

Sensitization to indoor allergens and the risk for asthma hospitalization in children

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Background: Hospitalization for asthma continues to present a major health problem despite advances in our understanding that asthma is an inflammatory disease of the bronchi and that exposure to specific allergens can induce and worsen this inflammation. The role of sensitization to specific indoor allergens and hospitalization for acute asthma in children is unclear.

Objective: The purpose of this study was to evaluate the independent contributions of sensitization to specific indoor allergens among children with asthma to the risk of hospitalization for asthma.

Methods: The charts of 138 consecutive children with asthma, aged 5 to 18 years, seen at pediatric allergy clinics were reviewed to obtain the results of skin tests to cat, dog, cockroach, and dust mite allergens and the history of hospitalization for asthma within the year prior to the clinic visit. Logistic regression analysis was used to examine the association between indoor allergen sensitivity and other factors, and the risk of hospitalization for asthma.

Results: In univariate analyses, hospitalization for asthma was significantly associated with cockroach sensitivity (odds ratio [OR] = 2.2; 95% confidence interval [CI] = 1.1, 4.3); cat sensitivity (OR = 2.9; CI = 1.3, 6.4); black race (OR = 2.4; CI = 1.1, 5.1); public aid/self pay (OR = 2.3; CI = 1.1, 4.9) and age, (OR [per year increase in age] = 0.8; CI = 0.7, 0.9). In a stepwise multiple logistic regression analysis, only cat sensitivity (OR = 3.8; CI = 1.5, 9.2), age (OR = 0.8; CI = 0.7, 0.9) and race (OR = 3.2; CI = 1.4, 7.5) entered into the model as significant independent predictors.

Conclusion: Sensitivity to cat allergen may be an important determinant for asthma hospitalization in children. Sensitization to cockroach allergen per se was not found to be an independent risk factor. As observed in previous studies, younger and black children were at increased risk of hospitalization for asthma.

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INTRODUCTION

There has been a great deal of concern in recent years about increases in asthma prevalence, hospitalization, and mortality in children.¹ Hospitalizations for asthma among all children in the United States increased by 28% from 1980 to 1993. In 1993, among persons aged 5 to 14 years, blacks were 3.4 times more likely than whites to be hospitalized for asthma, and 4 times more likely than whites to die

from asthma. It has been suggested that factors such as air pollution, poor compliance with medications, poor access to health care, and airway inflammation after exposure to inhaled allergens or respiratory viral infections may underlie these increases.¹⁻⁴ Studies have focused on the indoor environment because individuals spend a large part of their lives indoors. A wide variety of elements in the indoor environment, such as house dust mites, cat, dog and cockroach allergens, tobacco smoke, and nitrogen dioxide, have been associated with asthma.^{5,6} Even in children who have been asymptomatic and have no history of clinical allergy, airway hyperresponsive-

ness appears to be closely linked to an allergic diathesis.⁷

The prevalence of sensitization and the clinical relevance of the allergen found in houses vary greatly with regard to climate, living conditions, and racial background.^{5,6,8-10} In inner cities across the United States, and especially among blacks, cockroaches seem to be the major source of indoor allergen.^{6,9} Dust mite allergens seem to be more common in humid areas.^{8,10,11}

Although sensitization and exposure to indoor allergens have been suggested to be important risk factors for acute asthma requiring emergency treatment, few studies have evaluated the relationship between sensitization to indoor allergens and asthma hospitalization.¹² Sporik et al demonstrated that a majority of children admitted to a hospital in Dorset, United Kingdom were exposed and sensitized to dust mite and cat allergen. In that study, cockroach or dog allergen sensitivities were not evaluated. This report evaluates the role of specific sensitization to indoor allergens in relation to the risk of hospitalization for asthma in children.

