

- commercial house dust extracts: comparison with dust extracts from cat-containing environment. *J ALLERGY CLIN IMMUNOL* 1987;79:955-9.
21. Wood RA, Eggleston PA, Lind P, et al. Antigenic analysis of household dust samples. *Am Rev Respir Dis* 1988;137:358-63.
22. Swanson MC, Campbell AR, O'Hollaren MT, Reed CE. Role of ventilation, air filtration, and allergen production rate in determining concentrations of rat allergens in the air of animal quarters. *Am Rev Respir Dis* 1990;141:1578-81.
23. van der Brempt X, Charpin D, Haddi E, da Mata P, Vervloet D. Cat removal and *Fel d 1* levels in mattresses. *J ALLERGY CLIN IMMUNOL* 1991;87:596-7.

Atopic profile of inner-city asthma with a comparative analysis on the cockroach-sensitive and ragweed-sensitive subgroups

Bann C. Kang, MD, Jessie Johnson, BS, and Chris Veres-Thorner, MD
Chicago, Ill.

Background: Inner-city asthma is well known for its high risk of mortality. To better understand urban asthma, we examined clinical characteristics and aeroallergen sensitivities of 592 of 680 consecutive urban Chicago residents with asthma.

Methods: A total of 227 male and 453 female subjects who met the criteria for the study were registered. A comprehensive clinical evaluation was followed by allergy skin testing (prick and intradermal testing) with 10 groupings (5 indoor and 5 outdoor) of common aeroallergens. Serum total IgE and selective antigen-specific IgE levels, including cockroach-specific IgE, were routinely measured. A total of 592 (196 male and 396 female) subjects with an average age of 35 years were skin tested. The average duration of asthma was 12.6 years, and 31% of the population was receiving corticosteroids.

Results: Aeroallergen sensitivity was noted in 85%, and 94 subjects (15%) were nonallergic. House dust sensitivity (76%) was most prevalent, distantly followed by sensitivity to cockroach (48%), ragweed (45%), other weeds (42%), cat (40%), and dust mite (24%). The average number of aeroallergen sensitivities detected was 4 of 10 groupings of both indoor and outdoor allergens. Twenty percent of subjects were allergic to only indoor allergens, whereas 4% were allergic to outdoor allergens only. Serum IgE was 245 ± 17.3 IU/ml (geometric mean + SEM), and 74% of 444 serum samples assayed showed IgE antibody levels greater than or equal to 100 IU/ml. A cockroach-sensitive subgroup (283 subjects) had longer duration of asthma ($p < 0.0001$) and fewer additional aeroallergen sensitivities ($p < 0.0001$) than the ragweed-sensitive subgroup (264 subjects).

Conclusion: The results indicate that a great majority (85%) of inner-city Chicago residents with asthma have atopic asthma, as demonstrated by highly elevated IgE levels and multiple aeroallergen sensitivities. Sensitivity to indoor allergens is more prevalent than sensitivity to outdoor allergens. The subjects with cockroach-sensitive asthma appear to be a distinctive subgroup characterized by chronicity and elevated serum IgE antibody levels with fewer aeroallergen skin test sensitivities. (*J ALLERGY CLIN IMMUNOL* 1993;92:802-11.)

Key words: Inner-city asthma, aeroallergens, cockroach allergy, IgE antibody, indoor allergen

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Reprint requests: Bann C. Kang, MD, University of Kentucky, Department of Medicine, K528, Kentucky Clinic, Lexington, KY 40536-0084.

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Abbreviations used

ANOVA: Analysis of variance
CRa: Cockroach antigen
RGa: Ragweed antigen

Bronchial asthma is one of the most common chronic diseases with multifactorial causes. Although it was considered at one time to be a "slight ailment that promotes longevity" in Osler's words,¹ it is now recognized as one of the more costly diseases at both the personal and community levels because of increasing morbidity and mortality rates.²⁻³ In particular, inner-city residents with asthma usually have severe symptoms with frequent exacerbations. They commonly have lifelong disease, which can result in a fatal outcome at an early age.^{3,4} Consequently, this group of patients with asthma is depleting a significant portion of our national health resources by heavy use of emergency rooms and hospitals.³⁻⁵

Individual aeroallergens are known to induce immediate bronchospasm and late-phase responses that result from a complex inflammation mediated by allergen-IgE antibody reaction in subjects with asthma.⁶⁻⁹ In particular, late-phase inflammation is believed to be the cause of the chronic airway inflammation that is observed "day to day" in patients with chronic asthma.^{7,8} Allergens, such as grass pollen, house dust mite, and cat dander, are known risk factors for atopic sensitization and for acute exacerbation in patients with asthma.^{9,10} Furthermore, it is known that hospital admissions of patients with asthma are associated with seasonal and endemic exposures to outdoor allergens.^{11,12} However, unlike the causal relationship of a seasonal outdoor allergen, a causative element is not easily suspected or identifiable in patients with severely symptomatic perennial asthma. In fact, controversy exists over whether there is any significance of the noted aeroallergen sensitivities and over how many allergens should be tested in subjects with severe asthma. However, it is easily conceivable that patients with allergic asthma who have multiseasonal aeroallergen and/or indoor allergen sensitivities may have chronic symptoms perennially as a result of continuous inhalation of the multiple allergens. Particularly, an indoor allergen may have a more deleterious effect on patients with asthma because of the protracted duration of contact. One of the common allergens, the cockroach allergen (CRa), has been recently uncovered and is mostly considered as an indoor allergen highly prevalent among inner-city popula-

tions.¹³⁻¹⁶ Furthermore, it has been proven that CRa challenge in patients with cockroach-sensitive asthma produces early- and late-phase asthmatic responses.¹⁷⁻²⁰

