoides pteronyssinus*), cats, dogs, cockroaches, and molds were examined for relationships to demographic variables, home dust allergen exposures, number of other positive allergy skin test responses, total serum IgE levels, and smoking in the home.

Results: San Diego (78.5%) and Toronto (59.3%) had the topmost percentages of homes with moderate-to-high house dust mite levels. Boston (21.5%), St Louis (16.3%), and Baltimore (13.4%) had the highest percentages of homes with detectable levels of cockroach allergen. For house dust mites, the higher the level of allergen exposure, the more likely patients were to have positive allergy skin test responses, with relative odds of 9.0 (95% confidence interval, 5.4-15.1) for those exposed to high mite levels (>10.0 μg/g dust) relative to those unexposed. Even exposure to low levels of mite allergen (0.020-2.0 μg/g) was found to be a significant risk factor for sensitization. For cockroach allergen, those with detectable home exposure were more likely to have positive skin test responses (relative odds, 2.2; 95% confidence interval, 1.3-3.8) than those with undetectable exposure. In contrast, levels of exposure to cat, dog, and mold allergens were not related to sensitization rates. For cat allergen, this may reflect lower rates of cat ownership among highly sensitized subjects. Furthermore, the number of allergy skin test responses that were positive, excluding the test for the outcome of interest for each model, and total serum IgE levels were strong independent predictors of sensitization.

Conclusions: Levels of exposure determined by house dust analysis are important determinants of sensitization for dust mite and cockroach allergen. This relationship was not demonstrable for cat, dog, or mold allergens, possibly because of confounding factors. For all allergens studied, the degree of atopy, determined by the total number of positive skin test responses or by total serum IgE levels, is an important contributing risk factor for sensitization. (J Allergy Clin Immunol 2001;107:48-54.)

Key words: *House dust mites, childhood asthma, cockroach allergy, Childhood Asthma Management Program, allergy sensitization, indoor allergens, atopy, risk factors for asthma, allergen exposure*

This analysis was carried out on baseline data from 1041 children enrolled in the Childhood Asthma Management Program (CAMP) sponsored by the National Heart, Lung, and Blood Institute. CAMP was a 5-year, randomized, double-blind, placebo-controlled, multicenter clinical trial conducted at 8 centers throughout North America. The primary goal was to determine whether chronic anti-inflammatory therapy with inhaled nedocromil or budesonide, together with as-needed β-agonist, administered to 5- to 12-year-old children (median, 8 years) with mild-to-moderate asthma would alter lung growth, as determined by postbronchodilator FEV_1.

There is a dose-response relationship between increasing exposure to house dust mites and the likelihood of having positive allergy skin test responses to mites.[1-7] In children, higher cockroach allergen exposure in bedrooms is associated with an increased likelihood of positive cockroach skin test responses.[8,9] Individuals with positive allergy skin test responses are at higher risk for development of asthma than those with negative test responses.[1] Also, there is a higher risk of development of positive skin test responses to house dust mites or cockroaches with increasing degrees of atopy, as measured by the number of positive allergy skin test responses an individual has to allergens other than mites or cockroach-

From [a]Johns Hopkins Asthma and Allergy Center, Baltimore; [b]Johns Hopkins University School of Hygiene and Public Health, Baltimore; and [c]Serum Repository, DACI Reference Laboratory, Johns Hopkins Asthma and Allergy Center, Baltimore.

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Reprint requests: Karen Huss, DNSc, Johns Hopkins University, School of Nursing, 525 North Wolfe St, Room 416, Baltimore, MD 21205.

