UNIVERSITY OF CINCINNATI

Date:  7/10/06

I, Michelle D. Stevenson
hereby submit this work as part of the requirements for the degree of:

Master of Science

in:

Epidemiology, in the Department of Environmental Health

It is entitled:

Aeroallergen Sensitization in Healthy Children: Ethnic and Socioeconomic Correlates

This work and its defense approved by:

Chair: Gurjit K. Khurana Hershey, MD, PhD
Ranjan Deka, PhD
C. Ralph Buncher, PhD
Aeroallergen Sensitization in Healthy Children: Ethnic and Socioeconomic Correlates

A thesis submitted to the
Division of Research and Advanced Studies
of the University of Cincinnati

in partial fulfillment of the
requirements for the degree of

MASTER OF SCIENCE (M.S.)

In the Division of Epidemiology and Biostatistics
of the Department of Environmental Health
of the College of Medicine

July 10, 2006

By

Michelle D. Stevenson

BS, Indiana University 1993
MD, University of Kentucky 1997

Committee Chair: Gurjit K. Khurana Hershey, MD PhD
ABSTRACT

This study examined the ethnic and socioeconomic risk factors for allergic sensitization among children without a family or personal history of allergic diseases. 39% of subjects were sensitized to ≥ 1 panel. Multivariate logistic regression showed an increased risk among African American children for any sensitization (OR 2.18; [95% CI 1.3, 3.66]) and sensitization to any outdoor allergen (OR 2.69 [95% CI, 1.49, 4.86]). The Pediatric Allergic Disease Quality of Life Questionnaire (PADQLQ) showed little impact of sensitization on quality of life. PADQLQ scores from children with allergic diseases were examined for correlation to multiple allergic disease outcome measures. Total PADQLQ showed excellent correlation to asthma-related quality of life, but poor correlation to lung function and skin prick test results. Allergic sensitization, even among healthy children, is common. African American children are at greater risk for sensitization, especially to outdoor allergens. The PADQLQ may be a useful allergy assessment instrument.
ACKNOWLEDGEMENTS

I would like to thank the following individuals for their contributions to the successful completion of this thesis:

Gurjit K. Khurana Hershey, MD PhD
Richard M. Ruddy, MD
Ranjan Deka, PhD
C. Ralph Buncher, PhD
Stacey Sellins
Nola Clarke
Emilie Grube
Kathy Schroer
Jayanta Gupta

I would also like to thank my husband for his support, encouragement, and assistance with SAS.

This work was funded by NIH R01AI46652-01A1 (GKKH), University of Cincinnati, Molecular Epidemiology in Children’s Environmental Health - Institutional NIEHS T32 ES10957; and Cincinnati Children’s Hospital Medical Center - Institutional NICHD T32 HD43005

The following individuals contributed in the following ways to this project:

Project oversight and mentorship: Dr. Gurjit Khurana Hershey
Identification of eligible subjects: Michelle Stevenson, Stacey Sellins, Nola Clarke, Emilie Grube, Kathy Schroer, Jayanta Gupta
Skin prick testing of healthy subjects: Michelle Stevenson (270 subjects) and Jayanta Gupta (5 subjects)
Administration of PADQLQ to healthy subjects: Michelle Stevenson, Stacey Sellins, Nola Clarke, Emilie Grube, Kathy Schroer,
Administration of PADQLQ, CHSA to Allergy Clinic subjects: Michelle Stevenson, Stacey Sellins, Emilie Grube
Collection of SCORAD data: Jayanta Gupta
Creation of database of healthy subjects: Michelle Stevenson
Maintenance of database of healthy subjects: Michelle Stevenson, Kathy Schroer, Stacey Sellins
Maintenance of database of Allergy Clinic subjects: Emilie Grube
Data cleaning from Allergy Clinic database: Michelle Stevenson
Statistical analysis: Michelle Stevenson and Stacey Sellins
Manuscript writing: Michelle Stevenson
# TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>Section</th>
<th>Pages</th>
</tr>
</thead>
<tbody>
<tr>
<td>List of Tables and Figures</td>
<td>2</td>
</tr>
<tr>
<td>Introduction</td>
<td>3-5</td>
</tr>
<tr>
<td>Methods</td>
<td>5-9</td>
</tr>
<tr>
<td>Results</td>
<td>9-13</td>
</tr>
<tr>
<td>Discussion</td>
<td>13-17</td>
</tr>
<tr>
<td>Conclusion</td>
<td>17-18</td>
</tr>
<tr>
<td>Figure 1</td>
<td>19</td>
</tr>
<tr>
<td>Figure 2</td>
<td>19</td>
</tr>
<tr>
<td>Table 1</td>
<td>20</td>
</tr>
<tr>
<td>Table 2</td>
<td>20</td>
</tr>
<tr>
<td>Table 3</td>
<td>21</td>
</tr>
<tr>
<td>Table 4</td>
<td>21</td>
</tr>
<tr>
<td>Table 5</td>
<td>22</td>
</tr>
<tr>
<td>References</td>
<td>23-24</td>
</tr>
</tbody>
</table>
TABLES AND FIGURES

