

P. Plaschke
C. Janson
B. Balder
O. Löwhagen
B. Järvholm

Authors' affiliations:

P. Plaschke, Roskilde County Hospital, Denmark, and Allergy Research Centre, Sahlgrenska University Hospital, Göteborg, Sweden

C. Janson, Department of Lung Medicine and Asthma Research Centre, Akademiska sjukhuset, Uppsala, Sweden

B. Balder, O. Löwhagen, Allergy Research Centre, Sahlgrenska University Hospital, Göteborg, Sweden

B. Järvholm, Department of Occupational and Environmental Medicine, Umeå University, Umeå, Sweden

Correspondence to:

Dr P. Plaschke
Department of Medicine
Roskilde Amts Hospital
Køgevej 7-13
DK - 4000 Roskilde
Denmark

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Original article

Adult asthmatics sensitized to cats and dogs: symptoms, severity, and bronchial hyperresponsiveness in patients with furred animals at home and patients without these animals

Key words: allergy avoidance; asthma; bronchial hyperresponsiveness; cats; dogs; eosinophils; indoor allergens; peak-flow variability.

Background: Domestic furred animals are important sources of allergens in asthma, but few clinical studies have investigated the effects of exposure to or elimination of these allergens. The objective of this study was to investigate whether pet-sensitized asthmatics with pets at home have worsened asthma, compared with similar asthmatics without pets.

Methods: In a cross-sectional epidemiologic study, 129 adult asthmatics sensitized to cats or dogs were investigated by interviews, skin prick tests, specific IgE, eosinophil counts, and bronchial methacholine challenge tests. Patients with a cat or dog at home ($n=39$) were compared with subjects without pets ($n=90$).

Results: More subjects with pets had symptoms, inhaled or oral steroids, abnormal peak-flow records, higher eosinophil counts, and a higher degree of bronchial hyperresponsiveness than subjects without pets. Asthmatics with pets more frequently ascribed their symptoms to their home environment, but fewer of them reported that their symptoms were elicited by contact with cats or dogs.

Conclusions: This study strongly indicates that living with a cat or a dog aggravates symptoms and biomarkers of airway inflammation in asthmatics sensitized to cats or dogs. The study indicates that avoidance of these allergens may be an important measure in the treatment of sensitized asthmatics.

A reduction of exposure to allergens should be an obvious cornerstone in the treatment of allergic diseases such as atopic asthma and allergic rhinitis (1, 2), but there are few studies of the importance of such reductions. Cats and dogs are important sensitizers in patients visiting emergency

rooms with asthma (3, 4), and in Sweden, sensitization to pets is very common (5). Pet allergens are the allergens most closely related to asthma in Sweden and parts of the USA (6, 7). To our knowledge, there are no studies of allergen avoidance in asthmatics sensitized to pets. However, in asthmatics sensitized to house-dust mite (HDM) improvements such as reduction in sputum eosinophils and bronchial hyperresponsiveness (BHR) are seen when exposure to HDM is reduced (8–11).

The aim of this study was to investigate whether asthma was worsened by exposure to cats or dogs at home in persons sensitized to pets. In a cross-sectional epidemiologic study, the prevalence of symptoms and clinical findings was compared between sensitized asthmatics with and without pets.

Material and methods

Study design and patient material

The patients were recruited with the aim of establishing a cohort for a study of recent-onset adult asthma (12, 13). The inclusion criteria were onset of asthma 1983–6, age 18–60 years, and residence in Göteborg or its suburbs. Persons with asthma earlier in life were included if they had had no symptoms and no medication for at least 5 years before their actual onset of asthma. Criteria for the diagnosis of asthma were reversibility of FEV₁ of 15 % or more after a β -agonist or after a course of corticosteroids, PC₂₀ of 4 mg/ml methacholine or less, abnormal peak-flow record, or typical history of asthma. Subjects with chronic obstructive pulmonary disease or other cardiopulmonary diseases were excluded. The aim was to identify as many subjects as possible with onset of asthma during 4 years, 1983 to 1986. This was done by searching patient records of that period for all subjects seeking medical care for asthma or asthma-like symptoms at the emergency departments of the city, at the departments of allergology and respiratory medicine, and at the major primary health-care centers of the city. After evaluation of the medical records of 590 possible participants, 115 were excluded because they did not fulfil the inclusion criteria or because they refused to participate ($n=48$). A total of 475 subjects participated in the study investigations at the department of allergology, Sahlgrenska University Hospital. Of these subjects, 420 fulfilled all of the inclusion criteria. Additional inclusion criteria for this analysis were sensitization to cats, dogs, or both and either a cat or a dog at home and sensitization to that pet, or sensitization to cats and/or

dogs and no pet at home at all. Exclusion criteria in this analysis were sensitization to cats, and not to dogs, and a dog at home; sensitization to dogs, and not to cats, and a cat at home; and sensitization to cats or dogs and ownership of types of pet other than cats or dogs. Of 420 asthmatics, 142 were sensitized to cats and/or dogs; 129 patients fulfilled all the criteria and were included. Thirty-nine subjects had pets and 90 did not have pets at home. Among the patients without pets, a subgroup of 39 subjects had pets at the onset of their asthma, but they had removed their pets because of their allergy, and did not have pets at the time of the study.