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Abbreviations used
CAMP: Childhood Asthma Management Program
RO: Relative odds

es.[6,9] High total serum IgE, another measure of atopy, is associated with an increased risk of having positive skin test responses.[10-12] For cat allergen, a dose-response relationship between allergen levels and the presence of positive skin test responses has been described,[4] although others did not find such a relationship.[13,14]

In this cross-sectional analysis, we describe allergen levels in dust samples collected from homes of children with asthma in cities across North America. The purpose is to define risk factors associated with the presence of positive allergy skin test responses in a group of children with mild-to-moderate asthma. We analyzed data, including patients' demographic variables, home allergen exposures determined by house dust analysis, total serum IgE, and sensitivities to environmental allergens determined by allergy skin tests. We found that the risk of having positive allergy skin test responses in children with asthma is influenced by the quantity and types of indoor allergen exposures, atopic status, and total serum IgE levels.

METHODS

Patients

A description of the design, rationale, and methods of CAMP has been published.[15] To be enrolled, children met the following criteria: (1) age 5 to 12 years at initial interview; (2) chronic asthma symptoms for at least 6 months of the past year; (3) symptoms or morning or evening peak flow rates less than 80% of personal best on at least 8 days during a 4-week screening period; and (4) sensitivity to methacholine (PC_{20} FEV_1 ≤12.5 mg/mL).

Environmental assessment

A Home Environment Questionnaire was administered to parents or guardians gleaning information on the following: (1) type and number of any pets; and (2) pets allowed inside the home. We asked the following questions:

1. Do you ever see cockroaches in your home?
2. Do you currently smoke cigarettes?
3. Do you smoke a pipe or cigars?
4. Does anyone who visits at least 5 times per week smoke in your home?

Any positive response to these last 3 questions indicated "smoking in the home."

House dust specimen collection

Approximately 6 months after randomization, baseline house dust specimens were collected by local CAMP technicians. The delay in collections allowed specimens to reflect instruction in environmental control measures and placement of allergen-impermeable mattress and pillow encasings for children allergic to mites. A mixed house dust specimen was obtained from 969 (93.1%) homes. Areas vacuumed for 2 minutes each included the following: (1) 2 m^2 of the surface of each patient's mattress (if encased, the cover was vacuumed); (2) 1 m^2 of bedroom floor-carpet; (3) 1 m^2 of living room or family room floor-carpet; (4) 1 m^2 of kitchen floor; and (5) 1 major item of upholstered furniture.[15] After sieving dust, samples were quantitatively analyzed for the presence of major allergens from mites (Der p 1 and Der f 1), cats (Fel d 1), dogs (Can f 1), and German cockroaches (Bla g 1) by using standardized mAb-based immunoenzymetric assays.[16] Dust was plated on Sabouraud's dextrose agar plates containing penicillin, gentamicin, and streptomycin to enumerate viable fungal spores that were not further speciated.[17]

Total serum IgE

Total serum IgE was quantified by using a microparticle enzyme immunoassay with the IMx autoanalyzer (Abbott Laboratories, Abbott Park, Ill).[18] The autoanalyzer is a self-contained system delivering patient and control sera, specimen diluent, anti-human IgE antibody coated on microparticles, and substrate to the reaction cell at appropriate times. The assay is calibrated to the World Health Organization second international reference preparation for human IgE (75/502).[18] Trilevel control sera were analyzed in each assay to assess intra-assay and interassay variation. The working range of the assay was 1.2 to 500 ng/mL. Final results were reported in nanograms per milliliter (1 IU = 2.4 ng).

Allergy skin testing

Skin testing by pricking the skin with a bifurcated needle (Allergen Laboratories of Ohio, Columbus, Ohio) was performed during screening on all 1041 children. Tests were administered on the back, and results were read in 15 minutes. Patients avoided antihistamines or antidepressants for at least 72 hours before testing. Positive (5 mg/mL histamine base) and negative (50% glycerin) controls were simultaneously applied along with *Dermatophagoides pteronyssinus* and *Dermatophagoides farinae* (both 10,000 AU/mL); mixed breed dog allergen (1:20 wt/vol); *Penicillium* mix (1:20 wt/vol); *Aspergillus* mix (1:20 wt/vol); and *Alternaria tenuis* (1:20 wt/vol; all from Greer Laboratories, LaNoir, NC). Other allergens used were cat allergen (5000 BAU/mL; Allergologisk Labrationium, ALK USA, Milford, Conn); Timothy grass (1:20 wt/vol); German cockroach (1:20 wt/vol); American cockroach (1:20 wt/vol); and short ragweed (1:20 wt/vol; all from Meridian Bio-Medical Inc, Berkeley, Calif).