Considering these findings together with the fact that inner-city residents with asthma frequently live in crowded multidwellings that are heavily infested with pests and cockroaches,²¹⁻²³ it is plausible that patients with severe asthma may be sensitive to indoor allergens, multiseasonal aeroallergens, or both. Also, the increasing morbidity and mortality rates associated with urban asthma could be direct consequences of allergic asthma resulting from these aeroallergen sensitivities. Moreover, because few large-scale studies have investigated aeroallergen sensitivities of these urban residents with asthma in this country, we analyzed the skin test results of 592 of the 680 consecutive patients with asthma, documented over a period of 13 years in the Asthma Registry of the Mount Sinai Hospital Center in Chicago, Illinois. Two exemplary aeroallergen-sensitive groups, a cockroach-sensitive group as an example of indoor allergen sensitivity and a ragweed-sensitive group as an example of outdoor allergen sensitivity, were separated from the population of subjects with asthma, and characteristics were compared.

PATIENT SELECTION AND ASTHMA REGISTRY

The asthma registry was established at Mount Sinai Hospital Medical Center to record all known subjects with bronchial asthma as defined by the following criteria.⁶ Specifically, subjects were included if they had had recurrent symptoms of wheezing, shortness of breath, cough, and a sensation of chest tightness for longer than 1 year plus objective signs of obstructive airway disease as determined by chest x-ray films or spirometers. Reversibility of the obstructive airway disease was documented by physicians or proven by repeated measurements of simple spirometers. Most subjects were referred to the Allergy Service by primary care physicians, by emergency room physicians, and house staff in the tertiary care hospitals. The registry was active from September 1973 until November 1986. Subjects included all age groups of both genders. Social class or race was not discriminated. More adults than children were included by chance because of the structure of the department in which the registry was set up. Subjects with the following criteria were excluded: (1) subjects with questionable asthma, who required only periodic administration of antibiotics or cough syrup for infrequent attacks of

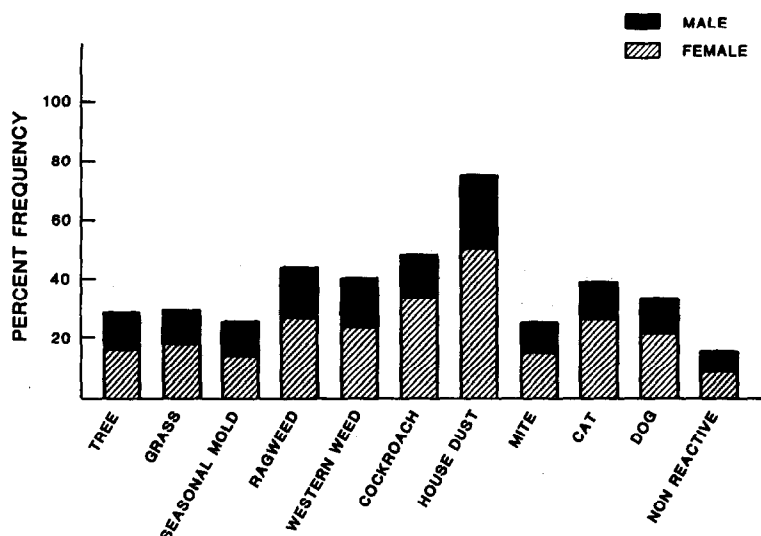


FIG. 1. The prevalence of inhalant allergen sensitivities in 592 Chicago residents with asthma.

"chest tightness" with or without coughing; (2) subjects who required occasional administration of bronchodilators for less than 30 days per year for control of infrequent "wheezing"; and (3) subjects who had irreversible chronic obstructive lung disease proven by repeated spirometers after an aggressive 10-day treatment with bronchodilators and corticosteroids. Corticosteroid dependency was defined as systemic corticosteroid use orally and/or parenterally for longer than 3 months continuously or on more than five separate occasions in a tapering mode, intermittently. This corticosteroid use was applied as a criterion for a sign of severity of asthma in this population because the drug was used only when the usual combined treatment, a sympathomimetic and a xanthine derivative, failed to control the asthma.

Subjects with cockroach-sensitive (CR+) asthma were defined as subjects with asthma who had positive skin test results to CRa as described previously.^{18-20, 23} Ragweed-sensitive (RG+) subjects with asthma were defined in the same manner. Both groups may or may not have had positive results to other aeroallergens tested.

