Exposure to Dogs and Cats in the First Year of Life and Risk of Allergic Sensitization at 6 to 7 Years of Age

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Context  Childhood asthma is strongly associated with allergic sensitization. Studies have suggested that animal exposure during infancy reduces subsequent allergic sensitization.

Objective  To evaluate the relationship between dog and cat exposure in the first year of life and allergic sensitization at 6 to 7 years of age.

Design, Setting, and Subjects  Prospective birth cohort study of healthy, full-term infants enrolled in a health maintenance organization in suburban Detroit, Mich, who were born between April 15, 1987, and August 31, 1989, and followed up yearly to a mean age of 6.7 years. Of 835 children initially in the study at birth, 474 (57%) completed follow-up evaluations at age 6 to 7 years.

Main Outcome Measures  Atopy, defined as any skin prick test positivity to 6 common aeroallergens (Dermatophagoides farinae, D pteronyssinus, dog, cat, short ragweed [Ambrosia artemisiifolia], and blue grass [Poa pratensis]); seroatopy, defined as any positive allergen-specific IgE test result for the same 6 allergens or for Alternaria species.

Results  The prevalence of any skin prick test positivity (atopy) at age 6 to 7 years was 33.6% with no dog or cat exposure in the first year of life, 34.3% with exposure to 1 dog or cat, and 15.4% with exposure to 2 or more dogs or cats (P =.005). The prevalence of any positive allergen-specific IgE test result (seroatopy) was 38.5% with no dog or cat exposure, 41.2% with exposure to 1 dog or cat, and 17.9% with exposure to 2 or more dogs or cats (P =.003). After adjustment for cord serum IgE concentration, sex, older siblings, parental smoking, parental asthma, bedroom dust mite allergen levels at 2 years, and current dog and cat ownership, exposure to 2 or more dogs or cats in the first year of life was associated with a significantly lower risk of atopy (adjusted odds ratio, 0.23; 95% confidence interval, 0.09-0.60) and seroatopy (adjusted odds ratio, 0.33; 95% confidence interval, 0.13-0.83).

Conclusion  Exposure to 2 or more dogs or cats in the first year of life may reduce subsequent risk of allergic sensitization to multiple allergens during childhood.

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risk of subsequent allergy to these animals.8,10–12 This assumption is primarily based on a few retrospective studies reporting an increased likelihood of allergic sensitization following exposure during infancy.10–12 Some studies, however, have suggested that exposure to dogs or cats during infancy is associated with reduced risk of allergic disease.13–18 Others have shown that children growing up on farms, especially farms with animals, were less likely to be allergic than were children growing up in urban environments.19,20

This analysis is part of the Childhood Allergy Study, a prospective birth cohort study designed to simultaneously evaluate multiple relationships between early environmental exposures and subsequent allergic sensitization and asthma.21–30 Among the variables considered were parental allergy histories, parental smoking, IgE levels in cord blood, month of birth, concentrations of dust mite and cat allergen in the child’s bedroom at age 2 years, and pet exposure. In this analysis, we specifically examined exposure to dogs or cats in the first year of life and a child’s risk of later allergic sensitization to common allergens after adjusting for potential confounding associations. We also examined relationships between early dog and cat exposure and allergen-specific serum IgE concentrations, lung function, methacholine airway responsiveness, and asthma.

METHODS

The selection of children for the Childhood Allergy Study has previously been described.21 Briefly, all pregnant women living in an area of northern, suburban Detroit, defined by contiguous ZIP codes, and belonging to a health maintenance organization, were eligible to participate if their infants were born between April 15, 1987, and August 31, 1989. Only infants born at term (36 or more weeks’ gestational age) with valid measurements of cord serum IgE concentration were entered into the study. The study was approved by the institutional human rights committee, and written informed consent was obtained when the mothers were enrolled, at the time of the first home visit, and prior to the clinical evaluations.

Study nurses interviewed mothers prior to delivery to obtain information concerning each parent’s level of education; presence of allergies in general and of hay fever and asthma specifically; and parental smoking habits. The number of siblings was also noted along with other data about the home. Cord serum IgE concentrations were measured for all infants as previously described.21

We contacted parents by telephone when infants were aged 1 year to obtain information on prespecified variables of interest, including the presence and number of pets in the home during the first year. The number of dogs and cats reported at this time was used for this analysis. When children were aged 2 years, nurses visited each child’s home to obtain information about the home environment and to collect dust samples from the child’s bedroom, as well as urine samples from the child for measurement of urinary cotinine as a biomarker of passive cigarette smoke exposure. The dust samples were analyzed for concentrations of mite (Der p 1 and Der f 1) and cat (Fel d 1) allergens using a monoclonal antibody-based enzyme-linked immunosorbent assay as previously described.28 We have documented the validity of parental smoking histories in this cohort with reference to children’s urinary cotinine concentrations.29 Questionnaire-based parental smoking histories from the first year of the child’s life were used for these analyses because there were fewer missing values than for urinary cotinine concentrations. Follow-up telephone interviews also were conducted when the children were aged 3, 5, and 6 years, and a second home visit was conducted when the children were aged 4 years.