METHODS

This is a retrospective study of children with asthma aged 5 to 18 years seen in the allergy outpatient clinics of the University of Chicago Children's Hospital over a 6½-year period. Those included in the study were consecutive patients who had their pulmonary function evaluated to confirm the diagnosis of asthma and assess the degree of severity of asthma. Children with specific respiratory diseases such as vocal cord dysfunction, cystic fibrosis, tuberculosis, bronchiectasis, sickle cell disease, congenital heart disease, im-

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munodeficiency, bronchopulmonary dysplasia, and anatomical variations were excluded. The study population included 159 children with a confirmed diagnosis of asthma; complete data about hospitalization was available on 138. The patients were classified as to whether they were hospitalized during the 12 months prior to their clinic visit or not. Suburban versus urban residence was determined by zip-code; if the home was in one of 55 zipcodes that lay within the Chicago city boundaries, residents were considered to be urban dwellers. Children were grouped as either on public aid/self pay or as having commercial insurance.

Immediate wheal and flare skin tests were performed on the forearm by the prick-puncture method with a bifurcated needle and glycerinated full strength mixed (German and American) cockroach, cat, dog, and dust mite (*D. farinae* and *pteronyssinus*) allergens (Bayer; Spokane, WA). The wheal diameters observed at 15 minutes were compared with skin test reactions produced by a positive response to histamine (10 mg/mL) control and a negative response to phenol-saline-human serum albumin control. Wheal diameters greater than or equal to the histamine control were considered positive. All the eligible patients denied use of oral medications containing antihistamine and had acceptable histamine responses (≥ 5 mm above the negative control).^{6,13}

Statistical Analysis

Analysis of the frequency of sensitization to cockroach, dust mite, dog and cat allergen, and its association with the risk of hospitalization for asthma was performed using chi-square tests and logistic regression.¹⁴ Odds ratios and 95% confidence intervals for the odds ratios were derived. Student's *t* test was used to compare the mean age of hospitalized and nonhospitalized children. Stepwise multiple logistic regression analysis was performed to evaluate and adjust for the effects of the following confounding variables: age, sex, race, area of residence, and

type of medical insurance. *P* values $\leq .05$ were regarded as statistically significant. The analyses were performed using the SAS statistical software package (SAS Institute; Cary, NC).

RESULTS

Factors Related to Hospitalization for Asthma

Of the 138 children who were evaluated, 76 (55%) were hospitalized for asthma within the previous year of the first clinic visit. Sixty-eight (49%) of the 138 children were sensitized to cockroach (Table 1). Forty-four (65%) of the 68 children who were sensitized to cockroach were hospitalized compared with 32 (46%) of the 70 who were not sensitized ($\chi^2 = 4.29$, *P* = .038). Similarly, there was a significant difference between cat-sensitized children and non-cat-sensitized children in the proportion who had been hospitalized; 29/40 (72%) versus 47/98 (48%) ($\chi^2 = 5.96$, *P* = .015). In contrast, sensitivity to dust mite or dog allergen was not significantly associated with hospitalization. Cockroach allergen sensitivity was significantly associated with the black race ($\chi^2 = 9.8$, *P* = .002) as well as with children who were on public aid/self pay ($\chi^2 = 7.1$, *P* = .008). Cat sensitivity was not related to race or insurance status.

One hundred (72%) of all the children were black. There was a significant difference between the black children and the non-black children in the

rate of hospitalization for asthma, 61/100 (61%) versus 15/38 (39%) ($\chi^2 = 4.32$, *P* = .038). Similarly, 60% of the children on public aid/self pay were hospitalized compared with 40% who had commercial insurance ($\chi^2 = 4.39$, *P* = .036). Sex and urban/suburban residency were not significantly related to hospitalization for asthma. The mean age of children hospitalized was lower than that for nonhospitalized children (9.5 versus 10.9 years, *t* = 2.91, *P* = .0004).

Risk Factors for Asthma Hospitalization

Table 2 presents the odds ratios for admission to the hospital for asthma within the previous 12 months when analyzed according to the subject's skin test reactivity to indoor allergens (cockroach, dust mite, dog, and cat), urban or suburban residence, race, type of insurance, age, and sex. In this study group, the odds of hospitalization were 2 times greater for a cockroach-sensitive child than for a child with negative sensitivity to cockroach allergen (*P* = .026). The odds for children sensitized to cat allergen were 2.9-fold greater than for those not sensitized (*P* = .010). Dust mite or dog allergen-sensitive children were not at increased risk of hospitalization for asthma.