FIGURES

Figure 1 - Number and percentage of positive skin test responses

Figure 2 - Type of allergen response among children sensitized to at least one allergen

TABLES

Table 1 - Univariate analysis of subjects of African American or Caucasian ethnicity

Table 2 – Adjusted odds ratios for allergic sensitization

Table 3 - Linear regression estimates of atopy index adjusted for age and class of annual household income

Table 4 - PADQLQ results for healthy subjects

Table 5
  a - PADQLQ and Skin Prick Test correlation among subjects with allergic rhinitis
  b - PADQLQ and CHSA and PFT correlation among subjects with asthma
  c - PADQLQ and objective SCORAD correlation among subjects with atopic dermatitis
INTRODUCTION

Asthma is a major public health problem affecting 15 million people in the United States alone (1). Allergic sensitization, as defined by $\geq 1$ 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 symptoms or overt disease are not known (5).

Children have many exposures to aeroallergens important in respiratory health both inside home and school environments and outdoors during play and sporting activities. These allergens include dust mite, cockroach, molds, pollens, and pet dander. In order to adequately understand the role of environmental allergens in disease etiology, it is helpful to first understand the socioeconomic and ethnic contribution to allergic sensitization. Children who have evidence of exposure to allergens as manifested by at least one positive skin prick test and yet who are asymptomatic to date represent an important phenotypic group in the study of the continuum of the allergic phenotype.

Allergic disorders cause significant morbidity in an estimated 300 million adults and children worldwide (6). The prevalence of asthma varies from 2 to 32% across the globe (7) and is increasing (8). 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 (9). Further, data from the Third National Health and Nutrition Examination Survey (1994) demonstrates that African-American children are more likely to be sensitized to important indoor allergens than Caucasian children even after adjustment for socio-economic factors (10). Poverty increases the likelihood of sensitization to some allergens, such as cockroach (11). African
American race and poverty have been independently associated with sensitization to cockroach allergen among children with asthma (12). It has been shown that even asymptomatic children who are sensitized to allergens may demonstrate bronchial hyperresponsiveness, a key component of asthma (13-16).

Despite numerous environmental and genetic investigations, reasons for worldwide and racial variations in allergic sensitization and respiratory allergy remain poorly understood (17). 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 ethnic and socioeconomic correlates to sensitization to indoor and outdoor aeroallergens in children aged 6 to 16 years without reported allergic disease.

In order to verify that occult allergic disease does not significantly impact the study population’s quality of life, the Pediatric Allergic Disease Quality of Life Questionnaire (PADQLQ, Appendix 1) (18) was administered to subjects between the age of 6-16 years. This questionnaire has been validated against individual asthma, allergic rhinitis, and atopic dermatitis symptoms and quality of life instruments in the United Kingdom. Permission from the author was obtained to replace the word “troubled” with “bothered”, as it was felt that “bothered” would be better understood by children in the United States. A series of 26 questions is self-administered by children and uses 7 point Likert-type responses to yield scores with a range of 0 to 6. Higher scores indicate worsening allergy-related quality of life.

Due to the small sample size in the initial validation study, the authors of the PADQLQ recommend further validation in clinical research settings (18). To that end, the second purpose of this study is to further validate this instrument in the Allergy and Immunology Clinic against other outcome measures of allergic diseases. These include the Children’s Health Survey for
Asthma (19), a reliable functional outcome measure for children with asthma, pulmonary function tests, the number of allergens to which children with allergic rhinitis are sensitized, and the objective SCORAD (20), a validated severity scoring instrument for atopic dermatitis.

In summary, the aims of the study are therefore threefold:

**Specific Aim 1** To establish the relationship between asymptomatic sensitization to indoor and outdoor aeroallergens and 1) ethnicity and 2) socioeconomic status.

**Specific Aim 2** To establish that children with asymptomatic allergic sensitization have low allergy-related quality of life, as measured by the Pediatric Allergic Disease Quality of Life Questionnaire (PADQLQ, Appendix 1). Age, socioeconomic status, and gender will be examined as potential covariates.

