

Addressing issues of asthma in inner-city children

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For children living in the inner city, asthma tends to be more frequent and severe. Although the causes for this heightened severity of asthma are not clearly established, environmental allergens likely play a major role. To characterize, understand, and treat children with asthma living in the inner city better, the National Institutes of Allergy and Infectious Diseases of the National Institutes of Health established an Inner City Asthma Program in 1991. Over the past 15 years, 3 separate inner-city asthma research networks have been formed and funded by this institute. The work from these programs has led to important observations including evidence that environmental allergens, particularly cockroach, are important for sensitization and severity of asthma of the affected children. Furthermore, reductions in the allergen load can lead to improved asthma control. The most recent program, the Inner City Asthma Consortium, was formed in 2002 with a goal to develop immune-based therapy for children with asthma in the inner city and to determine mechanisms of these therapies as well as immunopathogenesis of asthma in these high-risk children. This article reviews these programs and how they have begun the effort to understand and treat children with asthma who live in inner cities better and what their findings mean in relationship to unique features of asthma in inner city children. (*J Allergy Clin Immunol* 2007;119:43-9.)

Key words: *Asthma, inner city, allergens*

In the United States, asthma has a major effect on the health of inner-city children. A number of reasons likely account for the effect of asthma on these patients' lives, their lifestyle, and morbidity.¹⁻⁴ First, as identified in the late 1980s and early 1990s, the prevalence of asthma in these areas of large cities is greater and increasing more dramatically than in other locales.⁵⁻⁷ Furthermore, the severity of asthma in this population, particularly among

Abbreviations used

ACE: Asthma Control Evaluation
FeNO: Fraction of exhaled nitric oxide
ICAC: Inner City Asthma Consortium
ICAS: Inner City Asthma Study
NCICAS: National Cooperative Inner-City Asthma Study
NIAID: National Institute of Allergy and Infectious Diseases
NO: Nitric oxide

children, is greater than that found in patients of other locations.⁸ Third, the accessibility for asthma care is often burdensome and, as a consequence, may pose major limitations to ongoing care of this chronic illness and, possibly, its control.⁹ Finally, the at-risk population with asthma in the inner cities is more likely to be African American or Hispanic. Thus, healthcare disparities make this group of patients of particular need for new information to understand better the origins of their illnesses, risk factors associated not only with onset but persistence of their disease, and, perhaps most importantly, improvements in the effectiveness and management of their asthma. As a consequence of this very significant need, the National Institute of Allergy and Infectious Diseases (NIAID) of the National Institutes of Health formed special programs to investigate the causes of asthma in children living in the inner cities, establish research efforts, and develop interventions to understand and manage this respiratory illness better.

ASTHMA NETWORKS IN THE STUDY, CHARACTERIZATION, AND TREATMENT OF INNER-CITY CHILDHOOD ASTHMA

Over the past 15 years, the NIAID has funded 3 distinct inner-city networks: the National Cooperative Inner-City Asthma Study (NCICAS), the Inner City Asthma Study (ICAS), and the Inner City Asthma Consortium (ICAC; Table I). Although each of these individual programs has distinct research objectives, a common element is the promotion of asthma research in inner-city children to benefit the understanding and control of their illness. To accomplish this goal, selected sites for research in inner cities are identified throughout the United States. Second, the investigators at these sites have a demonstrated record in the recruitment and retention of patients in protocols designed to characterize features of asthma, to detect and

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TABLE I. Objectives and key findings of NIAID inner-city asthma programs

NCICAS: 1991-1997	<ul style="list-style-type: none"> • In studies designed to determine the relationship of allergic sensitization to asthma severity, cockroach was found to be a principal allergen associated with disease severity.
ICAS: 1994-2001	<ul style="list-style-type: none"> • With an environmental avoidance trial, decreases in household cockroach and house dust mite antigen were associated with reduction in asthma morbidity.
ICAC: 2002 to the present	<ul style="list-style-type: none"> • Studies designed to evaluate immune-based therapy on asthma in inner-city children are currently underway.

quantitate environmental risk factors, and to have a staff skilled in the care and communication with this at-risk group. These investigative groups are supported by a statistical and clinical coordinating center to facilitate, coordinate, and assist in the conduct of these investigations. Given these demographic and structural features, inner city asthma networks have been able to design, implement, and conduct studies to expand knowledge of what is unique about asthma in the inner city and what treatment approaches may be helpful.