A test result was considered positive if it produced either a wheal with a mean diameter of at least 3 mm with any size flare (criterion 1) or a wheal with a diameter of less than 3 mm with a flare with a mean diameter of at least 10 mm (criterion 2). These criteria are similar to others that have been described.[19] The percentages of patients who had positive skin test responses by criteria 2 were as follows: American cockroach, 15.0%; German cockroach, 13.9%; dog, 11.4%; Der p 1, 8.0%; Der f 1, 7.1%; and Fel d 1, 6.5%.

Statistical methods

All analyses were performed by using baseline data from the 969 CAMP participants for whom dust samples were collected, except regression models that used skin tests for analysis. These models required that patients have at least one positive allergy skin test response. Only 12% had no positive skin test responses. For cross-tabulation and logistic regression, dust levels for allergens other than cockroach were divided into 4 categories: high, moderate, low, and undetectable.[20] Logistic regressions were done to calculate the adjusted relative odds (RO) of children having positive outcome allergy skin test responses by levels of respective house dust allergen in the homes, number of positive allergy skin test responses, and total serum IgE levels.

For house dust mites, undetectable allergen level was used as the reference category for logistic regressions because there were sufficient samples below the limits of sensitivity of the assays for analysis. For cat, dog, and mold allergen, low allergen level was used because of insufficient samples with levels below limits to be labeled "undetectable." Cockroach allergen was classified as

TABLE I. Characteristics of CAMP participants

No. of subjects at clinical center location	
Albuquerque	121
Baltimore	128
Boston	124
Denver	144
St Louis	133
San Diego	122
Seattle	144
Toronto	125
Total participants	1041
Age at initial interview, y (median [range])	8 (5-12)
Ethnic representations	
White	69%
African American	13%
Hispanic	9%
Other	9%
Female sex	40%
Duration of asthma since diagnosis, y (median [range])	4.8 (0.3-12.1)
Prebronchodilator FEV_1, % predicted (mean ± SD)	94 ± 14
Postbronchodilator FEV_1, % predicted (mean ± SD)	103 ± 13
Skin prick test, % positive of total sample (n = 1041)	
Cat	48.9
D pteronyssinus and/or *D farinae*	48.5
Timothy grass	46.6
D pteronyssinus	43.4
D farinae	42.0
Ragweed	37.5
Alternaria species	36.9*
German and/or American cockroach	34.0
German cockroach	29.1
Penicillium species	24.4
American cockroach	23.7
Dog	22.8
Aspergillus species	22.3

*Tested at 7 clinics (n = 920).

detectable or undetectable. For linear regression analyses, the $\log_{10}$ concentration of dust levels was used; zero or undetectable values were imputed to half of the lowest detectable dust concentration to facilitate log transformation.

The number of positive allergy skin test responses was categorized into 3 groups: (1) 0 to 2 positive skin test responses (where zero positive skin test responses implies that the patient reacted only to the allergen associated with the outcome for that model); (2) 3 to 4 positive skin test responses; and (3) 5 or more positive skin test responses. For total serum IgE, reference value is low IgE (low, <243 ng/mL; moderate, 243-869 ng/mL; and high, >869 ng/mL), with levels determined by dividing the study population into 3 strata determined by tertiles.

