Morbidity in children with moderate-to-severe asthma. Thus far, there are no compelling candidates. The disease that will more favorably alter the course of childhood and adulthood. It remains to be seen whether there is any sort of intervention at a very early phase in childhood and adulthood. The prognosis of childhood allergic asthma is largely determined early in life. The degree of atopy seems to be a critical determinant of asthma persistence.

RESULTS. Thirteen (15.3%) of these young adults, aged 17 to 30 years, were in remission. Another 19 (22%) had only mild intermittent asthma. There were 12 (14%) with mild persistent asthma, 25 (29%) with moderate persistent asthma, and 16 (19%) with severe persistent disease. Subjects in remission, compared with subjects with mild intermittent or persistent asthma, had lower serum immunoglobulin E in childhood (412 vs 1136 vs 968 ng/mL, respectively) and fewer positive allergy skin tests (7 vs 9 vs 10, respectively, from a panel of 18 allergens). Subjects in remission also had milder childhood asthma, indicated by lower average daily medication usage scores and lower percentage of days on inhaled corticosteroids (13.7% vs 24.7% vs 40.9%). There was no association found between current asthma severity and childhood immunotherapy.

CONCLUSIONS. The prognosis of childhood allergic asthma in adulthood is largely determined early in life. The degree of atopy seems to be a critical determinant of asthma persistence.

REVIEWER COMMENTS. The authors point out that numerous studies of the natural history of asthma have suggested associations between childhood atopy and disease severity with risk of asthma persistence and severity in later childhood and adulthood. It remains to be seen whether there is any sort of intervention at a very early phase in the disease that will more favorably alter the course of asthma. Thus far, there are no compelling candidates.

METHODS. Eighty-five of the original subjects participated in the adult evaluation, underwent spirometry and inhalant allergy skin testing, and completed questionnaires regarding their interim medical history, asthma symptoms, and medications. Asthma severity was classified by using a modified version of the 1997 National Asthma Education and Prevention Program algorithm. Postbronchodilator spirometry was used for severity categorization. Subjects were categorized in the most severe category for which they qualified.

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Timothy Andrews, MD
James R. Banks, MD
Arnold, MD

ALLERGENS AND ENVIRONMENTAL EXPOSURES

Inner City Asthma Study: Relationships Among Sensitivity, Allergen Exposure, and Asthma Morbidity


PURPOSE OF THE STUDY. To describe the relationship between allergen sensitivities, allergen exposures, and asthma morbidity in children with moderate-to-severe asthma while also exploring geographic variations in indoor allergen levels.

STUDY POPULATION. Subjects were children aged 5 to 11 years (n = 937) from 7 inner-city and metropolitan areas across the United States participating in the Inner City Asthma Study.

METHODS. In a fully crossed factorial design, participants were randomly assigned to receive an allergen intervention, bimonthly feedback of the child’s health status to their primary care physicians, both interventions, or no intervention (control group, n = 234). At baseline, a clinical interview with the child’s primary caregiver (including demographics, asthma morbidity, home characteristics, and exposure to tobacco smoke) was conducted with skin-prick tests to aeroallergens. Morbidity was measured at 2-month intervals during a 24-month period. Home visits including a visual inspection and dust sample collection (dust mite, cockroach, cat and dog dander) were conducted at baseline and every 6 months.

RESULTS. Of 1059 children tested, 94% had at least 1 positive skin test. Allergen sensitivities varied widely across the study sites, with cockroach (69%), dust mites (62%), and molds (50%) being the most predominant. Cockroach sensitivity was highest in The Bronx, New York, New York City, New York, and Dallas, Texas (81%, 79%, and 79%, respectively), whereas dust mite sensitivities were highest in Dallas and Seattle, Washington (84% and 78%, respectively). At least 30% of the subjects were allergic to cats at all sites. Cockroach levels were highest (>50% of homes) in Chicago, Illinois, New York City, The Bronx, and Dallas and were lower in Seattle and Tucson, Arizona (8% and 11% of homes, respectively). Dust mite levels were highest in Seattle and Dallas. Cockroach levels were higher in high-rise and low-rise apartments, whereas dust mite levels were higher in detached homes. No correlation was seen between animal dander and housing type.

CONCLUSIONS. There were significant differences between geographic study sites and the type of indoor allergen exposure and skin-test sensitivity in this study group. Cockroach predominated in the Northeast, whereas dust mite predominated in the South and Northwest. Although most children in the study were allergic to dust mite and/or cockroaches, only the children who were sensitive and exposed to cockroach had increased asthma morbidity.

