

Pets, parental atopy, and asthma in adults

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Background: Studies of exposure to pets and the risk of asthma have provided conflicting results.

Objective: We conducted a population-based incident case-control study to assess the relationship of current and previous pet keeping with the risk of adult-onset asthma. We also investigated whether genetic propensity as a result of parental atopy modifies these relations.

Methods: From the source population of 441,000 inhabitants of a geographically defined area in South Finland, we systematically recruited, during a 2.5-year period, all new cases of asthma in 21- to 63-year-old adults and randomly selected control subjects. The clinically diagnosed case series consisted of 521 adults with newly diagnosed asthma and a control series of 932 control subjects. Information on current and past exposure to hairy pets was collected by using a self-administered questionnaire.

Results: In logistic regression analysis the risk of asthma was lower among subjects with pets during the past 12 months (adjusted odds ratio [OR], 0.74; 95% confidence interval [CI], 0.57-0.96) but higher among subjects with pets more than 12 months previously (adjusted OR, 1.39; 95% CI, 1.05-1.84). Parental atopy increased the risk of asthma (OR, 1.88; 95% CI, 1.47-2.41), but there was no interaction between parental atopy and pet exposure.

Conclusions: The present results are consistent with the hypothesis that both keeping furry pets and parental atopy increase the risk of asthma development in adulthood.

Parental atopy does not modify the effects of pet exposure. The negative association between current pets and the risk of asthma is consistent with selective avoidance of these pets by symptomatic individuals. (*J Allergy Clin Immunol* 2002;109:784-8.)

Key words: Parental atopy, pets, gene-by-environment interaction, asthma, adults

Studies of exposure to pets and the risk of asthma have provided conflicting results.¹ Controversial findings on the relationship between pet keeping and asthma could be explained by both methodological issues and by the complexity of the phenomenon. Individuals with symptoms of asthma tend to remove pets from their home as a

Abbreviations used

CI: Confidence interval

OR: Odds ratio

means of alleviating their conditions.² This could introduce a selection bias in cross-sectional and prevalent case-control studies, masking or even reversing a relationship between pet exposure and the risk of asthma.

In a recent meta-analysis, exposure to pets appeared to increase the risk of asthma and wheezing in children older than 6 years of age, but in younger children a lower risk of wheezing was observed in exposed than in unexposed children.¹ This finding could mean that the relation between keeping pets and asthma differs depending on the age of pet keeping and the age of asthma onset. Information on the role of pet keeping in adult-onset asthma is limited. We identified only 3 cross-sectional studies on pet keeping and the risk of asthma in adults.³⁻⁵ These studies did not separate asthma developing in adulthood from asthma developing in childhood, and the results were conflicting.

Family history of allergic diseases is associated with an increased risk of asthma, suggesting that genetic factors play a central role in the development of asthma.⁶⁻⁸ Some genetic markers could impose susceptibility to the effects of environmental factors. In a recent Norwegian cohort study the effect of exposure to environmental tobacco smoke on asthma was found to be stronger in children of atopic parents compared with children of nonatopic parents.⁸

We conducted a large population-based study in South Finland to assess the relations between current and past exposure to pets and the risk of developing asthma in adulthood. We also assessed the joint effect of genetic propensity to asthma, measured as parental atopy or asthma, and exposure to pets.

METHODS

Study design

This study was a population-based incident case-control study. The source population consisted of adults 21 to 63 years of age living in a geographically defined administrative area in South Finland with a population of 440,913 in 1997. The study was approved by the ethics committees of the Finnish Institute of Occupational Health and the Tampere University Hospital.

Definition and selection of cases

We systematically recruited all new cases of asthma, first in the city of Tampere beginning on September 15, 1997, and then from

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Supported by the Ministry of Social Affairs and Health of Finland and the Finnish Work Environment Fund.

Received for publication November 5, 2001; revised February 4, 2002; accepted for publication February 6, 2002.