Linear regression analyses were performed to evaluate relationships between allergy skin test reactivity (positive vs negative) and covariates, including house dust allergen levels, age at randomization, sex, clinic, race, total IgE level, season of dust collection, smoking in the home, and number of positive allergy skin test responses, excluding the test for the outcome of interest for each model. The regression models included only patients with at least one positive allergy skin test response. *P* values were derived from the Wald test, were nominal, and were not adjusted for multiple looks or multiple outcomes. Data were analyzed by using version 6.12 of the SAS System.[21]

RESULTS

Study population

Patients were recruited between November 1993 and September 1995 from 8 clinical sites in North America. Demographic characteristics of the 1041 patients are summarized in Table I. About one third of the patients came from self-declared minority groups. The mean percent predicted prebronchodilator FEV_1[22,23] was consistent with a population with mild-to-moderate asthma. A total of 30% of children lived in homes with a smoking parent or relative, and 70% had furred or feathered pets. Data on allergy skin tests are presented in Table I by descending frequency. A total of 88% of patients had at least one positive allergy skin test response.

Geography of house dust allergen levels

The quantitative levels of allergens among the 8 clinical sites were significantly different from each other ($P < .001$, Table II). The centers with the highest percentages of homes containing major allergens of combined house dust mites (Der p 1 plus Der f 1) in high or moderate levels were San Diego (78.5%), Toronto (59.3%), and Boston (56.2%). The lowest levels were found in Denver (0.7%), Albuquerque (2.1%), and St Louis (34.2%).

Of the 6 sites with the highest house dust mite allergen (high-moderate), *D farinae* prevailed in the East (Boston, Baltimore, and Toronto) and mid-West (St Louis), and *D pteronyssinus* prevailed in the West (San Diego and Seattle). The highest frequencies of homes with detectable cockroach allergen (Bla g 1) were Boston (21.5%), St Louis (16.3%), and Baltimore (13.4%). Mold colony counts of high-to-moderate levels in homes ranged from 90.8% in San Diego to 50.0% in Seattle.

Risk factors for positive allergy skin test responses

Of 9 variables examined, only house dust allergen levels of house dust mites and cockroach, the number of positive allergy skin test responses excluding the test for the outcome of interest for each model, and total IgE levels were found to be associated with having a positive allergy skin test response (Table III). For house dust mites, the higher the levels of allergen exposure, the more likely individuals were to have positive allergy skin test responses. The adjusted RO for a positive skin test response in children exposed to high levels of allergen versus undetectable levels was 9.0 for either mite (95% confidence interval, 5.4-15.1). Denver and Albuquerque, sites with the lowest levels of mites, also had the lowest percentage of children with positive mite skin test responses (33.1% and 21.5%, respectively). For cockroach allergen, children living in homes with detectable levels had significantly higher risks of experiencing positive allergy skin test responses (RO, 2.2; 95% confidence interval, 1.3-3.8) than children living in homes with undetectable levels of allergen.

There were no significant relationships between allergen levels and positive allergy skin test responses to cat,