INNER-CITY ASTHMA PROGRAMS

NCICAS

In the early 1990s, the NIAID established NCICAS with the goal of first identifying and then intervening in the factors responsible for this rapid increase in asthma among inner-city children. In a year-long epidemiologic study of 1528 children and their families from 8 major inner-city areas (Bronx, NY; East Harlem, NY; St Louis; Washington, DC; Baltimore; Cleveland; Chicago; and Detroit), a broad range of potential factors were examined that could be related to asthma morbidity in this population. The recruited children all lived in neighborhoods where 30% of the households had incomes below the 1990 poverty level. The children enrolled in NCICAS had a mean age of 6.2 years and were primarily black or Hispanic, and more than 60% had a household income of less than \$15,000/year. The children and their primary care givers were interviewed by NCICAS staff about access to healthcare, adherence to prescribed therapy, family, psychosocial problems, home environment, cigarette smoking by household members, and demographics of the household members. Prick-puncture skin testing was performed with extracts of house dust mites (*Dermatophagoides pteronyssinus* and *Dermatophagoides farinae*), cat pelt, a mixture of German and American cockroach, and 10 other common aeroallergens. Three, 6, and 9 months after baseline evaluations were made, each family was contacted to obtain information about asthma symptoms and healthcare use. The value of the network approach and structure of this study is noted in the highly successful follow-up rates that averaged 92% over the course of the follow-up year. This successful retention speaks to the

skills, training, and dedication of the network investigators and staff.

The results of this investigation indicated that there was not a single cause or factor associated with these high levels of asthma morbidity, but rather a variety of factors seemed to play a role in what was clearly found to be a multifactor, multicausal disease. Among the many factors found to be associated with asthma morbidity in the inner city were access to and quality of healthcare, psychological problems of the child and/or caregiver, family functioning, and adherence. Somewhat surprising was the very strong influence of allergen exposures and sensitivity on the symptoms and healthcare utilization of these children. More specifically, cockroach allergen exposure and sensitivity were found to be especially important as a factor associated with asthma morbidity in the inner city. Skin testing found a frequency of reactivity of 36.8% for cockroach, 34.9% for house dust mite allergen, and 22.7% for cat dander.

In a sample of 663 of these 1528 children, extensive home dust collections were conducted. Bedroom samples were analyzed for house dust mites, cat allergen, and cockroach antigen (Bl a g 1). Environmental allergens are important for sensitization, development, and possibly the persistence and severity of asthma.¹⁰ To a large extent, the importance of environmental allergens in asthma has been derived from studies in which house dust mite, animal dander, and mold exposure have been evaluated in relationship to features of asthma.¹¹⁻¹³ In some inner-city dwellings, however, cockroaches are ubiquitous, highly allergenic, and capable of inducing asthma symptoms.^{14,15} In contrast with other indoor allergens, the relationship between allergy to cockroach and asthma, as well as disease severity, was not fully established before NCICAS. The NCICAS Network hypothesized that asthma morbidity is highest among children who are both allergic to a specific allergen and exposed to high levels of this allergen.¹⁶

The majority of bedrooms sampled had detectable levels of all 3 allergens: 49.4% for house dust mite, 62.6% for cat dander, and 85.3% for cockroach. The investigators also evaluated the number of bedrooms where antigen concentrations were found above allergen levels that exceeded the proposed disease-induction thresholds. Under these clinically relevant stratified criteria, high levels of cockroach allergen were found in 50.2% of the bedrooms, whereas only 12.6% and 9.7% of the bedrooms, respectively, had high levels of cat and dust mite.

