Published in final edited form as:

Allergy. 2010 November ; 65(11): 1414–1422. doi:10.1111/j.1398-9995.2010.02412.x.

Allergen-specific IgE as a biomarker of exposure plus sensitization in inner-city adolescents with asthma

E. C. Matsui¹, H. A. Sampson², H. T. Bahnson³, R. S. Gruchalla⁴, J. A. Pongracic⁵, S. J. Teach⁶, P. J. Gergen⁷, G. R. Bloomberg⁸, J. F. Chmiel⁹, A. H. Liu¹⁰, M. Kattan¹¹, C. A. Sorkness¹², S. F. Steinbach¹³, R. E. Story⁵, C. M. Visness³, and behalf of the Inner-city Asthma Consortium

¹Johns Hopkins University School of Medicine, Baltimore, MD

²Mount Sinai School of Medicine, New York, NY

³Rho Federal Systems Division, Inc., Chapel Hill, NC

⁴University of Texas Southwestern Medical Center, Dallas, TX

⁵Children's Memorial Hospital, Chicago, IL

⁶Children's National Medical Center, Washington, DC

⁷Division of Allergy, Immunology, and Transplantation – NIH, Bethesda, MD

⁸Washington University School of Medicine, St. Louis, MO

⁹Rainbow Babies and Children's Hospital, Cleveland, OH

¹⁰National Jewish Health and University of Colorado Denver School of Medicine, Denver, CO

¹¹Columbia University College of Physicians and Surgeons, New York, NY

¹²University of Wisconsin School of Medicine and Public Health, Madison, WI

¹³Boston University School of Medicine, Boston, MA, USA

Abstract

Background—Relationships among allergen-specific IgE levels, allergen exposure and asthma severity are poorly understood since sensitization has previously been evaluated as a dichotomous, rather than continuous characteristic.

Methods—Five hundred and forty-six inner-city adolescents enrolled in the Asthma Control Evaluation study underwent exhaled nitric oxide (FE_{NO}) measurement, lung function testing, and completion of a questionnaire. Allergen-specific IgE levels and blood eosinophils were quantified. Dust samples were collected from the participants' bedrooms for quantification of allergen concentrations. Participants were followed for 12 months and clinical outcomes were tracked.

Results—Among sensitized participants, allergen-specific IgE levels were correlated with the corresponding settled dust allergen levels for cockroach, dust mite, and mouse ($r = 0.38, 0.34, 0.19$, respectively; $P < 0.0001$ for cockroach and dust mite and $P = 0.03$ for mouse), but not cat ($r = 0.02, P = 0.71$). Higher cockroach-, mite-, mouse-, and cat-specific IgE levels were associated

with higher FE_{NO} concentrations, poorer lung function, and higher blood eosinophils. Higher cat, dust mite, and mouse allergen-specific IgE levels were also associated with an increasing risk of exacerbations or hospitalization.

Conclusions—Allergen-specific IgE levels were correlated with allergen exposure among sensitized participants, except for cat. Allergen-specific IgE levels were also associated with more severe asthma across a range of clinical and biologic markers. Adjusting for exposure did not provide additional predictive value, suggesting that higher allergen-specific IgE levels may be indicative of both higher exposure and a greater degree of sensitization, which in turn may result in greater asthma severity.

Keywords

allergen exposure; allergen-specific IgE; biomarker; childhood asthma; Inner-city Asthma Consortium

Although there has been a reduction in asthma morbidity in the US overall, there has been little improvement in asthma morbidity among urban minority populations (1). Indoor allergens likely contribute to this disparity in asthma morbidity as exposure to certain allergens, such as cockroach, mouse, dust mite and cat; have been linked to worse asthma outcomes in inner-city children with asthma. Specifically, numerous studies have shown that among sensitized inner-city children, exposure to a high level of the corresponding allergen, defined as a level above a particular cut point, is associated with worse asthma (2–5).