Evaluations for Allergic Sensitization and Asthma

Clinical evaluations for allergic sensitization and asthma were performed when the children were aged 6 to 7 years. In addition to general medical histories and physical examinations, these evaluations included skin prick testing with commercial extracts of dust mites (Dermatophagoides farinae, D pteronyssinus), dog, cat, short ragweed (Ambrosia artemisiifolia), and blue grass (Poa pratensis), along with saline and histamine controls (all extracts and controls, Pharmaceutical Division, Bayer Inc, Spokane, Wash). Skin prick test results were considered positive if the product of perpendicular wheal diameters was 4 mm or more associated with a flare of at least 10 mm, and if there was no response to the negative control. Atopy was defined as a positive skin prick test result with any of the 6 allergens tested. Blood samples obtained during the evaluation were assayed for total serum IgE concentration and concentrations of allergen-specific IgE antibodies using a commercial assay (AlaSTAT, Diagnostic Products Corp, Los Angeles, Calif). Allergen-specific IgE testing included the same 6 allergens used for skin prick testing in addition to Alternaria species. Total and allergen-specific serum IgE levels were expressed in international units per milliliter (1 IU/mL corresponds to 2.4 ng/mL). Allergen-specific IgE levels of 0.35 IU/mL or higher were considered to be a positive test result in accordance with the manufacturer’s recommendation. Seroatopy was defined as any positive test result for an allergen-specific IgE concentration. Numbers of children with seroatopy may have been slightly higher than those with atopy because one additional allergen, Alternaria, was also used to define seroatopy. Because a study published after the start of this study suggested that cockroach sensitization may be associated with asthma,31 a random sample of 100 sera were assayed for cockroach-specific IgE and only 2 sera were positive.32 Given the low prevalence of detectable cockroach sensitization, no further testing for cockroach-specific IgE was performed.

At the time of skin prick testing, children were defined as having current asthma if a parent reported that they had been diagnosed by a physician as having asthma and that they had asthma...
EXPOSURE TO DOGS AND CATS AND ALLERGIC SENSITIZATION

Symptoms or used asthma medications in the preceding 12 months. Pulmonary function tests were performed as previously described, and the results are presented as the percentage of predicted using standard equations. Methacholine airway responsiveness was determined as previously described. After baseline spirometry and no response to a control saline challenge, 5 doses of methacholine (0.025-25 mg/mL) were administered through a dosimeter (Pulmonary Data Services, Louisville, Colo). Methacholine airway responsiveness was defined as a fall in forced expiratory volume in 1 second (FEV₁) of 20% or more from the postsaline challenge value at a concentration of administered methacholine of 10 mg/mL or less.²⁹

Statistical Analysis

The power of this study was originally based on the ability to detect a small to medium effect (0.2) for a χ² test as defined by Cohen. With this assumption, and assuming an α level of .05, the power to detect significant associations between outcomes in 3 exposure groups is greater than 90% with an overall sample size of 470. Given the same assumptions, it also is possible to stratify the data for a variable with approximately equal prevalences (ie, sex) and still have power greater than 70% with 235 in each group. If the prevalence of a variable is low in the cohort, such as current asthma, the power is much lower.

The collected data were first examined for potential imbalances between those children lost from the study and those who were retained. χ² Tests were used to compare the relative percentages. Pet exposure in the first year of life was defined as an ordinal variable with 3 categories: no dog or cat exposure, exposure to 1 dog or cat, and exposure to 2 or more dogs or cats. The highest strata was truncated at 2 or more because of the small sample size above this level. Information about pet exposure at age 6 to 7 years was used to create the same 3 categories of pet exposure as was used for the first year of life. Binary variables of interest (eg, atopy [yes or no], specific skin prick test positivity) were analyzed according to pet exposure category using a χ² test for 2 × 3 contingency tables. We did not have a preconceived hypothesis concerning a relationship between exposure to varying number of dogs and cats and the risk of allergic sensitization. Therefore, we tested the general hypothesis that outcomes differed across categories of dog and cat exposure rather than testing for trends with increasing exposure.

The relationships between pet exposure categories and continuous variables, such as percent predicted forced vital capacity (FVC) or total serum IgE, were evaluated with a 1-way analysis of variance technique. Each continuous variable was transformed to natural logarithmic equivalents to reduce positive skewing prior to analysis. If the range of the variable to be logarithmically transformed included zero, 1 was added to the variable prior to transformation. When logarithmic data transformation did not result in a near normal distribution, such as for dust mite concentrations, a Kruskal-Wallis test was used. The number of children in each analysis varied slightly because of missing data.

Atopy and seroatopy were each used as a dependent binary variable in a linear logistic regression assessing 2 indicator variables for pet exposure: exposure to 1 dog or cat or exposure to 2 or more dogs or cats. These models were fitted without other variables and with other potentially confounding variables, including cord serum IgE concentration, child’s sex, having older siblings, parental smoking, mother or father with a history of asthma, and total bedroom dust mite allergen levels at child age 2 years. The logistic model is appropriate for modeling binary dependent variables. It makes minimal assumptions about the distributional properties of the independent variables and the exponentiation of the coefficient allows for estimation of the odds ratio (OR). We chose to include the number of dogs and cats as 2 binary indicator variables avoiding assumptions concerning the direction of any associations. Using the Hosmer-Lemeshow test, we found no evidence to doubt the validity of the models.³⁵

We analyzed the entire data set and data sets defined by sex. In all analyses, an α = .05 criteria was used to determine statistical significance. There was no attempt to impute data; all analyses were performed on all available data. SAS v8.0 (SAS Institute Inc, Cary, NC) was used for all analyses.