METHODS

Allergy skin testing

Routine allergy skin testing was done by prick screening followed by intradermal injections as previously described.^{18-20, 23} Thirty-nine common inhalants in 10 groupings were routinely tested (see Appendix). Testing allergens (prick, 1:10, wt/vol) (intradermal, 500 to 1000 PNU) were obtained from Hollister-Stier Company (Spokane, Wash.). A negative control (buffered albuminized saline solution) and a positive control (histamine phosphate base, 0.1 mg/ml) were included. The sizes of wheal and erythema were measured and

recorded after 15 minutes. A test result was considered positive when the mean diameter of wheal was greater than or equal to 5 mm by prick screening or greater than or equal to 11 mm by intradermal screening. These are more stringent criteria than recommended²⁵ in order to increase the specificity of the testing.

Measurement of total IgE antibody

Total serum IgE, in nanograms per milliliter, was measured by Mayo Laboratory (Rochester, Minn.) from July 1975 until June 1980. Total IgE levels of subjects who were entered in the Asthma Registry during the period from September 1973 to June 1975 were measured from the collected and stored sera. During the period from 1980 to 1986, the test was done by the Allergy and Immunodiagnostics Laboratory, Ltd., (Kansas City, Mo.). IgE measured by the former laboratory (nanograms per milliliter) was converted to international units per milliliter with a formula described by Nye et al.²⁶ for the purpose of statistical analysis.

Statistical analysis

Data were analyzed by Statistical Analysis System main frame computer (SAS Institute Inc., Cary, N.C.). Significance was determined by chi square analysis, paired and unpaired Student's *t* tests, and McNemar's test for correlated proportions. Analysis of variance (ANOVA) was also performed. Arithmetic mean $\pm$ SD was calculated. Geometric mean ($\pm$ SE) and log₁₀ values were used for serum IgE.

RESULTS

Atopic profile of urban residents with asthma

Of the 680 consecutive patients with asthma (227 male and 453 female subjects) registered, 592 (196 male, 396 female subjects) completed the

TABLE I. Distribution of aeroallergen sensitivity of patients with asthma in relation to age

Age (yr)	Negative	Indoor*	Outdoor†	Both	Total
0-15	5	15	5	74	99
16-25	5	17	2	71	95
26-35	14	27	5	76	122
36-45	12	27	5	65	109
46-55	20	17	3	38	78
56-65	25	8	4	27	64
> 60	13	5	1	6	25
Total	94	116	25	356	592

*Indoor aeroallergens include house dust, mattress dust, feathers, kapok, dust mite (*Dermatophagoides farinae*), cockroach, perennial mold spores, and all animal danders except horse hair.

†Outdoor aeroallergens include all pollens and outdoor mold spores plus horse hair.

screening allergy skin test with the listed allergens. Female subjects were double the number of male subjects except in the age groups below 15 (more male than female subjects) and above 66 (equal number of male and female subjects). Forty percent of the population had at least coexisting chronic rhinitis, and 1% had chronic eczema as determined by questionnaire at entry. The average age and duration of asthma of the 592 subjects were 35 years and 12.6 years, respectively. Close to one third of the population had lifelong asthma, which began in childhood, and the rest had adult onset. Approximately one third were steroid-dependent (30.8%). Fig. 1 shows the overall prevalence of inhalant allergies in patients with asthma as determined by allergy skin testing: house dust (76%), cockroach (48%), ragweed (45%), other weed pollens (42%), cat (40%), seasonal molds (36%), dog (29%), grass pollens (29%), and dust mite (24%). Ninety-four subjects (15.8%) failed to show any positive skin test results. Eighty-five percent of 592 subjects had one or more positive skin test results to the tested aeroallergen groups, and the average number of detected allergens was 4.5. A majority (66%) had positive test results to two to seven aeroallergens, and 60% had positive reactions to both indoor and outdoor allergens when allergens were divided categorically into indoor allergens: (house dust, dust mite, cat and dog, feathers, perennial mold, and/or cockroach) and outdoor allergens (all pollens [trees, grasses, ragweeds, and western weeds], seasonal mold spores, and/or horse hair). The number of subjects sensitive to only indoor allergens (≥ 1 allergen) (116:20%) exceeded the number of those sensitive to only outdoor allergens (≥ 1 allergen) (25:4%) (Table I). The skin test reactivity in general declined with subject's age (chi square = 88.2, based on 18 degrees of freedom, $p < 0.001$). The highest frequency of positive skin test results was noted in

TABLE II. Distribution of IgE antibody ($\log_{10}$ IgE) of patients with asthma

Age (yr)	No. of subjects	Log IgE (mean $\pm$ SD)
0-15	59	2.622 $\pm$ 0.546
16-25	79	2.583 $\pm$ 0.557
26-35	101	2.452 $\pm$ 0.604
36-45	77	2.426 $\pm$ 0.601
46-55	56	2.105 $\pm$ 0.702
56-65	47	2.185 $\pm$ 0.563
> 66	25	2.076 $\pm$ 0.616

One-way ANOVA F test: 7.25 based on 6 and 437 degrees of freedom ($p < 0.001$).

subjects between the age of 26 and 45 (8.3 allergens on average).