Findings from these studies suggest that knowledge of both allergen sensitization and exposure status is important in gauging a child's risk for future exacerbations and for making recommendations regarding environmental control practices. Although sensitization status is routinely assessed by allergen-specific IgE levels or skin testing, assessment of allergen exposure in clinical practice is generally limited to patient reports because collection of a settled dust sample from patients' homes for allergen quantification is not practical. Sensitization is also routinely characterized as being present or absent (i.e. detectable vs. undetectable allergen-specific IgE), and more information may be available by using the continuous allergen-specific IgE measure. A more practical approach to estimating exposure, along with sensitization, could provide important information regarding a patient's relevant allergen exposures, and therefore provide insight into the causes of poor asthma control and the risk of future exacerbations in an individual patient. An understanding of both sensitization and exposure status could also guide environmental control practice recommendations.

We proposed a model in which allergen exposure drives allergen-specific IgE levels among individuals who are already sensitized. Under this model, we would expect that higher allergen-specific IgE levels would be associated with worse asthma health, independent of specific exposure measurements, since exposure is accounted for by the concentration of allergen-specific IgE. Specifically, we hypothesized that indoor allergen-specific IgE levels would be correlated with indoor allergen exposure among sensitized patients, and that specific IgE levels, as a measure for the combination of sensitization and exposure, would be related to asthma severity/control. We tested these hypotheses among inner-city adolescents with moderate to severe asthma enrolled in the Asthma Control Evaluation (ACE) study, a randomized, controlled trial utilizing the addition of (eNO) measurements to guidelines-based asthma care.

Methods

Details of the ACE study have been previously published (6). Briefly, a total of 546 participants, aged 12–20 years, with a physician diagnosis of asthma were enrolled at ten centers. Eligibility was limited to residents of urban census tracts in which at least 20% of households had incomes below the federal poverty threshold. Individuals receiving long-term controller therapy were required to have symptoms of persistent asthma or evidence of uncontrolled disease. Individuals not receiving long-term control therapy were required to have both symptoms of persistent asthma and evidence of uncontrolled disease defined by NAEPP guidelines (7, 8). The protocol was approved by all institutional review boards.

Study design

The ACE study was a randomized, double-blind, parallel-group trial with a 3-week run-in to characterize participants, establish treatment, and evaluate adherence. At the recruitment visit, symptoms, rescue medication use, pulmonary function, and adherence were used to assign a medication regimen based upon standardized treatment guidelines across sites. A home visit was conducted for dust sample collection and environmental evaluation after the recruitment visit. Participants returned after run in for the randomization visit. Skin testing to a panel of 14 aeroallergens (*Alternaria*, *Aspergillus*, cat, *Cladosporium*, cockroach mix, *Dermatophagoides farinae*, *Dermatophagoides pteronyssinus*, dog, German cockroach, mouse, *Penicillium*, ragweed mix, rat, and timothy grass) was performed at this visit using methods described previously (6). After run-in, subjects were randomly assigned to either a Reference Group (pharmaco-therapy titrated according to NAEPP guidelines) or the Fractional exhaled nitric oxide concentration (FE_{NO}) Group (pharmacotherapy titrated according to NAEPP guidelines as well as the fraction of eNO) at the randomization visit. Treatment recommendations were derived from protocol-defined treatment steps based on asthma control and adherence (6). FE_{NO} was measured (flow rate 50 ml/s) with a rapid-response chemiluminescent analyzer (NIOXTM System, Aerocrine, Sweden) following American Thoracic Society guidelines (9). Following the recruitment and randomization visits, participants made 6 clinic visits approximately 2 months apart for 1 year.

Biomarker, allergen-specific IgE, and allergen exposure data were collected once at the beginning of the study, either during the recruitment or the randomization visit. For the purposes of this report, these time points are considered baseline measurements. Data on exacerbations, hospitalization, and lung function are analyzed from both the recruitment visit and throughout the 1 year follow-up period.

Dust allergen collection and analysis

A vacuumed dust sample was collected from each participant's bed and bedroom floor following a standard protocol. Protein was extracted from the dust samples using standardized methods, and the samples were assayed for cockroach (*Bla g 2*), dust mites (*Der f 1* and *Der p 1*), cat (*Fel d 1*), and mouse (*Mus m 1*) allergens by ELISA (10–12).

