

## Inner City Asthma Study: Relationships among sensitivity, allergen exposure, and asthma morbidity

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**Background:** Asthma-associated morbidity is rising, especially in inner city children.

**Objective:** We evaluated the allergen sensitivities, allergen exposures, and associated morbidity for participants in the Inner City Asthma Study. We also determined geographic variations of indoor allergen levels.

**Methods:** Nine hundred thirty-seven inner city children 5 to 11 years old with moderate to severe asthma underwent allergen skin testing. Bedroom dust samples were evaluated for Der p 1, Der f 1, Bla g 1, Fel d 1, and Can f 1.

**Results:** Skin test sensitivities to cockroach (69%), dust mites (62%), and molds (50%) predominated, with marked study site-specific differences. Cockroach sensitivity was highest in the Bronx, New York, and Dallas (81.2%, 78.7%, and 78.5%, respectively), and dust mite sensitivity was highest in Dallas and Seattle (83.7% and 78.0%, respectively). A majority of homes in Chicago, New York, and the Bronx had cockroach allergen levels greater than 2 U/g, and a majority of those in Dallas and Seattle had dust mite allergen levels greater than 2 µg/g. Levels of both of these allergens were influenced by housing type. Cockroach allergen levels were highest in high-

rise apartments, whereas dust mite allergen levels were highest in detached homes. Children who were both sensitive and exposed to cockroach allergen had significantly more asthma symptom days, more caretaker interrupted sleep, and more school days missed than children who were not sensitive or exposed.

**Conclusion:** Geographic differences in allergen exposure and sensitivity exist among inner city children. Cockroach exposure and sensitivity predominate in the Northeast, whereas dust mite exposure and sensitivity are highest in the South and Northwest. Cockroach allergen appears to have a greater effect on asthma morbidity than dust mite or pet allergen in these children. (*J Allergy Clin Immunol* 2005;115:478-85.)

**Key words:** Asthma, allergen exposure, allergen sensitivity, morbidity, allergens, cockroach, dust mite, cat, dog

In the United States, morbidity as a result of asthma is disproportionately high among children living in less affluent urban communities.<sup>1,2</sup> It is also known that these children are exposed to high levels of indoor allergens,<sup>3,4</sup> that they are often sensitized to many of these allergens,<sup>5-7</sup> and that asthma-associated morbidity is related to this exposure.<sup>8-10</sup> Although cockroach, dust mite, and cat exposure has been most commonly associated with asthma exacerbations in sensitized individuals,<sup>8,11,12</sup> exacerbations also have been noted with dog, mouse, and *Alternaria* allergen exposure.<sup>6,13,14</sup>

The purpose of this report is to describe certain of the allergen sensitivities, allergen exposures, and associated asthma morbidity in 937 children with moderate to severe asthma who were enrolled in the Inner City Asthma Study (ICAS). In addition, the multiple study site structure of this project permitted an exploration of a broad range of geographic variation in allergen exposures and sensitivity among children with asthma across the United States. Thus, it expanded the population studied in the previous National Cooperative Inner City Asthma Study (NCICAS) to include not only children who resided in inner cities in the northeastern region of the United States but also children who lived in cities located in the southwestern and western areas of the country.

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#### Abbreviations used

BAU: Bioequivalent allergy units  
ICAS: Inner City Asthma Study  
NCICAS: National Cooperative Inner City Asthma Study

## METHODS

The ICAS enrolled 937 children (of 1059 children screened) age 5 to 11 years and their caretakers from 7 metropolitan inner city areas in the United States. In a fully crossed factorial design, study participants were randomized to receive an environmental allergen reduction intervention, an intervention providing bimonthly feedback regarding the child's clinical status to the children's primary care physician, both interventions, or neither intervention. The sample size was chosen on the basis of being able to detect a 0.6-day difference in maximum symptom days with 90% power. The study was conducted from August 1998 through August 2001. The environmental intervention is described in detail elsewhere.<sup>15</sup> Urban census tracts with at least 20% of households below the federal poverty guidelines were targeted. Eligibility for the study required that the child have at least 1 hospitalization or 2 emergency department visits for asthma during the 6 months before screening and have a positive skin test result (wheal size at least 2 mm greater than saline control<sup>7,8,12</sup>) to at least 1 of 11 common indoor allergens. Children also had to sleep in the primary caretaker's intervention home at least 5 nights per week.

After obtaining informed consent, trained bilingual interviewers administered a baseline clinical interview to the child's primary caretaker that included demographics, asthma morbidity, characteristics of the home environment, and the child's exposure to environmental tobacco smoke. Morbidity was measured at baseline and at 2-month intervals over a 24-month period. Morbidity was assessed by asking the caretaker to report 3 numbers: the number of days in the past 2 weeks that the child had wheezing, tightness in the chest, or cough; the number of nights that the child awoke because of asthma; and the number of days that the child had to slow down or discontinue play activities because of asthma. The primary outcome, the maximum symptom days per 2 weeks, is the largest value among these 3 reported numbers at each assessment. In addition, the caretaker reported the number of school days missed and caretaker days of lost sleep within the last 2 weeks, and the number of hospitalizations, scheduled and unscheduled clinic visits because of asthma, and emergency department visits for asthma within the last 2 months. Total unscheduled visits were calculated as the sum of unscheduled clinic visits and emergency department visits.