To determine the clinical implication of these allergen exposures, in particular cockroach, to this asthma population, the investigators assessed morbidity caused by asthma in terms of 4 factors: clinical symptoms, use of healthcare services, activities of daily life, and effect on the parent or other caregiver. The findings are of considerable interest to risk features of asthma and indicate that cockroach allergy, but not dust mite or cat, is associated with increased hospitalizations, wheezing, unscheduled medical visits, and change in caregiver's plans (Fig 1).

The findings of NCICAS were important to define environmental risk factors for asthma in children living in

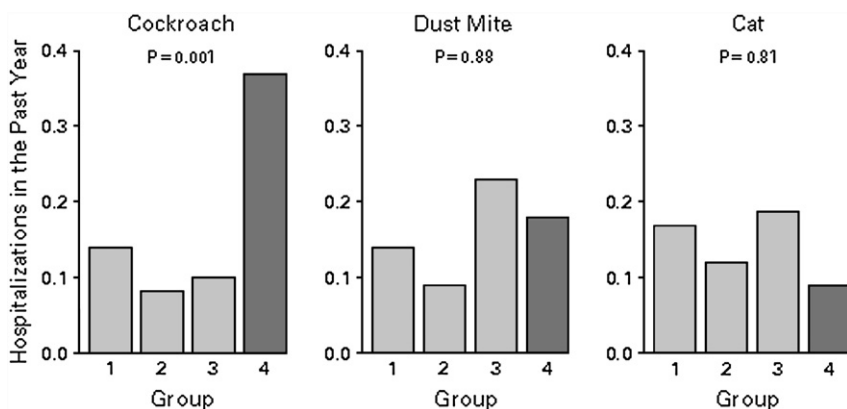


FIG 1. Number of hospitalizations in the past year according to the presence or absence of allergy to cockroach, dust mite, or cat allergen, and the degree of exposure. Group 1, no allergy and with low levels of exposure; group 2, no allergy and high exposure; group 3, allergy and low exposure; group 4, allergy and high exposure. Reprinted with permission from Rosenstreich DL, Eggleston P, Kattan M, Baker D, Slavin RG, 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;336:1356-63.¹⁶ © Copyright 1997 Massachusetts Medical Society. All rights reserved.

inner cities and were based on a large sample, multiple cities, and measurement of both sensitization and exposure. These studies have shown that the highest levels of asthma morbidity occurred in the presence of a positive skin test and allergen exposure. Moreover, asthma morbidity was reflected in healthcare services use, clinical symptoms, and effect on daily activities. Children measured peak expiratory flow rates, but no relationship was found between sensitization and exposure. The reasons for a lack of effect on a measure of lung function may reflect the precision of peak flow determinations, the short duration of the study, or a different effect of sensitivity and allergen exposure on measures of asthma control versus lung function. Also of interest was the absence of effects of sensitization and exposure to house dust mites and animal dander allergen on these asthma measures of morbidity. Therefore, for children with asthma who live in the inner city, cockroach appears to be the dominant allergen causing asthma morbidity.

Armed with these results, the second phase of the NCICAS project conducted an extensive multifactor intervention to address the many variables shown to influence asthma morbidity in the phase I epidemiologic investigation. This randomized intervention of 1033 families was tailored to the specific risks of each child and included guidance on reducing allergen exposures and exterminating cockroaches. Asthma counselors guided the year-long intervention process, and a clear reduction in asthma morbidity was observed.¹⁷

ICAS

The ICAS was a second major program designed to conduct multicenter intervention trials to reduce asthma morbidity among inner-city children. A number of key observations from this network have been published and provide insight into additional features of asthma in children living in inner cities. ICAS developed and

