

Presence and timing of cat ownership by age 18 and the effect on atopy and asthma at age 28

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Background: Asthma and allergic sensitization to cats frequently coexist, although recent studies show less atopic disease among people who had pets in infancy. However, no long-term evaluations have been performed thus far.

Objective: We sought to evaluate the relationship between cat ownership at different age periods (<18, >18, and both periods) and atopic disease at age 28.

Methods: Australian school children aged 8 to 10 years were recruited in 1982 and participated in follow-up surveys until 2002. Cat ownership was defined by surveys in 1992 and 2002 as having a cat before age 18 only, after age 18 only, or in both periods of life. Health outcomes were defined at a mean age of 28.5 years.

Results: Complete data were available for 224 subjects, 50 of whom had a cat before 18 years of age only, 14 after age 18 only, and 70 in both periods. Compared with 90 subjects that never had a cat, having a cat before age 18 protected against atopy to outdoor allergens, airway hyperresponsiveness (AHR) to histamine, current wheeze, and current asthma ($P < .05$). In contrast, subjects who acquired their first cat after age 18 showed a trend toward higher prevalence rates for asthma symptoms and AHR ($P > .10$).

Conclusions: Having had a cat before 18 years of age protects against adult asthma and atopy. (*J Allergy Clin Immunol* 2004;113:433-8.)

Key words: Childhood cat ownership, asthma, AHR, atopy, wheeze

Asthma is strongly associated with atopy in both children^{1,2} and adults.³⁻⁶ In different populations, the allergens that confer the greatest risk vary and are generally those to which high indoor exposure occurs. In temperate

Abbreviations used

AHR: Airway hyperresponsiveness
SPT: Skin prick test

climates, mite allergy is most frequently present in asthma,⁷⁻¹⁰ whereas in drier climates it is allergic sensitization to cockroach^{11,12} or *Alternaria*.^{13,14}

Sensitization to domestic pets, particularly cats, is also more often present in asthma.^{9-11,14-17} This observation might serve as a pointer toward prevention strategies for at least 1 of the triggers that induces asthma exacerbations. However, the situation with domestic pets is complex. In contrast to other indoor allergens, there is no clear dose-response relationship between cat allergen exposure and asthma severity.^{9,18,19} Because of the ubiquitous nature of cat allergen in many communities, low levels of exposure might be sufficient for sensitization to occur, even in the absence of a cat.²⁰⁻²³ The relationship between asthma and exposure to cats is further complicated by the apparent high-dose tolerance to cat allergens^{24,25} and the contradictory effects of cat ownership in infancy.²⁶⁻²⁹

A number of recent studies have shown a protective effect of childhood cat ownership against cat sensitization²⁶⁻²⁸ and asthma symptoms.²⁷⁻²⁹ In contrast, 2 birth cohort studies demonstrated that a high level of exposure to cat allergen in early life was a risk factor for the development of sensitization and asthma.^{30,31}

The onset of sensitization and asthma might be a function of both the intensity of allergen exposure and its timing. The risks and benefits of the acquisition of a cat, and the effect of timing of the exposure, is a subject of great practical interest for the general community and researchers trying to understand the etiologic mechanisms of allergy and asthma.

Since 1982, we have been monitoring asthma and allergy outcomes in a local cohort with a high prevalence of cat ownership. The aim of the current analysis is to assess the effects of cat ownership in different age periods (<18 only, >18 only, and both periods) on asthma and allergy outcomes at age 28.

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TABLE I. Baseline (1982) characteristics (%) in participants and nonparticipants of current analysis

	Participants (N = 224)	Nonparticipants (N = 494)
Girls	46	48
Age in 1992	18.5 (17-20)	18.5 (17-20)
Atopy, any allergen	23	23
Atopy, cat allergen	3	1
Ever asthma	10	9
Airway hyperresponsiveness	11	9
Parental atopic history	57	54
Passive smoking	55	63
Pet owner in 1990	84	80

TABLE II. Cat ownership by age by data collected in 1992 (at age 18) and in 2002 (at age 28)

	1992		2002	
	Ever cat	Current cat	Ever cat	Current cat
<18 y only	Yes	No	Yes	No
>18 y only	No	No	Yes	Either
<18 y & ≥18 y	Yes	Yes	Yes	Either
	Yes	No	Yes	Yes
Never	No	No	No	No

Note that a person who currently owned a cat in 1992 (age 17-20 years) is classified as owning a cat both <18 years and ≥18 years, on the assumption that cat ownership around 1992 was usually acquired before 18 years of age.