During the baseline clinical interview, children underwent skin testing (MultiTest II; Lincoln Diagnostics, Decatur, Ill) to the following 11 allergens: dust mite (*Dermatophyoides farinae* and *Dermatophyoides pteronyssinus*), cockroach (German and American mix), rat, mouse, mold (*Alternaria*, *Cladosporium*, *Aspergillus*, *Penicillium*), cat (standardized 10,000 bioequivalent allergy units (BAU)/mL), and dog (mixed breeds). Cockroach (German and American mix) extract was ordered from Bayer Corp (Spokane, Wash), and all other extracts were ordered from Greer Laboratories (Lenoir, NC). All extracts of each type were ordered from the same lot number. Specific allergens were chosen on the basis of findings from the NCICAS.<sup>7,8</sup> Because the studies of rat, mouse, and mold allergen sensitivity and exposure will be discussed elsewhere, they are not shown here.

One to 3 weeks after the baseline clinical evaluation, and every 6 months thereafter, a team of 2 trained research assistants performed an evaluation of each child's home. This included a home survey

**TABLE I.** Characteristics of participants and their homes, ICAS

|                                                                                                               | All ICAS participants (N = 937) | Control group only (N = 234) |
|---------------------------------------------------------------------------------------------------------------|---------------------------------|------------------------------|
| Race/ethnicity (%)                                                                                            |                                 |                              |
| Hispanic                                                                                                      | 40.3                            | 39.1                         |
| African American                                                                                              | 39.7                            | 42.5                         |
| White                                                                                                         | 7.0                             | 7.3                          |
| Asian                                                                                                         | 1.2                             | 0.9                          |
| Native American                                                                                               | 3.1                             | 2.6                          |
| Mixed/other                                                                                                   | 8.8                             | 7.7                          |
| Sex (%)                                                                                                       |                                 |                              |
| Male                                                                                                          | 62.6                            | 62.4                         |
| Female                                                                                                        | 37.4                            | 37.6                         |
| Age of child, y (mean)                                                                                        | 7.7                             | 7.6                          |
| Caretaker completed high school (%)                                                                           | 69.4                            | 71.2                         |
| At least 1 household member has a job (%)                                                                     | 75.9                            | 73.8                         |
| Household income <\$15,000 (%)                                                                                | 60.3                            | 63.7                         |
| Skin test positive to                                                                                         |                                 |                              |
| Mouse epithelia                                                                                               | 28.2                            | 27.8                         |
| Rat epithelia                                                                                                 | 18.9                            | 23.5                         |
| Cat standardized (10,000 BAU/mL)                                                                              | 44.1                            | 48.7                         |
| Dog epithelia (mixed breeds)                                                                                  | 21.1                            | 24.4                         |
| <i>D farinae</i>                                                                                              | 47.6                            | 47.0                         |
| <i>D pteronyssinus</i>                                                                                        | 57.1                            | 53.4                         |
| Either dust mite                                                                                              | 61.8                            | 61.5                         |
| Cockroach mix (American and German)                                                                           | 68.6                            | 70.4                         |
| <i>Alternaria tenuis</i>                                                                                      | 35.9                            | 36.9                         |
| <i>Cladosporium herbarum</i>                                                                                  | 18.1                            | 18.9                         |
| <i>Aspergillus</i> mix ( <i>flavus</i> , <i>fumigatus</i> , <i>glaucus</i> , <i>nidulans</i> , <i>niger</i> ) | 27.0                            | 24.0                         |
| <i>Penicillium notatum</i>                                                                                    | 13.1                            | 14.2                         |
| Any mold                                                                                                      | 50.1                            | 48.5                         |
| Type of dwelling (%)                                                                                          |                                 |                              |
| Detached house                                                                                                | 29.1                            | 30.3                         |
| Duplex/triplex                                                                                                | 9.2                             | 5.6                          |
| Row house                                                                                                     | 2.4                             | 1.3                          |
| Low-rise apartment (1-3 floors)                                                                               | 29.8                            | 31.2                         |
| High-rise apartment (>3 floors)                                                                               | 27.5                            | 28.6                         |
| Mobile home/trailer                                                                                           | 2.0                             | 3.0                          |
| One or more smokers in the home (%)                                                                           | 48.4                            | 46.2                         |
| Evidence of cockroaches in the home (%)                                                                       | 62.0                            | 63.2                         |
| Evidence of mice/rats in the home (%)                                                                         | 23.3                            | 25.0                         |
| Evidence of moisture or leaks (%)                                                                             | 49.4                            | 46.6                         |
| Cat in the home (%)                                                                                           | 13.1                            | 15.0                         |
| Dog in the home (%)                                                                                           | 16.6                            | 15.4                         |
| Other furry pet in the home (%)                                                                               | 4.7                             | 5.1                          |

involving both direct visual inspection and questions asked of the primary caretaker. Data on the entire home and on specific rooms (the child's sleeping area, the family/television room, the kitchen, and the bathroom) were collected. By using a standardized protocol and equipment, the home evaluation team collected separate vacuumed dust samples from the child's bedroom floor and bed. First, an area of 2 m<sup>2</sup> on the floor beside and under the child's bed was vacuumed for a total of 5 minutes. Then, a 1 m<sup>2</sup> area was delineated at the head of the child's bed for sampling. All bedding layers including the pillow were vacuumed for a total of 5 minutes. After vacuuming, sample collection thimbles were placed in separate sealed bags and shipped