Serum markers of allergy

At baseline, a blood sample was obtained from all study participants for measurement of allergen-specific IgE to cockroach (*Blatella germanica*), dust mites (*D. farinae* and *D. pteronyssinus*), cat (cat epithelium and dander), and mouse (mouse urine). Serum IgE was measured with the Immuno-CAP System® (Phadia; Uppsala, Sweden) in a central laboratory (Mount Sinai School of Medicine). The limit of detection was 0.10 kU_A/l and a level <0.10 kU_A/l was assigned a value of 0.05 kU_A/l for analyses. The sum of the specific IgE levels was calculated by summing the specific IgE levels for cockroach, cat, mouse, and

the maximum of the two dust mite species. Determination of total blood eosino-phil counts was performed by local clinical laboratories.

Spirometry

Spirometry was performed by certified technicians, according to American Thoracic Society standards (13), using a Jaeger Masterscreen (VIASYS Healthcare GmbH; Hoechberg, FRG).

Clinical outcomes

At recruitment, a standardized questionnaire was administered to ascertain the number of exacerbations and hospitalizations during the previous year. An exacerbation was defined as one or more of the following: hospitalization; prednisone course for asthma; or an unscheduled visit to an emergency department, urgent care facility, or physician's office or clinic. In addition, data on these same clinical outcomes were collected throughout the study. Since these events were rare, each subject was classified as to the presence or absence of these events during the 12-month follow-up period.

Statistical methods

As a first step in testing the hypothesis that the allergenspecific IgE level is a composite marker of both sensitization and allergen exposure, and therefore would be correlated with inflammatory, physiologic and clinical outcomes, we used an analytic approach taken in previous studies (2–5). Participants were stratified based on sensitization and exposure status, and the stratum that was both sensitized and exposed to the allergen tended to have more peripheral blood eosinophils and higher FE_{NO} concentrations, and was also at increased risk for exacerbations or hospitalizations (see Supporting Information).

After confirming that the combination of sensitization and exposure was associated with poorer outcomes in this population, we then examined the relationship between allergenspecific IgE concentrations and allergen levels and the relationship between allergen-specific IgE concentrations and the inflammatory, physiologic, and clinical outcomes.

The correlation between allergen-specific IgE measures and the corresponding settled dust allergen concentrations were analyzed using partial Pearson correlations. Partial correlations allow the strength of a relationship between two variables to be assessed, while controlling for the effect of other variables. The partial Pearson correlations were controlled for the effect of gender, age, race, study group and income above \$15 000 per year. We assessed linearity and normality of these data and subsequently performed log base 10 transformations. The linear and normal assumptions were found to be adequate following transformation. General linear and logistic models were used to examine separately the relationships between allergen-specific IgE levels and clinical outcomes, and allergen exposure and clinical outcomes. Additionally, models including both allergen-specific IgE and the matched exposure were considered to investigate the effects of each specific IgE measurement while controlling for the corresponding allergen exposure as well as the specified covariates. All models controlled for the effect of gender, age, race, study group and income above \$15 000 per year. Baseline (recruitment and randomization) and follow-up clinical outcomes (average over 1 year) are presented separately. The linear assumptions of the statistical methods were improved after log base 10 transformations of skewed data were performed on the following measures: FE_{NO} , blood eosinophils, sum of the specific IgE levels, allergen-specific IgEs, and allergen concentrations in settled dust. All statistical analyses were performed using sas statistical software version 9.2 (SAS Institute Inc; Cary, NC, USA) and the *R* system for statistical computing version 2.7.0.

Results

Study population

Five hundred and forty-six 12–20 year old inner-city adolescents with asthma were studied and their characteristics are presented in Table 1. The study population was predominantly (65%) African American and 48% had annual household incomes of <\$15 000. More than 88% were atopic, defined as having at least one positive skin test, with cockroach (61%), cat (58%), mold (52%), and dust mite (47%) being the most common sensitivities. Thirty-five percent had a positive skin test to mouse. The study population generally had moderate to severe asthma, with a mean number of symptom days in the previous 2 weeks of 2.3 (2.86) and the majority having had an unscheduled visit for asthma in the previous 12 months.