METHODS

Design

A random sample of third and fourth grade school children living in the coastal town of Belmont, New South Wales, Australia, was recruited in 1982 (N = 716, response rate 87%). Every other year the children were invited for a follow-up study until 1994, whereafter subsequent follow-up surveys were conducted in 1997 and 2002. All surveys were undertaken in the winter season (July through September). The Human Research Ethics Committee of the University of Sydney approved the protocols for these surveys.

Information on cat ownership was obtained in 1992 and 2002. For the present analysis, we used data on asthma and allergy outcomes collected in 2002. Hence, the study population for this analysis was based on subjects with complete data in 2002 and information on cat ownership in 1992 (N = 224). Characteristics at baseline (1982) and when first information on cat ownership was obtained (1992) were similar for participants and nonparticipants (Table I).

Questionnaire

Health outcomes were based on questionnaire data collected in 2002 as: current wheeze (a history of wheeze in the past 12 months) and current asthma (a history of wheeze in the past 12 months and ever been diagnosed as asthma by a doctor or currently using inhaled corticosteroid treatment). Cat ownership was defined by questionnaire data of 1992 and 2002, as shown in Table II.

Potential confounders were coded with available information collected at the various surveys: the presence of another pet (1990), passive smoking (1986, 1988, 1990), current (2002) and former smoking (1990, 1992, 1994, 1997, 2002), history of occupational dust exposure (1997, 2002), wheeze at job (1997, 2002), parental history of atopic disease (1982), sibling's history of atopic disease, (1997) and number of siblings (1997).

Skin prick tests

Atopic status was assessed by skin prick tests (SPT) using house dust, house dust mite (*Dermatophagoides pteronyssinus* and *D farinae*), cat dander, cockroach, rye grass, *Alternaria alternata*, and *Cladosporium* (all Hollister-Stier, Spokane, Australia). Histamine and 50% glycerol were used as positive and negative controls. A positive SPT was defined as a mean wheal diameter ≥3 mm. If this occurred for the negative control solution, all SPTs were set missing. Atopy was considered to be present if there was at least 1 positive SPT.

Airway hyperresponsiveness

Airway hyperresponsiveness (AHR) was assessed by histamine challenge. Subjects were asked to withhold β-agonist medication 6 hours before the test. Baseline lung function was assessed according European Respiratory Society guidelines using a dry rolling seal spirometer. Subjects with a baseline FEV₁ <70% of the predicted value were excluded. Histamine was administered in doubling or quadrupling doses, ranging from 0.03 to 3.92 μmoles by DeVilbiss No 45 hand-held nebulizers (DeVilbiss Co, Heston, UK).³² The test was stopped, and subjects were classified as having AHR if their FEV₁ had fallen ≥20% from the post saline value. Salbutamol aerosol was administered to relieve bronchoconstriction.

Statistical analyses

Odds ratios and 95% CI were calculated by use of the SAS8 package (SAS Institute, Cary, NC) to express the relationship between defined categories of cat ownership and health outcomes in 2002. The reference group consisted of subjects who never had owned a cat. All analyses were adjusted for potential confounding by sex, atopic history of parents or siblings, number of siblings, childhood passive smoking, current and past

TABLE III. Prevalence of atopy, airway hyperresponsiveness, and asthma at age 28 by cat ownership before and after age 18

	Cat ownership				All (N = 224)
	Never (N = 90)	< 18 y only (N = 50)	< 18 y and ≥18 y (N = 70)	> 18 y only (N = 14)	
Atopy					
Any allergen	67	58	61	71	63
Indoor allergen*	62	56	57	71	60
Outdoor allergen†	38	26	29	29	32
Cat	21	24	16	36	21
Current wheeze	34	18‡	33	43	31
Airway hyperresponsiveness	9	12	9	21	10
Current asthma	25	12	22	36	22

*House dust, *Dermatophagoides pteronyssinus*, *D farinae*, cat dander, cockroach.