TABLE II. Distribution of house dust allergen levels by clinic

House dust allergen	Allergen level	Percentage of homes									
		Albuquerque (n = 95)	Baltimore (n = 113)	Boston (n = 121)	Denver (n = 140)	San Diego (n = 121)	Seattle (n = 132)	St Louis (n = 129)	Toronto (n = 118)	All sites (n = 969)	*P* value*
Mite, *D pteronyssinus*, Der p 1	High†	0.0	8.9	12.4	0.0	35.5	18.2	7.8	2.5	10.8	.001
	Moderate	1.1	14.3	14.9	0.0	26.5	22.0	6.2	6.8	11.6	
	Low	10.5	42.5	57.0	10.7	31.4	54.6	30.2	38.1	34.7	
	Undetectable	88.4	34.5	15.7	89.3	6.6	5.3	55.8	52.5	42.9	
Mite, *D farinae*, Der f 1	High†	0.0	13.3	18.2	0.0	13.2	0.8	7.0	31.4	10.3	.001
	Moderate	1.1	26.6	28.1	0.7	23.1	10.6	19.4	19.5	16.1	
	Low	15.8	53.1	53.7	17.1	52.9	39.4	66.7	44.9	43.2	
	Undetectable	83.2	7.1	0.0	82.1	10.7	49.2	7.0	4.2	30.3	
Combined mite, Der Gr 1‡	High†	0.0	21.2	30.6	0.0	49.6	19.7	14.0	35.6	21.4	.001
	Moderate	2.1	27.4	25.6	0.7	28.9	34.1	20.2	23.7	20.5	
	Low	19.0	45.1	43.8	22.9	19.0	41.7	59.7	36.4	36.3	
	Undetectable	79.0	6.2	0.0	76.4	2.5	4.6	6.2	4.2	21.8	
Cat, Fel d 1	High§	14.7	14.2	9.9	12.1	14.1	17.4	10.9	14.4	13.4	.001
	Moderate	23.2	15.0	12.4	17.1	21.5	20.5	7.8	11.0	15.9	
	Low	62.1	65.5	76.9	70.7	63.6	62.1	79.1	73.7	69.5	
	Undetectable	0.0	5.3	0.8	0.0	0.8	0.0	2.3	0.9	1.2	
Dog, Can f 1	High‖	19.6	21.8	10.0	25.9	14.8	17.2	19.4	18.5	18.8	.001
	Moderate	34.8	20.9	15.0	26.6	27.3	31.2	27.1	13.9	24.7	
	Low	45.7	57.3	75.0	47.5	58.0	51.6	53.5	67.6	56.5	
	Undetectable	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	
German cockroach, Bla g 1	Positive¶	6.3	13.4	21.5	4.3	9.9	1.5	16.3	2.5	9.4	.001
	Undetectable	93.7	86.6	78.5	95.7	90.1	98.5	83.7	97.5	90.6	
Mold colony count	High#	26.6	15.9	5.9	16.6	43.7	14.4	21.4	22.2	20.6	.001
	Moderate	51.1	55.8	47.5	51.8	47.1	35.6	50.8	51.3	48.6	
	Low	22.3	28.3	46.6	31.7	9.2	50.0	27.8	26.5	30.8	
	Undetectable	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	

*P values were obtained by using the χ^2 test for intersite differences.
†High: Greater than 10.000 μg/g; moderate: 2.001-10.000 μg/g; low: 0.020-2.000 μg/g; undetectable: less than 0.020 μg/g.
‡Der Gr 1 = Der f 1 plus Der p 1.
§High: greater than 80.000 μg/g; moderate: 8.001-80.000 μg/g; low: 0.020-8.000 μg/g; undetectable: less than 0.020 μg/g.
‖High: greater than 80.000 μg/g; moderate: 8.001-80.000 μg/g; low: 0.150-8.000 μg/g; undetectable: less than 0.150 μg/g.
¶Positive: 0.4 U/g or greater; undetectable: less than 0.4 U/g.
#High: greater than 25,000 CFU/g; moderate: 10,001-25,000 CFU/g; low: 0-10,000 CFU/g.

dog, and mold allergens, respectively. For cat allergen, children exposed to the highest levels of allergen were 20% less likely to have positive skin test responses than those exposed to the lowest levels of allergen. Furthermore, increasing exposure to group 1 dust mite allergen, measured in deciles, was associated with a progressive increase in the prevalence of positive allergy skin test responses (Fig 1). A total of 72% of children exposed to the highest decile of allergen (>100.0 μg/g dust mite allergens) had positive allergy skin test responses.