**Specific Aim 3** To evaluate consistency of the Pediatric Allergic Disease Quality of Life Questionnaire (PADQLQ, Appendix 1) in a population of children aged 6 to 16 years with physician diagnosed asthma, allergic rhinitis, and atopic dermatitis.

**METHODS**

**Recruitment:** Children aged 2 to 18 years in this study were recruited as part of an ongoing case-control study regarding the genetics of asthma and allergy among children in the greater Cincinnati, Ohio area from January 2003 to May 2005. Asymptomatic children were enrolled at the Dental, Dermatology, Orthopedic or Neurology outpatient clinic sites at Cincinnati Children’s Hospital Medical Center. For the PADQLQ validation portion of the study, children with a physician diagnosis of asthma, allergic rhinitis, or atopic dermatitis, aged 6 to 16 years, were recruited from the Allergy and Immunology Clinics from September 2004 to May 2005.

Children with no personal or family history (parent or sibling) of either symptoms or diseases are eligible for the study. Eligible asymptomatic subjects were identified in the waiting
rooms of the above clinics using an Eligibility Screening Form and Control Data Form (Appendix 2) which, by parent report, establishes the absence of either diagnosed allergic diseases (asthma, allergic rhinitis, or atopic dermatitis), or symptoms of these diseases, either in the present or in the past in eligible children. Additional data regarding race, ethnicity, annual household income, type of health insurance, and parental education were also collected. Prior to enrollment, responses to these questions were verbally confirmed for each participant by the investigator who obtained informed consent.

**Sample size calculation:** Based upon a predicted ratio of 3:2 for healthy skin prick test (SPT) negative children to SPT+ asymptomatic subjects and a 1:1 ratio of African-American to Caucasian subjects, a sample size of 203 was required to detect a difference of 20% in the percentage of skin test positive patients between ethnic or socioeconomic groups, which was considered by the investigator to be clinically meaningful. Due to the demographics of Cincinnati, only a small percentage of Hispanic or other racial or ethnic groups was expected in the study population. Therefore, only differences between the Caucasian and African American populations were analyzed.

**Definitions of Allergic Sensitization:** Skin prick testing was performed using the GREERPick™ System as a prick test device (Greer Laboratories, Lenoir, North Carolina) on the volar aspect of the forearm in the absence of systemic antihistamines according to published guidelines. Sensitization was defined as present when the wheal of the allergen tested was greater than 3 mm and was also greater than the saline negative control. Tests were read at fifteen minutes after placement. Histatrol® (Center Laboratories, Port Washington, NY) 1 mg/mL was used as the positive control. Allergen panels were mixed by Hollister-Stier to include aeroallergens prevalent in the Ohio River Valley. Panels included mold mix (2), grass mix, ragweed (giant and
short), tree pollen mix (2), weed mix, dust mite (der f and der p), cat (fel d 1), dog (hair and dander), and cockroach (*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, and sensitization to any indoor allergen. The atopy index, a summary score of allergic sensitization (21) was utilized as a continuous variable.

**Validation of PADQLQ:** Children aged 6 to 16 years completed the PADQLQ during routine visits to the Allergy and Immunology Clinics as well as Dermatology Clinics. For subjects with a history of asthma, parents completed the Children’s Health Survey for Asthma, a validated parent-report functional outcome measure developed by the American Academy of Pediatrics (19). This instrument yields 5 quality of life scores regarding the physical health of the child, emotional health of the child and family, and activity of the child and family and has been shown to correlate with other measures of asthma status in low-income populations (22). Pulmonary function tests were also performed on subjects with asthma and interpreted according to published standardized criteria(23). The SCORAD, a validated a severity assessment of atopic dermatitis, was collected on each child with atopic dermatitis (20). Both the number of environmental allergens to which children were sensitized and the summary score for allergic response was calculated based upon skin prick test results and used to validate the allergic rhinitis component of the questionnaire. These variables were used to validate the PADQLQ.

**Data Analysis:** All statistical analysis was performed using SAS Version 8. Graphs and Tables were made in SPSS Version 13.0.

**Specific Aim 1** Univariate analysis using Chi-square was performed to examine for significant relationships between socioeconomic and ethnic factors and allergic sensitization using PROC FREQ. Those variables found to be significant were entered into a logistic regression model in
order to study ethnic and socioeconomic risk factors related to the probability of the occurrence of: 1) any allergic sensitization, 2) sensitization to any indoor allergen and 2) sensitization to any outdoor allergen. Factors determined significant in this model at a 0.05 statistically significant level were entered into a linear regression model using PROC REG in which the outcome variable will be the total atopy index based upon published methods (21) (a sum of the degree of positivity and total number of allergens to which the child is sensitized).