RESULTS

A total of 1194 pregnant women were potentially eligible for entry into this study, and consent for participation was obtained from 953 women. Infants of 106 of these women were not enrolled in the study because a cord blood sample was not obtained, leaving 847 eligible newborns. Six of the cord blood samples were thought to be contaminated by maternal blood,²¹,²³ and an additional 6 children were found to be ineligible when each child’s data were examined and verified prior to the 6- to 7-year evaluations, yielding 835 eligible children enrolled at birth. Of the 835 children initially enrolled, 235 had been lost to follow-up by age 6 years, and 126 of those contacted at age 6 years declined participation in the clinical evaluation. Thus, 474 (57%) of the 835 eligible children initially enrolled completed the clinical evaluation for allergic sensitization and asthma at an average age of 6.7 (SD, 0.17) years. Characteristics of children who were evaluated at 6 to 7 years did not differ significantly from those of children who did not undergo clinical evaluation at age 6 to 7 years, including whether the parent had a history of asthma or hay fever or whether there were dogs or cats in the household (Table 1). Also, interactions between each variable, any exposure to dogs and cats in the home in the first year of life, and whether the child participated in the clinical evaluation were not statistically significant (Table 1). When the relationship between maternal and paternal histories of asthma, allergies, and hay fever and presence of 2 or more dogs or cats in
the household was evaluated, no significant associations were found. The parents of the children in this study were relatively well educated and almost all (804 [96.3%]) described themselves as white, non-Hispanic. Characteristics of the children completing the study are presented in Table 2. Boys and girls were approximately equally represented. The presence of a dog or cat in the home did not differ significantly between parents with a history of asthma, allergies, or hay fever and those who did not report these conditions.

To investigate the relationships between dog and cat exposure and allergic sensitization, we initially compared the 184 children with any dog exposure in their first year of life to the 220 children without either dog or cat exposure. Children exposed to a dog were less likely to have a positive skin test result to dog allergen (3.3% vs 8.6%, \(P = .03\)) and detectable dog-specific IgE (3.7% vs 8.7%, \(P = .06\)) at follow-up. Any exposure to a dog was also associated with lower total serum IgE levels (geometric mean, 23.8 IU/mL vs 33.1 IU/mL for no dog or cat exposure; \(P = .04\)). The inverse association between dog exposure and allergic sensitization was further examined in relation to number of dogs (Table 3).

**Table 1.** Comparison of Children in the Cohort Who Underwent Clinical Evaluation at Age 6 to 7 Years With Those Not Evaluated*

<table>
<thead>
<tr>
<th>Variable</th>
<th>Not Evaluated</th>
<th>Evaluated</th>
<th>Evaluated vs Not Evaluated</th>
<th>For Cat and Dog Interaction†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Children</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>178/351 (50.7)</td>
<td>247/484 (51.0)</td>
<td>.93</td>
<td>.71</td>
</tr>
<tr>
<td>First-born</td>
<td>148/321 (46.1)</td>
<td>214/478 (44.8)</td>
<td>.71</td>
<td>.13</td>
</tr>
<tr>
<td>Exposure to dogs and cats in first year of life</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dogs or cats</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>139/285 (48.8)</td>
<td>223/474 (47.1)</td>
<td>.89</td>
<td>.54</td>
</tr>
<tr>
<td>1</td>
<td>88/285 (30.9)</td>
<td>173/474 (36.5)</td>
<td>.93</td>
<td>NA</td>
</tr>
<tr>
<td>≥2</td>
<td>58/285 (20.4)</td>
<td>78/474 (16.9)</td>
<td>.20</td>
<td>NA</td>
</tr>
<tr>
<td>Dogs only</td>
<td>113/252 (44.8)</td>
<td>184/407 (45.2)</td>
<td>.93</td>
<td>NA</td>
</tr>
<tr>
<td>Cats only</td>
<td>70/209 (33.5)</td>
<td>106/329 (32.2)</td>
<td>.76</td>
<td>NA</td>
</tr>
<tr>
<td>Parental Characteristics</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smoking ≥1 cigarette per day</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mother</td>
<td>66/351 (18.8)</td>
<td>78/484 (16.1)</td>
<td>.31</td>
<td>.46</td>
</tr>
<tr>
<td>Father</td>
<td>85/348 (24.4)</td>
<td>116/482 (24.1)</td>
<td>.90</td>
<td>.82</td>
</tr>
<tr>
<td>Asthma</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mother</td>
<td>24/351 (6.8)</td>
<td>41/483 (8.5)</td>
<td>.38</td>
<td>.87</td>
</tr>
<tr>
<td>Father</td>
<td>28/333 (8.4)</td>
<td>25/463 (5.4)</td>
<td>.09</td>
<td>.46</td>
</tr>
<tr>
<td>Either parent</td>
<td>47/335 (14.0)</td>
<td>64/463 (13.8)</td>
<td>.93</td>
<td>.42</td>
</tr>
<tr>
<td>Allergy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mother</td>
<td>99/351 (28.2)</td>
<td>141/483 (29.1)</td>
<td>.77</td>
<td>.18</td>
</tr>
<tr>
<td>Father</td>
<td>86/321 (26.8)</td>
<td>113/429 (26.3)</td>
<td>.89</td>
<td>.69</td>
</tr>
<tr>
<td>Either parent</td>
<td>159/333 (47.8)</td>
<td>219/447 (49.0)</td>
<td>.73</td>
<td>.18</td>
</tr>
<tr>
<td>Hay fever</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mother</td>
<td>62/350 (17.7)</td>
<td>76/483 (15.7)</td>
<td>.45</td>
<td>.09</td>
</tr>
<tr>
<td>Father</td>
<td>62/320 (19.4)</td>
<td>88/445 (19.8)</td>
<td>.89</td>
<td>.68</td>
</tr>
<tr>
<td>Either parent</td>
<td>108/329 (32.8)</td>
<td>142/453 (31.4)</td>
<td>.66</td>
<td>.83</td>
</tr>
<tr>
<td>Formal education beyond high school‡</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mother</td>
<td>219/351 (62.4)</td>
<td>299/484 (61.8)</td>
<td>.86</td>
<td>.25</td>
</tr>
<tr>
<td>Father</td>
<td>239/349 (68.5)</td>
<td>331/483 (68.5)</td>
<td>.99</td>
<td>.40</td>
</tr>
</tbody>
</table>