†Rye grass, *Alternaria alternata*, and *Cladosporium*.

‡P < .05 compared with “never cat.”

TABLE IV. Cat ownership in different periods of life and atopic disease at age 28: results of multiple logistic regression analyses*; reference: never cat

A. All participants (N = 224)	< 18 y only	< 18 and ≥18 y	> 18 y only
	Odds ratio (95% CI)	Odds ratio (95% CI)	Odds ratio (95% CI)
Atopy			
Any allergen	0.53 (0.13-2.18)	0.39 (0.10-1.48)	0.58 (0.10-3.30)
Indoor allergen†	0.68 (0.18-2.53)	0.49 (0.14-1.69)	0.74 (0.13-4.05)
Outdoor allergen‡	0.38 (0.10-1.44)	0.34 (0.10-1.18)	0.31 (0.04-2.15)
Cat allergen	0.57 (0.15-2.17)	0.31 (0.08-1.19)	2.43 (0.44-13.32)
Current wheeze	0.15 (0.03-0.63)§	0.50 (0.15-1.73)	1.34 (0.24-7.50)
Airway hyperresponsiveness	0.26 (0.04-1.64)	0.16 (0.02-1.01)	2.45 (0.28-21.16)
Current asthma	0.08 (0.01-0.46)	0.17 (0.04-0.77)§	2.62 (0.34-19.97)
B. Participants without childhood asthma at baseline (1982), N = 201	< 18 y only	< 18 and ≥18 y	
	Odds ratio (95% CI)	Odds ratio (95% CI)	
Atopy			
Any allergen	0.62 (0.14-2.72)	0.50 (0.12-2.07)	
Indoor allergen†	0.85 (0.21-3.39)	0.69 (0.18-2.58)	
Outdoor allergen‡	0.23 (0.05-0.74)§	0.18 (0.05-0.98)§	
Cat allergen	0.66 (0.16-2.80)	0.32 (0.08-1.40)	
Current wheeze	0.10 (0.02-0.49)	0.43 (0.11-1.67)	
Airway hyperresponsiveness	0.06 (0.01-0.77)§	0.13 (0.02-0.91)§	
Current asthma	0.03 (0.00-0.32)	0.14 (0.02-0.76)§	

*Adjusted for sex, atopic parents, atopic sibs, number of sibs, childhood passive smoking, adult current and past smoking, childhood other pet ownership, ever occupational dust exposure, wheeze at job.

†House dust, *D pteronyssinus*, *D farinae*, cat dander, cockroach.

‡Rye grass, *Alternaria alternata*, and *Cladosporium*.

§P < .05.

||P < .01.

smoking, childhood other pet ownership, a history of occupational dust exposure and wheeze while working.

To take into account the possibility of selective pet avoidance because of a childhood asthma diagnosis, we conducted a sensitivity analysis excluding subjects with an asthma diagnosis in 1982.

RESULTS

The final study population was composed of 224 subjects with complete data for cat ownership before and after 18 years of age (1992) and for health out-

comes measured in 2002. At age 18 (1992 survey), 120 subjects (54%) ever had a cat, and 62 (52%) of these still did. Introduction of a cat in the household between age 18 (1992) and age 28 (2002) occurred for 22 subjects. Eight of them also had had a cat before age 18, and thus 14 subjects acquired their first cat after 1992. Considering the entire study period, 134 of the 224 participants (60%) ever had a cat.

Table III shows prevalence rates of atopy, AHR, and asthma symptoms by age of cat ownership. Compared to subjects who never owned a cat, those who owned a cat before age 18 years only were less likely to report current wheeze at age 28 years ($P < .05$). Similarly, lower prevalence rates were observed for atopy and current asthma, although the difference from those who had never owned a cat did not reach statistical significance ($P > .05$).

In contrast, cat sensitization, current wheeze, AHR, and current asthma tended to occur more commonly in subjects who acquired a cat after 18 years, although not statistically significant ($P > .05$).

Results of multiple logistic regression analyses are shown in Table IV, with subjects who never had a cat as a reference group. Table IVA shows the results for all subjects and Table IVB for those without a childhood asthma diagnosis in 1982. Having had a cat before 18 years only was associated with a reduced risk of current wheeze and current asthma ($P < .05$).