Four hundred forty-four of the 592 subjects with asthma had total serum IgE antibody measured, which showed widely variable results (5 to 3390 IU/ml), (geometric mean $\pm$ SEM: 245.6 $\pm$ 17.3 IU/ml; log IgE, 0.7 to 3.9). Seventy-four percent of the serum IgE levels were abnormal (≥ 100 IU/ml). IgE antibodies ($\log_{10}$ IgE) were highest in subjects below the age of 15 (Table II) and declined with age; regression lines for log IgE on age were male subjects: 2.8388 + (-0.0119) age, female subjects: 2.7213 + (-0.0093) age (one-way ANOVA F = 7.25 based on 6 and 443 degrees of freedom, $p = 0.0001$). The serum IgE antibody was also well correlated with the number of positive skin test results of the subjects with asthma (one-way ANOVA, F = 4.85, based on 9 and 591 degrees of freedom, $p < 0.0001$).

Comparative characteristics of two subgroups of residents with asthma, cockroach-allergic versus ragweed-allergic

To assess the role of the identified aeroallergen sensitivities in this population, we selected two representative allergen-sensitive subgroups and

TABLE III. Comparative characteristics of patients with asthma among CR+RG−, CR−RG+, and CR+RG+ groups

Group	Sex		Age (yr)	Duration of asthma (yr)	IgE antibody (log ₁₀)	No. of allergens positive*
	F	M				
CR+RG−	97† (128)	31	32.2 ± 1.38	14.6 ± 1.13	2.54 ± 0.50‡	2.73 ± 0.13§
CR−RG+	62 (109)	47	30.0 ± 1.19	9.6 ± 1.22	2.55 ± 0.52‡	4.33 ± 0.16
CR+RG+	97 (155)	58	28.3 ± 1.25	14.7 ± 1.02	2.68 ± 0.48	4.63 ± 0.16

Values are expressed as means ± SEM.

*Number of additional aeroallergen sensitivities.

†Female subjects are frequently affected ($p = 0.006$).

‡Number of allergens positive is significantly lower in CR+RG− as compared with those in CR−RG+ and CR+RG+ ($p = 0.0001$).

§Duration of asthma is shorter in CR−RG+ as compared with either CR+RG+ ($p = 0.0016$) or CR+RG− ($p = 0.0031$).

||Log IgE antibody is lower in CR−RG+ than that in CR+RG+ ($p = 0.0047$).

compared some of the characteristics. We chose CRa to represent indoor allergens because it is a defined allergen that is highly concentrated indoors and the well-known ragweed antigen (RGa) to represent outdoor allergens. Prevalence of cockroach sensitivity (CR+) and ragweed sensitivity (RG+) were similar (48% vs 45%) among subjects listed in the Chicago Asthma Registry (see Fig. 1). The CR+ group included 194 female and 89 male subjects, and the RG+ group included 159 female and 115 male subjects. Average ages of both groups were similar (30.4 and 29.5 years), and both groups had highly elevated serum IgE antibodies (geometric mean ± SEM: 413.1 ± 3.8 IU/ml and 425.9 ± 7.4 IU/ml). However, the frequency of raised serum IgE antibodies (>100 IU/ml) was 87% in patients with CRa-sensitive asthma, whereas it was 78% in patients with RGa-sensitive asthma ($p < 0.05$). Both groups had a similar proportion of dust mite (*Dermatophagoides farinae*) sensitivity (35% vs 31%) ($p > 0.05$). Both CR+ and RG+-sensitive subjects had a wide range of other aeroallergen sensitivities (0 to 9). Cockroach hypersensitivity was prevalent among female subjects (76% vs 62%), whereas RG+ was high in male subjects (77% vs 65%) (chi square = 10.12 based on 2 degrees of freedom, $p \leq 0.006$).

The characteristics of both aeroallergen-sensitive groups were analyzed in further detail: (1) cockroach-sensitive and ragweed-nonsensitive (CR+ RG−); (2) cockroach-nonsensitive and ragweed-sensitive (CR− RG+); and (3) cockroach- and ragweed-sensitive (CR+ RG+)

groups (data shown in Table III). The cockroach-sensitive groups (CR+ RG+ and CR+ RG−) experienced a significantly longer duration of asthma (14.6 and 14.7 years) than the cockroach-nonsensitive group (CR− RG+) (9.6 years) ($p = 0.0016$ and 0.0031). The CR+ RG− group showed an average of 2.7 additional aeroallergen sensitivities, whereas ragweed-sensitive groups, CR− RG+ and CR+ RG+, reacted with 4.3 and 4.6 additional aeroallergens, respectively ($p = 0.0001$, both). The CR+ RG− group consisted of six subjects who were only allergic to CRa, and the rest had positive reactions to house dust plus other inhalants. IgE levels in all three were highly elevated, yet the CR+ RG+ group showed slightly higher values than those of both CR+ RG− and CR− RG+ ($p = 0.0047$). However, the IgE antibody of the CR+ RG− group was similar to that of CR− RG+ group, which had many aeroallergen sensitivities. Distributions of IgE antibody (scattergram) of both subgroups showed similar slopes ($r = -0.04$, $r = -0.13$) with a significant difference between intercepts of the lines ($p = 0.03$).