implemented an environmental intervention to address the many allergen and irritant exposures found in the inner city environment. For this randomized trial, the ICAS investigators recruited 937 children with moderate-to-severe asthma who ranged in age from 5 to 11 years. These children had specific clinical features including at least 1 hospitalization or 2 emergency department visits for asthma during the 6 months before the initial evaluation at study enrollment. In addition, the children had an immediate positive skin test response to at least 1 of the 11 common indoor allergens tested: dust mite (*D farinae* and *D pteronyssinus*), cockroach (a German and American mixture), rat, mouse, mold (*Alternaria cladosporium* and *Aspergillus penicillium*), and dog. Children needed to sleep in the primary caretakers' intervention home at least 5 nights per week. After completion of these baseline evaluations, and every 6 months thereafter, a trained team of research assistants conducted a detailed evaluation of each child's home including a direct visual assessment and obtained samples, primarily from the bedroom, for antigen detection. From these data, interactions between the children's asthma morbidity, home environment, and exposure to environmental tobacco smoke could be made. Morbidity was determined at baseline and at 2-month intervals over a 24-month period.

In a recent report, Gruchalla et al¹⁸ found considerable variability in sensitization from city to city, with cockroach reactivity lowest in Seattle and highest in the Bronx; house dust mite sensitivity, in contrast, was the highest in Dallas and lowest in Chicago. As noted in NCICAS, a strong correlation existed between allergen exposure and the degree and frequency of allergic sensitivity. For example, if *Bla g 1* was found in the bed or on the floor at a 39.5% exposure rate, skin test reactivity occurred in 81.4% of the subjects. Importantly, positive skin test responses to cockroach were also found (60.1%) even when there was no apparent exposure at home. Thus, allergen

exposure that leads to sensitization was more likely to occur if the antigen existed in the home environment; however, other sites of exposures were equally effective in leading to sensitization.

When determinants of allergen exposure and sensitization were evaluated in relationship to asthma morbidity, cockroach exposure and sensitivity were more likely to be associated with asthma symptom days, caretaker loss of sleep, or school days missed. Similarly, the rate of unscheduled medical visits was greatest with children sensitive and exposed to cockroach antigen. Both NCICAS and ICAS indicate that cockroach antigen is likely the environment allergen with greatest effect on asthma in inner-city children.

To extend these studies, the ICAS group designed a protocol to determine whether an environmental intervention that was tailored to each child's allergen sensitization and environmental risk factors could improve asthma-related outcomes.¹⁹ From the previously identified and characterized group of 937 inner city children with asthma, an intervention (n = 469) and control group (n = 468) were selected. After baseline clinical evaluations, members of the ICAS investigative teams conducted home evaluations and collected samples to determine the presence of *D pteronyssinus* (Der p 1) and *D farinae* (Der f 1), cockroach allergen (Bla g 1), cat allergen (Fel d 1), and dog allergen (Can f 1). Families who were randomized to the control group received visits at 6-month intervals throughout the study but did not have an environmental intervention. A unique feature of the ICAS protocol was the method for environmental modification, which was structured to provide the child's caretaker with knowledge skills, motivation, equipment, and supplies to perform the environmental remediation. The intervention was designed to focus on remediation of exposure to dust mites, passive smoking, cockroaches, pets, rodents, and molds and, importantly, was tailored to the sensitivity of the patients.

In the findings reported by Morgan et al,¹⁹ the interventional strategies were effective and reduced home allergen exposure. These efforts also translated into improved asthma control with significant reductions in the maximal number of days with asthma symptoms (3.39 vs 4.2; $P = .001$) and unscheduled asthma-related healthcare use (unscheduled visits to a clinic for asthma [number/year], 2.22 vs 2.57; $P = .04$), but no change in lung function values (Table II). Moreover, the benefits of the intervention in year 1 carried into the second year, even though the intervention was not active at this time.

The results of this study have important implications for asthma care and causative features of asthma in inner-city children. First, a reduction in key environmental allergen exposure, such as house dust mite and cockroach, is possible. Second, a reduction in bedroom exposure to these allergens, either in the bed or on the floor, had a positive impact on relevant features of asthma morbidity. Third, the benefits of this intervention had lasting effects, because the improvement persisted for at least 12 months after cessation of the active intervention. Last, the benefit

on asthma in the at-risk child was an improvement in asthma control, for example, symptoms and need for acute care, not greater lung function. Possibly this lack of effect on lung function reflects an absence of severe airflow obstruction at enrollment in the children, or that allergen acts primarily to sensitize the airway toward the development of symptoms. Nonetheless, this was an important study and demonstrated the beneficial effects of antigen avoidance and the translation of this therapy to key outcomes of asthma treatment and asthma symptom control. In addition, the feasibility of this approach linked the importance of inner-city allergen exposure, associated disease sensitivity, and a lessening of asthma symptoms to a reduction in a relevant allergen load.