Each person was investigated by interview, skin prick test, specific IgE (RAST), eosinophil count, peak-flow monitoring, spirometry, and bronchial methacholine challenge test. Investigations took place at a maximum of 4 years after the onset of asthma.

Structured interviews

All the patients were interviewed with a questionnaire including questions on medical history, respiratory symptoms, medication, occupation, smoking habits, type of housing, and ownership of domestic furred animals. The structured interview was administered in a standardized manner by trained nurses and physicians. The interview took place before the skin test and the bronchial methacholine challenge test. The questions used in this part of the study are shown in Appendix 1.

Skin prick test, specific IgE, and eosinophils

Skin prick tests were performed according to the recommendations of the Standardization Committee of the Nordic Society of Allergology and included the standard panel of the Allergy Laboratory at Sahlgrenska University Hospital (cat, dog, horse, *Dermatophagoides pteronyssinus*, *D. farinae*), timothy grass, ryegrass, birch, mugwort, *Cladosporium herbarum*, *Aspergillus fumigatus*, and a negative control (diluent) and histamine 10 mg/ml). A wheal of 2+ (half the size of the histamine reference) was defined as positive (14, 15). Specific IgE was measured if the SPT was 1+, or if there was clinical suspicion of a certain allergy and a negative SPT. Specific IgE was measured by the Phadebas RAST[®] test (Pharmacia Diagnostics, Uppsala, Sweden). A RAST class of ≥ 2 (0.7 kU/ml) was categorized as positive. Sensitization was defined as a positive SPT and/or a positive RAST. A total of 115 subjects were classified as sensitized to cat or dog by SPT of at least 2+, 12 had SPT of 1+ and a positive RAST, and two had a negative SPT and a positive RAST.

Bronchial methacholine challenge

BHR was measured by a standardized methacholine challenge test performed according to Löwhagen (16, 17). Concentrations of methacholine chloride solution increasing by twofold were prepared before the challenge and inhaled by tidal-volume breathing from a Pari-Boy nebulizer (Paul Ritzan, Pariwerk, Starnberg am See, Germany) (18). The inhalation time was 2 min with 5-min intervals. FEV₁ was measured twice after each dose, and the best value was used. Before the inhalations of methacholine started, isotonic NaCl (diluent) was inhaled, and a baseline FEV₁ was measured. The starting concentration of methacholine was 0.03 mg/ml. The dose was increased fourfold as long as the decrease in FEV₁ was less than 10%. When the fall was 10–19%, a double dose was used. The provocation test was stopped when the reduction in FEV₁ was 20% or more or when the maximum dose of 16 mg/ml was given. The PC₂₀ values were calculated from the dose-response curve by interpolation between the two last concentrations. Subjects without a reduction in FEV₁ of 20% or more after the challenge test were considered not to have BHR. FEV₁ was measured on a computerized Jäger spirometer. When PC₂₀ was included in the multivariate analysis, adjustments were made for FEV₁ (19).

Peak-flow measurements

Peak flow was registered for 2 weeks every morning and evening before and 10 min after two doses of a pressurized nebulizer of salbutamol 0.1 mg/ml (Ventolin®) or terbutaline (Bricanyl®). Mini Wright peak-flow meters were used. The best of three values was registered each time. The peak-flow registration was categorized as pathologic if there were more than three amplitudes of $\geq 20\%$ during a period of 2 weeks. Amplitudes were calculated as the highest value – the lowest value/mean of the two values, or the post β -agonist value – the pre- β -agonist value/mean of the two values. Mean peak-flow variation was calculated as the sum of daily premedication highest values – the sum of daily premedication lowest values/the sum of the means of the two values (20).