**TABLE II.** Percentages of positive skin test results to tested allergens by study site, ICAS (N = 937)\*

|                                     | Boston<br>(N = 119) | Bronx<br>(N = 134) | Chicago<br>(N = 141) | Dallas<br>(N = 135) | New York<br>(N = 141) | Seattle<br>(N = 127) | Tucson<br>(N = 140) | Total<br>(N = 937) |
|-------------------------------------|---------------------|--------------------|----------------------|---------------------|-----------------------|----------------------|---------------------|--------------------|
| Cockroach mix (American and German) | 67.2                | 81.2               | 69.5                 | 78.5                | 78.7                  | 44.4                 | 58.6                | 68.6               |
| <i>D farinae</i>                    | 46.2                | 45.9               | 27.7                 | 72.6                | 32.6                  | 67.7                 | 43.6                | 47.6               |
| <i>D pteronyssinus</i>              | 52.9                | 54.5               | 33.3                 | 83.7                | 48.9                  | 73.2                 | 55.0                | 57.1               |
| Either dust mite                    | 58.8                | 60.2               | 39.0                 | 83.7                | 55.3                  | 78.0                 | 59.3                | 61.8               |
| Cat standardized (10,000 BAU/mL)    | 60.5                | 60.4               | 29.8                 | 30.4                | 39.7                  | 52.8                 | 38.6                | 44.1               |
| Dog epithelia (mixed breeds)        | 25.2                | 27.6               | 7.8                  | 15.6                | 22.0                  | 34.6                 | 17.1                | 21.1               |

\*All differences by site are significant at  $P < .0001$  by Pearson  $\chi^2$ .

**TABLE III.** Percent of study homes with significant exposure to assayed allergens by study site, ICAS (N = 937)\*

|                                         | Boston<br>(N = 119) | Bronx<br>(N = 134) | Chicago<br>(N = 141) | Dallas<br>(N = 135) | New York<br>(N = 141) | Seattle<br>(N = 127) | Tucson<br>(N = 140) | Total<br>(N = 937) |
|-----------------------------------------|---------------------|--------------------|----------------------|---------------------|-----------------------|----------------------|---------------------|--------------------|
| Bla g, bed or floor, >2 U/g             | 36.8                | 54.3               | 55.1                 | 47.7                | 62.2                  | 7.6                  | 11.0                | 39.5               |
| Der p, bed or floor, >2 $\mu$ g/g       | 11.8                | 9.4                | 7.9                  | 60.2                | 2.9                   | 62.7                 | 5.0                 | 22.5               |
| Der f, bed or floor, >2 $\mu$ g/g       | 33.9                | 14.1               | 13.8                 | 27.5                | 6.7                   | 7.2                  | 22.3                | 17.7               |
| Either mite, bed or floor, >2 $\mu$ g/g | 39.8                | 21.4               | 16.7                 | 69.9                | 8.2                   | 65.1                 | 24.5                | 34.7               |
| Fel d, bed or floor, >8 $\mu$ g/g       | 14.0                | 12.4               | 5.9                  | 1.6                 | 12.6                  | 32.8                 | 5.8                 | 12.0               |
| Can f, bed or floor, >10 $\mu$ g/g      | 9.1                 | 17.5               | 7.7                  | 9.7                 | 13.8                  | 25.4                 | 19.9                | 14.8               |

\*All differences by study site are significant at  $P < .001$  by Pearson  $\chi^2$ .

**TABLE IV.** Housing types and humidity by study site, ICAS (N = 937)\*

|                                             | Boston<br>(N = 119) | Bronx<br>(N = 134) | Chicago<br>(N = 141) | Dallas<br>(N = 135) | New York<br>(N = 141) | Seattle<br>(N = 127) | Tucson<br>(N = 140) | Total<br>(N = 937) |
|---------------------------------------------|---------------------|--------------------|----------------------|---------------------|-----------------------|----------------------|---------------------|--------------------|
| Detached house/trailer                      | 11.8                | 13.4               | 14.2                 | 53.2                | 0.0                   | 52.0                 | 72.9                | 31.2               |
| Low-rise apartment/row house/duplex/triplex | 74.0                | 11.9               | 82.3                 | 46.7                | 3.6                   | 48.0                 | 27.1                | 41.3               |
| High-rise apartment                         | 14.3                | 74.6               | 3.6                  | 0                   | 96.4                  | 0                    | 0                   | 27.5               |
| Humidity >50%                               | 28.6                | 26.1               | 28.4                 | 58.5                | 21.3                  | 29.1                 | 12.9                | 29.1               |

\*All differences by study site are significant at  $P < .0001$  by Pearson  $\chi^2$ .

to a central laboratory for evaluation of levels of Der p 1, Der f 1, Bla g 1, Fel d 1, and Can f 1 by ELISA. Humidity was measured in the child's bedroom at the time of the dust sample collection by using a handheld hygrometer.