ICAC

In 2002, the ICAC was formed. ICAC has 4 structural components: (1) an administrative unit, (2) a statistical and clinical coordinating center, (3) investigative sites, and (4) programmatic support at the NIAID. The goals of this inner-city network are distinct from the previous programs, but build on earlier findings that the activation of immune responses by environmental allergens is linked to the expression of asthma, a likely or causative determinant of disease severity, and a highly relevant target for therapy for children with asthma of the inner-city. The ICAC research program has 2 lines of investigation: (1) to design and implement immune-based therapies for asthma, and (2) to conduct studies directed toward defining the immunopathogenesis of asthma in inner-city children.

The first phase of the consortium has focused on the development of immune-based therapy protocols that (1) contain a plan to identify molecular targets for immune-based therapies, (2) test the effectiveness of such interventions in children in the inner city with asthma, and (3) complement these clinical protocols with evaluations of relevant biomarkers and design studies to establish mechanisms of asthma and effects of the intervention studies on these processes. Two studies have been designed to meet the objectives of this ICAC initiative. The first study is entitled Asthma Control Evaluation (ACE): A Biomarker-based Approach to Improving Asthma Control. The primary objective of this study is to evaluate the use of biomarkers as a supplemental approach to asthma therapy and is based on the hypothesis that this approach would improve asthma outcomes (asthma symptom days and asthma exacerbations) compared with a guideline-based approach without the benefit of a specific biomarker. In the ACE protocol, the fraction of exhaled nitric oxide (FeNO) is used as a biomarker of allergic inflammation in asthma.

ACE

The ACE is a randomized, parallel study with a group of inner-city participants, 12 to 20 years of age, with persistent asthma. Spirometry and FeNO will be measured at all visits by all participants. After a 3-week run-in period, the subjects are randomized to the reference treatment groups (Guideline Based) or Biomarker Strategy Group. In the conduct of this study, a research assistant collects data