**Specific Aim 2** The PADQLQ scores were calculated according to published methods by obtaining a mean score which was calculated as the sum of all responses 0 to 6 and divided by the total number of items answered (18). Because the subjects enrolled in this portion of the study did not have allergic disease or asthma the last two questions (#25 and #26) were not included in the final scoring. Questions #25 asked subjects how bothered they were about feeling frightened by the thought of an asthma attack and was left blank by 22% of children completing the instrument. Question #26 asked children to think about how bothered they were by their allergies during recent activities and was not answered by 34% of children completing the instrument. The mean 24-item score in the children who have no personal family history of allergic sensitization but who are sensitized to an allergen was compared to the mean score of children in the validation arm of the study using PROC TTEST. Log transformations of the mean PADQLQ 24 item score plus a coefficient of 1 were investigated because the distributions were found to be non-normal.

**Specific Aim 3** For evaluation of internal consistency of the PADQLQ, the Cronbach α coefficient was calculated using PROC CORR to compare agreement between individual items in the PADQLQ. Cross sectional validity was assessed by comparing the PADQLQ total score and its disease component score (allergic rhinitis, asthma, or eczema) to the pertinent scores from
the other valid clinical assessment tools (% predicted FEV1, the physical health score of the Children’s Health Survey for Asthma, degree of skin prick test positivity, and the objective SCORAD) using PROC CORR to obtain Pearson correlation coefficients. When indicated, skin prick testing to allergens was collected as part of routine clinical care according to the methods described above. Skin prick test results, physician diagnoses, objective SCORAD, Children’s Health Survey for Asthma, and pulmonary function data were extracted from a larger allergy clinic research database, cleaned and merged with PADQLQ data. P values were modified for multiple testing using Bonferroni transformation in PROC MULTTEST.

RESULTS

As of June 2005, 275 children aged 18 years or less without a first degree family member with a history of allergic disease or asthma had been recruited. The Children’s Hospital Medical Center Dental Clinic served as the primary recruitment site for 93% of subjects. Approximately 57% of subjects were female. The child’s ethnicity 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%) or other ethnicity. Parents of 2 children (0.7%) did not provide ethnicity data. While 54% of children were of ages 6 to 11 years, 15% were of ages 2 to 5 years and the remainder (31%) was aged 12 to 18 years.

Approximately 93% of parents provided information regarding the type of health insurance coverage for the subject and 90% indicated their annual household income and level of mother’s education. The sample population was primarily of low socioeconomic status, with 72% of parents reporting less than $30,000 in annual household income and 76% receiving some form of public health insurance for their child. Approximately 45% of mothers had received some form of education beyond high school.
Figure 1 depicts the number of positive skin prick test panels. Despite having no personal or family history of allergic disease or symptoms, 39% of children were positive to at least one allergen panel tested. Strikingly, two-thirds of children (68%) who were sensitized to at least one allergen panel were positive to more than one allergen panel. Among children who were sensitized to any allergen tested, 54% were sensitized to the dust mite mix and 44% were sensitized to the Tree pollen panel #2. Figure 2 further depicts the percentage of children who were positive to each allergen panel among only children who were sensitized to any allergen (n=108).

Specific Aim 1 Due to the infrequency of ethnicities other than Caucasian or African American in the enrolled study group (6.2%), children from other ethnicities were not included in the univariate analysis and the regression model, resulting in a total sample size of 256. Table 1 depicts the results of the univariate analysis comparing class of subject age, sex, ethnicity, insurance status, class of annual household income, and class of maternal education to allergic sensitization (at least one positive skin prick test). Only class of subject age and ethnicity were significant in the univariate analysis. When age was treated as a continuous variable via student’s t-test, the difference in mean age between groups of sensitized and non-sensitized children was also significant (p=0.016). The mean age in the group of children without evidence of sensitization was 8.78 years and the mean age in the group of sensitized children was 9.87 years, with a mean difference of 1.09 years [95% CI, 0.21 to 1.97].

In the logistic regression model, increasing age was found to be significantly associated with allergic sensitization to any allergen panel and any indoor allergen panel (molds, cockroach, or dust mite). As shown in Table 2, African American ethnicity was significantly associated with allergic sensitization to any aeroallergen after adjustment for age. The magnitude of this
association was higher when sensitization to any outdoor allergen (tree pollens, ragweed, weed and grass pollens) was analyzed separately, with an increase in odds ratio from 2.18 to 2.69.

