Effect of Pet Removal on Pet Allergic Asthma*

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Background: **Allergen avoidance has been recommended in the management of allergic asthma. Very few studies have assessed the effect of pet removal on pet allergic asthma.**
Objective: **We examined the effect of pet removal from homes on pulmonary function testing, airway hyperresponsiveness, and medication use.**
Design: **Prospective, nonrandomized, nonblinded observational study.**
Patients and methods: **Subjects included 20 symptomatic patients with newly diagnosed pet allergic asthma who were keeping domestic animals, including hamsters, cats, dogs, and ferrets, and were sensitized to the animals. They were treated with inhaled corticosteroids or other medications according to recommendations by level of severity of the Global Initiative for Asthma. Methacholine inhalation tests were performed regularly before and after starting medication. Clinical features were compared between the patients who gave away their pets according to recommendations by the clinician (removal group) and the patients who refused to give away their pets (keeping group).**
Results: **There were 10 patients in both the removal group and the keeping group. After ≥ 1 year of follow-up with or without pet removal, a 5.9-fold increase in the provocative concentration of methacholine causing a 20% fall in FEV_1 was observed in the removal group compared with a 2.3-fold increase in the keeping group ($p = 0.04$). There were no significant differences in the changes in FEV_1 and peak flow variability. Finally, no patient received inhaled corticosteroids in the removal group, whereas all but one of the patients needed beclomethasone dipropionate (mean dose, 600 μg/d) in the keeping group.**
Conclusion: **This study indicates that removal of pets from homes reduces airway responsiveness in patients with pet allergic asthma more than optimal pharmacotherapy alone, thereby enabling a decrease in inhaled corticosteroid doses.** ***(CHEST 2005; 127:1565–1571)***

Key words: allergen avoidance; domestic animal; inhaled corticosteroids; methacholine; pharmacotherapy

Abbreviations: ANOVA = analysis of variance; ECP = eosinophil cationic protein; GINA = Global Initiative for Asthma; PC_{20} = provocative concentration of methacholine causing a 20% fall in FEV_1; PEF = peak expiratory flow

Domestic animals, including cats, dogs, and rodents, release allergens in secretions, excretions, and danders.[1] A consensus is emerging that animal allergens play a significant role in the development of asthma, although some studies have suggested that early contact with pets may prevent the development of allergy and asthma in children.[2] If the patient is sensitive, removal of the animal from the home has been recommended as a method to reduce exposure. However, patients often refuse to give away their pets, and adequate pharmacotherapy and various allergen control measures are needed.[3] Very few studies[4–8] have assessed the effect of animal allergen avoidance on symptoms of asthma, objective measurements of airflow obstruction, or airway hyperresponsiveness. Concerning the usefulness of air cleaners, some studies[5,6] demonstrated an improvement in airway hyperresponsiveness, whereas other studies[7,8] did not detect significant effects on clinical findings or reduction of allergen exposure levels, suggesting limitations in the use of air cleaners in the management of pet allergic asthma. The discrepancy may be derived in part from the differences in medication use, *ie*, whether patients whose medication altered over the course

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were withdrawn from the final analysis or changes in medication use were based on outcome measures. To our knowledge there are no studies exploring the effect of pet removal from homes.[4]

The purpose of this study was to clarify the clinical features of patients with pet allergic asthma who were sensitized to hamsters, cats, dogs, and ferrets and gave away their pets according to recommendations compared with those of patients who insisted on keeping their pets, and to determine whether pet removal is effective for improving airway hyperresponsiveness under optimal pharmacotherapy based on asthma treatment guidelines.