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0091-6749/2002 \$35.00 + 0 1/81/123870

doi:10.1067/mai.2002.123870

March 10, 1998, to March 31, 2000, in the whole Pirkanmaa Hospital District. Patients were recruited at all health care facilities diagnosing asthma, including the Department of Pulmonary Medicine at the Tampere University Hospital, offices of the private-practicing pulmonary physicians in the region, and public health care centers. As an additional route of case selection, the National Social Insurance Institution of Finland invited all patients whose reimbursement rights for asthma medication began during the period from September 1, 1997, through May 1, 1999, and who had not yet participated. The following diagnostic criteria were applied for asthma: (1) history of at least one asthma-like symptom (prolonged cough, wheezing, attacks of or exercise-induced dyspnea, or nocturnal cough or wheezing) and (2) demonstration of reversibility of airways obstruction in lung function investigations, including spirometry, bronchodilation testing, and a 2-week peak expiratory flow follow-up. The same lung function protocol was applied for all patients with suspected asthma. The only exceptions were patients recruited through the National Social Insurance Institute, for whom lung function data were obtained by abstracting from the medical records. The measurements were carried out according to the standards of the American Thoracic Society.⁹ The details of lung function measurements and criteria for bronchial obstruction are given elsewhere.¹⁰ Presence of obstruction was judged by using the reference values derived from a Finnish population.¹¹ A total of 362 case subjects (response rate of 90%) participated through the health care system, and 159 case subjects (response rate of 78%) participated through the National Social Insurance Institution, totaling 521 case subjects.

Selection of control subjects

The control subjects were randomly drawn from the source population by using the national population registry, which has a full coverage of the population. The general eligibility criteria were applied for control subjects. After up to 3 invitation letters and phone calls, 1016 control subjects participated in the study (response rate of 80% of those who had a phone number in the Pirkanmaa area). Previous or current asthma was reported by 76 (7.5%), 6 persons were older than 63 years, and 2 returned incomplete questionnaires. After excluding these persons, our study population included 932 control subjects.

Data collection

At the Tampere University Hospital, case subjects were recruited at their first visit because of suspected asthma, and the diagnosis was then verified by means of clinical examinations. At the other health care facilities, case subjects were recruited immediately when the asthma diagnosis was verified. The National Social Insurance Institution invited the case subjects half a year to 2 years after their diagnoses were established. For these patients, the date and criteria of the asthma diagnosis were confirmed from their medical records. For all case subjects, we verified from their medical records that they did not have an asthma diagnosis previously. Eligible subjects were invited to participate in the study by their physician or through a letter sent by the National Social Insurance Institution. Recruitment of control subjects took place by letter at regular intervals throughout the study period. The participants were asked to fill out a self-administered questionnaire at their first visit. The questionnaire was modified from the Helsinki Office Environment Study questionnaire for use in a general population.^{10,12}

Genetic and environmental determinants of interest

Parental atopy was defined as a history of maternal or paternal asthma, hay fever, allergic eczema, or allergic conjunctivitis. Infor-

mation on these was obtained in the questionnaire. Exposure to pets was assessed on the basis of questionnaire information on the presence of cats, dogs, birds, rodents, or other hairy animals during the past 12 months and more than 12 months previously. Information on the duration of pet keeping was also requested.

Statistical methods

We used the exposure odds ratio (OR) to quantify the relations between determinants of interest and the risk of asthma. We estimated adjusted ORs in logistic regression analyses. Sex, age, education (as an indicator of socioeconomic status), personal smoking, mold problems in the home or at work, exposure to environmental tobacco smoke, and self-reported occupational exposure to sensitizers, dusts, or fumes were used as covariates. We studied the relation of asthma to parental atopy and to current and past exposures to individual pets or any pet combined.

