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Aeroallergen Sensitization in Healthy Children: Racial and Socioeconomic Correlates

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Abstract

Objective—Allergic sensitization is very prevalent and often precedes the development of allergic disease. This study examined the association of race with allergic sensitization among healthy children with no family history of atopy.

Study design—275 children, predominantly from lower socioeconomic strata, from Cincinnati, OH aged 2 to 18 years without a family or personal history of allergic diseases, underwent skin prick testing to eleven allergen panels. The Pediatric Allergic Disease Quality of Life Questionnaire (PADQLQ) was used to examine the impact of sensitization on quality of life.

Results—39% of healthy children were sensitized to ≥ 1 allergen panels. Multivariate logistic regression showed increased risk among African American children for any sensitization (OR 2.17; [95% CI; 1.23, 3.84]) and sensitization to any outdoor allergen (OR 2.96 [95% CI; 1.52, 5.74]). 86% of children had PADQLQ scores ≤ 1 (0 to 6 scale).

Conclusion—Allergic sensitization is prevalent even among children who do not have a personal or family history of asthma, allergic rhinitis, or atopic dermatitis, and who have no evidence of current even subtle effects from this sensitization on allergic-disease related quality of life. African American children are at greater risk for presence of sensitization, especially to outdoor allergens.

Keywords

Allergic sensitization; atopy; race; quality of life; child

Asthma is a major public health problem affecting 15 million people in the United States alone (1). Allergic sensitization, as defined by ≥ 1 positive skin test responses to allergens, is a critical step in the pathogenesis of asthma. It is the major determinant for the development of childhood asthma (2–4), yet sensitization alone is not sufficient to cause disease. The biologic and genetic factors that prevent children who are sensitized to environmental allergens from manifesting

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symptoms or overt disease are not known (5). Children who have evidence of exposure as manifested by at least one positive skin prick test and yet who are asymptomatic represent an important group in the study of the continuum of the allergic phenotype.

In order to adequately understand the role of environmental allergens in disease etiology, it is helpful to understand the socioeconomic and racial contribution to allergic sensitization. In the U.S., African American children, those receiving Medicaid insurance, and children living in poverty are more likely to have ever been diagnosed with asthma (6). African American race and poverty have been independently associated with sensitization to cockroach allergen among children with asthma (7). It has been shown that even asymptomatic children who are sensitized to allergens may demonstrate bronchial hyperresponsiveness, a key component of asthma (8–11).

Despite numerous environmental and genetic investigations, reasons for worldwide and racial variations in allergic sensitization and respiratory allergy remain poorly understood (12). This study contrasts to previously published literature by focusing on a cohort of children without allergy related symptoms. The objective of this study was to determine racial and socioeconomic correlates to sensitization to indoor and outdoor aeroallergens in children aged 2 to 18 years *without* reported allergic disease.

METHODS

Study Subjects

This study was approved by the Cincinnati Children's Hospital Medical Center Institutional Review Board. Children aged 2 to 18 years in this study were recruited from January 2003 to May 2005 as part of a case-control study regarding the genetics of asthma and allergy among children in the greater Cincinnati, Ohio area. Asymptomatic children were enrolled at the Dental, Dermatology, Orthopedics, or Neurology outpatient clinic sites at Cincinnati Children's Hospital Medical Center. Informed consent from the parent or legal guardian and age appropriate child assent was obtained for all enrolled study subjects.

The Pediatric Allergic Disease Quality of Life Questionnaire (PADQLQ) (13) was used to evaluate the potential impact of allergic disease on the study population's quality of life. This questionnaire has been validated against individual asthma, allergic rhinitis, and atopic dermatitis symptoms and quality of life instruments. PADQLQ scores from children with allergic disorders have been shown to be significantly associated with both pollen counts and fractional exhaled nitric oxide levels (14). The validity of the PADQLQ was also further evaluated using data from subjects with allergic conditions enrolled at Cincinnati Children's Hospital Medical Center Allergy and Immunology clinics (data not shown).

