

Indoor pet exposure and the outcomes of total IgE and sensitization at age 18 years

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Background: Early-life exposure to household pets has been shown to be protective against allergic sensitization in childhood. **Objective:** We sought to evaluate the association between early-life pet exposure and allergic sensitization at age 18 years.

Methods: Teenagers who had been enrolled in the Detroit Childhood Allergy Study birth cohort in 1987-1989 were contacted at age 18 years. Serum total and allergen-specific IgE levels to 7 common allergens (dust mite, cat, dog, ragweed, Timothy grass, *Alternaria* species, and peanut; atopy was defined as any specific IgE level ≥ 0.35 kU/L) were measured at age 18 years. Annual interview data from childhood were used to determine indoor dog and cat ($\geq 50\%$ of their time in the home) exposure during early life. Exposure was considered in various ways: first year, cumulative lifetime, and age groups, as well as multiple pets.

Results: Dog or cat exposure in the first year of life was not associated with atopy (relative risk, 0.97; 95% CI, 0.83-1.12). Those living with pets in the first year and atopic at 18 years had lower total IgE levels. Neither cumulative exposure nor exposure at a particular age was strongly and consistently associated with either outcome. Although not statistically significant, there was a pattern of decreased odds of sensitization among those with 2 or more pets versus no pets in the first year of life.

Conclusions: Early-life pet exposure can be associated with lower total IgE levels among atopic subjects but is not strongly associated with decreased likelihood of sensitization to common allergens at age 18 years. (*J Allergy Clin Immunol* 2010;126:274-9.)

Key words: *Pets, allergy, epidemiology*

Abbreviations used

CAS: Childhood Allergy Study

ETS: Environmental tobacco smoke

Exposure to pets has received much attention as a potential risk or protective factor in allergic disease research.¹⁻²² Various measures of exposure (timing, duration, and type) and outcomes (IgE measurement, skin prick testing, and symptom reporting) have been investigated across studies, and results have been mixed. No single study has examined all of these numerous components of pet exposure for associations with allergy risk. Additionally, few studies have been able to examine whether the effects seen in early life persist beyond childhood.

Meanwhile, parents frequently ask physicians whether they should allow their children to have pets, usually dogs and cats, in the home because they worry that cat and dog exposure increases the risk of allergies. There are no clear answers because evidence has been mixed over the years and research results have been as variable as the study approaches. The analyses presented here use a systematic approach to study this important exposure. In a recent text Strachan and Sheikh²³ discussed the life-course epidemiology of respiratory and allergic diseases. They concluded that early-life events affect the development of the immune system during poorly defined critical periods, which in turn can affect the risk of allergic disease. In the life-course epidemiology approach, there are various models of how a factor might be considered to cause subsequent disease.²⁴ These approaches include, but are not limited to, the following: (1) a critical period model (ie, Exposure to a factor or occurrence of an event during a specific time window of development leads to the disease) and (2) a cumulative dose model (ie, the cumulative exposure [or lack of exposure] to a factor over a period of time leads to the disease).

It is probable that disease causation can be linked to multiple models or versions of these models that are likely not mutually exclusive.

The purpose of this study was to extensively evaluate the possible role that indoor pets play in allergic sensitization in teenagers by using these principles of disease causation to guide us. Specifically, using data from our birth cohort study with follow-up of participants to age 18 years, we examined whether the following exposure patterns are associated with total IgE levels and the risk of sensitization (positive allergen-specific IgE level ≥ 0.35 kU/L) at age 18 years: (1) presence of pets in the first year of life and (2) high lifetime cumulative exposure to pets in the home. We also examined whether exposure to pets in any of

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the following age periods was more strongly associated with outcomes: first year of life, 1 to 5 years, 6 to 12 years, and 13 years and older. In prior analyses of this cohort, we reported that having multiple pets in the first year of life was associated with a decreased risk of allergic sensitization at age 6 years.¹ This current work will allow us to examine whether this protective association persisted to age 18 years.

METHODS

The relationship between pet keeping and allergy is complex, and the questions are factorial, with various ways to consider exposure associated with various outcomes. With respect to pet exposure, at least 4 primary elements can be identified: timing (eg, first year of life), duration (number of years), dose (number of pets), and type of animal (cat, dog, and both). A cluster of outcomes has been hypothesized to be affected by these exposures, including both allergic symptoms and allergic sensitization (as measured based on the presence of allergen-specific IgE) and whether symptoms or sensitization are related to the exposure-specific animal, both animals, or other nonpet allergens. All these exposure and outcome elements might be studied separately or in combination with each other. Because of sample size constraints, we chose to focus on exposure to either dogs or cats and the outcomes of total IgE levels and allergic sensitization to any of 7 common allergens (including dog and cat) at 18 to 20 years of age.