We also studied independent and joint effects of parental atopic diseases and pet keeping by comparing the risk of asthma in 4 exposure categories: (1) no parental atopy and never kept pets (reference category); (2) parental atopy and never kept pets; (3) no parental atopy and kept pets (current, only >12 months previously); and (4) parental atopy and kept pets (current, only >12 months previously). We calculated ORs contrasting each of the 3 exposure categories with the reference category. Estimates for the independent effects of parental atopy and pet keeping and their joint effect were derived from the same logistic regression model, adjusting for the covariates.

RESULTS

Characteristics of case subjects and control subjects

A larger proportion of patients than control subjects were women, were young, were current smokers, were exposed to environmental tobacco smoke and to visible mold or mold odor at work, and had lower education (Table I).

Parental atopy and exposure to pets

Table II shows the distributions of parental atopic diseases and pet keeping in case subjects and control subjects. The parents of case subjects had any history of atopic disease (36%) more commonly than the parents of control subjects (22%). In all, the case subjects had a pet at some time slightly more often (74%) than the control subjects (71%). However, a comparison of current pet keeping and pet keeping only more than 12 months previously showed a difference. The prevalence of current pets was lower in case subjects than in control subjects (43% vs 45%), whereas the prevalence of pets only in the past was higher in case subjects (32% vs 26%). A similar pattern was observed for cats and dogs but not for other less frequent pets.

Effects of parental atopy and exposure to pets

Table III presents the risk of asthma in relation to parental atopic disease and the presence of current or past pets in the home. The risk estimates shown in the first column were adjusted for other parental atopic diseases or for other pets, and the estimates shown in the second column were adjusted for a set of other covariates as

TABLE I. Characteristics of the study population

Characteristics	Case subjects n (%)	Control subjects n (%)
Total	521	932
Sex		
Male	175 (33.6)	438 (47.0)
Female	346 (66.4)	494 (53.0)
Age (y)		
21-29	108 (20.7)	141 (15.1)
30-39	107 (20.5)	224 (24.0)
40-49	125 (24.0)	254 (27.3)
50-59	140 (26.9)	240 (25.8)
60-64	41 (7.9)	73 (7.8)
Education*		
No vocational schooling	107 (20.6)	154 (16.6)
Vocational course	89 (17.2)	104 (11.2)
Vocational institution	149 (28.7)	271 (29.2)
College-level education	113 (21.8)	261 (28.1)
University or corresponding	61 (11.8)	138 (14.9)
Smoking†		
No	239 (46.1)	487 (52.4)
Ex	133 (25.7)	203 (21.8)
Current (regular or occasional)	146 (28.2)	240 (25.8)
ETS in the workplace	89 (17.1)	130 (13.9)
ETS in the home	30 (5.9)	52 (5.6)
Visible mold or mold odor in the home	70 (13.4)	118 (12.7)
Visible mold or mold odor in the workplace	70 (13.4)	99 (10.6)
Any work exposure‡	313 (60.1)	579 (62.1)

ETS, Environmental tobacco smoke.

*Information on education was missing for 6 subjects.

†Information on smoking was missing for 5 subjects.

‡Self-reported exposure to sensitizers, dusts, and/or fumes.

well. Parental atopy was a strong determinant of asthma (adjusted OR, 1.88; 95% confidence interval [CI], 1.47-2.41). Paternal asthma was the strongest predictor of asthma (adjusted OR, 2.16; 95% CI, 1.39-3.35), followed by maternal asthma (adjusted OR, 1.84; 95% CI, 1.23-2.76). The presence of pets currently at home was inversely related to the risk of asthma (adjusted OR, 0.74; 95% CI, 0.57-0.96), whereas the presence of any pet more than 12 months previously was related to an increased risk of asthma (adjusted OR, 1.39; 95% CI, 1.05-1.84). A similar pattern was observed when studying cats and dogs separately, whereas the risk of asthma was elevated for both current and previous keeping of birds and rodents.

Table IV shows that for both cat and dog exposure, there seemed to be an exposure-related increase in the asthma risk from the lowest quintile (<20%) to the fourth quintile (60% to <80%), but for the highest quintile, the risk was lower. Excluding the subjects with a pet during the past 12 months resulted in an exposure-response pattern without a lower risk in the highest exposure category.