## Statistical analyses

$\chi^2$  Tests were used to test for differences across sites. Risk ratios were calculated for risk of sensitivity according to exposure and risk of high allergen levels according to housing type and pet ownership by using contingency tables and a Mantel-Haenszel adjustment where indicated.

Only children who did not receive either intervention (control group, N = 234) were used in the morbidity analyses so that the observed outcomes would not be influenced by any changes caused by the interventions. The effect of sensitivity and exposure on 2-year morbidity was examined by using a longitudinal model with a generalized estimating equation approach to adjust for the correlation between measurements on each individual child. Morbidity measurements were averaged to the closest of the 5 home evaluation visits, such that there were as many as 5 records per child in this analysis. On the basis of previous studies, allergen exposure cutoffs were set at 2 U/g for Bla g 1, 2  $\mu$ g/g for Der f 1 and Der p 1, 8  $\mu$ g/g for Fel d 1, and 10  $\mu$ g/g for Can f 1.<sup>8-11,16</sup>

Children were classified at each of the 5 time points with respect to each allergen: sensitive and exposed, sensitive but not exposed, not sensitive but exposed, and neither sensitive nor exposed. Mean morbidity outcomes were calculated for each group and tested with an

a priori planned comparison of the sensitive and exposed group against the other 3 groups, adjusting for study site and month of the first home evaluation. Because of the distribution of outcomes, a Poisson model was used to calculate the rate ratio for unscheduled visits, and a binomial regression model was used to calculate the risk ratio for hospitalization with the same a priori planned comparison. The hospitalization model could not be adjusted for seasonality because of the infrequent number of hospitalizations.

Models were also run to examine the effect of using a wheal 3 mm greater than negative control to denote sensitivity. Although data for all allergens were generated, only results for cockroach are shown.

## RESULTS

Of 1059 children skin tested, 994 (93.9%) had a positive skin test result to 1 or more of the allergens used in the testing. Of these 994 children, 937 (94.3%) successfully completed the baseline home evaluation and were enrolled. Table I describes the characteristics of all of the participants and their homes. As shown, the children in the control group, the only group examined in the morbidity analysis, had characteristics that were not appreciably different from the entire population enrolled.

The ICAS involved study sites that were more widely distributed around the United States than the previous

**TABLE V.** Relationship of housing type and pet ownership to allergen levels, ICAS (N = 937)

|                                                  | Percent exposed | Crude RR (95% CI)       | Study site-adjusted RR (95% CI) |
|--------------------------------------------------|-----------------|-------------------------|---------------------------------|
| Cockroach allergen (Bla g 1 > 2 U/g)             |                 |                         |                                 |
| High-rise apartment (>3 floors)                  | 58.9            | <b>2.64 (2.07-3.36)</b> | <b>1.50 (1.07-2.09)</b>         |
| Low-rise apartment (1-3 floors)                  | 40.1            | <b>1.80 (1.40-2.31)</b> | <b>1.33 (1.03-1.71)</b>         |
| Detached house                                   | 22.0            | 1                       | 1                               |
| Dust mite allergen (Der f 1 or Der p 1 > 2 µg/g) |                 |                         |                                 |
| High-rise apartment (>3 floors)                  | 13.6            | <b>0.29 (0.21-0.41)</b> | 0.66 (0.41-1.08)                |
| Low-rise apartment (1-3 floors)                  | 39.4            | 0.85 (0.72-1.02)        | 1.02 (0.87-1.19)                |
| Detached house                                   | 46.2            | 1                       | 1                               |
| Cat allergen (Fel d 1 > 8 µg/g)                  |                 |                         |                                 |
| High-rise apartment (>3 floors)                  | 10.8            | 0.87 (0.54-1.41)        | 0.51 (0.24-1.10)                |
| Low-rise apartment (1-3 floors)                  | 12.3            | 0.99 (0.66-1.49)        | 0.95 (0.63-1.42)                |
| Detached house                                   | 12.5            | 1                       | 1                               |
| Dog allergen (Can f 1 > 10 µg/g)                 |                 |                         |                                 |
| High-rise apartment (>3 floors)                  | 13.9            | <b>0.65 (0.44-0.96)</b> | 0.57 (0.29-1.14)                |
| Low-rise apartment (1-3 floors)                  | 10.2            | <b>0.47 (0.32-0.69)</b> | <b>0.57 (0.38-0.86)</b>         |
| Detached house                                   | 21.5            | 1                       | 1                               |
| Cat allergen (Fel d 1 > 8 µg/g)                  |                 |                         |                                 |
| Cat in home                                      | 66.7            | <b>21.2 (14.0-32.0)</b> | <b>14.9 (10.0-22.0)</b>         |
| No cat in home                                   | 3.2             | 1                       | 1                               |
| Dog allergen (Can f 1 > 10 µg/g)                 |                 |                         |                                 |
| Dog in home                                      | 65.5            | <b>16.7 (11.4-24.5)</b> | <b>14.4 (10.0-20.8)</b>         |
| No dog in home                                   | 3.9             | 1                       | 1                               |