Materials and Methods

Subjects

Subjects consisted of 20 patients with newly diagnosed pet allergic asthma keeping domestic animals including hamsters, cats, dogs, and ferrets. These consecutive patients first visited Fujinomiya City General Hospital from February 1997 to October 2001. All subjects satisfied the American Thoracic Society criteria[9] and had asthmatic symptoms within 1 week prior to the first visit. Severity of asthma was classified according to the Global Initiative for Asthma (GINA).[10] Sensitization to the animals was confirmed by the presence of specific IgE antibodies (CAP System; Pharmacia; Uppsala, Sweden), positive skin-prick test results (Bayer; Elkhart, IN), as well as a suggestive history of pet allergy, including bronchial, nasal, ocular, or cutaneous symptoms. No inhalation challenge with animal allergen solution was done. Sensitization to house dust mites, cedar pollen, grass pollens, molds, and cockroach were also confirmed by the positive specific IgE antibodies (CAP System).

Study Design

At the first visit, the patients underwent spirometry, blood tests, and skin-prick tests. They were also instructed to record their peak expiratory flow (PEF) values using a flowmeter (Miniwright Peak Flowmeter; Clement Clarke; Harlow, UK) twice daily at home. An inhaled, rapid-acting β_2-agonist on an as-needed basis was prescribed at this time. At the second visit, within 1 week after the first visit, the patients underwent a methacholine inhalation test. All patients were advised to remove their pets from their homes by the clinician. Even when the patients had more than one of a kind or several different species of pets, all pets were removed. None received information on cleaning, air purification, use of hypoallergenic products, and cessation of smoking. Regular follow-up and medication, including inhaled corticosteroids, theophylline, and pranlukast, were started from the second visit according to the recommendations of the GINA guidelines. Spirometry and a methacholine inhalation test were repeated every 3 to 6 months. If there was a marked improvement in clinical findings, methacholine tests were performed at 1- to 2-month intervals. Thus, the patients attended on at least three occasions. According to the stepwise approach of the GINA guidelines, the number and frequency of medications, especially inhaled corticosteroid doses, increased (step up) as the need for asthma therapy increased, and decreased or ceased (step down) when asthma was under control. The patients were followed up as long as possible even after medication was ceased. Finally, the patients' data were analyzed in November 2003. Clinical features, pulmonary function testing, and airway hyperresponsiveness were compared between the patients who gave away their pets according to recommendations of the clinician (removal group) and the patients who refused (keeping group). Furthermore, measurement of induced sputum and peripheral blood eosinophils and serum eosinophil cationic protein (ECP) was done to assess parameters of airway inflammation after treatment.

Methacholine Inhalation Challenge

Airway responsiveness to methacholine was assessed with nebulizer (model 646; DeVilbiss; Somerset, PA; output, 0.3 mL/min) at tidal volume breathing for 2 min according to the standard method proposed by the Japanese Society of Allergology.[11] Pretreatment and posttreatment values of FEV_1 and provocative concentration of methacholine causing a 20% fall in FEV_1 (PC_{20}) represent the data measured at the second visit and on the day of the final methacholine challenge, respectively. All subjects were without medication that might influence the test results and did not report any acute viral infections for at least 1 month before the challenges. Informed consent was obtained from all subjects prior to the test.

PEF Variability

Diurnal PEF variation was calculated by the following formula: (evening − morning PEF/the mean of the evening and morning PEF) × 100, and the results are shown as the mean daily variation. Pretreatment and posttreatment PEF variability show the mean values during 1 week since the first visit and during the last week prior to the final methacholine challenge, respectively.

Assessment of Airway Inflammation After Treatment

Sputum induction was performed according to the method described previously[12] with minor modifications, and the induced sputum and peripheral blood eosinophil count were measured. Serum ECP levels were determined with an ECP radioimmunoassay kit (Pharmacia; Uppsala, Sweden). These posttreatment parameters were measured within 1 week of the final methacholine challenge.

Statistical Analysis

All data are expressed as mean ± SD. PC_{20} is expressed as geometric mean ± SD, and logarithmic transformation was used for further analyses. Comparisons between groups were made with unpaired or paired *t* tests. Comparisons between groups and between preteatment and posttreatment were performed by two-way analysis of variance (ANOVA) for repeated measures. The Fisher exact test was used for independence. Correlations between variables were done using the Pearson correlation coefficient; software (Stat View Version 5.0; SAS Institute; Cary, NC) was used for the statistical calculations. A p value < 0.05 was considered significant; all tests were two tailed. Since the total number of patients in this study was small, the statistical power was 52.6%.