*NA indicates not applicable.
†For interaction between any exposure to cats and dogs in the first year of life, the variable of interest, and being evaluated at age 6 to 7 years.
‡Includes some college or technical school training.

The reference group remained the 220 children with neither dog nor cat exposure in the first year of life. An apparent dose-response effect for atopy and seroatopy was found across the 3 exposure categories. Atopy was present in 33.6% of the children without dog or cat exposure, in 29.7% with exposure to 1 dog, and in only 8.3% with exposure to 2 or more dogs (\(P = .009\)). The prevalence of seroatopy was 38.5% with no pet exposure, 36.7% with exposure to 1 dog, and 12.9% with exposure to 2 or more dogs (\(P = .02\)).

Based on finding similar relationships between dog and cat exposures in the first year of life and allergic sensitization at age 6 to 7 years, relationships were further analyzed by simultaneously considering combined dog and cat exposure. Combining dogs and cats increased the number of children in each category, allowing further exploration of the relationships through stratification of the data by sex. Atopy and seroatopy were each present in about one third of children. When all children were considered, the prevalence of skin prick test positivity to dog allergen, outdoor and indoor allergens, atopy, and seroatopy was significantly different across the 3 exposure categories and generally decreased with increasing pet exposure (Table 4).

The pattern of decreasing skin prick test positivity to cat allergen with increasing exposure was similar but the relationship(s) failed to reach statistical significance.
When boys and girls were considered separately, different patterns emerged from the data (Table 4). Exposure to a single dog or cat in the first year of life was associated with an increased prevalence of atopy and serum atopy in girls while both outcomes declined in boys exposed to a single dog or cat. Lower prevalences of skin prick test positivity to dog, cat, and indoor and outdoor allergens, and of methacholine airway responsiveness were consistently found in association with exposure to a single dog or cat with boys but not with girls. Measurements of lung function were also related to dog and cat exposure for boys but not for girls. The prevalence of methacholine airway responsiveness in boys was 25.5% when there had been no dog or cat exposure, 11.8% with exposure to 1 dog or cat, and 5.1% with exposure to 2 or more dogs or cats (P= .03). In girls, the prevalence of methacholine responsiveness was unchanged across pet exposure categories. Similarly, the mean percent predicted FVC and FEV1 increased significantly across pet exposure categories among boys but not among girls, and were highest with exposure to 2 or more dogs or cats. Thirty-three (7%) of 473 children had current asthma. The prevalence of current asthma was lower in boys who had been exposed to 2 or more dogs or cats in infancy compared with no exposure (5.1% vs 11.8%, respectively), but the difference across exposure categories was not statistically significant (P=.43) and no difference was seen for girls.

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Table 4. Relationship Between Number of Dogs and Cats in the Home in the First Year of Life, Prevalence of Allergic Sensitization, and Measures of Lung Function or Presence of Current Asthma at Age 6 to 7 Years