As shown in Table IVB, exclusion of subjects with an asthma diagnosis in 1982 increased the protective effects of cat ownership before 18 years against atopy to outdoor allergens and against AHR (Table IVB). Separate analyses for children without a paternal history of atopy could only be performed for a limited number of outcomes and yielded similar results. A cat might have been removed because of allergic sensitization in 1 of the previous surveys, though exclusion of children sensitized to cat in 1982 did not change the results. Extending the exclusion with subjects sensitized in 1 of the surveys before 1992 resulted in a stronger protection against cat sensitization in 2002 (age 28) of having a cat both before and after age 18 (odds ratio, 0.19; 95% CI, 0.04-1.06).

DISCUSSION

This follow-up study from childhood until adulthood shows that having a cat before 18 years of age reduces the risk of having asthma symptoms and probably also protects against allergic sensitization in adulthood. Our study is novel in including data from childhood until adulthood, and the design of the study allowed us to evaluate a number of atopic outcomes and consider the role of confounders in more detail.

The prevalence of atopy and asthma at age 28 was high in this population. Nevertheless, we did not find evidence for selection bias directed to atopic subjects, because prevalence rates among participants and nonparticipants were similar both at age 8 and at age 18. We also

found no evidence of selective participation of subjects with respect to other personal and environmental characteristics at baseline.

In this study, we found that having had a cat before age 18 protected against atopy to outdoor allergens, AHR, current wheeze, and asthma at age 28. Two models have been proposed to explain this interesting observation. First, the "hygiene hypothesis," which proposes that microbial exposure in early life might protect against atopic disease by shifting the immature immune response of a T_H2 type toward a nonallergic T_H1 type.³³ The link between early life pet ownership and the "hygiene hypothesis" is the observation of higher endotoxin levels in houses with pets.^{34,35}

A second explanation for the inverse relationship between pet ownership and atopic disease is the induction of immune tolerance.^{24,25} Under conditions of high exposure, the T_H2 response is expressed as IgG4 rather than specific IgE antibodies. Other studies have supported this hypothesis, showing that high exposure to multiple pets was protective against allergic sensitization³⁶ and that protective effects of pet ownership and endotoxin exposure on asthma symptoms were independent of each other.²⁹ We did not collect data on cat allergen or endotoxin in these subjects' houses and hence cannot directly test these alternative hypotheses.

Because of the design of our study, we had to define childhood cat ownership by a cutoff age of 18 years. In earlier surveys, no data were collected on cat ownership. According to the "hygiene hypothesis," pet exposure reflects exposure to microbes and might protect against disease if occurring in early childhood (ie, the time window of immune maturation). This is supposed to occur in the first 2 years of life, although a recent review has suggested that this period might be up to 6 years.³⁷ Our cutoff at age 18, therefore, might have resulted in conservative odds ratios and thus underestimation of the protective effect of childhood cat ownership.

Our results strongly suggest that the achieved protection lasts into adulthood, irrespective of the presence of a cat in adulthood as well. Others have also found protection of childhood cat ownership by use of a rather broad time window.²⁶ This might suggest that immunologic adaptation by pet ownership might occur beyond early infancy.

An inverse relationship, such as that demonstrated here, might be the result of selective avoidance of pets because of previously diagnosed allergic disease.^{38,39} We performed separate analyses after excluding subjects with childhood asthma at enrollment in 1982 ($N = 23$). In case of selective avoidance, one would expect a reduction in the observed protective associations. In our study, the protective effects actually increased after excluding subjects with childhood asthma or those with cat sensitization in surveys before 1992. This suggests that selective cat avoidance is not the explanation for the observed associations. However, we have no direct information on whether parents did avoid purchasing a cat (or got rid of

an existing cat) because their child or one of the parents had asthma, and hence we cannot completely exclude this as a source of bias.

In this study population, the protection of childhood cat ownership was most pronounced in children without childhood asthma. This is in agreement with our results of a trend toward higher prevalence rates of asthma characteristics in subjects who acquired their first cat after age 18. Unfortunately, the number of subjects was too low ($N = 14$) to perform further statistical analyses.

We conclude that cat ownership before 18 years of age reduces the risk of atopic disease. The protection seems to last beyond childhood, irrespective of whether a cat is re-introduced in adult life.

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