Joint effect of parental atopy and exposure to pets

In subjects without pets, parental atopy alone significantly increased the risk of asthma, with an adjusted OR of

TABLE II. Parental atopy and pet keeping by case and control subjects

Characteristics	Case subjects n (%)	Control subjects n (%)
Total	521	932
Parental atopic diseases		
Maternal allergy	85 (16.3)	108 (11.6)
Paternal allergy	47 (9.0)	48 (5.2)
Maternal asthma	66 (12.7)	64 (6.9)
Paternal asthma	62 (11.9)	48 (5.2)
Any	186 (35.7)	204 (21.9)
Pets		
Never	134 (25.7)	269 (28.9)
Currently	222 (42.7)	420 (45.1)
Only >12 mo previously	165 (31.7)	243 (26.1)
Sometimes	387 (74.3)	663 (71.1)
Currently (previous 12 mo)		
No pets	299 (57.4)	512 (54.9)
Cats	108 (20.7)	191 (20.5)
Dogs	124 (23.8)	252 (27.0)
Birds	7 (1.3)	8 (0.9)
Mice, guinea pigs, or rabbits	23 (4.4)	30 (3.2)
Other	12 (2.3)	19 (2.0)
Only >12 mo previously		
No pets	221 (42.4)	662 (71.0)
Cats	90 (17.3)	122 (13.1)
Dogs	111 (21.3)	142 (15.2)
Birds	31 (6.0)	32 (3.4)
Mice, guinea pigs, or rabbits	50 (9.6)	73 (7.8)
Other	18 (3.5)	29 (3.1)

2.02 (95% CI, 1.28-3.19), which corresponds to a 102% excess risk. The effect of pet keeping more than 12 months previously was significant in subjects with nonatopic parents, with an OR of 1.46 (95% CI, 1.04-2.05), corresponding to a 46% excess risk. The adjusted OR of asthma was 2.39 (95% CI, 1.55-3.69), a 139% excess risk, in subjects with both atopic heredity and pets more than 12 months previously compared with subjects of the reference category. The combined effect of parental atopy and exposure to pets was approximately as expected on the basis of their independent effects in additive scale.

DISCUSSION

The incident case-control study is very efficient compared with a cohort study, yielding a similar amount of information. Our study includes the largest number of new asthma cases among all the studies addressing the relations between pet keeping and the risk of development of asthma in adults. The present study corresponds to a follow-up of approximately 100,000 adults for 5 years if we assume a realistic asthma incidence of 1 case per 1000 person-years. Our results provide evidence that keeping pets at home, including dogs, cats, rodents, and birds, increases the risk of development of asthma in adulthood. Applying a biologically meaningful timing

TABLE III. Adjusted ORs of asthma in relation to parental atopy and current or previous pet keeping

	Adjusted OR (95% CI)	Adjusted OR* (95% CI)
Parental atopic diseases		
None	1.00	1.00
Maternal allergy	1.31† (0.94-1.82)	1.11 (0.79-1.59)
Paternal allergy	1.37† (0.87-2.15)	1.32 (0.82-2.12)
Maternal asthma	1.76† (1.19-2.60)	1.84 (1.23-2.76)
Paternal asthma	2.29† (1.50-3.48)	2.16 (1.39-3.35)
Any	1.98 (1.56-2.51)	1.88 (1.47-2.41)
Any pets		
Never (reference)	1.00	1.00
Currently (12 mo)	0.77‡ (0.60-0.99)	0.74 (0.57-0.96)
Only >12 mo previously	1.44‡ (1.10-1.89)	1.39 (1.05-1.84)
Specific pets		
Never pets (reference)	1.00	1.00
Cats		
Currently	0.86‡ (0.62-1.19)	0.81 (0.58-1.15)
Only >12 mo previously	1.27‡ (0.96-1.69)	1.23 (0.92-1.65)
Dogs		
Currently	0.68‡ (0.50-0.92)	0.72 (0.52-0.99)
Only >12 mo previously	1.35‡ (1.03-1.77)	1.27 (0.96-1.68)
Birds		
Currently	1.12‡ (0.37-3.41)	1.23 (0.39-3.87)
Only >12 mo previously	1.52‡ (0.91-2.57)	1.30 (0.75-2.25)
Rodents		
Currently	1.17‡ (0.64-2.14)	1.33 (0.71-2.51)
Only >12 mo previously	1.25‡ (0.86-1.81)	1.13 (0.77-1.66)
Other		
Currently	1.06‡ (0.48-2.34)	1.13 (0.49-2.62)
Only >12 mo previously	1.06‡ (0.61-1.86)	1.06 (0.59-1.90)