When the atopy index (total number of allergens out of eleven to which subjects had a positive response), was used as the outcome variable in a linear regression model, the strength of the association between African American ethnicity and increasing atopy index still held, even after adjustment for age and class of annual household income (p < 0.001) (Table 3).

Specific Aim 2 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 zero on the 24 item PADQLQ. Scores were overall very low, with 86% of scores falling below 1 and 97% of scores falling below 2. Because of the high degree of skewness observed in this data (3.71) and a large number of scores equaling zero, a coefficient of 1 was added to PADQLQ score and a log transformation was performed. This improved the skewness to 1.47. As shown in Table 3, there was no significant difference in mean PADQLQ score or log transformed mean PADQLQ score+1 (LOGPADQLQ+1) between subjects who were positive to any allergen panel and subjects who were negative to all allergens.

Specific Aim 3 A total of 167 PADQLQ instruments were completed among subjects in the Allergy or Dermatology Clinics for PADQLQ evaluation. Twenty-one of these were completed by subjects during more than one visit. For the 26 item questionnaire, Cronbach’s alpha measuring internal consistency was 0.92 for the 167 subjects in the Allergy or Dermatology Clinics. When combined with the 131 instruments from healthy subjects, Cronbach’s alpha was 0.96. The original authors of the instrument also computed practical problem, symptoms, and emotion domain scores. The Cronbach’s alpha coefficients for these domains for all 298 subjects were 0.83, 0.94, and 0.74 respectively.
Cross-sectional consistency was assessed by calculating the Pearson correlation coefficients between 1) the total PADQLQ score and 2) the PADQLQ allergic rhinitis subscore which was calculated as the mean score of the 4 questions pertaining to nasal symptoms with 3) the total number of positive skin tests and 4) the mean of the degree of positiviy (scale 0-4). This was performed on a subset of 56 patients who had a complete 11 panel set of allergens tested with a physician diagnosis of allergic rhinitis. Table 5a shows these results after Bonferroni correction for multiple testing.

Cross sectional consistency was further assessed by comparing the PADQLQ total score and asthma subscore with the physical health score of the Children’s Health Survey for Asthma (CHSA). This was performed on data from 120 subjects with a physician diagnosis of asthma who completed the PADQLQ and whose parents had completed the CHSA. These results are shown in Table 5b with the Bonferroni correction and demonstrate a high degree of negative correlation between the PADQLQ total and asthma subscores and physical functioning. Higher scores for the CHSA indicate better functioning, whereas higher PADQLQ scores indicate poorer allergic disease related quality of life. Table 5b also depicts the Pearson correlation coefficients for the percent predicted FEV1 and the percent predicted of the ratio of FEV1/FVC the PADQLQ total score and asthma subscore. This was performed using data from 71 patients who had pulmonary function testing performed at any time as part of their Allergy Clinic evaluation. Although there was significant correlation between the parent reported physical function score of the CHSA and the PADQLQ and asthma subscore, there were no significant correlations between pulmonary function tests and the PADQLQ. Table 5c shows the results for the correlation between the objective SCORAD and the total PADQLQ score and the atopic dermatitis domain score. Higher scores in the objective SCORAD indicate worsening objective
skin disease in patients with atopic dermatitis. Twenty two patients with atopic dermatitis completed the PADQLQ and had the objective SCORAD assessed. Again, while there is no significant correlation with the total PADQLQ and the objective SCORAD, there is a significant negative correlation between the atopic dermatitis subscore of the PADQLQ and the objective SCORAD.

**DISCUSSION**

The objective of this study was to determine ethnic and socioeconomic correlates to sensitization to indoor and outdoor aeroallergens in children aged 6 to 16 years without reported allergic disease. We demonstrated a high degree (39%) of allergic sensitization among children with no previous history or 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. In this study, African-American children were significantly more likely to be sensitized than Caucasian children to any allergen. This association held true in regression models adjusting for age and annual household income. These data are consistent with other population based studies regarding ethnicity 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 (24). In contrast, a study of NHANES III (1988-1994) data showed that 54.3% of the population aged 6 to 59 years were sensitized to at least one of ten allergens (25). Further, non-Hispanic blacks were significantly more likely than non-Hispanic whites to have a positive skin test response to seven of the ten allergens tested.
Another study of NHANES III data utilized multivariate models to demonstrated 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 (10). 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) (10).