**TABLE VI.** Relative risk of skin test reactivity (2-mm wheal > control) according to exposure to allergen at baseline visit, ICAS (N = 937)

|                                    | % Exposed | % Positive among exposed | % Positive among nonexposed | Risk ratio (95% CI)     |
|------------------------------------|-----------|--------------------------|-----------------------------|-------------------------|
| Bla g, bed or floor, >2 U/g        | 39.5      | 81.4                     | 60.1                        | <b>1.36 (1.24-1.48)</b> |
| Der p, bed or floor, >2 µg/g       | 22.5      | 82.1                     | 49.8                        | <b>1.65 (1.50-1.82)</b> |
| Der f, bed or floor, >2 µg/g       | 17.7      | 62.4                     | 44.9                        | <b>1.39 (1.20-1.60)</b> |
| Either mite, bed or floor, >2 µg/g | 34.7      | 78.6                     | 52.8                        | <b>1.49 (1.35-1.63)</b> |
| Fel d, bed or floor, >8 µg/g       | 12.0      | 44.3                     | 43.9                        | 1.01 (0.80-1.27)        |
| Can f, bed or floor, >10 µg/g      | 14.8      | 21.9                     | 20.5                        | 1.07 (0.75-1.53)        |

NCICAS, and we determined whether there were study site-specific differences with respect to the allergen sensitivities in the children evaluated and the allergen levels in their home environments. As shown in Table II, allergen sensitivities varied widely across the study sites. Cockroach sensitivity was highest in the Bronx, New York, and Dallas (81%, 79%, and 79%, respectively), and dust mite sensitivity was highest in Dallas and Seattle (84% and 78%, respectively). At least 30% of children at all study sites were allergic to cat.

Table III presents the allergen exposure data by study site. As shown, more than 50% of the homes in Chicago, New York, and the Bronx had Bla g 1 allergen levels greater than 2 U/g, and nearly 50% of homes in Dallas had levels in this range as well. However, most of the homes evaluated in Seattle and Tucson had lower Bla g 1 allergen levels, with only 7.6% and 11% of homes, respectively, having levels greater than 2 U/g. Dust mite levels were highest in Seattle and Dallas, with Der p 1 the most

prevalent dust mite allergen in the homes of children with asthma in these cities. Fewer than 20% of homes in all cities except Seattle had Fel d 1 allergen levels greater than 8 µg/g and Can f 1 levels greater than 10 µg/g.

Table IV shows housing types by study site, and Table V demonstrates the relationship of housing type to allergen levels. There were no high-rise apartments in Dallas, Seattle, or Tucson and very few in Chicago. At these study sites, except for Chicago, the majority of participants lived in detached homes. As shown in Table V, elevated cockroach allergen levels (Bla g 1 > 2 U/g) were seen significantly more often in high-rise and low-rise apartments, whereas elevated dust mite allergen levels (Der f 1 or Der p 1 > 2 µg/g) were seen more often in detached houses. Study site location is related to both housing type and allergen levels and thus confounds this relationship. As Table V indicates, controlling for study site differences affects the relationship between housing type and allergen level. Nevertheless, cockroach allergen

**TABLE VII.** Two-year morbidity outcomes by sensitivity and exposure to each allergen over time, ICAS, control group only (N = 234)