Ragweed-sensitive subjects (CR+RG+ and CR−RG+ groups) exhibited mostly an identifiable history of seasonal exacerbation during the late fall, from September to the beginning of November, whereas cockroach-sensitive subjects (CR+RG− group) manifested year-round symptoms of asthma, and some experienced exacerbations in winter. Table IV shows distribution of subjects with CR+ asthma. Cockroach hypersensitivity affected more female subjects except in the

TABLE IV. Age-related distribution of cockroach hypersensitivity among 592 patients with asthma who had skin tests

Sex	Age (yr)						
	≤ 15	16-25	26-35	36-45	46-55	56-65	66 ≥
M = 45% (196 tested)	41/61*	9/23	18/31	10/29	5/19	4/21	2/12
F = 49% (396 tested)	17/38	42/72	54/91	44/80†	23/59	11/13	3/13
Total 48% (Tested 592)	58/99	51/95	72/122	54/109	28/78	15/34	5/25

Number indicates positive rate (%) by allergy skin testing.

*Male subjects in this age group show significantly higher prevalence ($p = 0.027$) than female subjects.

†Female subjects in this group show tendency of higher prevalence ($p = 0.058$) than male subjects.

age group below 15 years (67% in male vs 45% in female subjects, $p = 0.027$). Its prevalence in patients with asthma was over 50% up to the age of 45 in both genders, and gradually decreased with age, 20% in the group aged 66 years and older ([female: chi square = 23.13, $p < 0.001$], [male: chi square = 28.14, $p < 0.0001$]). Seventy percent of cockroach-sensitive and 50% of nonsensitive subjects with asthma had one or more first-degree relatives with asthma. Unlike RGA-sensitive subjects, the CRA-sensitive subjects were mostly allergic to house dust; a few were allergic to other outdoor or indoor aeroallergens. Six subjects reacted to no other allergens. Steroid dependency was 32% in the CRA-positive group and only 24% in the RGA-positive group ($p < 0.05$).

DISCUSSION

This study describes a strong association of atopic causes, particularly inhalant allergies, among urban Chicago residents with asthma. The Chicago residents with asthma in this study are largely representative of the low socioeconomic class so called "clinic population" of the inner city living near the Southwest section of metropolitan Chicago as described earlier.²⁷ Although we did not have a specific ethnic breakdown, over one half of the subjects were African-Americans, and there was a significant number of Hispanics. Similar aeroallergen sensitivities in general populations with asthma have been described in a study from Australia,²⁸ which reports overall that 60% of 8071 cases of asthma were related to extrinsic causes. Hendrix et al.²⁹ reported that 84% of 656 patients with asthma in London showed sensitivity to one or more allergens, which was well correlated with history of asthma exacerbations. Seventy-two percent of adults with "asthma" in Tucson³⁰ had positive skin test results, and Schulaner³¹ reported that 78% of children with asthma

in Manhattan had positive test results to Germany cockroach extract. Recently, Kalliel et al.³² observed that 58.3% of the population with asthma in a pulmonary clinic showed aeroallergen sensitivities by prick skin tests. The comparatively high rate (85%) of aeroallergen sensitivities noted in our study could have resulted in part from the fact that we tested with many more allergens including a new allergen, CRA, than other studies used. It may also be in part an indication that inner-city Chicago residents with asthma may be more atopic than other populations reported previously. The strong atopy in our study is also reflected in the highly elevated levels of serum total IgE antibodies as compared with other available data³² (Table II).

A significant finding in this study is the revelation of prevalent cockroach hypersensitivity that is not found in other studies. This finding, however, most likely comes from the fact that other studies missed it simply because it was not tested, since it is known that cockroach infestation has been a worldwide phenomenon including flats in London and tropical islands.^{16, 33} In this study it could have been also easily missed or could have been a "hidden factor" if the cockroach allergen was not included in the screening panel. Prevalence of the cockroach sensitivity in this study seems to be similar to that reported on atopic populations from New York City (44%)^{13, 14} and the midwestern United States (58%)³⁴ but higher than those from Puerto Rico (21%).³⁵ Patients with cockroach-sensitive asthma have been reported sporadically^{15, 18-20} and are particularly prevalent among low socioeconomic urban populations.^{13, 14, 17-20, 34-36}

An indoor aeroallergen, house dust, was highest among the tested allergen sensitivities, which is similar to results of other studies.^{23, 27-29, 34, 35} Less than 6% of the subjects in the study had an

"isolated dust allergy," which is higher than that of the "isolated CRa-allergy." However, the significance of the house dust sensitivity in these subjects is not clear, particularly because its content of dust extracts is uncertain. Moreover, unlike patients with "isolated Cra allergy, a few patients with "isolated dust allergy" responded positively to dust challenge tests. The CRa hypersensitivity, on the other hand, even in the "isolated CRa allergy" was proven for its causal relationships with asthma by the positive asthmatic responses (87%).^{18, 19, 36} Cat and dog sensitivities seem to correlate well with the clinical symptoms of the subjects with asthma. Among indoor aeroallergens, dust mite (*Dermatophagoides farinae*) sensitivity was found in a relatively low rate in this study, similar to results of some previous studies.^{27, 36, 37} This sensitivity is lower than others reported from different parts of the country.^{32, 34, 38, 39} The reason for the low prevalence is not clear at present. It could be in part caused by the test antigen used (i.e., one species of mite), our stringent criteria, and/or a relatively low indoor humidity frequently found in Chicago during severe winter. The low prevalence of cat allergy could also have been due to the characteristics of inner-city residents related to the low rate of pet ownership among the patients with asthma living in high-rise buildings in Chicago.^{37, 40}