*Adjusted for sex, age, parental atopy-asthma, education, visible mold or mold odor in the home or in the workplace, self-reported occupational exposures, personal smoking, environmental tobacco smoke (workplace or home), and other parental atopy and pet variables.

†Adjusted for other parental atopic diseases.

‡Adjusted for other pet variables.

between exposure and outcome revealed an increased risk of asthma, whereas assessing only current pets at home suggested selection bias so that symptomatic individuals avoided pets. The risk estimates of asthma for having dogs and cats during the previous 12 months were below unity, whereas having these pets more than 12 months previously was related to an increased risk of asthma. There was an exposure-response pattern according to the duration of exposure when focusing on individuals without current exposure.

Validity of results

We reduced the likelihood of selection bias both in the design and analysis phase. Our study of incident, rather than prevalent, cases and use of different exposure periods reduced potential bias related to avoidance of pets. Because parental atopy is likely to be related to both risk of asthma and keeping pets, we adjusted for parental atopy and elaborated both independent and joint effects of parental atopy and exposure to pets.

The study was introduced to the participants as a study on environmental factors in general (the Finnish Envi-

TABLE IV. Adjusted ORs of asthma in relation to duration of cat and pet keeping separately for all subject and subjects without pets during the previous 12 months

	All, adjusted OR* (95% CI)	No current exposure, adjusted OR* (95% CI)
Duration of cat keeping (in % of lifetime)		
Never (reference)	1.00	1.00
<20%	1.16 (0.86-1.56)	1.44 (0.90-2.30)
20%-<40%	1.19 (0.80-1.77)	1.44 (0.73-2.86)
40%-<60%	1.25 (0.64-2.45)	1.12 (0.38-3.34)
60%-<80%	1.53 (0.52-4.55)	3.47 (0.52-23.1)
≥80%	0.96 (0.29-3.10)	—†
Duration of dog keeping (in % of life)		
Never (reference)	1.00	1.00
<20%	0.93 (0.29-3.10)	1.19 (0.73-1.93)
20%-<40%	1.26 (0.90-1.78)	1.80 (1.05-3.09)
40%-<60%	1.04 (0.64-1.70)	1.17 (0.47-2.90)
60%-<80%	1.41 (0.52-3.83)	1.57 (0.19-13.2)
≥80%	1.14 (0.42-3.08)	2.06 (0.11-38.0)

*Adjusted for sex, age, parental atopy-asthma, education, visible mold or mold odor in the home or in the workplace, self-reported occupational exposures, personal smoking, environmental tobacco smoke (workplace or home), and other pet variables.

†No estimate was given because of too few observations (1 exposed control subject and no exposed case subjects).

ronment and Asthma Study), with no special focus on keeping pets, to reduce information bias. Information on exposures was collected from case subjects and control subjects in a similar way. We cannot fully exclude the possibility that case subjects and control subjects provide differential information on current and previous pet keeping. However, clear factual information on the presence of a pet, often considered as a member of the family, is likely to be less sensitive to bias than information on some more ambiguous exposures. Defining asthma on the basis of objective clinical findings was performed to eliminate information bias concerning the outcome, which could result if persons with pets would interpret their own respiratory symptoms as asthma.