TABLE II. Effect of intervention on symptoms of asthma and health care use*

Variable	Intervention group	Control group	Difference†	P value
Year 1				
No. of children	444	425		
Days with symptoms of asthma (no./wk)				
Maximal number of days with symptoms	3.39 ± 0.12	4.20 ± 0.12	-0.82	<.001
Days of wheeze	2.65 ± 0.11	3.43 ± 0.11	-0.78	<.001
Days child had to slow down or stop play because of asthma	2.34 ± 0.10	2.84 ± 0.10	-0.49	<.001
Nights child woke up because of asthma	1.55 ± 0.08	2.17 ± 0.08	-0.62	<.001
Nights caretaker woke up because of child's asthma	1.70 ± 0.09	2.32 ± 0.10	-0.61	<.001
Days caretaker changed plans	0.91 ± 0.07	1.22 ± 0.07	-0.31	<.001
School days missed	0.65 ± 0.04	0.82 ± 0.04	-0.17	.003
Asthma-related health care use				
Unscheduled visits to ED or clinic for asthma (N/y)	2.22 ± 0.12	2.57 ± 0.13	-0.35	.04
ED	0.93 ± 0.07	1.08 ± 0.07	-0.14	.17
Clinic	1.28 ± 0.09	1.48 ± 0.09	-0.21	.11
≥1 Hospitalizations for asthma (%)	17.1	15.5	1.6	.56‡
Pulmonary function				
FEV ₁ at 12 mo (% of predicted value)	87.0 ± 0.77	87.4 ± 0.78	-0.4	.69
Forced vital capacity at 12 mo (% of predicted value)	97.3 ± 0.72	98.1 ± 0.73	-0.8	.48
Daily variability in PEF in 1st y (%)	16.6 ± 0.83	15.0 ± 0.81	1.6	.09
Days with > 20% variability in PEF in 1st y (%)	26.8 ± 2.00	23.3 ± 1.96	3.48	.14
PEF in morning in 1st y (L/min)	216.7 ± 3.11	219.3 ± 2.96	-2.61	.51
Year 2				
No. of children	407	414		
Maximal number of days with symptoms of asthma (no./wk)				
Days with maximal symptoms	2.62 ± 0.12	3.21 ± 0.13	-0.60	<.001
Days of wheeze	2.28 ± 0.11	2.87 ± 0.11	-0.60	<.001
Days child had to slow down or stop play because of asthma	1.67 ± 0.10	2.13 ± 0.10	-0.46	.001
Nights child woke up because of asthma	1.27 ± 0.08	1.57 ± 0.08	-0.30	.01
Nights caretaker woke up because of child's asthma	1.31 ± 0.09	1.68 ± 0.09	-0.37	.006
Days caretaker changed plans	0.72 ± 0.06	0.87 ± 0.06	-0.15	.09
School days missed	0.54 ± 0.04	0.71 ± 0.04	-0.17	.009
Asthma-related health care use				
Unscheduled visits to ED or clinic for asthma (N/y)	1.39 ± 0.10	1.66 ± 0.10	-0.26	.07
ED	0.55 ± 0.06	0.62 ± 0.06	-0.07	.38
Clinic	0.85 ± 0.08	1.03 ± 0.08	-0.19	.09
≥1 Hospitalizations for asthma (%)	10.6	13.5	-2.6	.19‡

ED, Emergency department; PEF, peak expiratory flow.

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*Plus-minus values are means ± SEs, adjusted for site and baseline levels.

†Unrounded values were used to determine the difference between groups.

‡The P value was calculated by means of the Cochran-Mantel-Haenszel test.

from the participant and, through a series of blind staff and 1 unblind staff member, determines the treatment level on the basis of a clinical assessment and treatment algorithm centered on the National Asthma Education and Prevention Program Guidelines. In the biomarker group, the treatment can be adjusted on the basis of the value of FeNO.

This approach for study was selected for a number of reasons. First, nitric oxide (NO) is an inflammatory product and biomarker that is hypothesized to reflect an immune-based response that results in airway inflammation, that is, after allergen exposure.²⁰⁻²² Second, NO has been shown to reflect ongoing airway inflammation, presumably from allergen exposure, and has been helpful as a guide to therapy.²¹ Furthermore, if a biomarker-developed approach to therapy is successful, it might be an

effective means to monitor and direct therapy in the high-risk child with asthma.²³ Finally, if devices can be developed for simple but accurate detection of NO, a more effective monitor of asthma activity and directive for therapy could be implemented.

Some of the ICAC centers will also conduct mechanistic studies to gain insight into basic features of this population's asthma and to evaluate possible mechanisms of disease and response to treatment. A hypothesis to be tested in ACE is the possibility that "inner city asthmatic adolescents who are highly sensitized to house-dust mite, cockroach, and/or *Alternaria* will have more severe asthma at ACE enrollment and throughout the study compared to weakly sensitized asthmatic patients." Sensitization will be based on allergen specific IgE levels.

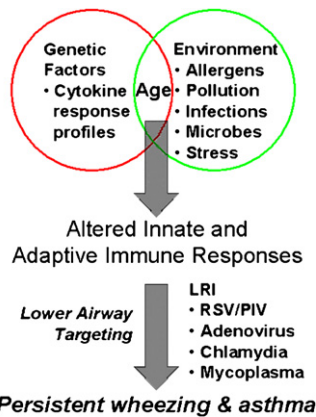


FIG 2. Factors in the development of recurrent wheezing and asthma. *LRI*, Lower respiratory infection; *RSV*, respiratory syncytial virus; *PIV*, parainfluenza virus.