Children with no personal or family history (parent or sibling) of allergic disease or symptoms were eligible for the study. Eligible asymptomatic subjects were identified during visits to the aforementioned clinics using an Eligibility Screening Form and Control Data Form. Parents were asked if the subject, the subject's parents or brothers or sisters had a history, either now or at any time in the past, of asthma or frequent wheezing or environmental allergies (sneezing/runny nose to dust, pollen, pets or mold). During the informed consent process, the parents of subjects with negative responses then completed the Control Data Form. On the Control Data Form, parents were asked to report if the subject had any history of asthma, wheezing, allergic rhinitis, atopic dermatitis, eczema, or food allergy. Parents were also asked to report if the subject ever had a history of a frequent runny, stuffy nose, water and/or itchy eyes, frequent sneezing, recurrent cough or wheezing, nasal polyps, red or itchy dry skin, or recurrent sinusitis. Only subjects with all negative responses were eligible for the study. Medications were recorded and any subject with any current or previous history of receiving asthma- or allergy-

related medication also was excluded. Any questions regarding whether or not previous or present symptoms represented possible wheezing or asthma, allergic rhinitis or atopic dermatitis were addressed by the study physician and in cases of uncertainty, the patient was deemed ineligible. Prior to enrollment, the study physician verbally confirmed Control Data Form responses and medications with the parent and subject. Additional data such as race, annual household income, type of health insurance, and parental education were also collected. The child's parent or legal guardian reported on a written form one of the following racial or ethnic groups: 1) White/Caucasian, 2) Black/African American, 3) Asian 4) Hispanic/Latino, 5) Native Hawaiian/Pacific Islander, 6) American Indian/Alaska Native, 7) Other (written description requested).

Definitions of Allergic Sensitization

Skin prick testing was performed using the GREERPick™ System (Greer Laboratories, Lenoir, North Carolina) on the volar aspect of the forearm in the absence of systemic antihistamine use according to published guidelines. Sensitization was defined as present when the wheal around the allergen tested was greater than 3 mm and was also greater than the saline negative control. Tests were read 15 minutes after placement. Histatrol® (Center Laboratories, Port Washington, NY) 1 mg/mL was used as the positive control. Subjects without a positive response to the Histatrol® were excluded (n=1). Allergen panels were mixed by Hollister-Stier to include 11 aeroallergens prevalent in the Ohio River Valley. Panels included mold mixes (2), grass mix, ragweed (giant and short), tree pollen mixes (2), weed mix, dust mite mix (der f and der p), cat (fel d 1), dog (hair and dander), and cockroach mix (*P. americana* and *B. germanica*). Dichotomous outcome variables (expressed as the presence or absence of sensitization) were sensitization to any allergen, sensitization to any outdoor allergen (grass, tree, ragweed, or weed) and sensitization to any indoor allergen (molds, cockroach, or dust mite). The atopy index, a summary score of allergic sensitization (15) was utilized as a continuous variable.

Data Analysis

Statistical analysis was performed using SAS Version 8 or SPSS Version 13. Univariate analysis using Chi square was performed to examine the relationship between socioeconomic and racial factors and allergic sensitization. Logistic regression models were used to examine racial and socioeconomic associations with the probability of the occurrence of: 1) any allergic sensitization, 2) sensitization to any indoor allergen and 2) sensitization to any outdoor allergen. Linear regression models in which the outcome variable was the total atopy index (15) were also performed. PADQLQ scores were calculated according to published methods (13). Questions #25 and #26 were not included in the final scoring because the questions directly referred to the subject's asthma or allergies, which was irrelevant for healthy subjects. The mean 24-item score in children who were sensitized to any allergen was compared with the mean score of children who were not sensitized to any allergens.