We found that the larger the size of skin test wheal to cat allergen (categorized in tertiles), the less likely children were to have a cat. Of 161 children who were in the highest tertile of wheal size, only 14.9% had a cat, whereas of 199 children in the lowest tertile, 26.1% had a cat ($P = .034$, χ^2 test). No such relationship was found for dog allergen. Also, the more atopic children were, as measured by the number of positive allergy skin test responses other than the outcome skin test, the more likely they were to have positive responses to any of the indoor allergens tested (Table III). The effects on skin test reactivity of the number of positive allergy skin test responses for each allergen was higher for those with 5 or more positive skin test responses than for those with 3 to 4 positive test responses ($P = .0004$ for dog; $P = .0001$ for others). Similar effects of the same magnitude were observed for the highest tertile of total serum IgE, except for mold skin tests (Table III).

DISCUSSION

The highest levels of house dust mites (combined Der p 1 and Der f 1) in the CAMP study are found in San Diego, Toronto, Boston, and Seattle (Table II). Coastal cities like San Diego, with warm temperatures and high humidity during most of the year, have high levels of house dust mites.[24,25] The lowest levels are found in Albuquerque and Denver, cities located more than 5000 feet above sea level, where total humidity is low, and few house dust mites are found.[13,26,27] In 4 cities, from 9.9% to 21.5% of homes have detectable levels of the cockroach allergen Bla g 1 (Table II). In studies of inner-city

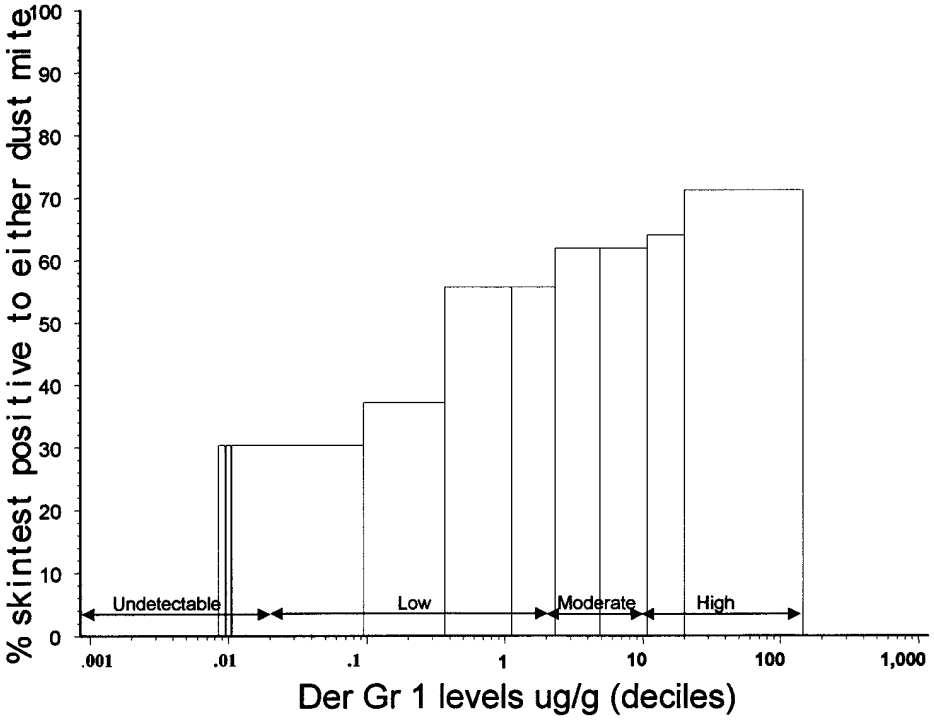

FIG 1. Increasing exposure to group 1 dust mite allergen measured in deciles, demonstrating a progressive increase in the percentage of CAMP patients with positive allergy skin test responses to either mite. The allergen classification levels for dust mites are defined in the footnote to Table II. *Der Gr 1,* Sum of group 1 mite allergen (Der p 1 plus Der f 1).

children, the highest levels of morbidity caused by asthma have been associated with the presence of positive skin test responses to cockroach allergen and current exposure to high levels of allergen in bedrooms.[28] CAMP included 2 cities (Albuquerque and Denver) where many houses contained high levels of dog and cat allergen. In the mountainous states of the United States, sensitization to dog and cat allergens, not mite allergen, is the strongest risk factor associated with the development of asthma.[13,26,27]