Results

The number of patients enrolled in the study each year ranged from two to seven between 1997 and

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2001. There were 10 patients in both the removal group and the keeping group. The clinical characteristics of the study population are shown in Table 1. The removal group had a higher frequency of current smokers and initial onset of asthma than the keeping group, but this did not reach statistical significance by the Fisher exact test. There were no differences in age, sex, and severity of asthma between the two groups. There was a tendency that the keeping group was sensitized to more allergens, including house dust mites, cedar pollen, grass pollens, molds, and cockroach compared to the removal group. However, there was no difference in sensitization to domestic animal allergens between the two groups. Patient 6 had kept two hamsters at home, and exposure to a cat and a dog was away from home and intermittent. This patient had bronchial and nasal symptoms whenever he got in contact with each animal. There were no significant differences in duration of exposure to pets before onset of asthmatic symptoms and after onset to the first visit between the two groups. The causative pets were removed soon after the first visit in five patients and after 1 to 16 months in the remaining five patients. Patient 6 removed hamsters from the home and intended to keep away from the cat and the dog completely. These patients were followed up after pet removal for 1 to 28 months (mean, 10 months). There was no difference in the mean duration of follow-up from the first visit to the final methacholine challenge: 14 months (range, 1 to 43 months) in the removal group and 16 months (range, 1 to 41 months) in the keeping group, respectively. No patients gave away their pets and got another pet later.

The results of treatment with or without pet removal are shown in Table 2. There was no significant difference in the initial treatment between the two groups. However, no patient was administered inhaled corticosteroids finally in the removal group, which was significant compared with the keeping group ($p < 0.001$). In patient 5, pet removal alone improved her asthma. Two patients in the keeping group had acute exacerbation, one of whom required hospitalization. The removal group had a significantly lower frequency of regular follow-up visits and medication than the keeping group did 6 months after the final methacholine challenge ($p < 0.01$). Patient 6 had intermittent asthma and required medication several times a year.

There were no differences in the pretreatment values of FEV_1, PC_{20}, or PEF variability between the two groups (Table 3). No significant correlation was found between duration of exposure to pets and the pretreatment values of FEV_1 or PC_{20} in the removal group. The FEV_1 in the removal group increased significantly after medication with pet removal, but there was no difference compared with the keeping group (difference was not significant, two-way ANOVA). The number of additional methacholine tests ranged from 1 to 11 tests (mean, 4 tests). Six patients in the removal group had a greater than fourfold increase in PC_{20}, while two patients in the keeping group did. Overall, a 5.9-fold increase in PC_{20} was observed in the removal group (from 1.4 ± 1.4 mg/mL [range, 0.3 to 4.7 mg/mL] to 8.3 ± 8.1 mg/mL [range, 1.8 to 20.0 mg/mL]; $p < 0.05$), in comparison with a 2.3-fold increase in the keeping group (from 0.9 ± 1.4 mg/mL [range, 0.3 to 4.6 mg/mL] to 2.1 ± 6.3 mg/mL [range, 0.3 to 15.5 mg/mL]; the difference was not significant), which was statistically significant ($p < 0.05$, two-way ANOVA; Fig 1, Table 3). There were no significant changes in PEF variability in each group (difference was not significant, two-way ANOVA). No significant correlation was found between duration of elapsed time since pet removal and the changes in FEV_1 or PC_{20}. Concerning the posttreatment status, there were no differences in the parameters of airway inflammation, including induced sputum and peripheral blood eosinophils, or serum ECP, between the two groups.