Allergen-specific IgE concentration and allergen exposure, partial correlations

Pearson correlations between specific IgE levels and settled dust allergen concentrations were examined among sensitized participants, i.e. those having a detectable level (>0.10 kU_A/l) of IgE to the allergen (Fig. 1). There were highly statistically significant correlations between allergen-specific IgE levels and settled dust allergen concentrations for dust mite, cockroach and mouse among sensitized participants (Fig. 1). There was no relationship between cat-specific IgE levels and settled dust Fel d 1 levels.

Specific IgE levels and inflammatory and physiologic biomarkers

In adjusted models, higher allergen-specific IgE levels were associated with higher FE_{NO} concentrations and a greater number of blood eosinophils for practically all allergens assessed – cockroach, mouse, dust mite, cat, and the sum of the allergen-specific IgE levels (Fig. 2). For example, for every 1 unit (log base 10) increase in mouse-specific IgE (kU_A/l), there was a 0.06 log base 10 increase in ppb of FE_{NO} (P value <0.01). None of the allergen-specific IgE measures, including the sum of the allergen-specific IgE levels, was consistently a better predictor of FE_{NO} or blood eosinophils than the others. Notably, consistent and significant relationships were not seen between the corresponding exposure measures and blood eosinophils or FE_{NO} (Fig. 2).

Higher allergen-specific-IgE levels, as well as the sum of the allergen-specific IgE levels, were also associated with lower lung function for all allergens assessed, although not all associations reached statistical significance (Fig. 3). For example, a 1 unit increase in cat-specific IgE (log₁₀, kU_A/l) was associated with a 1.42% point decrease in FEV₁/FVC (P value <0.001) measured at baseline. None of the allergen-specific IgE measures, including the sum of the allergen-specific IgE levels, was consistently a better predictor of lung function than the others. Cat and cockroach allergen exposure were inversely associated with some lung function measures, but overall, measurements of allergen exposure were less consistently associated with lung function than allergen-specific IgE levels (Fig. 3). In addition, the few inverse relationships between exposure and lung function disappeared after accounting for the allergen-specific IgE level. Figure 4 depicts the linear relationships of allergen-specific IgE levels to biomarker and lung function outcomes.

Allergen-specific IgE levels and clinical outcomes

Among the 546 subjects who were randomized, 431 had exacerbations, and 80 had hospitalizations in the previous year; 225 had exacerbations and 20 had hospitalizations during the follow-up year. The sum of the specific IgE was associated with increased exacerbations and hospitalizations in the previous 12 months. Higher cat-specific IgE levels were associated with a greater risk of having an exacerbation over the previous year. Higher dust mite-specific IgE levels were associated with a greater risk of hospitalization in the

previous 12 months while mouse-specific IgE levels were associated with a hospitalization in the subsequent 12 months (Fig. 5).

Relationships between continuous measures of allergen exposure and clinical outcomes were also examined in adjusted models. Overall, dust mite, cockroach, mouse and cat allergen concentrations were not correlated with exacerbations or hospitalization (Fig. 5).

Independent effects of exposure and sensitization on asthma outcomes

In adjusted models including allergen exposure, the allergen-specific IgE concentration remained a predictor of the inflammatory, physiologic, and clinical outcomes. In these models, exposure did not provide any additional predictive value for the outcomes, suggesting that any contribution of allergen exposure to these outcomes was captured by the allergen-specific IgE level (See Supporting Information).

Discussion

In this population of inner-city adolescents with asthma, allergen-specific IgE levels were positively correlated with bedroom allergen exposure for dust mite, cockroach and mouse allergens. In addition, higher allergen-specific IgE levels, independent of allergen exposure, were associated with worse asthma across a range of clinical and biologic markers among sensitized inner-city adolescents with asthma. Taken together, these findings suggest that allergen-specific IgE is a surrogate measure of the combination of sensitization plus exposure, and ultimately reflects asthma severity.