<table>
<thead>
<tr>
<th>Variable</th>
<th>No. of Dogs and Cats</th>
<th>Sex</th>
<th>0</th>
<th>1</th>
<th>≥2</th>
<th>P Value†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin prick test positivity</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dog</td>
<td>All</td>
<td>19/220 (8.6)</td>
<td>6/172 (3.5)</td>
<td>2/78 (2.6)</td>
<td>.04</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Girls</td>
<td>6/112 (5.4)</td>
<td>4/90 (4.4)</td>
<td>1/39 (2.6)</td>
<td>.77</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Boys</td>
<td>13/108 (12.0)</td>
<td>2/82 (2.4)</td>
<td>1/39 (2.6)</td>
<td>.02</td>
<td></td>
</tr>
<tr>
<td>Cat</td>
<td>All</td>
<td>34/220 (15.5)</td>
<td>20/172 (11.6)</td>
<td>4/78 (5.1)</td>
<td>.76</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Girls</td>
<td>12/112 (10.7)</td>
<td>13/90 (14.4)</td>
<td>2/39 (5.1)</td>
<td>.30</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Boys</td>
<td>22/108 (20.4)</td>
<td>7/82 (8.5)</td>
<td>4/39 (10.3)</td>
<td>.05</td>
<td></td>
</tr>
<tr>
<td>Outdoor allergens‡</td>
<td>All</td>
<td>62/206 (30.1)</td>
<td>37/160 (23.1)</td>
<td>8/66 (12.1)</td>
<td>.01</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Girls</td>
<td>25/104 (24.0)</td>
<td>20/84 (23.8)</td>
<td>2/32 (6.3)</td>
<td>.08</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Boys</td>
<td>37/102 (36.3)</td>
<td>17/76 (22.4)</td>
<td>6/34 (17.7)</td>
<td>.04</td>
<td></td>
</tr>
<tr>
<td>Indoor allergens§</td>
<td>All</td>
<td>60/220 (27.3)</td>
<td>49/172 (28.5)</td>
<td>8/78 (10.3)</td>
<td>.005</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Girls</td>
<td>23/112 (20.5)</td>
<td>28/90 (31.1)</td>
<td>2/39 (5.1)</td>
<td>.004</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Boys</td>
<td>37/108 (34.3)</td>
<td>21/82 (25.6)</td>
<td>6/39 (15.4)</td>
<td>.07</td>
<td></td>
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<tr>
<td>Atopy‡</td>
<td>All</td>
<td>74/220 (33.6)</td>
<td>59/172 (34.3)</td>
<td>12/78 (15.4)</td>
<td>.005</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Girls</td>
<td>30/112 (26.8)</td>
<td>24/90 (37.8)</td>
<td>3/39 (7.5)</td>
<td>.002</td>
<td></td>
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<tr>
<td></td>
<td>Boys</td>
<td>44/108 (40.7)</td>
<td>25/82 (30.5)</td>
<td>9/39 (23.1)</td>
<td>.10</td>
<td></td>
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<tr>
<td>Seroatopy‡</td>
<td>All</td>
<td>74/192 (38.5)</td>
<td>61/148 (41.2)</td>
<td>12/66 (18.2)</td>
<td>.003</td>
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<tr>
<td></td>
<td>Girls</td>
<td>28/93 (30.1)</td>
<td>32/76 (42.1)</td>
<td>6/37 (16.2)</td>
<td>.02</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Boys</td>
<td>46/99 (46.5)</td>
<td>29/72 (40.3)</td>
<td>6/30 (20.0)</td>
<td>.04</td>
<td></td>
</tr>
<tr>
<td>Methacholine airway responsiveness§</td>
<td>All</td>
<td>53/220 (24.1)</td>
<td>40/166 (24.1)</td>
<td>12/76 (15.8)</td>
<td>.29</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Girls</td>
<td>25/110 (22.7)</td>
<td>24/87 (27.6)</td>
<td>10/37 (27.0)</td>
<td>.71</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Boys</td>
<td>28/110 (25.5)</td>
<td>16/79 (20.3)</td>
<td>2/39 (5.1)</td>
<td>.03</td>
<td></td>
</tr>
</tbody>
</table>

FVC % predicted, mean (SD) [No. of children]

<table>
<thead>
<tr>
<th>Value</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
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</thead>
<tbody>
<tr>
<td>All</td>
<td>93.9 (11.7) [222]</td>
<td>96.5 (11.4) [169]</td>
<td>95.1 (12.4) [77]</td>
<td>.10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Girls</td>
<td>94.4 (11.4) [112]</td>
<td>95.4 (10.7) [88]</td>
<td>91.0 (12.7) [38]</td>
<td>.14</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Boys</td>
<td>93.5 (12.1) [110]</td>
<td>97.7 (12.1) [81]</td>
<td>99.0 (10.9) [39]</td>
<td>.01</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

FEV₁ % predicted, mean (SD) [No. of children]

<table>
<thead>
<tr>
<th>Value</th>
<th></th>
<th></th>
<th></th>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>93.1 (11.6) [222]</td>
<td>94.5 (12.2) [169]</td>
<td>94.7 (12.6) [77]</td>
<td>.41</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Girls</td>
<td>92.3 (11.0) [112]</td>
<td>91.8 (11.0) [88]</td>
<td>89.1 (12.0) [38]</td>
<td>.29</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Boys</td>
<td>93.8 (12.2) [110]</td>
<td>97.4 (12.8) [81]</td>
<td>100.1 (10.7) [39]</td>
<td>.01</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Current asthma# | | | | | | |