Parameters marking greater asthma severity will include airway responsiveness, sputum eosinophils and selected cytokine mRNA, peripheral blood eosinophil values, and peripheral blood lymphocyte stimulated responses to allergen and modulation by corticosteroids. The effect of treatment on these measures and clinical outcomes will then be evaluated. Thus far, 547 subjects have been randomized in the ACE protocol; results from this study will be available in the spring of 2007.

Inner-City Anti-IgE Therapy in Asthma

The primary objective of Inner-City Anti-IgE Therapy in Asthma will be an evaluation of the efficacy of the mAb against IgE, omalizumab, compared with placebo, when administered to inner-city children and adolescents with moderate-to-severe allergic asthma who are receiving standard specialist care and basic asthma education. Efficacy of this immune-based intervention will be measured by differences in the maximum number of asthma symptom days as defined as the highest value among the 3 variables: (1) number of days of wheezing, tightness in the chest, or cough; (2) number of nights with disturbed sleep as a result of asthma; and (3) number of days on which the participant had to slow down or discontinue play/physical activities over a 2-week period, evaluated monthly. Parallel mechanistic studies will accompany the study, which begins September 2006.

Urban Environment and Childhood Asthma

In addition, ICAC has designed and initiated the Urban Environment and Childhood Asthma protocol, which is a birth cohort study designed to address a number of key fundamental questions about the basic immunopathogenesis of these children's asthma and asthma in the inner city population.

1. Does dysregulation of innate immune response, which may already be present at birth, increase the risk of allergen sensitization (adaptive immune responses) and asthma, and if so, which cytokines are key in this process?

2. How do lower respiratory tract infections in infancy affect the subsequent risk of recurrent wheezing and asthma in inner-city children?
3. Is the immune system of inner-city children already abnormal at birth, because of a unique prenatal environment?
4. Of the many unique features associated with the inner-city environment, which are the principal factors that adversely affect immune development, and thereby increase the risk of asthma?
5. Does the inner-city environment (eg, increased stress and pollution) increase the frequency or severity of lower respiratory infections, and if so, what are the relevant mechanisms (immune modulation versus lung-specific effects)?
6. Do environmental factors interact at a critical time point to establish a particular wheezing phenotype with future infections and/or exposures?

The study design is a longitudinal prospective evaluation over a 3-year period, beginning at birth. The initial study will involve a 3-year follow-up of study participants. If the initial phases of the study are successful, the children will be followed to 6 years of age to assess the development of bona fide childhood asthma. Thus far, 493 newborn infants have been enrolled. The recruited newborns all have 1 parent with asthma or allergies. The Urban Environment and Childhood Asthma study will provide an extensive amount of information on environmental factors, including allergen exposure, respiratory tract infections, and stress along with data on innate and adaptive immune activity. These studies will provide unique and critical insight into the genetic (cytokine dysregulation), environmental, and developmental aspects that are eventually associated with asthma in inner-city children (Fig 2).

CONCLUSION

For many children living in the inner cities of the United States, asthma poses an all too frequent risk to their normal health and development. The NIAID of the National Institutes of Health has established programs over the past 15 years whose efforts have included the development of collaborating research centers and teams in the inner city with the goal to define the characteristics and features of asthma in these children and design treatment protocols aimed at controlling the allergic responses to environmental allergens, particularly the cockroach, to improve asthma control and thus their quality of life. Through the efforts of NCICAS and ICAS, the importance of inner-city allergens, particularly as they relate to sensitization and asthma severity, has been convincingly shown. The design and implementation of these networks have illustrated the benefit and effectiveness of patient recruitment and retention in well conceived studies, and provided a model to accomplish research on the influence of special circumstances and environment on asthma. ICAC is the

most recent inner-city program and will extend the efforts of this NIAID program by studies that are directed toward immune-based therapy and correlating these outcomes with mechanistic investigations. Through these comprehensive approaches will emerge greater insight into mechanisms and management of asthma in this high-risk and underserved group of patients.

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