Consistent with our findings, a previous study examined relationships between the allergen-specific IgE level and risk of wheeze in a population-based birth cohort and found that the risk of current wheeze increased with increasing allergen-specific IgE levels to dust mite, cat, and dog (14). Our study extends the findings from the birth cohort study because of the focus on inner-city adolescents with established asthma and the demonstrated correlations between allergen-specific IgE levels and settled dust allergen levels among sensitized study participants. In our study, higher allergen-specific IgE levels were associated with higher FE_{NO} concentrations, higher numbers of blood eosinophils and worse lung function. Because these biomarkers are not tightly correlated with clinical outcomes (15), we also examined direct measures of asthma morbidity and found that higher allergen-specific IgE levels were associated with a greater number of exacerbations and hospitalizations. As expected, we also found relationships between the sum of the specific IgE levels and the inflammatory, physiologic and clinical outcomes, suggesting that the sum may reflect burden of allergic sensitization plus exposure to these major indoor allergens. However, the sum of the allergen-specific IgE levels was not a consistently better predictor of the outcomes examined than any of the allergen-specific IgE measures.

Although the presence of detectable allergen-specific IgE was not associated with future unscheduled doctor visits, exacerbations or hospitalizations in a previous report from this study (15), mouse allergen-specific IgE levels were associated with risk of future hospitalization when examined as a continuous variable in this analysis. Overall, however, allergen-specific IgE measures in this analysis were more often associated with morbidity in the previous year than during the 1 year follow-up period. The associations with morbidity measures over the previous year were more likely to be statistically significant because after enrollment and implementation of guidelines-based asthma care, asthma symptoms and other measures of morbidity were minimal. With the striking improvement in asthma and reduction in morbidity, the power to detect relationships between allergen-specific IgE measures and these outcomes was reduced.

We also found that dust mite-, cockroach-, and mouse-specific IgE levels were positively correlated with settled dust allergen levels among sensitized participants. Although others have examined relationships between sensitization and measured allergen, most studies have examined specific IgE (or skin test results) as dichotomous outcomes and have demonstrated some relationships between directly measured home allergen levels and risk of having IgE-sensitization (rather than the actual degree of sensitization as reflected by the level of IgE or wheal size) (16–20). For example, in the National Cooperative Inner-city Asthma Study, the prevalence of a positive cockroach skin test increased with increasing settled dust cockroach allergen levels. Few studies have examined relationships between measured home allergen concentrations and the *level* of allergen-specific IgE among sensitized individuals, as done in this study. Our findings suggest, at least for some allergens, that higher exposure is associated with higher allergen-specific IgE levels, so that IgE levels may be a composite measure of the combination of exposure plus degree of sensitization.

In contrast, cat-specific IgE levels were not correlated with settled dust Fel d 1 levels, suggesting that exposure outside of the home may be a more important determinant of cat-specific IgE levels. It is also possible that correlations between specific IgE levels and settled dust allergen levels are weakest among furred animal allergens because settled dust measures of these allergens may be a less accurate measure of true exposure, since these allergens are typically airborne. Another possibility is that our exposure metric is valid, but that higher cat allergen exposure attenuates cat-specific IgE responses as has been previously suggested (21, 22). Although cat-specific IgE levels were not correlated with settled dust Fel d 1 levels, cat-specific IgE levels were correlated with markers of inflammation, pulmonary physiology and clinical outcomes.

Not surprisingly, when allergen exposure was examined as a predictor of the outcomes of interest, exposure was not associated with inflammatory, physiologic or clinical outcomes. This finding is consistent with the effects of allergen exposure being mediated by IgE so that exposure would only be expected to be a predictor among participants with matched sensitization. In studies that have isolated the effects of exposure by examining relationships between allergen exposure and outcomes among non-sensitized asthmatics only (3, 5), the exposed and non-sensitized groups do not have greater morbidity than the non-exposed groups, underscoring the importance of sensitization in conferring susceptibility to the affects of allergen exposure.