A black child was more likely to be hospitalized for asthma than a non-black child, (OR = 2.4, *P* = .025). Similarly, a child on public aid/self pay was more likely to be hospitalized for asthma than a child on commercial insurance (OR = 2.3, *P* = .024). Younger children were more likely to be hospitalized for asthma than older children (*P* = .005). There was no increased risk of hospitalization for asthma in boys or children living in the urban area. When the relative contributions of the subject's skin test reactivity to indoor allergens and other factors were analyzed by stepwise multiple logistic regression analysis (Table 3), only cat allergen sensitivity (OR = 3.8, *P* = .004), black race (OR = 3.2, *P* = .008), and age (OR = 0.8, *P* = .001) entered into the model.

Table 1. Characteristics of Study Subjects

Variable	Number (%)
Positive skin test	
Cockroach	68 (49)
Dust mite	75 (54)
Dog*	23 (17)
Cat	40 (29)
Residence (urban)	110 (80)
Race (black)	100 (72)
Insurance (Medicaid/self pay)	96 (70)
Age mean $\pm$ SD#	10.1 $\pm$ 2.9
Sex (male)	89 (65)

* 2 cases had missing data.

SD = standard deviation.

Table 2. Odds Ratio for Admission to the Hospital for Asthma Exacerbation (Univariate)

Risk Factor	Odds Ratio	95% CI*	P Value
Positive skin test			
Cockroach	2.18	(1.10, 4.32)	0.026
Dust mite	0.86	(0.44, 1.68)	0.654
Dog	1.66	(0.65, 4.22)	0.290
Cat	2.86	(1.29, 6.36)	0.010
Residence (urban)	1.86	(0.80, 4.29)	0.149
Race (black)	2.40	(1.12, 5.15)	0.025
Insurance (Medicaid/self pay)	2.34	(1.12, 4.92)	0.024
Age (per year)	0.83	(0.73, 0.95)	0.005
Sex (male)	1.29	(0.64, 2.60)	0.478

* CI = confidence interval.

DISCUSSION

These data extend previous findings, showing not only that sensitivity to indoor allergens is common in children with asthma, but also that hospitalization for asthma is significantly associated with specific IgE response to cat and cockroach allergens. This relation persisted in the case of sensitization to cat but not to cockroach allergen after we have controlled for potentially confounding sociodemographic factors. Furthermore, we have confirmed findings that younger and black children are at increased risk of hospitalization for asthma.¹ A limitation of this study is that respiratory viral infections, allergen exposure, air pollution, and access to and compliance with medical care were not evaluated. The use of clinic populations may also limit the generalizability of the results.

Clinical and epidemiologic studies have demonstrated that sensitization and exposure to indoor allergens are risk factors for acute asthma requiring treatment in the emergency department.^{10,15} Geographic and sociodemo-

graphic variations in the distribution of allergens in homes of children with asthma have resulted in some discrepancies in the results of these studies.⁶ For example, Nelson et al demonstrated that cat allergen may not be associated with acute asthma in children in Tampa, Florida, possibly confounded by dust mite and cockroach allergens.¹⁵ On the other hand, Gelber et al found that the presence of specific IgE to mite, cat, and cockroach was associated with acute asthma in 114 adults who visited an emergency department in Wilmington, Delaware.¹⁰

Most previous studies have not gone beyond the emergency department or clinics to hospitalized children to evaluate the risk of allergen sensitization for asthma admission. In one study, Sporik et al evaluated 82 children admitted to the hospital with exacerbations of asthma and suggested that continued exposure to house dust mite or cat allergen in sensitized children with asthma may be associated with the risk of admission to the hospital in the

United Kingdom.¹² In their study exposure to cat allergen alone at home was not a risk factor for asthma admission, but strong sensitization to cat allergen alone was an important determinant for asthma admission. In our study, a skin test was considered positive if the wheal diameter was at least 5 mm larger than the negative control wheal.