<table>
<thead>
<tr>
<th>Value</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>17/223 (7.6)</td>
<td>12/172 (7.0)</td>
<td>4/78 (5.1)</td>
<td>.76</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Girls</td>
<td>4/113 (3.5)</td>
<td>5/89 (5.6)</td>
<td>2/39 (5.1)</td>
<td>.77</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Boys</td>
<td>13/110 (11.8)</td>
<td>7/83 (8.4)</td>
<td>2/39 (5.1)</td>
<td>.43</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*All data are No./Total (%) unless indicated otherwise. FVC indicates forced vital capacity; FEV₁, forced expiratory volume in 1 second.
†From χ² analysis except where noted.
‡See Table 3 footnote for definitions of outdoor and indoor allergens, atopy, and seroatopy.
§Defined as a provocative dose of ≤10 mg/mL for decreasing FEV₁ by 20%.
¶From analysis of variance.
||Results are presented as mean (SD) of the percent predicted from standard equations (see Ownby et al for details).
#Defined as physician diagnosis of asthma and symptoms of asthma or use of asthma medications in the previous 12 months.
cats using the same exposure categories as in the first year of life (no exposure; exposure to 1 dog or cat; exposure to 2 or more dogs or cats at age 6-7 years), the risk of atopy and seroatopy associated with exposure in the first year of life remained significantly decreased (atopy: OR, 0.23; 95% CI, 0.09-0.60; seroatopy: OR, 0.33; 95% CI, 0.13-0.83) (Table 6, model 2). When the variable for dog or cat exposure at age 6 to 7 years replaced the variable for exposure in the first year of life, no statistically significant associations were found. For example, with all children included in the analysis, risks of atopy and seroatopy among children with 2 or more dogs or cats at age 6 to 7 years were not significantly different than those among children with no current pet exposure (for atopy: OR, 0.79; 95% CI, 0.44-1.85; P = .79; for seroatopy: OR, 0.81; 95% CI, 0.43-1.94; P = .81).

**COMMENT**

In this prospective study we found that exposure to 2 or more dogs or cats in the first year of life was associated with a lower prevalence of allergic sensitization at age 6 to 7 years regardless of exposure to dogs and cats at age 6 years. This inverse relationship was consistent whether skin prick tests for 6 common allergens or tests for 7 allergen-specific IgE concentrations were considered as primary outcomes. The inverse relationship was present for both indoor (dust mites, dog, and cat) and outdoor (ragweed, grass, and *Alternaria*) allergens. The relationships remained significant after adjusting for a number of variables that may be risk factors for atopy and seroatopy.

### Table 5. Relationship Between Number of Dogs and Cats in the Home in the Child’s First Year of Life and Total Serum IgE Concentration at Age 6 to 7 Years*

<table>
<thead>
<tr>
<th>No Dogs or Cats</th>
<th>1 Dog or Cat</th>
<th>≥2 Dogs or Cats</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>Mean†</td>
</tr>
<tr>
<td>All children</td>
<td>204</td>
<td>32.8</td>
</tr>
<tr>
<td>Girls</td>
<td>100</td>
<td>24.0</td>
</tr>
<tr>
<td>Boys</td>
<td>104</td>
<td>43.8</td>
</tr>
<tr>
<td>Child’s parents free of asthma</td>
<td>163</td>
<td>29.4</td>
</tr>
<tr>
<td>Child’s parent has asthma</td>
<td>41</td>
<td>48.9</td>
</tr>
</tbody>
</table>

*Ln indicates natural logarithm.  †Geometric mean of the total serum IgE for each group, in IU/mL.  ‡Natural logarithm of the mean serum IgE and SD of the Ln mean.  §P value from analysis of variance comparing the 3 Ln means.

### Table 6. Adjusted Relationships Between Dog and Cat Exposure, Atopy, and Seroatopy*

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR (95% CI)</th>
<th>P Value</th>
<th>Adjusted OR (95% CI)</th>
<th>P Value</th>
<th>Adjusted OR (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All children</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atopy</td>
<td>1.03 (0.68-1.57)</td>
<td>.89</td>
<td>1.01 (0.61-1.67)</td>
<td>.97</td>
<td>0.85 (0.48-1.52)</td>
<td>.58</td>
</tr>
<tr>
<td>Seroatopy</td>
<td>1.12 (0.72-1.73)</td>
<td>.62</td>
<td>1.20 (0.71-2.02)</td>
<td>.50</td>
<td>0.93 (0.51-1.68)</td>
<td>.80</td>
</tr>
<tr>
<td>Girls</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atopy</td>
<td>1.66 (0.91-3.02)</td>
<td>.10</td>
<td>1.99 (0.95-4.17)</td>
<td>.07</td>
<td>2.02 (0.84-4.84)</td>
<td>.11</td>
</tr>
<tr>
<td>Seroatopy</td>
<td>1.69 (0.89-3.19)</td>
<td>.11</td>
<td>2.21 (1.03-4.72)</td>
<td>.04</td>
<td>1.78 (0.73-4.34)</td>
<td>.20</td>
</tr>
<tr>
<td>Boys</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atopy</td>
<td>0.64 (0.35-1.17)</td>
<td>.15</td>
<td>0.54 (0.25-1.15)</td>
<td>.11</td>
<td>0.36 (0.15-0.87)</td>
<td>.02</td>
</tr>
<tr>
<td>Seroatopy</td>
<td>0.78 (0.42-1.44)</td>
<td>.42</td>
<td>0.63 (0.29-1.37)</td>
<td>.25</td>
<td>0.46 (0.19-1.12)</td>
<td>.09</td>
</tr>
<tr>
<td>Exposure to 2 Dogs or Cats in First Year of Life</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All children</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atopy</td>
<td>0.36 (0.18-0.71)</td>
<td>.003</td>
<td>0.31 (0.14-0.72)</td>
<td>.007</td>
<td>0.23 (0.09-0.60)</td>
<td>.003</td>
</tr>
<tr>
<td>Seroatopy</td>
<td>0.35 (0.18-0.69)</td>
<td>.003</td>
<td>0.43 (0.19-0.96)</td>
<td>.04</td>
<td>0.33 (0.13-0.83)</td>
<td>.02</td>
</tr>
<tr>
<td>Girls</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atopy</td>
<td>0.23 (0.07-0.80)</td>
<td>.02</td>
<td>0.21 (0.04-1.00)</td>
<td>.05</td>
<td>0.15 (0.02-0.90)</td>
<td>.04</td>
</tr>
<tr>
<td>Seroatopy</td>
<td>0.45 (0.17-1.20)</td>
<td>.11</td>
<td>0.62 (0.20-1.96)</td>
<td>.42</td>
<td>0.54 (0.14-2.08)</td>
<td>.37</td>
</tr>
<tr>
<td>Boys</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atopy</td>
<td>0.44 (0.19-1.01)</td>
<td>.05</td>
<td>0.37 (0.13-1.05)</td>
<td>.06</td>
<td>0.23 (0.07-0.79)</td>
<td>.02</td>
</tr>
<tr>
<td>Seroatopy</td>
<td>0.29 (0.11-0.77)</td>
<td>.01</td>
<td>0.30 (0.09-0.96)</td>
<td>.04</td>
<td>0.21 (0.08-0.79)</td>
<td>.02</td>
</tr>
</tbody>
</table>