The clinical applicability of allergen-specific IgE levels remains unclear. For example, it is unclear whether the allergen-specific IgE level could serve as a tool to gauge the level of home allergen exposure and to guide environmental control practice recommendations to patients as well as to assess effectiveness of such control measures. It is possible, though, that the allergen-specific IgE level could be a more accurate reflection of an individual's total exposure than a single settled dust measurement from an individual's home, since individuals are exposed to allergens in multiple environments (school, work, other homes, public places, etc.) throughout any given time period. It is also unclear if changes in allergen-specific IgE levels can predict impending exacerbations or identify the highest risk patients who might merit closer follow-up. Future studies which include repeated measurements of allergen-specific IgE levels, exposure, and clinical status will be required to examine temporal relationships between these variables and to assess the clinical applicability of allergen-specific IgE levels. Intervention studies that include allergen-specific IgE as an outcome, particularly allergen abatement trials, will also provide important insight into the role of allergen-specific IgE as a biomarker.

In sensitized inner-city adolescents with moderate to severe asthma, dust mite, cockroach and mouse-specific IgE levels are directly correlated with settled dust levels of these

allergens. Specific IgE levels for these allergens, in addition to cat, are also correlated with a range of inflammatory, physiologic, and clinical markers, highlighting the potential use of indoor allergen-specific IgE levels as clinical biomarkers. These findings suggest that, for some allergens, the allergen-specific IgE level could be a composite measure of exposure plus degree of sensitization, and therefore ultimately, disease severity. Future studies should be designed to prospectively evaluate relationships between allergen-specific IgE levels and both exposure and disease markers in patients with asthma.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Funding

This project has been funded in whole or in part with Federal funds from the National Institute of Allergy and Infectious Diseases, National Institutes of Health, under Contracts number NO1-AI-25496 and NO1-AI-25482, and from the National Center for Research Resources, National Institutes of Health, under grants RR00052, M01RR00533, M01 RR00071, 5UL1RR024992-02, and 5M01RR020359-04.

Abbreviations

ACE	Asthma Control Evaluation
CI	confidence interval
ELISA	enzyme-linked immunosorbent assay
FE_{NO}	fractional exhaled nitric oxide concentration
LLOD	lower limit of detection
MDI	metered dose inhaler
NAEPP	National Asthma Education and Prevention Program
OR	odds ratio

References

1. Ginde AA, Espinola JA, Camargo CA Jr. Improved overall trends but persistent racial disparities in emergency department visits for acute asthma, 1993–2005. *J Allergy Clin Immunol.* 2008; 122:313–318. [PubMed: 18538382]
2. Gruchalla RS, Pongracic J, Plaut M, Evans R 3rd, Visness CM, Walter M, et al. Inner City Asthma Study: relationships among sensitivity, allergen exposure, and asthma morbidity. *J Allergy Clin Immunol.* 2005; 115:478–485. [PubMed: 15753892]
3. Matsui EC, Eggleston PA, Buckley TJ, Krishnan JA, Breyse PN, Rand CS, et al. Household mouse allergen exposure and asthma morbidity in inner-city preschool children. *Ann Allergy Asthma Immunol.* 2006; 97:514–520. [PubMed: 17069107]
4. Pongracic JA, Visness CM, Gruchalla RS, Evans R 3rd, Mitchell HE. Effect of mouse allergen and rodent environmental intervention on asthma in inner-city children. *Ann Allergy Asthma Immunol.* 2008; 101:35–41. [PubMed: 18681082]
5. Rosenstreich DL, Eggleston PA, Kattan M, Baker D, Slavin R, Gergen P, et al. The role of cockroach allergy and exposure to cockroach allergen in causing morbidity among inner-city children with asthma. *N Engl J Med.* 1997; 336:1356–1363. [PubMed: 9134876]
6. Szeftler SJ, Mitchell H, Sorkness CA, Gergen PJ, O'Connor GT, Morgan WJ, et al. Management of asthma based on exhaled nitric oxide in addition to guideline-based treatment for inner-city

adolescents and young adults: a randomised controlled trial. *Lancet*. 2008; 372:1065–1072. [PubMed: 18805335]