Discussion

This is a nonrandomized study, which may introduce a source of bias, *eg*, unexplained reason related to outcome that prompts some patients to remove pets. Lack of blinding of patients and physicians could bias outcome, unless all outcomes were totally objective. However, pet removal depends on patients' own decision making and involves behavioral changes on their part. Making pet removal randomized and blinded is almost impossible. Actually, according to the recommendations by the clinician, the patients made their own choice on what to do with their pets irrespective of disease severity. The reasons the subjects gave for their decision on pet removal included death of the pets, knowledge of the cause of their asthma, and failure to achieve asthma remission without medication even in the less severe patients. The reasons for insisting on keeping the pets included love and attachment to their pets, and an improvement in asthma with medications even in the severe patients. So that individual biases could not influence the outcome, we also chose exacerbation or hospitalization as an objective independent outcome measure. Another approach was to have outcomes collected by staff who are not involved in patient care or in measuring airway hyperresponsiveness.

In this study, we showed that removal of pets from homes and optimal pharmacotherapy significantly reduced airway responsiveness to methacholine in

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Table 1—*Characteristics of the Study Population

Patient No.	Age, yr	Sex	Smoking	Onset of Asthma	Severity of Asthma†	Sensitization to Allergens Other Than Pet	Sensitization to Pet	Pets, No.	Duration of Exposure to Pets, mo			Duration of Follow-up, mo	
									Before Onset of Asthmatic Symptoms	After Onset to the First Visit	From the First Visit to Pet Removal	From Pet Removal to the Final Methacholine Challenge	From the First Visit to the Final Methacholine Challenge
Removal group													
1	28	M	S	Initial	Step 2	HDM	Hamster	12	6	0	6	17	23
2	32	F	S	Initial	Step 2		Ferret	1	36	2	6	28	34
3	26	F	S	Initial	Step 2	Cedar pollen	Hamster	2	10	2	0	1	1
4	22	F	S	Recurrent	Step 2	HDM, cedar pollen	Cat	1	1	2	1	2	3
5	28	F	S	Initial	Step 1		Hamster	20	4	4	0	3	3
6	26	M	S	Recurrent	Step 2	HDM, cedar pollen, grass pollens	Hamster	2	1	1	11	9	20
							Cat	1					
							Dog	1					
7	24	F	NS	Initial	Step 2	HDM, cedar pollen	Hamster	1	12	0	0	2	2
8	28	F	S	Initial	Step 1		Cat	5	120	48	16	27	43
9	40	F	S	Initial	Step 2	Cedar pollen	Hamster	1	36	12	0	4	4
10	39	F	S	Initial	Step 2	HDM, cedar pollen, molds	Hamster	1	4	3	0	8	8
Mean (SD)	29 (6)								23 (37)	7 (15)	4 (6)	10 (10)	14 (15)
Keeping group													
11	32	F	S	Recurrent	Step 2	HDM, cedar pollen	Cat	1	36	1	—	—	21
12	29	F	S	Initial	Step 2	HDM, cedar pollen, grass pollens	Hamster	4	12	1	—	—	1
13	30	M	S	Recurrent	Step 1	HDM, cedar pollen, grass pollens, molds, cockroach	Dog	1	5	1	—	—	15
14	38	F	NS	Initial	Step 2	HDM, cedar pollen, grass pollen	Hamster	3	10	4	—	—	12
15	48	F	Ex-S	Recurrent	Step 2	HDM	Cat	2	3	1	—	—	11
16	52	F	NS	Initial	Step 2	HDM, cedar pollen, grass pollens	Dog	1	84	2	—	—	24
17	42	M	S	Initial	Step 2		Hamster	2	37	2	—	—	2
18	34	F	NS	Initial	Step 2	HDM, cedar pollen, grass pollens, molds	Cat	1	1	2	—	—	32
19	31	M	Ex-S	Recurrent	Step 2	HDM, cedar pollen, grass pollens, molds	Hamster	1	11	0	—	—	2
20	26	F	NS	Recurrent	Step 2	HDM, cedar pollen, grass pollens	Dog	1	96	0	—	—	41
Mean (SD)	36 (3)								30 (11)	1 (1)			16 (13)

*M = male; F = female; S = smoker; NS = nonsmoker; HDM = house dust mite.