In this large cohort of 5- to 12-year-old children with asthma, we found that allergic sensitivity to inhalant allergens is strongly related to home dust allergen content for house dust mites and cockroach, but not for cat, dog, or mold. In other studies of children with asthma, most,[1-7] but not all,[29] researchers have found the prevalence of positive allergy skin test responses to dust mites increased as levels of mite allergen exposure increased, with a similar degree of risk as in our study. In a cohort in which 38% of infants had a double-positive family history for atopy, increased cord blood IgE, or both, investigators found a dose-response relationship between early mite and cat allergen exposure (within the first 3 years of life) and specific sensitization.[4] Subjects with positive family histories of allergy required exposure to much lower concentrations of allergens to achieve sensitization.

We found that even low levels of exposure to mites (0.020-2.0 μg/g) is a risk for sensitization. Others report that low mite allergen concentrations are associated with sensitization in susceptible individuals.[4,5] Our results indicate that as exposure levels exceed 20 μg/g, the percentage of children who have positive skin test responses continues to rise, up to a total of 73%. Also, the risk of development of positive allergy skin test responses in these children depends independently on atopic status. As atopy increases, defined by an increasing number of positive skin test responses, children are more likely to be allergic to any of the indoor allergens studied. The RO ranges from 1.8 for cat allergen to 4.2 for either cockroach allergen for those allergic to 5 or more allergens compared with those with only 1 or 2 positive responses (Table III). Also, the highest tertile of IgE (>869 ng/mL) is a good predictor for positive allergy skin test responses for all allergens except mold (RO, 2.2-3.1).

Concerning house dust mites, our results are similar to those of a longitudinal study involving 1812 school children.[4] Investigators found that the incidence of positive skin test responses to house dust mites during a 2-year period was related to the levels of mite allergen exposure during that period and was strongly dependent on the atopic status of the children. For children with asthma who have positive allergy skin test responses to inhalant allergens other than house dust mites, the minimal avoidance aim to prevent primary sensitization is 2.0 μg/g.[4] Our results are comparable with those of a study involving 500 inner-city children with asthma aged 4 to 9 years.[9] Investigators found an additive effect between

TABLE III. Adjusted* RO of positive skin test response by house dust allergen and selected other factors (among patients with at least one positive skin test response)

Skin test allergen	House dust allergen	House dust allergen level†			No. of positive skin test responses‡		Total IgE§	
		Low	Moderate	High	3-4	≥5	Medium	High
Either mite	Der Gr 1	3.34	6.29	8.97	1.14	2.05	1.62	2.17
95% CI		2.16-5.14	3.78-10.47	5.35-15.07	0.79-1.65	1.36-3.10	1.09-2.41	1.43-3.29
Trend *P* value			.0001		.0001		.0011	
Cat	Fel d 1	NA¶	1.02	0.80	1.44	1.82	1.95	3.02
95% CI			0.68-1.52	0.52-1.26	1.01-2.03	1.26-2.63	1.34-2.82	2.05-4.46
Trend *P* value			.324		.0001		.0001	
Dog	Can f 1	NA¶	0.83	1.16	1.59	2.63	1.50	2.94
95% CI			0.55-1.26	0.74-1.82	0.98-2.56	1.67-4.14	0.90-2.48	1.79-4.82
Trend *P* value			.342		.0004		.0001	
Either cockroach	Bla g 1		2.24‖		1.56	4.16	2.46	3.11
95% CI			1.31-3.83		1.04-2.33	2.77-6.27	1.57-3.87	1.97-4.89
Trend *P* value			.0023		.0001		.0001	
Any mold skin test	Mold count	NA¶	1.03	1.41	1.11	2.13	1.39	1.10
95% CI			0.74-1.45	0.91-2.18	0.77-1.60	1.42-3.20	0.94-2.06	0.73-1.68
Trend *P* value			.515		.0001		.130	

CI, Confidence interval.