Adjustment for an extensive number of potential confounders in logistic regression analysis reduced the probability that these results were due to confounding.

Synthesis with previous knowledge

In general, inhalation of aeroallergens is considered to increase the risk of asthma development, and sensitization to specific allergens is part of the underlying mechanism. For example, there is strong evidence that occupational exposure to high-molecular-weight allergens increases the risk of asthma.¹³ Individuals may become sensitized to specific allergens in the workplace and then experience symptoms and signs of asthma when exposed to these allergens. Typically, these reactions can be reproduced in controlled conditions. Our findings of an increased risk of asthma in relation to keeping pets in the past are consistent with this generally accepted theory.

Recently, this theory has been challenged by a proposition that exposure to allergenic and infectious factors in

Asthma, rhinitis,
other respiratory
diseases

early life favors the development of tolerance to environmental allergens and reduces the risk of asthma and allergies. Promotion of T_H1 , as opposed to T_H2 , cells that mediate allergic reactions has been suggested as the mechanism for the favorable effects of early life exposure.^{14,15} Two cohort studies provide evidence of a lower risk of asthma among children exposed to pets in early life compared with unexposed children.^{16,17} In a Swedish 5-year cohort study of 402 school children 7 to 8 years of age at baseline, the cumulative incidence of asthma was lower among children who had a pet in the home during the first year of life, with an adjusted OR of 0.34 (95% CI, 0.07-0.77).¹⁶ In a Norwegian cohort study of 2531 children followed for 4 years from birth, the risk of asthma was lower in children with any pet at birth, with an adjusted OR of 0.7 (95% CI, 0.5-1.1).¹⁷ Recently, childhood in a farming environment has been reported to be associated with a lower risk of asthma later in life.¹⁸⁻²¹ On the other hand, avoidance of allergenic exposures may take place by symptomatic individuals, as well as by children of atopic parents. Thus it is important to ensure that a relevant time period has taken place between the exposure and onset of asthma and to make an effort to assess any selection as a result of a family history of atopic diseases.

It is possible that asthma appearing in childhood is different from asthma in adulthood as to genetic and environmental causes. To our knowledge, only 3 previous cross-sectional studies have assessed the role of pet exposure in the cause of adult-onset asthma.³⁻⁵ In an Italian study the age of the study population ranged from 0 to 69 years.³ The relations were given for the whole study population, and apparently, only current pet keeping was considered. The occurrence of asthma was not related to pet keeping. In a Canadian study of 20- to 44-years-old adults,⁴ the risk of asthma was related to current pet ownership, with an OR of 1.6 for cats (95% CI, 1.1-2.4) and dogs (95% CI, 0.9-2.9) and 1.7 for other pets (95% CI, 0.9-3.1). The presence of pets in childhood had no influence on the risk of asthma in adulthood. The European Respiratory Health Survey of 20- to 44-year-old adults in 35 centers in 16 countries found an increased risk of asthma in communities in which the average level of cat-specific IgE was elevated.⁵ However, reported childhood exposure to pets, including cats, was associated with lower sensitization to cats in adulthood.

Previous studies have shown that parental atopic diseases are important determinants of asthma.⁶⁻⁸ The present results show, to our knowledge and for the first time, that parental atopy also increases the risk of adult-onset asthma. We found paternal asthma to be the strongest determinant of asthma development in adulthood. Maternal asthma and other parental allergies also predicted adult-onset asthma. These findings suggest strongly that genetic background is an important determinant of asthma in adulthood. The results show that the joint effect of hereditary propensity to atopy, representing genetic constitution, and exposure to pets was not stronger than expected on the basis of their independent effects in additive scale.

Conclusion

Our results are consistent with the hypothesis that both keeping furry pets and parental atopy increase the risk of developing asthma in adulthood. Parental atopy does not modify the effects of pet exposure. A negative association between current keeping of dogs and cats and the risk of asthma is consistent with selective avoidance of these pets by symptomatic individuals.

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