RESULTS

Eligibility

The Children's Hospital Medical Center Dental Clinic served as the primary recruitment site for 93% of enrolled subjects. Although data regarding ineligible subjects was not available for the entire study period, for six consecutive weeks, data regarding the total number of parents approached for the study and reasons for exclusion were recorded. Over the six week period, 279 parents or guardians were approached and asked to undergo screening to determine their child's eligibility. Of those, 150 (54%) children were not eligible due to a positive personal or family history of asthma, allergic rhinitis or atopic dermatitis. Another 102 (37%) parents refused participation in either screening or the study. Reasons most commonly cited were lack

of time and unwillingness to have their child undergo skin prick testing. Six (2%) of the adults approached were not legally able to provide informed consent. In total, 21/279 (7.5%) of screened patients were eligible and agreed to participate in the study. Due to lack of time after completion of the Dental Clinic visit, 3/21 (14%) eligible subjects subsequently withdrew.

Enrolled Subjects

275 children aged 18 years or less without a first degree family member with a history of allergic disease or asthma were enrolled. Approximately 57% of subjects were female. The child's race was reported as Caucasian by 48% of parents, African American by 46% of parents, with the remainder of subjects being of Biracial (2.5%), Hispanic (1.1%), not provided (0.7%), or other. 54% of children were of ages 6 to 11 years, 31% were of ages 12 to 18 years, and the remainder (15%) was aged 2 to 5 years. The sample population was primarily of low socioeconomic status (Table I).

Despite having no personal or family history of allergic disease or symptoms, 39% (108/275) of children were positive to at least one allergen panel tested. Strikingly, 68% (73/108) of children who were sensitized to at least one allergen were positive to more than one allergen. Further, 41% (44/108) of children who were sensitized to at least one allergen were positive to three or more allergens. Among children who were sensitized to any allergen tested, the Figure further depicts the percentage of children who were positive to each allergen group (n=108). Notably, 54% were sensitized to dust mite mix and 44% were sensitized to Tree pollen panel #2.

Due to the infrequency of races other than Caucasian or African American in the enrolled study group (6.2%), children from other racial groups were not included in the univariate analysis and regression models, resulting in a total sample size of 256. Table I depicts the results of the univariate analysis comparing sex, race, insurance status, class of annual household income, and class of maternal education to allergic sensitization (at least one positive skin prick test). When age was examined as a continuous variable, the difference in mean age between groups of sensitized and non-sensitized children was also significant ($p=0.016$). The mean age in children without allergic sensitization was 8.78 years and the mean age among sensitized children was 9.87 years, with a mean difference of 1.09 years [95% CI, 0.21, 1.97]. Only age and race were significant in the univariate analysis.

In the logistic regression models, increasing age was found to be significantly associated with allergic sensitization to any allergen panel and any indoor allergen panel. As shown in Table II, African American race was significantly associated with allergic sensitization to any aeroallergen after adjustment for age and annual household income. Adjustment was made for annual household income due to previous literature suggesting that socioeconomic status alone may contribute to sensitization (7). The magnitude of the association between African American race and any outdoor allergen was higher than to any allergen, with an increase in the odds ratio from 2.17 to 2.96.

The atopy index (total number of allergens out of eleven to which subjects had a positive response) was also used as an outcome variable. The mean atopic index (\pm SD) was 0.63 (\pm 1.24) among Caucasian children, and 1.54 (\pm 2.14) in African American children ($p < 0.001$ by t-test). In a linear regression model with atopy index as the outcome, the strength of the association between African American race and increasing atopy index still held, even after adjustment for age and class of annual household income ($p < 0.001$).

A total of 131 healthy subjects aged 6 to 16 years completed the PADQLQ. Out of a possible score of 6, 10 % of subjects had a mean score of 0 on the 24 item PADQLQ. Scores were overall very low, with 86% of scores falling below 1 and 97% of scores falling below 2. There

was no significant difference in mean PADQLQ score between subjects who were positive to any allergen panel (mean score $.54 \pm .6$) and subjects who were negative to all allergens (mean score $.55 \pm .72$).

DISCUSSION

We demonstrated a high degree (39%) of allergic sensitization among children with no previous history or current symptoms of allergic disease. Further, 68% of children who were found to be sensitized were positive to at least one of eleven common aeroallergen panels. Among subjects who completed the Pediatric Allergic Disease Quality of Life Questionnaire (PADQLQ), results demonstrate that study subjects were not likely experiencing important subclinical or underreported allergic symptoms.