| Outcome                                                  | Sensitivity/<br>exposure group | Cockroach                   |      |             | Dust mite                   |      |             | Cat                         |      |             | Dog                         |      |             |
|----------------------------------------------------------|--------------------------------|-----------------------------|------|-------------|-----------------------------|------|-------------|-----------------------------|------|-------------|-----------------------------|------|-------------|
|                                                          |                                | Adjusted<br>Mean            | SE   | P<br>value* | Adjusted<br>Mean            | SE   | P<br>value* | Adjusted<br>Mean            | SE   | P<br>value* | Adjusted<br>Mean            | SE   | P<br>value* |
| Maximum<br>symptom<br>days                               | Exposed/sensitive              | 4.36                        | 0.31 | <b>.02</b>  | 3.56                        | 0.31 | .30         | 4.54                        | 0.56 | .31         | 4.58                        | 0.55 | .22         |
|                                                          | Exposed/not sensitive          | 3.08                        | 0.49 |             | 3.97                        | 0.53 |             | 4.18                        | 0.71 |             | 4.12                        | 0.36 |             |
|                                                          | Not exposed/sensitive          | 3.95                        | 0.25 |             | 3.61                        | 0.27 |             | 3.48                        | 0.28 |             | 3.92                        | 0.40 |             |
|                                                          | Not exposed/not<br>sensitive   | 3.24                        | 0.35 |             | 4.29                        | 0.34 |             | 4.08                        | 0.31 |             | 3.79                        | 0.23 |             |
| Caretaker<br>lost sleep                                  | Exposed/sensitive              | 2.74                        | 0.26 | <b>.001</b> | 2.14                        | 0.26 | .93         | 2.11                        | 0.40 | .98         | 2.62                        | 0.41 | .34         |
|                                                          | Exposed/not sensitive          | 1.47                        | 0.44 |             | 2.10                        | 0.41 |             | 2.08                        | 0.64 |             | 2.61                        | 0.36 |             |
|                                                          | Not exposed/sensitive          | 2.23                        | 0.21 |             | 2.13                        | 0.21 |             | 1.98                        | 0.22 |             | 2.07                        | 0.31 |             |
|                                                          | Not exposed/not<br>sensitive   | 1.43                        | 0.23 |             | 2.10                        | 0.30 |             | 2.32                        | 0.26 |             | 2.07                        | 0.18 |             |
| School days<br>missed                                    | Exposed/sensitive              | 1.11                        | 0.12 | <b>.04</b>  | 0.77                        | 0.10 | .81         | 0.93                        | 0.21 | .66         | 1.27                        | 0.28 | .19         |
|                                                          | Exposed/not sensitive          | 0.77                        | 0.30 |             | 0.60                        | 0.14 |             | 0.82                        | 0.16 |             | 0.99                        | 0.17 |             |
|                                                          | Not exposed/sensitive          | 0.84                        | 0.08 |             | 0.88                        | 0.10 |             | 0.83                        | 0.09 |             | 0.94                        | 0.12 |             |
|                                                          | Not exposed/not<br>sensitive   | 0.62                        | 0.10 |             | 0.92                        | 0.12 |             | 0.86                        | 0.09 |             | 0.78                        | 0.06 |             |
|                                                          |                                | <b>RR†<br/>(95% CI)</b>     |      |             | <b>RR†<br/>(95% CI)</b>     |      |             | <b>RR†<br/>(95% CI)</b>     |      |             | <b>RR†<br/>(95% CI)</b>     |      |             |
|                                                          |                                | <b>1.40<br/>(1.02-1.92)</b> |      |             | <b>0.94<br/>(0.70-1.28)</b> |      |             | <b>1.39<br/>(1.00-1.92)</b> |      |             | <b>1.45<br/>(0.98-2.14)</b> |      |             |
| Rate of<br>unscheduled<br>visits per 1000<br>person-days | Exposed/sensitive              | 7.14                        | 0.82 |             | 5.51                        | 0.76 |             | 7.94                        | 1.15 |             | 8.10                        | 1.44 |             |
|                                                          | Exposed/not sensitive          | 5.35                        | 1.43 |             | 5.35                        | 1.12 |             | 6.19                        | 1.50 |             | 6.12                        | 1.10 |             |
|                                                          | Not exposed/sensitive          | 6.44                        | 0.56 |             | 5.56                        | 0.62 |             | 4.69                        | 0.51 |             | 4.77                        | 0.70 |             |
|                                                          | Not exposed/not<br>sensitive   | 3.86                        | 0.64 |             | 6.68                        | 0.80 |             | 6.46                        | 0.62 |             | 5.95                        | 0.55 |             |
|                                                          |                                | <b>RR†<br/>(95% CI)</b>     |      |             | <b>RR†<br/>(95% CI)</b>     |      |             | <b>RR†<br/>(95% CI)</b>     |      |             | <b>RR†<br/>(95% CI)</b>     |      |             |
|                                                          |                                | <b>1.45<br/>(0.86-2.46)</b> |      |             | <b>1.31<br/>(0.80-2.16)</b> |      |             | <b>1.20<br/>(0.62-2.32)</b> |      |             | <b>1.37<br/>(0.57-3.33)</b> |      |             |
| Risk of<br>hospitalization<br>in 2 y (%)                 | Exposed/sensitive              | 26.0                        | 0.05 |             | 25.9                        | 0.05 |             | 25.5                        | 0.08 |             | 29.8                        | 0.13 |             |
|                                                          | Exposed/not sensitive          | 17.5                        | 0.06 |             | 26.8                        | 0.08 |             | 21.9                        | 0.08 |             | 21.9                        | 0.06 |             |
|                                                          | Not exposed/sensitive          | 19.2                        | 0.05 |             | 18.3                        | 0.05 |             | 25.2                        | 0.05 |             | 23.3                        | 0.06 |             |
|                                                          | Not exposed/not<br>sensitive   | 16.9                        | 0.06 |             | 15.7                        | 0.04 |             | 17.6                        | 0.04 |             | 20.1                        | 0.04 |             |

\*Repeated measures analysis of variance comparing group 1 (sensitive/exposed group) to the mean of the other 3 groups.

†Relative risk (rate ratio or risk ratio) of unscheduled visits or hospitalization in group 1 compared with the mean rate or risk in the other 3 groups.

levels continue to be significantly higher in high-rise apartments than in detached homes. In the crude analysis, high dust mite levels were significantly less likely to be found in high-rise apartments than detached homes; however, this relationship was not significant after controlling for study site. There was no relationship between housing type and cat allergen levels in either the crude or the adjusted analysis. High dog allergen levels were significantly less likely to be observed in apartments than in detached homes, although this relationship is not significant for high-rise apartments after controlling for study site. Cat and dog allergen levels were significantly higher in those homes where a cat or dog was reported to be living.

By using the bed or floor allergen concentrations in the child's bedroom as the independent variable, we determined the relative risk for having a positive skin test

result to each of the allergens evaluated. As shown in Table VI, associations were demonstrated between cockroach and dust mite allergen levels and skin test responses to these allergens. The relative risk of having a positive skin test response to cockroach was 1.36 (95% CI, 1.24-1.48) when exposed to at least 2 U/g cockroach allergen and the relative risk of having a positive skin test response to either Der p 1 or Der f 1 was 1.49 (95% CI, 1.35-1.63) when exposed to at least 2 µg/g dust mite allergen. In contrast, we saw no relationship between current dog and cat allergen levels and skin test sensitivity.