REVIEWER COMMENTS. This study demonstrates the association of allergen sensitivities and exposures (particularly cockroach allergens) to increased asthma morbidity in children with moderate-to-severe asthma living in inner-city areas. Physicians can use this knowledge to identify significant risk factors in asthmatic patients, implement appropriate prevention measures (ie, environ-
moral intervention), and more aggressive medical management to decrease the level of asthma morbidity.

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Michael Le Bras, DO
Stacie M. Jones, MD
Little Rock, AR

Initial High-Dose Nasal Allergen Exposure Prevents Allergic Sensitization to a Neoantigen

PURPOSE OF THE STUDY. Epidemiologic studies have suggested that high-dose allergen exposure may protect against primary allergic sensitization—the formation of immunoglobulin E (IgE) after initial antigen exposure. This study uses a human nasal allergic sensitization model to evaluate the effect of the dose of the antigen on the rate of primary sensitization to a neoantigen, keyhole limpet hemocyanin (KLH).

STUDY POPULATION. Fifty-one healthy nonsmoking atopic subjects aged 18 to 55 years. Atopic status was defined by a positive skin-prick test to at least one Aeroallergen; the subjects therefore had a propensity to mount an allergic (IgE) response to respiratory antigen exposure.

METHODS. Subjects underwent a 33-day sensitization protocol including initial exposure to 0.1-, 10-, 1000-, or 100 000-µg doses of intranasal KLH as well as later exposure to adjuvant intranasal diesel exhaust particles. At the conclusion of protocol, antigen-specific IgE, IgG, and IgG4 were measured in nasal lavage samples.

RESULTS. The rates of allergic sensitization, defined as detectable KLH-specific IgE, for the 0.1-, 10-, 1000-, or 100 000-µg dose groups were 0, 100, 57, and 11%, respectively. Furthermore, the mean KLH-specific IgE levels decreased with increasing doses of initial antigen exposure. Antigen-specific IgG and IgG4 were produced by all subjects, with the highest levels observed in the high-dose group.

CONCLUSIONS. Initial high levels of respiratory antigen exposure may prevent primary allergic sensitization through induction of an antigen-specific non-IgE humoral immune response.

REVIEWER COMMENTS. In children at high risk of allergic sensitization, a means of preventing primary sensitization and inducing durable allergic tolerance would be of great value. This study found that initial high-dose exposure to a neoantigen, KLH, results in a humoral immune response with high levels of antigen-specific IgG, including IgG4, and low levels of KLH-specific IgE. Whether these findings apply to other respiratory antigens remains unclear. The mechanism underlying this induction of tolerance remains unclear, and it is also not known whether this immune response represents durable allergic tolerance. Future studies investigating these issues are needed to move toward potential primary prevention therapy for allergic disease.

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Hemant Sharma, MD
Elizabeth Matsui, MD
Baltimore, MD

FOOD ALLERGY

The Natural History of Tree Nut Allergy

PURPOSE OF THE STUDY. To estimate the proportion of children who outgrow tree nut (TN) allergy and examine predictors of outgrowing it.

STUDY POPULATION. All children with TN allergy followed at the authors’ pediatric allergy clinic.

METHODS. Patients with TN allergy, defined as a history of reaction on ingestion and evidence of TN-specific immunoglobulin E (TN-IgE) or positive TN-specific IgE level but no history of ingestion, were evaluated. If all current TN-IgE levels were <10 kU/L of antibody (kU/L), double-blind, placebo-controlled food challenges were offered. Patients who had undergone open oral TN challenges as part of routine clinical care were also included.

RESULTS. Two hundred seventy-eight patients with TN allergy were identified. One hundred one (36%) had a history of acute reactions, 12 (12%) of whom had reactions to multiple TNs and 73 (63%) of whom had a history of moderate-to-severe reactions. Nine of 20 patients who had previously reacted to a TN passed challenges, so that 9 (8.9%; 95% confidence interval: 4%–16%) of 101 patients with a history of previous TN reactions outgrew TN allergy. Of 19 patients who had never ingested TNs but had detectable TN-specific IgE levels, 14 passed challenges. One hundred sixty-one did not meet the challenge criteria, and 78 met the criteria but declined challenges. Looking at specific TN-IgE values, 58% with TN-IgE levels of ≤5 kU/L and 63% with TN-IgE levels of ≤2 kU/L passed challenges.

CONCLUSIONS. Approximately 9% of patients outgrow TN allergy, including some who had previous severe reactions. Although ideal cutoffs for challenge cannot be firmly recommended on the basis of these data, patients aged 4 years or older with all TN-IgE levels of ≤5 kU/L should be considered for physician-supervised oral food challenges.

REVIEWER COMMENTS. This is the first study to comprehensively address the natural history of TN allergy. Although
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