*OR indicates odds ratio; CI, confidence interval.  †Odds ratio and 95% CI with reference to no dog or cat exposure in the first year of life adjusted for cord serum IgE concentration, total dust mite allergen (Der f 1 + Der p 1) in child’s bedroom at age 2 years, child’s sex, older siblings, parental smoking, and parental history of asthma.  ‡Odds ratio and 95% CI adjusted for variables in model 1 plus dog and cat exposure at age 6 to 7 years.
factors for allergic sensitization or that could have been associated with pet ownership, including cord serum IgE concentration, house dust mite exposure, older siblings, parental smoking, and parental history of asthma.\textsuperscript{3,37-42}

Other studies have also reported lower prevalences of allergic sensitization or symptoms related to allergic diseases in association with early exposure to dogs and cats.\textsuperscript{13,15,16,43,44} but a systematic review of the literature concerning this question concluded that previous exposure to dogs and cats increased the risk of asthma and wheezing in children older than 6 years.\textsuperscript{45} The conclusions of this systematic review differ from the results of 2 large prospective birth cohort studies.\textsuperscript{43,44} Nafstad et al\textsuperscript{43} found that after using logistic regression to adjust for potential confounders, being exposed to pets in early life reduced the risk of asthma (OR, 0.7; 95% CI, 0.5-1.1) and allergic rhinitis (OR, 0.6; 95% CI, 0.4-1.0) in a birth cohort of 2531 children followed to age 4 years. In a birth cohort of 1246 children in Arizona followed up to age 13 years, Remes et al\textsuperscript{44} reported that children who had 1 or more dogs in the home at birth were significantly less likely to develop frequent wheeze than children without early dog exposure, but neither early exposure to dogs or to cats was associated with skin prick test positivity or total serum IgE concentrations. Remes et al did not find a difference between children exposed to 1 dog compared with those exposed to 2 or more dogs. They also found that the inverse relationship between dog exposure and frequent wheeze was predominantly among children without a parental history of asthma. Reasons for the differences in allergic sensitization outcomes between our study and the study by Remes et al are not clear, but may include differences in climate where the birth cohorts were located and differences in keeping pets inside the home.

In a recent cross-sectional study in children by Platts-Mills et al,\textsuperscript{48} and also in a subsequent study in adults,\textsuperscript{49} a bell-shaped dose-response relationship between cat allergen exposure and cat-specific sensitization was observed. Decreased levels of cat-specific sensitization were associated with both the lowest and the highest cat allergen exposure groups. Platts-Mills and colleagues also found that cat-specific IgG antibody levels increased with increasing cat exposure, and were highest in the highest cat exposure group. They suggested that high levels of cat allergen exposure induced a modified T helper cell type 2 (Th2) response with production of cat allergen–specific IgG and IgG4 antibodies without allergic sensitization. This interesting hypothesis is not entirely consistent with the data presented in our study because we found that allergen-specific IgE antibodies to dust mites, ragweed, and grass (allergens unrelated to dog and cat) were also less prevalent in children exposed to dogs and cats in the first year of life.

Other researchers have suggested that the protective effect of dogs and cats is not related to allergen exposure but rather to increased exposure to bacterial endotoxin associated with household pets.\textsuperscript{53,54} Endotoxin exposure is hypothesized to shift the developing immune system away from a Th2-type pattern of response, which favors development of allergic sensitization, toward a Th1-type response. Studies in animals have shown that concomitant exposure to endotoxin and allergen will prevent allergic sensitization normally induced by the allergen.\textsuperscript{48} Recent studies have shown that endotoxin levels in homes are inversely related to Th2-type cytokine production by lymphocytes of children residing in the homes and that the presence of household dogs is related to higher levels of indoor endotoxin.\textsuperscript{47,49} Our data are consistent with the hypothesis that exposure to 2 or more dogs or cats, and therefore exposure to higher levels of endotoxin, is associated with a Th1 pattern of immune response and less allergic sensitization.