Statistics

Fisher's exact test was used to analyze differences between groups in terms of categorical variables. The answers to the questions Q.1 and Q.2 (Appendix 1) were dichotomized to mild or moderate-severe symptoms. Differences between groups in terms of continuous variables were tested by the unpaired *t*-test. Mean values for peak-flow variation, PC₂₀,

and eosinophil counts were used after logarithmic transformation. The adjusted analysis was done with multiple linear regression analysis when the dependent variable was continuous, and with multiple logistic regression when the dependent variable was categorical. *P*-values of <0.05 (two-tailed test) were regarded as statistically significant. The statistical analysis was performed with the StatView 4.0 (Abacus Concepts, Inc., Berkeley, CA, USA) and Statistica 4.0 (StatSoft Inc., Tulsa, OK, USA) software packages.

Ethics

The study was approved by the ethics committee at Sahlgrenska University Hospital. All the patients gave their informed consent to participate in the study.

Results

Of the 39 asthmatics with pets, 22 had cats, 15 had dogs, and two had both animals. Subjects with pets were slightly older and reported childhood asthma/bronchitis significantly less frequently than subjects without pets (Table 1). The duration of asthma was similar in the two groups. Almost all asthmatics had rhinitis in both groups. The prevalence of current smokers was similar in the groups, while the percentage of lifelong nonsmokers was lower among subjects with pets. More than 80% were sensitized to cats in both groups. While pet owners were somewhat more commonly sensitized to horse, those without pets were more often sensitized to birch. Sensitization to other allergens was similar.

Symptoms and medication (Figs. 1 and 2)

More subjects with pets had daytime and nocturnal symptoms, oral steroids, and inhaled steroids than subjects without pets. In contrast, fewer subjects with pets had nasal symptoms elicited by cats or dogs, and fewer subjects with pets found it difficult to visit friends who were pet owners than subjects without pets. However, it was more common for subjects with pets to report nasal symptoms elicited by dust at home and to suspect that something in their home environment aggravated their bronchial symptoms. Self-reported allergy to cats or dogs was reported more commonly by non-pet owners. When these comparisons were adjusted for age, sex, smoking habits, and asthma or bronchitis in childhood, all differences were statistically significant, with the exception of the questions relating to nocturnal

Table 1. Basic characteristics of two groups: pet owners and non-pet owners

	Pet owners n=39	Non-pet owners n=90
Age (years)	32.8±10.4 ^a	29.4±10.8
Women (%)	56	53
Current smokers (%)	28	27
Never smokers (%)	28	44
Living in apartment (%)	62	63
Living in own house (%)	38	37
Asthma/bronchitis as child (%)	13	32*
Current rhinitis (%)	85	94
Asthma duration 0–2 years (%)	41	41
Asthma duration 2–4 years (%)	59	59
Sensitization to (%)		
Cat	82	87
Dog	69	61
Horse	26	16
Mites	21	29
Birch	33	52
Grass	28	30
Mugwort	10	17
Molds	0	2

^aMean ± SD. **P*<0.05.

symptoms (*P*=0.05), oral steroids (*P*=0.07), and nasal symptoms elicited by cats or dogs (*P*=0.06).

Peak-flow, eosinophil counts, and BHR (Table 2)

Subjects with pets more often had abnormal peak-flow recordings, higher peak-flow variation, higher eosinophil counts, and lower PC₂₀ than subjects without pets. After adjustments for age, sex, smoking habits, and asthma or bronchitis in childhood, all these differences were still statistically significant.

Subgroups

In a separate analysis, cat-sensitized cat owners (*n*=24) were compared with cat-sensitized asthmatics without pets (*n*=78). Similarly, dog-sensitized dog owners (*n*=17) were compared with dog-sensitized asthmatics without pets (*n*=55). In addition, pet owners (*n*=39) were compared with the subgroup of patients who were former pet owners (*n*=33). The results of these subgroup analyses were basically the same as in the main analysis, although the groups were smaller and not all the differences were statistically significant.

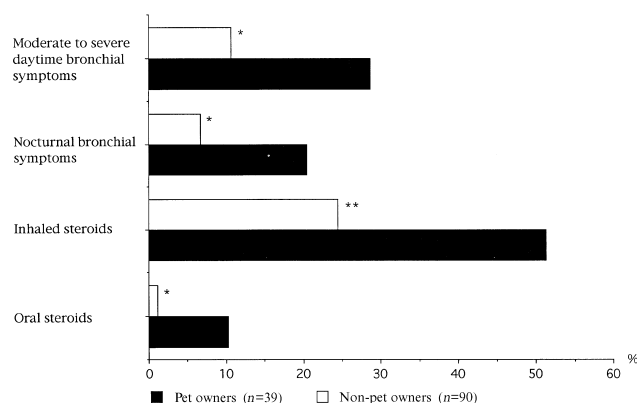


Figure 1. Prevalence of medication with oral and inhaled steroids and daytime symptoms and nocturnal symptoms among pet owners and non-pet owners. **P*<0.05; ***P*<0.01.