Abnormally high IgE antibody levels in this study need to be investigated further. Subjects with asthma in general and patients with atopic diseases are expected to have elevated IgE antibody levels.^{6, 32, 41-43} Yet, residents of metropolitan Chicago who have asthma seem to have particularly high IgE levels, higher than those of patients with asthma in Providence, Rhode Island³² or Lexington, Kentucky.⁴⁰ Although not all subjects were screened for parasitic diseases, no reasons, other than asthma and other atopic complaints, for the high IgE levels were apparent. There was no case of allergic bronchopulmonary aspergillosis. Although we do not know the reasons clearly, the antibody levels in this atopic population are consistently high in the previous studies of inner-city asthma, as well as in the patients with cockroach-sensitive asthma.^{27, 36} Such high levels could be caused by their strong atopic status, apparent by multiple aeroallergen sensitivities, which are generally well correlated with number of positive allergens by skin test (ANOVA, $F = 38.70$, $p < 0.0001$). However, an exception is the cockroach-sensitive subgroup, which had a disproportionately high number of positive skin test results.

Patients with cockroach-sensitive asthma collectively seem to have a few distinctive characteristics. They have elevated IgE antibody levels yet few additional aeroallergen sensitivities. This subgroup has more chronic and perennial symptoms, which are the same characteristics of high-risk inner-city asthma. Another characteristic seems to be relative severity, which is also a known characteristic of inner-city asthma. The characteristics of the inner-city Chicago residents with asthma appear to be related largely to the cockroach sensitivity, because the subgroup is a major proportion of this population. Such severity and chronicity of the asthma in this study, particularly for the CRa subgroup, could be explained by both the prolonged exposure time and heavy content of indoor allergens noted, particularly of the cockroach allergen in Chicago dwellings.^{27, 37} It is plausible to assume that CRa and/or any strong indoor allergen sensitivities would induce a protracted airway inflammation when individuals spend long hours indoors every day. Significance of and reasons for the disproportionately elevated IgE antibody levels in cockroach-sensitive asthma are not clear, as yet. It is, however, attractive to think that it could be caused by the large quantities of circulating cockroach-specific IgE antibody as noted.^{36, 37}

The reason that the cockroach sensitivity affects young male and adult female subjects more frequently is not clear. It could be related to the fact that young children and less mobile adults (older women) are sensitized more by their lifestyle (staying indoors for relatively longer period), which is similar to causes of dust mite sensitivities in young children.^{9, 38, 39} Winter exacerbations of symptoms noted in this subgroup might also be related to the amount and time of the exposure to airborne CRa at home in winter, while insects gather more indoors.^{27, 37, 44} Cockroach infestation in Lexington, Kentucky, for example, is said to be as heavy as that in Chicago, yet the insect hypersensitivity is less prevalent in Lexington (winter is milder and shorter).⁴⁰ The noted gender differences between the cockroach-sensitive and the ragweed-sensitive subjects with asthma may also be related to the duration of allergen exposure, CRa, indoors versus RGa, outdoors.

Admittedly, this descriptive study has inherent weaknesses because clinical and laboratory data were collected from a selected population without a control group for comparison (as a registry) over a long time. Therefore in order to minimize and overcome the effect of inherent weakness, we tried to adhere to the original criteria diligently

throughout the period. Furthermore, in order to maintain similar potencies of skin testing reagents, we used the same vendor throughout the period and maintained the same criteria for skin testing. We also minimized the personnel changes for skin testing and had the same principal investigator throughout the period. The lack of control group has been compensated for in part by the large patient pool and use of relevant statistical analysis. In spite of the inherent weaknesses, this study nonetheless shows the significant facts that urban Chicago residents with asthma, specifically those with relatively severe asthma (as defined), have multiple aeroallergen sensitivities, and a comprehensive atopic evaluation is a good start to a better understanding of inner-city asthma.

Although this study per se does not provide direct evidence that each of these aeroallergens causes allergic asthma, the majority of these aeroallergens are known to play causative roles in asthma.^{10-12, 27-29, 41, 45} Therefore it may be prudent to consider that these identified aeroallergens contribute to the symptoms of asthmatic inflammation. In particular, the revelation of the high prevalence of cockroach hypersensitivity could explain a part of the morbidity and severity of the disease in this population because the allergen is well known for inducing dual allergic asthmatic reactions.^{18-20, 36} By inference, these indoor and outdoor allergen sensitivities may be directly or indirectly linked to the morbidity and mortality rates of these patients with asthma. If so, avoidance of these allergens and/or manipulations of the hypersensitivities could help in reducing the morbidity and/or mortality rates of inner-city residents with asthma. For instance, subjects with cockroach-sensitive asthma have either sustained bronchospasm or severe dual asthmatic responses lasting up to 72 hours after a single inhalation challenge test with CRa.^{18-20, 35} Furthermore, patients with such severe and chronic cockroach-sensitive asthma experienced significant relief of asthmatic symptoms with cockroach allergen immunotherapy, and they were able to maintain "normal" quality of life.⁴⁵ Moreover, avoidance of cockroach allergens by patients with cockroach-sensitive asthma, when it is identified, is easy and may reduce the risk of asthma attacks, in a manner similar to that reported for patients with dust mite-sensitive asthma.⁴⁶

We need more definitive well-controlled studies to elucidate the role or roles of each identified aeroallergen individually and collectively and also more comparative studies among urban and rural residents with asthma.