Table VII depicts the 2-year morbidity outcomes for the children in the control group (children who received neither intervention). Significant relationships were found for cockroach allergens. Children who were sensitive and exposed to cockroach allergen had more maximum symptom days, more caretaker lost sleep, more missed

**TABLE VIII.** Two-year morbidity outcomes by sensitivity to cockroach allergen (wheal 3 mm greater than negative control) and exposure to cockroach (>2 U/g) over time, ICAS, control group only (N = 234)

|                                                 |                            | Cockroach     |      |                  |
|-------------------------------------------------|----------------------------|---------------|------|------------------|
| Outcome                                         | Sensitivity/Exposure Group | Adjusted Mean | SE   | P value*         |
| Maximum symptom days                            | Exposed/sensitive          | 4.25          | 0.36 | .18              |
|                                                 | Exposed/not sensitive      | 3.92          | 0.28 |                  |
|                                                 | Not exposed/sensitive      | 3.72          | 0.44 |                  |
|                                                 | Not exposed/not sensitive  | 3.50          | 0.30 |                  |
| Caretaker lost sleep                            | Exposed/sensitive          | 2.72          | 0.30 | .01              |
|                                                 | Exposed/not sensitive      | 1.92          | 0.36 |                  |
|                                                 | Not exposed/sensitive      | 2.26          | 0.23 |                  |
|                                                 | Not exposed/not sensitive  | 1.60          | 0.21 |                  |
| School days missed                              | Exposed/Sensitive          | 1.07          | 0.14 | 0.13             |
|                                                 | Exposed/Not Sensitive      | 0.94          | 0.21 |                  |
|                                                 | Not Exposed/Sensitive      | 0.76          | 0.09 |                  |
|                                                 | Not Exposed/Not Sensitive  | 0.78          | 0.09 |                  |
| RR† (95% CI)                                    |                            |               |      |                  |
| Rate of unscheduled visits per 1000 person-days | Exposed/sensitive          | 7.06          | 0.89 | 1.27 (0.93-1.73) |
|                                                 | Exposed/not sensitive      | 5.90          | 1.15 |                  |
|                                                 | Not exposed/sensitive      | 6.23          | 0.56 |                  |
|                                                 | Not exposed/not sensitive  | 4.69          | 0.68 |                  |
| RR† (95% CI)                                    |                            |               |      |                  |
| Risk of hospitalization in 2 years (%)          | Exposed/sensitive          | 27.4          | 0.05 | 1.54 (0.93-2.54) |
|                                                 | Exposed/not sensitive      | 17.3          | 0.06 |                  |
|                                                 | Not exposed/sensitive      | 20.1          | 0.06 |                  |
|                                                 | Not exposed/not sensitive  | 16.4          | 0.06 |                  |

\*Repeated measures analysis of variance comparing group 1 (sensitive/exposed group) with the mean of the other 3 groups.

†Relative risk (rate ratio or risk ratio) of unscheduled visits or hospitalization in group 1 compared with the mean rate or risk in the other 3 groups.

school days, and a higher rate of unscheduled visits for asthma than children in the remaining 3 categories. The risk of being hospitalized over the period of 2 years was 45% higher among these children, but that increase is not statistically significant. A relationship among exposure, sensitization, and morbidity could not be demonstrated for dust mite allergen (Table VII), even when evaluating only those study sites where dust mite exposure was high (Dallas, Seattle; data not shown). There is an increased rate of unscheduled visits of borderline significance among children sensitive and exposed to cat allergen and to dog allergen.

To determine whether more stringent criteria for allergy would increase the relative risk of morbidity, we used a 3-mm wheal greater than control instead of the 2-mm wheal criterion used in other tables. When a 3-mm wheal greater than control was used to denote skin test sensitivity, the morbidity relationships for cockroach were attenuated, with the exception of the risk of hospitalization, which was somewhat increased, albeit not to the level of statistical significance (Table VIII).

## DISCUSSION

Results from the ICAS demonstrate that skin test reactivity and allergen levels vary widely depending on location in the country. The majority of enrolled children

were allergic to dust mite and/or cockroach allergens, and positive skin test responses were related to the levels of these allergens in the child's bedroom. In addition, we found that children who were allergic to cockroach and exposed to cockroach allergen had more asthma symptoms, more school days missed because of asthma, and more unscheduled visits for asthma than children in the other categories of exposure and sensitization. We did not find this relationship for dust mites and asthma. Moreover, our data suggest that children who are sensitive and exposed to dog allergen or cat allergen have more unscheduled asthma healthcare visits than children who are not exposed and/or who are not sensitive.

Allergen levels were found to vary dramatically across the inner city sites. Northeastern homes had the highest concentrations of cockroach allergen, whereas dust mite allergen was more prevalent in Dallas and Seattle. Huss et al<sup>17</sup> also found that allergen levels vary depending on inner city location. In their study, most of the homes in San Diego and Toronto had moderate to high dust mite levels, whereas Boston, St Louis, and Baltimore had the highest number of homes with detectable cockroach allergen.