Study population

Details of recruitment for the Childhood Allergy Study (CAS), have been fully described elsewhere.²⁵ Briefly, pregnant women 18 years and older from a geographically defined area of metropolitan Detroit, Michigan, who belonged to a health maintenance organization, were seeing a Henry Ford Health System provider, and were to deliver between April 15, 1987, and August 31, 1989, were eligible for study inclusion. Study enrollment included providing written informed consent, completing a prenatal interview, and having cord blood collected at delivery. Women completed annual telephone questionnaires on the anniversary of their children's birth until (and including) each child's sixth birthday. Of the 1,194 women who were eligible for CAS, 953 consented to participate. Infants from 106 of these women were excluded from the study because their cord blood was not obtained for analysis. Of the remaining 847 infants, 6 had cord blood that was believed to be contaminated by maternal blood, and 6 more were determined to be ineligible at subsequent review of eligibility criteria. Mothers of the remaining 835 children were asked to complete interviews annually to discuss the health of the child for the previous year. Recently, we contacted these 835 children to obtain updated health information through age 18 years. After their 18th birthday, teenagers were contacted to complete (1) a telephone-administered interview and (2) a clinic visit with blood sample collection.

Of the 835 teenagers eligible at age 6 years of age, 15 withdrew from the study, died, or otherwise became ineligible before the follow-up at age 18 years. Of the remaining 820 teenagers, 40 were missing valid telephone numbers and were not contacted, 3 were enlisted in the military and unable to participate in the study, 3 had physical disabilities precluding them from completing interviews, and 2 were incarcerated, leaving a total of 772 teenagers eligible to provide interviews. Of these 772 teenagers, 671 (86.9%) consented to study enrollment, although blood was not collected from all participants. The Henry Ford Health System Internal Review Board approved this research.

Exposures

Current pet keeping was reported by families (usually the mother) at each annual interview through age 6 years. The question about pets in the house was as follows: "Have you had any pets in your home for more than 2 weeks?" If yes, the type of animal (eg, cat, dog, or bird) and the number of each type of animal were recorded, as well as whether these animals were kept mostly indoors, outdoors, or equally indoors and outdoors. Two weeks was chosen to differentiate household pets versus those being cared for on a temporary basis.

Additional information collected through interviews included tobacco smoke exposure throughout childhood, family size, and parental allergy history.

The telephone interview administered to teenagers at age 18 years addressed questions on lifetime exposure to animals, cigarette or other forms of smoking, family history of allergic disease, and demographic questions. Teenagers were asked, "Have you ever lived with any pets or outdoor animals?" Follow-up questions included the type of animals owned and whether these animals were indoor or outdoor animals. Animals were categorized as indoor animals if the teenager reported that the animal stayed indoors for 12 or more hours per day. If the teenager had any pets other than fish, they were asked, "Please list all [indoor/outdoor] pets that you have ever lived with for at least 1 month." For each pet listed, information on the type of pet, ages lived with, and categorization of amount of contact with the animal was queried. We did not have data on dog or cat allergen levels across the teenagers' life spans.

Parental report of dogs or cats in the first 6 years of life and the teen's report of dog or cat exposure from ages 6 through 18 years were used to define the exposures. The exposure definitions are as follows:

- (1) Lived with dogs or cats in the first year of life (critical period): Teenagers whose parents reported there was an indoor dog or cat that was "in their home for at least 2 weeks" in the child's first year of life.
- (2) Cumulative exposure to dog or cat: Cumulative exposure was calculated as the total number of years in which a child lived in a home in which a dog or cat was kept indoors at least half the day. The years did not have to be contiguous.
- (3) Additional critical periods: Exposure to pets during specific ages was calculated based on whether during each age period (first year of life, 1-5 years, 6-12 years, and ages 13 years and older) the child lived in a home in which a dog or cat was kept indoors at least half the day. These groupings were chosen *a priori* based on the interest in exposure in the first year of life, which is a period of rapid immune development, as well as ages before entering school, after entering school, and around the likely peripubertal period. An indicator variable was created for each age period, and a teenager was defined as exposed for any specific age period if there was sufficient pet contact during at least 1 of the years in that age period.

A teen's sex, parental allergy history (maternal, paternal, or both), and firstborn status were considered potential effect modifiers or confounders. Women were asked during the prenatal interview whether a physician had ever given them a diagnosis of "allergies" or told them that they had "hay fever." They were also asked if they had ever had "immunotherapy (allergy shots)." If the mother reported yes to any of these questions, she was classified as having an allergic history. A paternal allergic history was defined as the mother reporting the father being given a diagnosis of "hay fever" or "allergies" in the past. Information to define firstborn status was taken from parental report.

We also considered the role (effect modification and confounding) of exposure to environmental tobacco smoke (ETS) exposure in the first year of life in the association between dogs or cats and sensitization. ETS was defined as routine contact with a cigarette-smoking adult who smoked at least 1 cigarette per day (included mother, father, female guardian, male guardian, other adult living in the home, and babysitter if they smoked in the child's home for at least 20 days in the past month at the time of the interview). This information was taken from the parental interview.

Outcomes

Venous blood was collected for assessment of both total and allergen-specific IgE levels at age 18 years and stored at -80°C until assayed. Measurements of total and allergen-specific IgE levels were performed according to the standard manufacturer's protocols with the Pharmacia UniCAP system (Phadia, Portage, Mich). Allergen-specific IgE levels were analyzed for *Dermatophagoides farinae*, peanut, dog, cat, Timothy grass, *Ambrosia artemisiifolia* (ragweed), and *Alternaria alternata*. For savings, we removed *Dermatophagoides pteronyssinus* from the 18-year panel because only 5 (0.9%) of the 565 teenagers were sensitized to *D pteronyssinus* and no other allergens in the 6-year panel. Sensitization was defined as having at least 1 allergen-specific IgE result of 0.35 kU/L or greater.

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