Discussion

This study clearly indicates that asthmatics sensitized to cats or dogs would improve if their exposure to pets were reduced. In addition, we found that sensitized pet owners less often associated their symptoms with pet exposure, although their asthma was aggravated by their home environment.

However, this is an epidemiologic study, and an experimental, randomized study would be the method of choice, although such a study would not be ethical since it is generally accepted that exposure to allergens should be lowered in sensitized asthmatics. Furthermore, pet owners who associate their symptoms with pets may avoid exposure to them, making randomization difficult.

Aspects of validity

It is important to determine whether selection and information bias influenced the results. The difference in some outcomes, e.g., occurrence of nocturnal bronchial symptoms and use of steroids, was large, and only substantial confounding may explain such differences. Subjects with pets did not have a higher frequency of sensitization to other allergens such as house-dust mites or pollens. Furthermore, the groups were similar in terms of the prevalence of rhinitis, type of housing, sex, age, and duration of asthma. Pet owners were less frequently lifelong nonsmokers and less frequently had a history of asthma or bronchitis in childhood. It is possible that patients who had childhood asthma are more aware of their allergy and less inclined to be pet owners. It is also possible that the allergic symptoms differed between patients with previous asthma in childhood and primarily adult-onset asthmatics. We

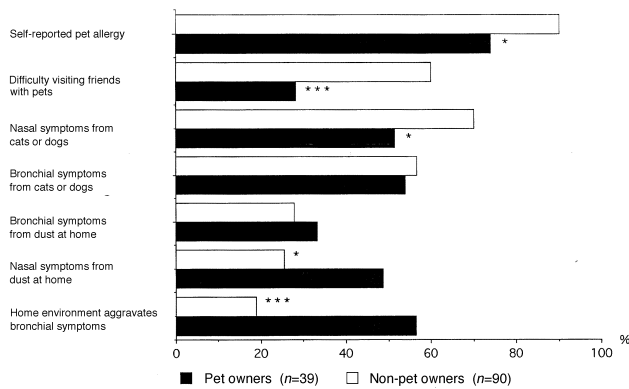


Figure 2. Prevalence of allergy-related symptoms among pet owners and non-pet owners. * $P<0.05$; ** $P<0.01$; *** $P<0.001$.

controlled for these differences in the adjusted analysis, and the differences between the groups persisted. It does not seem likely that the most severe asthmatics would be the least inclined to remove their pets and thus bias our results. The opposite is more probable. Thus, it is not probable that selection bias would explain more severe asthma in pet owners. Pet owners were less aware of their allergy to pets and less often associated symptoms with pets (Fig. 2), but pet owners had more symptoms in general, used more steroids, and had more often abnormal peak flow. One might assume that pet owners liked their pets and underestimated the symptoms associated with them. Thus, information bias seems to be a very improbable cause of more severe asthma in pet owners.

Reduction of pet allergens

In our study, we have assumed that pet owners have a higher exposure to pet allergens than asthmatics without pets. It would have improved our study if we had measured the levels of cat and dog allergens in the homes of patients. In

particular, it would have been of interest to know the allergen levels in patients who had removed their pets. However, at the time of the study, we did not have the necessary resources to determine this.

The allergens may persist for a very long time after the removal of a pet, and allergens from furred animals are widespread in our environment (21–26). However, Wood et al. found reduced allergen levels after the removal of cats (21). In addition, studies of allergen levels have shown the highest levels in homes with pets (27). In our study, fewer than 20% of the asthmatics who had removed their pets had symptoms elicited by dust at home or by their home environment, but 70% had symptoms when visiting friends with pets. This indicates that the allergen levels in their house dust had been significantly reduced after removal of their pets. Experimental studies have shown reduced levels of cat allergen with the cat *in situ* after repeated washings, with uncarpeted floors and air cleaning (28–30). The effect of these procedures on the asthma itself has not been shown. In clinical practice, it might help some patients who are reluctant to remove their pets. However, this type of advice might also prolong the delay of effective allergen avoidance, i.e., removing the animal from the home, and increase the risk that the asthma severity would progress.