NHANES data is representative of the entire population, including those with asthma, allergic rhinitis, and atopic dermatitis. Allergic rhinitis is the most common chronic disease in children (26) and 12% of children in the United States have ever been diagnosed with asthma (9) and children with these diagnoses were represented in the study of NHANES data (25). Our subjects have no history or recent 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 which suggest a genetic basis for racial differences in susceptibility to allergic diseases such as asthma (27).

Two other studies have suggested that African American children are more likely to be sensitized to outdoor allergens than Caucasian children (28, 29). One study was performed only in children with asthma, which showed strong association with African American ethnicity and sensitization to mixed tree pollen, mixed grass pollen, ragweed and mugwort/sage, even after adjustment for confounders such as area of residence and heath insurance type (28). 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 (29). Our study is the first to describe the high prevalence of allergic sensitization in children without a personal or family history of allergic disorder and demonstrate a predisposition for sensitization among African American children in the same group.

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 even among children who never had a history of asthma, wheeze or hay fever has been described (14). 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 (30). The incidence of new atopic disorders among children who are asymptomatic but show evidence of allergic sensitization is currently unknown.

In this study, the Pediatric Allergic Disease Quality of Life Questionnaire (PADQLQ) was used to assess possible subclinical effects of allergic symptoms among subjects. The PADQLQ is unique in that it encompasses changes in quality of life related to all allergic diseases including asthma, allergic rhinitis, and atopic dermatitis. When this survey was administered to subjects with no personal or family history of allergic disease, there was no significant difference in the mean of log transformed scores between children who were sensitized and those who were not sensitized to allergens. Further, 86% of the study population had scores less than one on a zero to six scale. These results demonstrate that study subjects were not experiencing important subclinical or underreported allergic symptoms.
Additional evaluation of the PADQLQ was undertaken as recommended by the authors in the initial publication (18). Internal consistency, as measured by cronbach’s alpha, was similar to values previously reported (18). In patients with asthma, allergic rhinitis, or atopic dermatitis, the PADQLQ total score correlated most closely with the Children’s Health Survey for Asthma physical function score. The Children’s Health Survey for Asthma is administered to the parent, while the PADQLQ is administered to the child. This study demonstrates that the PADQLQ may be a good indicator of disease related quality of life in children with asthma. Interestingly, only FEV1/FVC had a weak inverse correlation with the asthma subscore which was not statistically significant. Percent predicted FEV1 had no correlation with total PADQLQ or the asthma subscore. These results may be significantly influenced by the fact that not all pulmonary function tests were performed at the same time as the PADQLQ. FEV1 is known to change with medication use and clinical status, and this may have affected our results. However, other adult (31) and pediatric (22, 32-34) studies have also found minimal correlation with other asthma quality of life measures and pulmonary function tests. Multiple important clinical outcomes including both objective assessments of lung function and quality of life are recommended for pediatric asthma outcomes research (35).

The total degree of allergen sensitization was also not significantly correlated to the total PADQLQ score. Again, this may have been due to the fact that the skin prick tests were not always performed on the same day as the PADQLQ. However, skin prick test results are less likely than pulmonary function tests to change with time or therapy. The allergic rhinitis subscore, however, was modestly correlated to the total number of positive skin prick tests and the total SPT score. A similar pattern was noted with the objective SCORAD, in that the total PADQLQ score was not correlated to the objective SCORAD but it’s correlation to the atopic
dermatitis subscore was significant. Additional factors besides degree of atopy as measured by skin prick tests or objective measures of skin disease are therefore important in determining a child’s total allergic disease quality of life. Some of those factors might include the degree of control of allergic inflammation or current exposure to relevant allergens. Indeed, Roberts, et al, has recently shown that the PADQLQ score in children is significantly correlated with both the pollen count in the previous week and fractional exhaled nitric oxide levels (36).

CONCLUSIONS

These data add to the growing body of literature (25) which suggests that a high proportion of children in a predominantly low income group are sensitized to important allergens. Our study is the first to show that this is also true even among children who do not have a personal or family history of asthma, allergic rhinitis, or conjunctivitis, and who have no evidence of current subtle effects from this sensitization on allergic-disease related quality of life. The prognosis of this sensitization is unclear. However, this group of asymptomatic sensitized children is important to include in future studies. Evaluation of these children may elucidate protective mechanisms that prevent expression of allergic disease which may serve as important therapeutic targets.

Our study also demonstrates that even asymptomatic African American children are more likely than Caucasian children to be sensitized to important aeroallergens. This study’s data does not suggest that this has an environmental etiology since the relationship is more pronounced for sensitization to outdoor allergens.