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REFERENCES

1. Sigel SC. History of asthma death from antiquity. *J ALLERGY CLIN IMMUNOL* 1987;80:458-62.
2. Panlozzi LJ, Coleman JJ, Buist AS. A recent increase in asthma mortality in the Northwestern United States. *Ann Allergy* 1984;56:392-5.
3. Weiss KB. Seasonal trends in US asthma hospitalizations and mortality. *JAMA* 1990;263:2323-8.
4. Mak H, Johnston P, Abbey H, Talamo R. Prevalence of asthma and health service utilization of asthmatic children in an inner city. *J ALLERGY CLIN IMMUNOL* 1982;70:367-72.
5. Perrin JM, Homer CJ, Berwick DM, Woolf AD, Freeman JL, Wennberg JE. Variations in rates of hospitalizations of children in three urban communities. *N Engl J Med* 1982;320:1183-7.
6. Busse WW, Reed CE. Bronchial asthma. In: Middleton E Jr, Reed CE, Ellis EF, Adkinson NF Jr, Yunginger JW, eds. *Allergy: principles and practice*. 3rd ed. St. Louis: CV Mosby, 1988: 969-71; 1064-7.
7. Cockcroft DW. Hypothesis, mechanism of perennial allergic asthma. *Lancet* 1983;2:253-5.
8. Kaliner M. Hypothesis on the contribution of late-phase allergic responses to the understanding and treatment of allergic diseases. *J ALLERGY CLIN IMMUNOL* 1984;73:311-5.
9. Sears MR, Hershovitz GP, Holdaway MD, Hewitt CJ, Flannery EM, Silva PA. The relative risks of sensitivity to grass pollen, house dust mite, and cat dander in the development of childhood asthma. *Clin Exp Allergy* 1989;19:419-24.
10. Van Metre TE Jr, Marsh DG, Adkinson NF, et al. Dose of cat (Felis domestic allergen) (*Fel d*) that induces asthma. *J ALLERGY CLIN IMMUNOL* 1986;78:62-75.
11. Pollart SM, Chapman MD, Fiocco GP, Rose G, Platts-Mills TAE. Epidemiology of acute asthma: IgE antibodies to common inhalant allergens as a risk factor for emergency room visits. *J ALLERGY CLIN IMMUNOL* 1989;83:875-82.
12. Reid MJ, Moss RB, Hsu Y-P, et al. Seasonal asthma in Northern California: allergic causes and efficacy of immunotherapy. *J ALLERGY CLIN IMMUNOL* 1989;78:590-600.
13. Berntson HS, Brown H. Cockroach allergy II, the relation of infestation to sensitization. *South Med J* 1967;60:852-5.
14. Mendoza J, Snyder RD. Cockroach sensitivity in children with bronchial asthma. *Ann Allergy* 1970;28:159-63.
15. Berntson HS, Brown H. Insect allergy: the allergenicity of the excrement of the cockroach. *Ann Allergy* 1970;28: 543-7.
16. Kang BC. Cockroach allergy. *Clin Rev Allergy* 1990;8:87-98.
17. Berntson HS, McMahon TF, Brown H. Cockroach asthma. *Br J Dis Chest* 1972;66:61-6.
18. Kang B. Study on cockroach antigen as a probable causative agent in bronchial asthma. *J ALLERGY CLIN IMMUNOL* 1976;58:357-65.