*RO adjusted for house dust allergen level, age, sex, clinic, race, IgE levels, season of dust collection, smoking in the home, and number of other positive skin test responses, excluding the test for the outcome of interest for each model.

†Reference value is undetectable allergen level unless otherwise noted.

‡Reference value is 2 or fewer positive skin test responses other than the outcome skin test.

§Reference value is low total IgE levels (high: >869 ng/mL; medium: 243-869 ng/mL; and low: <243 ng/mL). Levels are determined by dividing the study population into tertiles.

¶Reference value is low (allergen was detected in at least 98% of all homes).

‖Cockroach levels were classified as detectable versus undetectable.

cockroach allergen exposure and atopic status. Children exposed to the highest levels of allergen who have 5 or more positive skin test responses have a 69% prevalence of having a positive cockroach skin test response.

In contrast to mite and cockroach allergen, the risk of having positive skin test responses to cat, dog, or mold allergens is not associated with currently measured home exposures. Investigators have reported no association between high levels of cat and dog allergen and the frequency of positive allergy skin test responses.[13] Others found that children sensitized to cat allergen early in life, especially during the first year, were exposed to higher levels of allergen than those not sensitized.[4] Also, these children were observed to become sensitized to cat allergen at an earlier age than to mite and other allergens.

The reasons we did not find a dose-response relationship between current cat exposure and sensitivity may be that (1) exposure early in life is more important than later exposure; (2) exposure in places other than homes, such as schools, induces sensitization[30,31]; and (3) airborne cat allergen is a more valid determiner of sensitization than reservoir dust allergen.[31] Also, our finding that children with the largest wheal sizes on skin testing had significantly fewer cats in their homes than those with smaller or negative wheal sizes suggests that as greater sensitivity to cat allergen develops in children, some families may be willing to give up cats for the health of their children. That there is no relationship between the degree of skin test sensitivity and the presence of dogs suggests that either dogs are less allergenic than cats, so that people are unlikely to remove them from homes, or avoidance measures are more successful at reducing symptoms than for cats.

Our study has several limitations. First, although CAMP was a randomized trial with long-term follow-up, the data here are cross-sectional and obtained at the beginning of the study. Therefore prior exposures cannot be assessed. However, that 46% to 60% of patients living in houses with low cat allergen levels (0.020-2.0 μg/g) are nevertheless sensitized to cat allergen suggests that prior exposures are clinically relevant. Second, CAMP patients were a select group of children with mild-to-moderate asthma and not a random sample of individuals from each city. Therefore the prevalence of sensitization must be interpreted cautiously. Third, at the time of home visit to collect dust specimens, approximately 80% of patients living where dust mites are endemic had allergen-impermeable encasings on mattresses and pillows. Also, they may have been taking other measures to reduce allergen burden. Carrying out these measures could have lowered dust mite allergen compared with levels just before the study.

In summary, we found that children with asthma become sensitized to house dust mite allergen at a frequency proportional to levels of current exposure, even with cross-sectional sampling. This suggests that at-risk children may be spared sensitization by reducing house dust mite burden in their homes if it is high or by maintaining already low levels. Having low mite allergens in homes would be particularly important for those who are presently atopic to other inhalant allergens because they

are at added risk of becoming sensitized to mites. Significant reductions of dust mite load can be accomplished by using relatively simple measures.[17] A similar situation may pertain to cockroach allergen. However, measures to reduce cockroach allergen in homes are not as established as those for mite allergen.[28,32] For furred pets and molds, the dose-response relationships are more complex. However, atopy, as measured by the total number of positive allergy skin test responses or total IgE levels, is an important contributor to sensitization rates to any of these indoor allergens.

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