Finally, the Pediatric Allergic Disease Quality of Life Questionnaire has been shown to have excellent consistency and correlates significantly with asthma-related quality of life as
measured by the Children’s Health Survey for Asthma. The individual disease subscores correlate modestly with other important allergic disease measures such as the objective SCORAD and degree of allergy as measured by total number of skin tests. This adds additional support to the utility of this instrument in assessing the quality of life of children with asthma, allergic rhinitis and atopic dermatitis.
Figure 1. Number and percentage of positive skin tests (n=275)

Number of Positive Skin Tests (n=275)
- None (60.7%)
- 1 (12.7%)
- 2 (10.5%)
- 3 (4.4%)
- 4 (3.3%)
- 5 (2.9%)
- 6 (2.9%)
- 7 (1.8%)
- 8 (0.4%)
- 10 (0.4%)

Figure 2. Type of allergen response among children sensitized to at least one allergen (n=108)

% positive to individual allergen panel
Table 1. Univariate analysis of subjects of African American or Caucasian ethnicity (n=256)

<table>
<thead>
<tr>
<th>Class Age</th>
<th>number</th>
<th>Total % of sample</th>
<th>at least one positive skin prick test (%)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-5 years</td>
<td>256</td>
<td>14.5</td>
<td>13.5</td>
<td>0.003</td>
</tr>
<tr>
<td>6-11 years</td>
<td></td>
<td>55</td>
<td>41.8</td>
<td></td>
</tr>
<tr>
<td>12-17 years</td>
<td></td>
<td>30.5</td>
<td>44.9</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td>0.56</td>
</tr>
<tr>
<td>Female</td>
<td>256</td>
<td>57.8</td>
<td>37.2</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td></td>
<td>42.2</td>
<td>40.7</td>
<td></td>
</tr>
<tr>
<td>Ethnicity (%)</td>
<td></td>
<td></td>
<td></td>
<td>0.003</td>
</tr>
<tr>
<td>Caucasian</td>
<td>256</td>
<td>51.2</td>
<td>29.8</td>
<td></td>
</tr>
<tr>
<td>African American</td>
<td></td>
<td>48.8</td>
<td>48</td>
<td></td>
</tr>
<tr>
<td>Insurance Status</td>
<td></td>
<td></td>
<td></td>
<td>0.78</td>
</tr>
<tr>
<td>Public or self pay</td>
<td>238</td>
<td>74.4</td>
<td>37.3</td>
<td></td>
</tr>
<tr>
<td>Private</td>
<td></td>
<td>25.6</td>
<td>39.3</td>
<td></td>
</tr>
<tr>
<td>Annual Household Income</td>
<td></td>
<td></td>
<td></td>
<td>0.52</td>
</tr>
<tr>
<td>&lt;$30,000</td>
<td>229</td>
<td>71.6</td>
<td>35.4</td>
<td></td>
</tr>
<tr>
<td>≥$30,000</td>
<td></td>
<td>28.4</td>
<td>40</td>
<td></td>
</tr>
<tr>
<td>Mother's Education</td>
<td></td>
<td></td>
<td></td>
<td>0.24</td>
</tr>
<tr>
<td>≤ High School Graduate</td>
<td>231</td>
<td>55.4</td>
<td>35.2</td>
<td></td>
</tr>
<tr>
<td>&gt; High School Graduate</td>
<td></td>
<td>44.6</td>
<td>42.7</td>
<td></td>
</tr>
</tbody>
</table>

Table 2. Adjusted odds ratios for allergic sensitization

Outcome variable = allergic sensitization to **any allergen**

<table>
<thead>
<tr>
<th>Variable</th>
<th>β</th>
<th>SE</th>
<th>Odds Ratio [95% CI]</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethnicity (Caucasian = reference group)</td>
<td>0.78</td>
<td>0.27</td>
<td>2.18 [1.3, 3.66]</td>
<td>0.003</td>
</tr>
<tr>
<td>Age</td>
<td>0.09</td>
<td>0.04</td>
<td>1.09 [1.02, 1.18]</td>
<td>0.02</td>
</tr>
</tbody>
</table>

Outcome variable = allergic sensitization to **any indoor allergen**

<table>
<thead>
<tr>
<th>Variable</th>
<th>β</th>
<th>SE</th>
<th>Odds Ratio [95% CI]</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethnicity (Caucasian = reference group)</td>
<td>0.53</td>
<td>0.29</td>
<td>1.7 [0.97, 2.97]</td>
<td>0.06</td>
</tr>
<tr>
<td>Age</td>
<td>0.11</td>
<td>0.04</td>
<td>1.12 [1.03, 1.21]</td>
<td>0.007</td>
</tr>
</tbody>
</table>