19. Kang B, Vellody D, Homburger H, Yuninger JW. Cockroach cause of allergic asthma. *J ALLERGY CLIN IMMUNOL* 1979;63:80-6.
20. Chang JL, Kang B, Theodorescu M, Ryo UY. Circulating free histamine in peripheral blood following cockroach antigen challenge in relationship to leucocyte sensitivity in vitro. *Mt Sinai J Med* 1984;51:197-202.
21. A Report by Committee on Urban Pest Management. Major urban arthropod pests in the United States. Washington DC: National Academy Press, 1980:261-71.
22. Toms EM, Robinson WH. Distribution, seasonal abundance and pest status of the Oriental cockroach (Orthoptera: Blattidae) and an evaniid wasp (Hymenoptera: Evaniidae) in urban apartments. *J Econ Entomol* 1986;79:431-6.
23. Kang B, Sulit N. A comparative study of prevalence of skin hypersensitivity to cockroach and house dust antigens. *Ann Allergy* 1978;41:333-6.
24. American Thoracic Society Committee on Diagnostic Standards for Nontuberculous Diseases. Definition and classification of chronic bronchitis, asthma, and pulmonary emphysema. *Am Rev Respir Dis* 1962;85:762-74.
25. Bousquet J. In vivo methods for study of allergy: skin tests, techniques, and interpretation. In: Middleton E Jr, Reed CE, Ellis EF, Adkinson NF Jr, Yunginger JW, eds. *Allergy: principles and practice*. 3rd ed. St. Louis: CV Mosby, 1988:425-36.
26. Nye L, Merrett TG, Landon J, White RJ. A detailed investigation of circulating IgE levels in a normal population. *Clin Allergy* 1975;1:13-24.
27. Kang B, Jones J, Johnson J. Analysis of indoor environment and characteristics of the urban bronchial asthma on one hundred consecutive asthmatics. *Ann Allergy* 1989;62:30-4.
28. Ford RM. Etiology of asthma. A continuing review (8071 cases seen from 1970-1980). *Ann Allergy* 1983;50:47-50.
29. Hendrix DJ, Davies FJ, D-Sonza MF, Pepys J. An analysis of skin prick test reactions in 656 asthmatic patients. *Thorax* 1975;30:2-8.
30. Burrows B, Lobowitz MD, Barbee RA. Respiratory disorders and allergy skin test reactions. *Ann Intern Med* 1976;84:134-9.
31. Schulaner FA. Sensitivity to the cockroach in three groups of allergic children. *Pediatrics* 1970;45:465-6.
32. Kalliel JN, Goldstein BM, Braman SS, Settupane GA. High frequency of atopic asthma in a pulmonary clinic population. *Chest* 1989;96:1336-40.
33. Roth LM, Willis ER. The medical and veterinary importance of cockroaches. *Smithsonian Miscellaneous Collection* 1957;134:1-149.
34. Hulett AC, Dockhorn RJ. House dust, mite (*D. farinae*) and cockroach allergy in a midwestern population. *Ann Allergy* 1979;42:160-5.
35. Marchand AM. Allergy to cockroaches. *Bol Asoc Med P R* 1966;58:49-53.
36. Kang BC, Wu CW, Johnson J. Characteristics and diagnosis of cockroach-sensitive bronchial asthma. *Ann Allergy* 1992;68:237-44.
37. Kang BC, Chang JL, Johnson J. Characterization and partial purification of the cockroach antigen in relation to housedust and housedust mite (*D.f.*) antigens. *Ann Allergy* 1989;63:207-12.
38. Lau S, Falkenhorst G, Weber A, et al. High mite-allergen exposure increases the risk of sensitization in atopic children and young adults. *J ALLERGY CLIN IMMUNOL* 1989;84:718-25.
39. Platts-Mills TAE, de Weck AL. Dust mite allergens and asthma—a worldwide problem. *J ALLERGY CLIN IMMUNOL* 1989;83:415-27.
40. Yun DK, Mayer L, Kambara T, Grizz V, Johnson J, Kang BC. Characteristics of bronchial asthmatics of two cities, atopy and indoor environment [Abstract]. *J ALLERGY CLIN IMMUNOL* 1990;85:181.
41. Burrows B, Martinez FD, Halonen M, Barbee RA, Cline MG. Association of asthma with serum IgE levels and skin-test reactivity to allergens. *N Engl J Med* 1989;320:271-7.
42. Barbee RA, Halonen M, Kaltenborn W, Lebowitz M, Burrow B. A longitudinal study of serum IgE in a community cohort: correlations with age, sex, smoking, and atopic status. *J ALLERGY CLIN IMMUNOL* 1987;79:919-27.
43. Wittig HJ, Bellort J, Fillippi I, Royal G. Age-related serum immunoglobulin E levels in healthy subjects and in patients with allergic disease. *J ALLERGY CLIN IMMUNOL* 1980;66:305-13.
44. Swanson MC, Argawal MK, Reed CE. An immunochemical approach to indoor aeroallergen quantitation with a new volumetric air sampler: studies with mite, roach, cat, mouse, and guinea pig antigens. *J ALLERGY CLIN IMMUNOL* 1985;76:724-9.
45. Kang BC, Johnson J, Morgan C, Chang JL. Role of immunotherapy in cockroach asthma. *J Asthma* 1988;25:205-18.
46. Platts-Mills TAE, Tovey ER, Mitchell EB, Mozarro H, Nock P, Wilkins SR. Reversal of bronchial reactivity during prolonged allergen avoidance. *Lancet* 1982;2:675-8.

APPENDIX

Inhalant allergens

Group I: Trees

Elm
Maple
Box elder
Willow
Sycamore
Walnut
Hickory
Oak
Cottonwood
Mulberry

Group II: Grasses

June
Orchard
Timothy
Bermuda

Group III: Ragweeds

Ragweed, short
Ragweed, giant

Group IV:

English plantain
Lamb's quarter
Russian thistle
Marsh elder
Sage brush

Group V: Animal danders

Dog dander
Cat dander
Guinea pig dander
Rabbit dander
Gerbil dander
Horse hair

Group VI: Dusts

House dust I
Mattress dust
Feathers
Kapok

Group VII: Seasonal molds

Alternaria
Hormodendrum
Fusarium
Helminthosporium

Group VIII: Perennial molds

Aspergillus
Penicillium

Group IX:

Mite (*D. farinae*)

Group X:

*Cockroach (CRa-M)

*Cockroach antigen used is an equal mixture of whole body extract of American, German, and Oriental cockroaches.