7. Expert Panel Report 3 (EPR-3). Guidelines for the Diagnosis and Management of Asthma-Summary. Aug 28. 2007 <http://www.nhlbi.nih.gov/guidelines/asthma/asthdln.pdf> 2007
8. Busse WW, Lemanske RF Jr. Expert Panel Report 3: moving forward to improve asthma care. *J Allergy Clin Immunol*. 2007; 120:1012–1014. [PubMed: 17983868]
9. American Thoracic Society. ATS/ERS recommendations for standardized procedures for the online and offline measurement of exhaled lower respiratory nitric oxide and nasal nitric oxide, 2005. *Am J Respir Crit Care Med*. 2005; 171:912–930. [PubMed: 15817806]
10. Chapman MD, Aalberse RC, Brown MJ, Platts-Mills TA. Monoclonal antibodies to the major feline allergen Fel d I. II. Single step affinity purification of Fel d I, N-terminal sequence analysis, and development of a sensitive two-site immunoassay to assess Fel d I exposure. *J Immunol*. 1988; 140:812–818. [PubMed: 3276780]
11. Ohman JL Jr, Hagberg K, MacDonald MR, Jones RR Jr, Paigen BJ, Kacergis JB. Distribution of airborne mouse allergen in a major mouse breeding facility. *J Allergy Clin Immunol*. 1994; 94:810–817. [PubMed: 7963149]
12. Wood RA, Eggleston PA, Lind P, Ingemann L, Schwartz B, Graveson S, et al. Antigenic analysis of household dust samples. *Am Rev Respir Dis*. 1988; 137:358–363. [PubMed: 3341627]
13. Miller MR, Hankinson J, Brusasco V, Burgos F, Casaburi R, Coates A, et al. Standardisation of spirometry. *Eur Respir J*. 2005; 26:319–338. [PubMed: 16055882]
14. Simpson A, Soderstrom L, Ahlstedt S, Murray CS, Woodcock A, Custovic A. IgE antibody quantification and the probability of wheeze in preschool children. *J Allergy Clin Immunol*. 2005; 116:744–749. [PubMed: 16210045]
15. Gruchalla RS, Sampson HA, Matsui E, David G, Gergen PJ, Calatroni A, et al. Asthma morbidity among inner-city adolescents receiving guidelines-based therapy: role of predictors in the setting of high adherence. *J Allergy Clin Immunol*. 2009; 124:213–221. [PubMed: 19615730]
16. Donohue KM, Al-alem U, Perzanowski MS, Chew GL, Johnson A, Divjan A, et al. Anti-cockroach and anti-mouse IgE are associated with early wheeze and atopy in an inner-city birth cohort. *J Allergy Clin Immunol*. 2008; 122:914–920. [PubMed: 19000580]
17. Eggleston PA, Rosenstreich D, Lynn H, Gergen P, Baker D, Kattan M, et al. Relationship of indoor allergen exposure to skin test sensitivity in inner-city children with asthma. *J Allergy Clin Immunol*. 1998; 102:563–570. [PubMed: 9802363]
18. Matsui EC, Eggleston PA, Breyse PN, Rand CS, Diette GB. Mouse allergen-specific antibody responses in inner-city children with asthma. *J Allergy Clin Immunol*. 2007; 119:910–915. [PubMed: 17337296]
19. Phipatanakul W, Eggleston PA, Wright EC, Wood RA. Mouse allergen. II. The relationship of mouse allergen exposure to mouse sensitization and asthma morbidity in inner-city children with asthma. *J Allergy Clin Immunol*. 2000; 106:1075–1080. [PubMed: 11112889]
20. Simpson A, John SL, Jury F, Niven R, Woodcock A, Ollier WE, et al. Endotoxin exposure, CD14, and allergic disease: an interaction between genes and the environment. *Am J Respir Crit Care Med*. 2006; 174:386–392. [PubMed: 16614348]
21. Custovic A, Simpson BM, Simpson A, Hallam CL, Marolia H, Walsh D, et al. Current mite, cat, and dog allergen exposure, pet ownership, and sensitization to inhalant allergens in adults. *J Allergy Clin Immunol*. 2003; 111:402–407. [PubMed: 12589363]
22. Platts-Mills T, Vaughan J, Squillace S, Woodfolk J, Sporik R. Sensitisation, asthma, and a modified Th2 response in children exposed to cat allergen: a population-based cross-sectional study. *Lancet*. 2001; 357:752–756. [PubMed: 11253969]

Figure 1.