In this study, African American children were significantly more likely to be sensitized than Caucasian children to any allergen. This association remained after adjusting for age and annual household income. These data are consistent with other population based studies regarding race and allergic sensitization. The National Health and Nutrition Examination Survey (NHANES) II included assessment of skin test reactivity to 8 common allergens in individuals aged 6 to 74 years from 1976 to 1980. Age adjusted prevalence of sensitization to one or more allergens was higher in non-Hispanic blacks (23.2%) than in non-Hispanic whites (19.8%) but the difference was not statistically significant (16). In contrast, a study of NHANES III (1988–1994) data showed that 54.3% of the population aged 6 to 59 years was sensitized to at least one of 10 allergens (17). Further, non-Hispanic blacks were significantly more likely than non-Hispanic whites to have a positive skin test response to seven of the 10 allergens tested in NHANES III (17). Another study of NHANES III data utilized multivariate models to demonstrate that African American children aged 6 to 16 years were more likely to be sensitized to common indoor allergens after adjustment for multiple socioeconomic factors (18). These differences were especially pronounced in central city regions. Although adjustments were made for housing and income in their multivariate models, the authors postulated that racial differences in housing quality and environment explained the racial differences in skin test responses to indoor allergens. Outdoor allergens were not examined in that study (18).

NHANES data represents the entire population, including subjects with asthma, allergic rhinitis, and atopic dermatitis. Allergic rhinitis is the most common chronic disease in children (19) and 12% of children in the United States have ever been diagnosed with asthma (6) and children with these diagnoses were represented in the study of NHANES data (17). Our subjects had no history or symptoms of allergic disease and yet the prevalence of allergic sensitization is still 39%. Further, the association of African American race and allergic sensitization is stronger for outdoor allergens in our study, even after adjustment for household income. Racial disparities in housing and environmental factors would be less likely to play a role in sensitization to outdoor allergens. Therefore, our data supports other family-based genetic studies that postulate a genetic basis for racial differences in susceptibility to allergic diseases such as asthma (20).

Two other studies have suggested that African American children are more likely than Caucasian children to be sensitized to outdoor allergens (21,22). One study, performed only in children with asthma, showed a strong association with African American race and sensitization to mixed tree pollen, mixed grass pollen, ragweed and mugwort/sage, even after adjustment for confounding factors such as area of residence and type of health insurance (21). The other study included a group of middle class children from suburban Detroit with and without asthma, and noted that that African American children were more likely to be sensitized to bluegrass than European American children (22). Our study is the first to our knowledge to describe a high prevalence of allergic sensitization in children without a personal

or family history of allergic disorder, and to demonstrate a predisposition for sensitization among African American children in this group.

This study has several limitations. Subjects were enrolled from clinic sites within one urban hospital and were primarily of low socioeconomic status. Although the study population is similar to children at high risk of asthma and environmental allergy, additional evaluation in other sites and populations would be helpful to confirm these findings. Information regarding personal or family history of allergy related disease was collected in a cross sectional format by parent report of diagnosis and symptoms rather than by medical record or prospective symptom diary. Subjects were tested to only 11 allergen panels. It is possible that some children could be sensitized to other important environmental allergens that were not included or those that were negative at the time of testing could become sensitized. Finally, an estimated one-third of eligible subjects' parents declined participation, with unknown effect on results.

The clinical significance of allergic sensitization without symptoms deserves further study. A significant relationship between airway hyperresponsiveness and sensitization to house dust mite or cat allergens has been described, even among children who never had a history of asthma, wheeze or hay fever (9). Longitudinal data from a cohort of college freshmen followed for 23 years suggests that positive skin test responses are significantly associated with the development of both allergic rhinitis and asthma later in adult life (23). The incidence of new atopic disorders among children who are asymptomatic but show evidence of allergic sensitization is currently unknown. Long-term outcome studies in well-defined study populations will be important.