Our findings are in agreement with surveys that have found that 15% to 30% of allergic populations have positive skin tests to cats and dogs, and that positive skin tests to cats are twice as common as to dogs.¹⁶ Possibly, because of the low prevalence of dog sensitization, there was no demonstrable relation between dog sensitization and asthma hospitalization. Since we did not measure the cat allergen on the clothing of these children on arrival at the hospital (assuming that was the clothing they were wearing at the time of onset of the acute asthma) or the cat allergen level in the environment in which the acute asthma occurred, we can only speculate that they may have been exposed to cat allergen prior to their hospitalization. Because cat allergen is sticky, and may be carried on clothing, clinically significant concentrations in schools and also homes with and without cats have been demonstrated in a number of studies.¹⁷⁻¹⁹ Alternatively, cat allergen sensitivity may select the highly atopic child who is reported to be prone to severe chronic asthma.²⁰

Dust mite sensitization was the most common among the four allergens we tested, which is consistent with the literature.^{8,15} Despite the high prevalence of sensitivity, dust mite allergens are barely detectable in the homes of children with asthma living in Chicago.⁹ Michel et al have also recently suggested that sensitivity and high exposure to dust mite allergen without concomitant exposure to endotoxin in house dust may not be clinically relevant in asthma.²¹ Cross reactivity between dust mite and other allergens like cockroach has been reported.²² Despite these reports, it was surprising to us to find no relation between dust

Table 3. Odds Ratio for Admission to the Hospital for Asthma Exacerbation (stepwise multiple logistic regression analysis)

Risk Factor	Odds Ratio	95% CI*	P Value
Positive skin test			
Cat	3.77	(1.53, 9.25)	0.004
Race (black)	3.18	(1.35, 7.49)	0.008
Age (per year)	0.77	(0.67, 0.90)	0.001

* CI = confidence interval.

mite sensitivity and hospitalization for asthma, which is in contrast with previous reports.¹² Dust mite is the only indoor allergen for which it has been demonstrated that avoidance leads to beneficial results.²³ It could therefore be possible that these children were in homes with low levels of the allergen due to avoidance measures or more likely due to regional or seasonal differences in the distribution of dust mite allergen. More prospective studies evaluating consecutive children hospitalized with asthma are needed to clarify the clinical relevance of dust mite sensitivity in asthmatic children in homes with low prevalence of the allergen.

Our results are consistent with studies showing that sensitization to cockroach allergen is common in children with asthma.^{6,15} It further confirms the reports of others that cockroach allergen sensitization is associated with asthma morbidity in children with asthma.¹⁵ Despite these findings, skin test reactivity to cockroach allergen was not independently associated with hospitalization for asthma possibly due to sample size or intensity of exposure. Our results are consistent with studies showing that cockroach allergen sensitization is higher in disadvantaged and black children, a population that has been identified as having increased asthma morbidity.^{1,6}

These results suggest that sensitization to indoor allergens like cat and to some extent cockroach allergen may partly explain the increased morbidity in children with asthma. Avoidance of cockroach allergens by patients with cockroach sensitive asthma may reduce the risk of acute asthma episodes as has been demonstrated with dust mite-related asthma.^{23,24} Although we would like to think that removing an animal from a home should be a relatively simple matter, virtually all families respond to this recommendation with some degree of emotion. Further, even if a child is able to avoid animal exposure at home, the danders are so common that some degree of exposure outside the home, for example in the school, is inevitable.¹⁸ Medications

will usually be effective in these situations and, if not, immunotherapy may provide added relief and should therefore be considered.²⁵