There were several associations with dog and cat exposure that were evident for boys but not for girls, including lower total serum IgE concentrations, lower prevalence of methacholine airway responsiveness, and better lung function. These differences in associations between boys and girls are puzzling, but others have also observed differences between boys and girls in factors related to asthma.\textsuperscript{50-52} Consistent with the pattern of the results of total serum IgE concentrations, methacholine airway responsiveness, and FEV\textsubscript{1}, in boys, the prevalence of asthma was also lower in those boys exposed to 2 or more dogs or cats compared with those who were unexposed (5.1% vs 11.8%). This difference was not statistically significant across pet exposure categories; however, only 39 boys were exposed to 2 or more dogs or cats in the first year of life. Assuming prevalences that we found in our cohort, a study designed to detect a statistically significant difference in the prevalence of asthma among boys exposed to 2 or more dogs or cats would have required a final cohort of at least 1327 children followed up to age 6 to 7 years.

An important strength of this study is the prospective design using a population-based cohort of children followed yearly from birth. The prevalences of allergic sensitization, methacholine airway responsiveness, and asthma found in our cohort were similar to those reported by others studying children of similar ages.\textsuperscript{53-55} The mean values for total serum IgE were also similar to those reported by others.\textsuperscript{53,56} Animal exposure was ascertained when the child was 1 year old, not years later.\textsuperscript{10,14,15} Assessing animal exposure prior to assessing outcomes reduces concern of misclassification of exposure and recall bias. Information on other factors potentially related to risk of allergic sensitization, most importantly family history, was collected, allowing adjustment for the potential confounding effects of these other variables.\textsuperscript{57} Another strength is the multiple objectively measured outcomes.\textsuperscript{10,14} The association between pet exposure and less allergic sensitization was found with both in vivo (skin prick test reactivity) and in vitro (allergen-specific IgE levels) tests. The per-
EXPOSURE TO DOGS AND CATS AND ALLERGIC SENSITIZATION

sons performing the skin prick tests, al- 
lergen-specific IgE tests, spirometry, 
and methacholine challenges were un- 
aware of study hypotheses at the time 
the tests were performed, making sys- 
tematic measurement bias unlikely.

Bronchial hyperresponsiveness is fre- 
quently stated to be a major compo- 
nent of asthma that can be objectively 
measured. Our findings of re- 
duced methacholine airway re- 
sponsiveness in boys with exposure to 2 
or more dogs or cats suggest that ex- 
posure to dogs and cats may be associ- 
ated with a reduced risk of asthma, at 
least in boys. While we did not find a 
statistically significant association for 
current asthma in this study, the preva- 
ience of asthma in boys exposed to 2 
or more dogs or cats was 57% lower 
than in unexposed boys, a difference 
that would likely be significant in a 
larger population.

There are limitations to our study. As 
with most prospective studies, some 
children did not complete the entire 
study. However, we found no impor- 
tant differences between children ex- 
amined at age 6 to 7 years and those 
who were not examined. In addition, 
we could not detect differences in the 
relationship between dog and cat own- 
ership and parental history of asthma, 
allergy, or hay fever among those 
examined and not examined. A sec- 
ond caveat is the limited racial, socio- 
economic, and geographic diversity of 
our study population, suggesting that 
our conclusions can only be applied to 
similar populations of white children. 
Since our follow-up was limited to an 
average age of 6.7 years, we do not 
know if the associations we found will 
persist as the children grow older, but 
others have found that the association 
between dog and cat exposure and a 
lower risk of allergy-related symp- 
toms persisted to age 12 to 13 years. Sample size is another limitation of the 
study. A larger sample would have al- 
lowed more reliable estimates and de- 
tailed examinations of the differences 
between boys and girls and between 
children with and without parental his- 
tories of asthma. A final caveat is that 
we did not consider exposure to dogs 
and cats outside the child’s home.

In this prospective study designed to 
examine multiple potential risk factors 
for allergic sensitization, we found that 
exposure to 2 or more dogs or cats in 
the first year of life was associated with 
a significantly lower probability of sub- 
sequent allergic sensitization to com- 
mmon aeroallergens. Exposure to 2 or 
more dogs or cats was also associated 
with significantly lower serum IgE con- 
centration. In boys, we also observed 
less methacholine airway re- 
sponsiveness, and better lung function 
in boys but not in girls. The association 
between pet exposure and decreased 
prevalence of allergic sensitization re- 
mained unchanged after adjustment for 
potentially confounding variables. These 
findings suggest that exposure to more 
than 1 dog or cat in the first year of life 
may reduce a child’s risk of allergic 
disease.

Author Contributions: Study concept and design: Ownby, Johnson. Acquisition of data: Ownby, Johnson. Analysis and interpretation of data: Ownby, Johnson, Peterson. Drafting of the manuscript: Ownby, Johnson, Peterson. Critical revision of the manuscript for important in- tellectual content: Ownby, Johnson, Peterson. Statistical expertise: Peterson. Obtained funding: Ownby, Johnson. Administrative, technical, or material support: Ownby, Johnson. Study supervision: Ownby, Johnson.

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