In contrast with dust mite and cockroach allergens, cat and dog allergen levels were elevated in a minority of homes. This latter finding is similar to that recently published by Arbes et al,<sup>18</sup> who found that cat and dog allergen levels are most commonly associated with homes inhabited by non-Hispanic whites who have higher incomes.

We also corroborated the findings of Tunnicliffe et al<sup>9</sup> and Arbes et al,<sup>18</sup> who both showed that pet ownership is highly predictive of pet allergen levels.

Like Chew et al,<sup>19</sup> we found that allergen levels vary by housing type. This group found that in Boston, building type predicted average concentrations of dust mite and cockroach allergens. High-rise apartments had higher levels of cockroach allergen, whereas houses had higher dust mite allergen levels. We have corroborated these findings and have extended them to include other inner city areas throughout the United States.

Like others,<sup>6,12,17,20</sup> we demonstrated that positive skin test responses to cockroach and/or dust mite allergens are related to allergen exposure. However, we were not able to demonstrate a similar relationship for pet allergens. Recent studies have demonstrated that very high levels of cat allergen do not increase sensitization to that allergen but actually decrease both sensitization and the likelihood of having asthma.<sup>21,22</sup> We too were not able to demonstrate an increased risk of skin test reactivity with exposure to increasing levels of current cat or dog exposure in the home (Fel d 1 > 8 µg/g or Can f 1 > 10 µg/g; Table VI). It should be noted that our study population, consisting only of children with moderate and severe asthma, is not comparable with the populations studied by Platts-Mills et al.<sup>22</sup>

In this study, allergen exposure was measured at enrollment and at time points thereafter in the child's bedroom (both bed and bedroom floor). Thus, our measurements do not reflect exposure before enrollment or exposure in places other than the home (eg, school) and may not reflect total household exposure (cockroach allergen levels may be higher in the kitchen, for example). These alternative exposures may explain why some children had a positive skin test result despite having low allergen levels in their bedrooms. Bedroom allergens were measured in ICAS because it had been previously noted that bedroom exposures may be a better predictor of morbidity than other exposures.<sup>8</sup>

The previous NCICAS demonstrated a relationship between cockroach allergen concentrations in the home and several measures of asthma morbidity: asthma symptom days, school days missed, unscheduled visits for asthma, and caretaker lost sleep.<sup>8,20</sup> We have found similar but somewhat more moderate results, presumably because of the more diverse geographic distribution of the current study sites. Our findings regarding dust mite are similar to those of Rosenstreich et al<sup>8</sup> and Lewis et al,<sup>20</sup> none of whom were able to demonstrate a relationship between dust mite allergen exposure and asthma morbidity in sensitized subjects. It is possible that, in these previous studies, an association was not demonstrated because the number of individuals in the exposed and sensitive group was too small to see a statistically significant relationship. However, compared with these previous 2 studies, we had a larger number of children in the exposed and sensitive group ( $n = 65$  at baseline), and we were still unable to demonstrate a relationship between dust mite allergen exposure and asthma morbidity in

sensitive individuals. Moreover, a relationship between dust mite exposure and morbidity was not found in study sites where dust mite exposure was high (Dallas, Seattle). Thus, although both dust mite and cockroach allergen exposures were found to be risk factors for the development of positive skin test responses, only cockroach allergen exposure, in conjunction with cockroach sensitivity, was associated with increased asthma morbidity. These results suggest that cockroach allergens may have a greater effect on asthma morbidity than dust mite allergens among sensitized children with asthma children in an inner city environment.

Exposure to other indoor allergens has also been shown to be associated with increased asthma severity in sensitized individuals. Lewis et al<sup>20</sup> found a strong positive correlation between cat allergen exposure and asthma symptoms in women with asthma allergic to cat. Ingram et al<sup>16</sup> demonstrated a similar positive correlation between dog and cat allergen exposure and asthma morbidity in sensitized children with asthma in Los Alamos, NM. Although we were not able to demonstrate a positive correlation between cat or dog allergen levels and asthma symptoms, we did see a relationship between Fed d 1 or Can f 1 allergen exposure and asthma-associated health-care utilization in children who were allergic to that pet.

In summary, we found that there are marked site-specific differences with respect to indoor allergen exposures and skin test reactivity to these allergens among children with asthma who reside in inner cities in the United States. Moreover, although both dust mite allergen and cockroach allergen exposures were found to be risk factors for the development of positive skin test responses, only cockroach allergen exposure, in conjunction with cockroach sensitivity, was associated with increased asthma morbidity. Pet exposure (cat or dog) was not a risk factor for the development of a positive skin test response. These results suggest that cockroach allergens have a greater effect on asthma morbidity than dust mite or pet allergens among children with asthma with a positive skin test who live in inner city environments.

The ICAS was a collaboration of the following institutions and investigators. Principal investigators are indicated by asterisks.

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## Correction

With regard to the January 2005 editorial entitled "Breathing for two: Now we can all breathe a little easier" (2005;115:31-3): The second paragraph should have appeared as follows:

First, specific prevalence data have now suggested that asthma is more common in pregnant women in this country than previously thought, affecting 3.7% to 8.4% of this population.<sup>2</sup> Moreover, the prevalence of asthma during pregnancy appears to be increasing.<sup>2</sup>