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REFERENCES

- Centers for Disease Control. Asthma mortality and hospitalization among children and young adults—United States, 1980–1993. *MMWR* 1996;45: 350–3.
- Carr W, Zeitel L, Weiss K. Variation in asthma hospitalizations and deaths in New York City. *Am J Pub Health* 1992;82:59–65.
- Crane J, Pearce N, Burgess C, et al. Markers of risk of asthma death or readmission in the 12 months following a hospital admission for asthma. *Int J Epidemiol* 1992;21: 737–44.
- Friday GA, Fireman P. Morbidity and Mortality of Asthma. *Pediatr Clin N Am* 1988;35:1149–69.
- Wood RA, Eggleston PA, Lind P, et al. Antigenic analysis of household dust samples. *Am Rev Respir Dis* 1988; 137:358–63.
- Sarpong SB, Hamilton RG, Eggleston PA, Adkinson NF, Jr. Socioeconomic status and race as risk factors for cockroach allergen exposure and sensitization in children with asthma. *J Allergy Clin Immunol* 1996;97: 1393–1401.
- Sears MR, Burrows B, Flannery EM, et al. Relation between airway responsiveness and serum IgE in children with asthma and in apparently normal children. *N Engl J Med* 1991;325: 1067–71.
- Sporik R, Holgate S, Platts-Mills TAE, Cogswell J. Exposure to house dust mite allergen (Der p 1) and the development of asthma in childhood: a prospective study. *N Engl J Med* 1990; 323:502–7.
- Eggleston P. For the National Cooperative Inner City Asthma Study. Allergens in inner city homes [Abstract]. *J Allergy Clinical Immunol* 1996;97: 301.
- Gelber LE, Seltzer LH, Bouzoukis JK, et al. Sensitization and exposure to indoor allergens as risk factors for asthma among patients presenting to hospital. *Am Rev Respir* 1993;174: 573–8.
- Hamilton RG, Chapman MD, Platts-Mills TAE, Adkinson NF Jr. House dust aeroallergen measurement in clinical practice: a guide to allergen free home and work environments. *Immunol Allergy Pract* 1992;14: 96–112.
- Sporik R, Platts-Mills TAE, Cogswell JJ. Exposure to house dust mite allergen of children admitted to hospital with asthma. *Clin Exp Allergy* 1992; 23:740–6.
- Kang B, Johnson J, Vere-Thorner C. Atopic profile of inner-city asthma with a comparative analysis on the cockroach-sensitive and ragweed-sensitive subgroups. *J Allergy Clin Immunol* 1993;92:802–11.
- Hosmer DW, Lemeshow SL. *Applied logistic Regression*. New York, Wiley, 1989.
- Nelson RP, DiNicolo R, Fernandez-Caldas E, et al. Allergen-specific IgE levels and mite allergen exposure in children with acute asthma first seen in an emergency department and in non-asthmatic control subjects. *J Allergy Clin Immunol* 1996;98:258–63.
- Murray AB, Fergusson AC, Morrison BJ. The frequency and severity of cat vs dog allergy in atopic children. *J Allergy Clin Immunol* 1983;72: 145–9.
- Bollinger ME, Eggleston PA, Flanagan E, Wood RA. Cat allergen in homes with and without cats may induce allergic symptoms. *J Allergy Clin Immunol* 1996;97:907–14.
- Munir AKM, Einarsson R, Schou C, Dreborg SKG. Allergens in school dust; The amount of the major cat (Fel d 1) and dog (Can f 1) allergens in dust from Swedish schools is high enough to probably cause perennial symptoms in most children with asthma who are sensitized to cat and dog. *J Allergy Clin Immunol* 1993;91: 1067–74.
- D'Amato G, Gennaro L, Russo M, et al. Clothing is a carrier of cat allergens. *J Allergy Clin Immunol* 1997;99: 577–8.
- Zimmerman B, Chambers C, Forsyth S. Allergy in asthma: II. The highly atopic infant and chronic asthma. *J Al-*

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- lergy Clin Immunol 1988;81:71-7.
21. Michel O, Kips J, Duchateau J, et al. Severity of asthma is related to endotoxin in house dust. *Am J Rev Respir Crit Care Med* 1996;154:1641-6.
22. Witteman AM, Akkerdaas JH, Leewen J, et al. Identification of a cross-reactive allergen (presumably tropomyosin) in shrimp, mite, and insects. *Int Arch Allergy Immunol* 1994;105:56-61.
23. Platts-Mills TAE, Tovey E, Mitchell EB. Reduction of bronchial reactivity during prolonged allergen avoidance. *Lancet* 1982;2:675.
24. Sarpong SB, Wood RA, Eggleston PA. Cockroach allergen (Bla g 2) environmental control with cleaning and extermination. *Ann Allergy Asthma Immunol* 1996;76:257-60.
25. Ohman JL Jr, Findlay SR, Leitermann KM. Immunotherapy in cat-induced asthma: double-blind trial with evaluation of in vivo and in vitro responses. *J Allergy Clin Immunol* 1984;74:230-9.
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