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ABBREVIATIONS

PADQLQ

Pediatric Allergic Disease Quality of Life Questionnaire

CHSA

Children's Health Survey for Asthma

SCORAD

Scoring Atopic Dermatitis tool

SPT

Skin Prick Test

SD

Standard Deviation

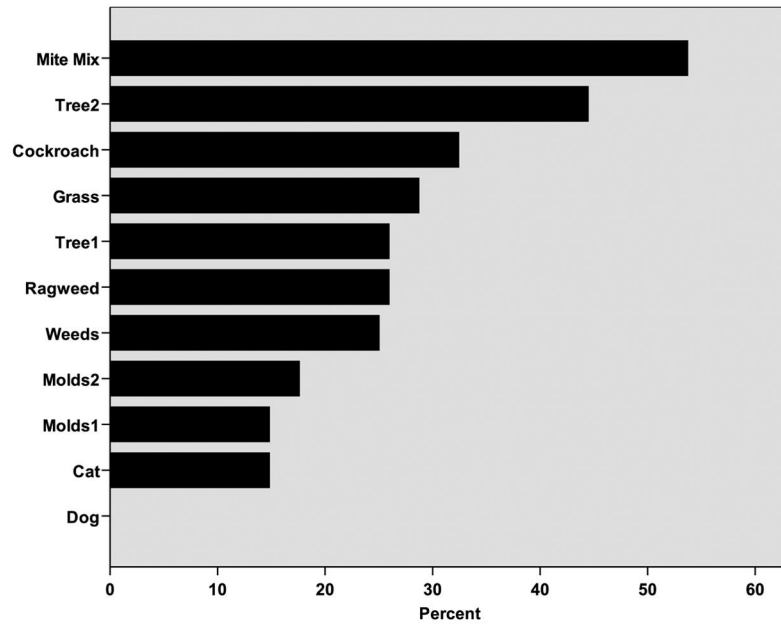


Figure.
Type of allergen response among children sensitized to at least one allergen (n=108)

Table 1
Demographic Characteristics and Univariate Analysis of Subjects of African American or Caucasian Race (n=256)

	n (%) number responding	n (%) among all responding	n (%) with ≥ 1 positive skin test response	n (%) with no positive skin test response	p value*
Sex	256 (100)				0.56
Female		148 (58)	55 (37)	93 (63)	
Male		108 (42)	44 (41)	64 (59)	
Race	256 (100)				0.003
Caucasian		131 (51)	39 (30)	92 (70)	
African American		125 (49)	60 (48)	65 (52)	
Insurance Status	238 (93)				0.78
Public or self pay		177 (74)	66 (37)	111 (63)	
Private		61 (26)	24 (39)	37 (61)	
Annual Household Income	229 (89)				0.51
< \$30,000		164 (72)	58 (35)	106 (65)	
\geq \$30,000		65 (28)	26 (40)	39 (60)	
Mother's Education	231 (90)				0.24
\leq High School Graduate		128 (55)	45 (35)	83 (65)	
> High School Graduate		103 (45)	44 (43)	59 (57)	

* p values refer to the 2x2 Chi square comparison between children sensitized to at least one allergen and children without sensitization

Table 2
Association Between Allergic Sensitization and Race

Modeled Outcome Variable	Adjusted Odds Ratio [95% CI] [*] African American Race
Sensitization to Any Indoor Allergen	1.63 [0.88, 3.02]
Mold mix 2	6.14 [1.52, 24.69] [†]
Cockroach mix	2.67 [1.11, 6.4] [†]
Dustmite mix	1.15 [0.58, 2.29]
Sensitization to Any Outdoor Allergen	2.96 [1.52, 5.74] ^{††}
Grass mix	3.78 [1.37, 10.51] [†]
Ragweed mix	2.11 [0.83, 5.38]
Weed mix	3.99 [1.34, 11.9] [†]
Tree mix 1	1.54 [0.58, 4.13]
Tree mix 2	6.51 [2.57, 16.47] ^{††}
Sensitization to Any allergen	2.17 [1.23, 3.84] ^{††}

* Caucasian = reference group, model adjusted for age and annual household income. The OR for Mold mix 1 was unable to be calculated because all sensitized subjects were African American.

[†] p value < 0.05;

^{††} p value < 0.01