Outcome variable = allergic sensitization to **any outdoor allergen**

<table>
<thead>
<tr>
<th>Variable</th>
<th>β</th>
<th>SE</th>
<th>Odds Ratio [95% CI]</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethnicity (Caucasian = reference group)</td>
<td>0.99</td>
<td>0.3</td>
<td>2.69 [1.49, 4.86]</td>
<td>0.001</td>
</tr>
<tr>
<td>Age</td>
<td>0.08</td>
<td>0.04</td>
<td>1.08 [0.997, 1.18]</td>
<td>0.06</td>
</tr>
</tbody>
</table>
Table 3. Linear regression estimates of atopy index adjusted for age and class of annual household income

Outcome variable = atopy index

<table>
<thead>
<tr>
<th>Variable</th>
<th>β</th>
<th>SE</th>
<th>95% CI for β</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethnicity (Caucasian = reference group)</td>
<td>0.87</td>
<td>0.22</td>
<td>[0.44, 1.30]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age</td>
<td>0.07</td>
<td>0.03</td>
<td>[0.01, 0.13]</td>
<td>0.03</td>
</tr>
<tr>
<td>Class of Annual Household Income</td>
<td>0.25</td>
<td>0.18</td>
<td>[-0.12, 0.61]</td>
<td>0.18</td>
</tr>
</tbody>
</table>

Table 4. PADQLQ results for healthy subjects

PADQLQ Scores (Scale = 0 to 6, higher numbers = worsening allergic symptoms)

<table>
<thead>
<tr>
<th>Allergic Status</th>
<th>n</th>
<th>Mean</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>No allergic sensitization</td>
<td>77</td>
<td>0.55</td>
<td>0.72</td>
</tr>
<tr>
<td>Sensitization to at least one allergen</td>
<td>53</td>
<td>0.53</td>
<td>0.6</td>
</tr>
</tbody>
</table>

Mean difference = 0.02, 95% CI [-0.21, 0.26]

LOGPADQLQ+1

<table>
<thead>
<tr>
<th>Allergic Status</th>
<th>n</th>
<th>Mean</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>No allergic sensitization</td>
<td>77</td>
<td>0.164</td>
<td>0.14</td>
</tr>
<tr>
<td>Sensitization to at least one allergen</td>
<td>53</td>
<td>0.159</td>
<td>0.14</td>
</tr>
</tbody>
</table>

Mean difference = 0.005, 95% CI [-0.04, 0.05]
Table 5.

a) PADQLQ and Skin Prick Test correlation among subjects with allergic rhinitis

<table>
<thead>
<tr>
<th>Total Number of Positive SPTs</th>
<th>Mean SPT Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>n 56</td>
<td>56</td>
</tr>
<tr>
<td>PADQLQ (total) 0.125</td>
<td>0.149</td>
</tr>
<tr>
<td>Allergic Rhinitis Subscore 0.370*</td>
<td>0.367*</td>
</tr>
</tbody>
</table>

Pearson correlation coefficients, * p<0.05 modified with the Bonferroni transformation

b) PADQLQ and CHSA and PFT correlation among subjects with asthma

<table>
<thead>
<tr>
<th>Physical Health</th>
<th>% Predicted</th>
<th>Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHSA</td>
<td>FEV1</td>
<td>FEV1/FVC</td>
</tr>
<tr>
<td>n 120</td>
<td>71</td>
<td>71</td>
</tr>
<tr>
<td>PADQLQ (total) -0.623 ***</td>
<td>-0.007</td>
<td>-0.166</td>
</tr>
<tr>
<td>Asthma Subscore -0.623 ***</td>
<td>-0.057</td>
<td>-0.231</td>
</tr>
</tbody>
</table>

Pearson correlation coefficients, *** p<0.001 modified with the Bonferroni transformation

c) PADQLQ and objective SCORAD correlation among subjects with atopic dermatitis

<table>
<thead>
<tr>
<th>SCORAD</th>
</tr>
</thead>
<tbody>
<tr>
<td>n 22</td>
</tr>
<tr>
<td>PADQLQ (total) 0.198</td>
</tr>
<tr>
<td>Atopic Dermatitis Subscore 0.693***</td>
</tr>
</tbody>
</table>

Pearson correlation coefficients, *** p<0.001 modified with the Bonferroni transformation
REFERENCES