Pet-related symptoms

It was expected that pet-sensitized asthmatics would have airway symptoms elicited by pets and problems visiting friends with pets. The lower frequency of pet-elicited symptoms among pet owners could hypothetically be explained by neglect of symptoms elicited by pets. Pet owners had nasal symptoms elicited by dust at home more frequently than patients without pets. This could support some degree of neglect – dust, and not the pet, was seen as

Table 2. Prevalence of abnormal peak-flow records, peak-flow variations, eosinophil counts, PC₂₀ (methacholine), and FEV₁ %predicted in pet owners and non-pet owners

	Pet owners n=39	Non-pet owners n=90	P value adjusted*
Abnormal peak-flow records (%)	47	16	0.004
Peak-flow variation (%)	10.4±8.5 ^a	5.9±5.6	0.01
Eosinophils (counts/ml)	0.414 (0.23) ^a	0.313±0.23	0.004
PC ₂₀ (mg/ml)	0.43±3.4 ^b	0.81±4.7	0.023
FEV ₁ %predicted	87.3±17 ^a	91.6±14	NS

^aMean ± SD. ^bgeometric mean ± SD. Eosinophil counts, PC₂₀, and mean peak-flow variations were compared after log transformation.
*Adjusted for age, sex, asthma/bronchitis in childhood, and smoking habits. PC₂₀ was also adjusted for FEV₁.

the offending agent. Another hypothetical explanation could be that pet owners did not experience immediate allergic reactions as often as the asthmatics without chronic allergen exposure. It is possible that repeated or continuous inhalations of a relatively high dose of allergens create a reaction pattern dominated by late-phase reactions (31). As a result, they might have become less aware of the importance of their allergy and consequently less prone to remove the animal. It is also possible that some of the asthmatic pet owners could tolerate their pets in spite of their positive allergy test, because they had only latent allergy. In particular, in older subjects, the sensitization could be a trace left from previous clinical allergy without present importance. However, young subjects could have an allergy with increasing clinical relevance. Eight of the 39 patients with pets had no or mild daily bronchial symptoms, no nocturnal symptoms, and no abnormal peak-flow records, and their only medication was a short-acting β -agonist. They were young (mean age 23 years), five had a cat, three had a dog, and one had both animals at home. Four of them reported bronchial symptoms, and six reported nasal symptoms elicited by pets. However, six of these subjects had pronounced hyperresponsiveness ($PC_{20} \leq 1$ mg/ml methacholine), and a longer observation period might have shown worsening of their asthma (32).

Importance of allergen exposure and allergen avoidance

In experimental studies, Ihre & Zetterström found an increase in BHR after repeated low-dose inhalations of allergens (33). In addition, bronchial variability with low peak-flow values was observed several days after a late-phase reaction (34). Gibson et al. found that an increase in BHR after allergen inhalation was associated with an

increase in circulating eosinophils after 24 h (35). The high eosinophil counts, the pronounced BHR, and the peak-flow variability among the pet owners in our study could therefore be a consequence of repeated or continuous allergen stimulation. There were also non-pet owners with asthma of considerable severity. In some cases, the major cause could be other allergens such as HDM or nonallergic factors. However, very sensitive patients could be affected by indirect exposure to pet allergens spread in the environment by pet owners (22–26).

If the pet owners in our study should have the same severity of disease as the asthmatics without pets, the use of inhaled steroids would decrease from a prevalence of around 50% to about 25%, a considerable reduction (Fig. 1). Ten percent of the pet owners used oral steroids, but hardly any would need them if their disease was similar to that of the non-pet owners. Furthermore, the prevalence of pet owners with moderate to severe daytime symptoms would be reduced from about 30% to 10%.

These results indicate that allergen avoidance in the form of removing the pet from the home should be recommended in cat- or dog-sensitized asthmatics. Some patients with pets might not be aware of their sensitization. Others know about their allergy, but might underestimate its importance, because they do not directly experience a worsening as a result of their pet.

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Appendix 1. Questions used in this part of the study

Q.1. To what extent do you have bronchial symptoms during the daytime?

Q.2. To what extent do you have nocturnal bronchial symptoms?

Q.3. Do you have a pet at home?

Q.4. If yes, what kind?

Q.5. Do you think you are allergic to cats?

Q.6. Do you have nasal symptoms caused by cats?

Q.7. Do you have bronchial symptoms caused by cats?

Q.8. Do you think you are allergic to dogs?

Q.9. Do you have nasal symptoms caused by dogs?

Q.10. Do you have bronchial symptoms caused by dogs?

Q.11. Did you get rid of a furred animal because of your allergy?

Q.12. Do you have nasal symptoms caused by dust at home?

Q.13. Do you have bronchial symptoms caused by dust at home?

Q.15. Do you suspect that something in your home environment aggravates your bronchial symptoms?

Q.16. Has it become difficult for you to visit friends with furred animals?

Possible answers to Q.1 and Q.2 were: none=0, mild=1, moderate=2, and severe=3.

Bronchial symptoms included wheezing, breathlessness, and coughing.

The answer to Q.3 was any kind of pet. Answers to all other questions were yes or no.