Partial correlations of Specific IgE and Settled Dust Allergen Concentrations. Correlations of each specific IgE (*y*-axis) and matching exposures (*x*-axis) are depicted with regression lines and 95% confidence limits. The Partial Pearson correlations and *P*-values head each cell and are adjusted for gender, age, race, study group and income above \$15 000 per year. IgE and exposure data are log base 10 transformed and only include subjects with detectable IgE levels (≥ 0.10 kUA/l). The Dust Max cell displays the maximum value of Der f 1- or Der p 1-specific IgE level and allergen concentrations.

Figure 2.

Effects of Exposure and Allergen-specific IgE on Inflammatory Biomarkers. Beta coefficients and 95% Confidence intervals are depicted with '○' for allergen-specific IgE and with '+' for allergen exposure. The sample size is approximately 534 for all estimates and varies slightly due to randomly missing data across each outcome and predictor. All models adjust for income above \$15 000 a year, study group, gender, age, and race. Both IgE and exposure measures are log base 10 transformed and entered as independent covariates in separate models.

Figure 3.

Effects of Exposure and Allergen-specific IgE on Lung Function. Beta coefficients and 95% Confidence intervals are depicted with '○' for allergen-specific IgE and with '+' for allergen exposure. The sample size is approximately 534 for all estimates and varies slightly due to randomly missing data across each outcome and predictor. All models adjust for income above \$15 000 a year, study group, gender, age, and race. Both IgE and exposure measures are log base 10 transformed and entered as independent covariates in separate models.

Figure 4.

Linear relationships between Allergen-specific IgE levels and Biomarker and Lung Function Measures. The sample size is approximately 534 for all estimates and varies slightly due to randomly missing data across each outcome and predictor. All models adjust for income above \$15 000 a year, study group, gender, age, and race.

Figure 5.

Effects of Exposure and Allergen-specific IgE on Clinical Outcomes. Odds ratios and 95% Confidence intervals are depicted with 'O' for allergen-specific IgE and with '+' for allergen exposure. The sample size is approximately 534 for all estimates and varies slightly due to randomly missing data across each outcome and predictor. All models adjust for income above \$15 000 a year, study group, gender, age, and race. Both IgE and exposure measures are log base 10 transformed and entered as independent covariates in separate models.

Table 1**Baseline characteristics**

Demographics	
Male (%)	53
Age at Visit 1 (year), mean $\pm$ SD	14.4 $\pm$ 2.1
Race/ethnic group (%)	
African American	64.7
Hispanic	23.5
Other or mixed	14
Household income <\$15 000 (%)	48
Outcomes	
Number of positive skin tests (of 14), mean $\pm$ SD	4.8 $\pm$ 3.35
Blood eosinophils (per μ l), median (IQR)	210 (118 – 373)
FEV ₁ (% of predicted value), mean $\pm$ SD	95.8 $\pm$ 15.7
FEV ₁ /FVC, mean $\pm$ SD	80.1 $\pm$ 8.68
FE _{NO} (ppb), mean $\pm$ SD	34.3 $\pm$ 37
1 Exacerbation at Recruitment (%)	79
1 Hospitalization at Recruitment (%)	15
1 Unscheduled Visit at Recruitment (%)	69

Allergen	Specific IgE (kU _A /l) Median (IQR)	Settled dust concentration (μ g/g) Median (IQR)
Cat	0.40 (<0.10–6.70)	4.2 (1.35–22.51)
Der p 1	0.31 (<0.10–2.78)	<LLOD (<LLOD–<LLOD)
Der f 1	0.29 (<0.10–2.69)	1.19 (<LLOD–8.16)
Cockroach	0.25 (<0.10–4.16)	<LLOD (<LLOD–0.51)
Mouse	<0.10 (<0.10–0.18)	0.695 (0.130–5.08)

LLOD, lower limit of detection; FE_{NO}, fractionalexhaled nitric oxide concentration.