†According to the classification of the Global Initiative for Asthma: step 1, intermittent; step 2, mild persistent.

Table 2—*Results of Inhaled Corticosteroids Treatment With or Without Pet Removal*

Patient No.	Initial			Final			Duration of Treatment, mo	Exacerbation or Hospitalization	Regular Follow-up Visits and Medication†
	Use	Dose*, μg/d	Other	Use	Dose*, μg/d	Other			
Removal group									
1	No		Pranlukast	No		Pranlukast	23	No	Quit
2	No		Pranlukast	No			18	No	Quit
3	Yes	400		No			1	No	Quit
4	Yes	400		No			3	No	Quit
5	No			No			0	No	Quit
6	No		Pranlukast Theophylline Procaterol	No		Pranlukast Theophylline	20	No	Continue
7	Yes	400		No			2	No	Quit
8	No		Pranlukast	No		Theophylline	22	No	Quit
9	Yes	400		No			4	No	Quit
10	Yes	800		No			4	No	Quit
Mean (SD)							10 (10)		
Keeping group									
11	Yes	200		Yes	1,600		21	No	Continue
12	Yes	400		No			1	No	Quit
13	No	0	Theophylline	Yes	400		15	No	Quit
14	Yes	800	Theophylline	Yes	400	Theophylline	12	No	Continue
15	Yes	400		Yes	200		11	No	Continue
16	No		Pranlukast Theophylline	Yes	200	Pranlukast Theophylline	24	No	Continue
17	No		Pranlukast	Yes	400	Pranlukast	2	Yes	Continue
18	Yes	800	Theophylline	Yes	800	Theophylline	32	No	Continue
19	Yes	400	Theophylline	Yes	400	Theophylline	2	Yes	Continue
20	No		Theophylline	Yes	1,600	Salmeterol	41	No	Continue
Mean (SD)							16 (13)		

*Beclomethasone dipropionate or equivalent.
†Six months after the final methacholine challenge.

patients with pet allergic asthma more than optimal pharmacotherapy alone. The improvement in PC_{20} was not influenced by alterations in baseline airway caliber, since no significant differences in the change of FEV_1 were detected between the two groups. We also found that pet removal allowed reduced doses of inhaled corticosteroids, a stepping down of medications, and a decrease in the frequency of follow-up visits. The consistency of the improvement in airway hyperresponsiveness and medication requirements suggests clinical as well as statistical significance.

Six patients in the removal group and eight patients in the keeping group were sensitized to cedar pollen, suggesting the possibility that seasonal pollinosis might affect the changes in airway hyperresponsiveness. However, methacholine tests were performed out of season in these patients, particularly in the five patients with intervals between initial and final methacholine tests of ≤ 4 months.

The frequency of hamsters was highest as the causative pet in this study. Horiguchi et al[13] reported six patients with hamster-induced asthma who had the following features: (1) earlier onset than for keeping other pets; (2) adults ranging from 30 to 40 years old; (3) apartment dwelling; (4) high levels of total IgE and serum ECP; (5) dual asthmatic responses on inhalation challenges; (6) rapid remission after removal; and (7) smokers. It is possible that the higher frequency of current smokers and initial onset of asthma, which were found in the removal group but were not statistically significant, may reflect the features of hamster-induced asthma and were the reason for the different effect between the groups. Larger studies will clarify this.

Other measures, including air cleaners and pet washing, have been proposed as alternatives to pet removal to lower the amount of allergens in the air and on the floor of the home.[5–8,14,15] Very few studies have assessed the usefulness of air cleaners, which is controversial. In a study by van der Heide et al,[5] the improvement in airway responsiveness was only a 1.2 doubling-dose increase, whereas Wood et al[7] found no significant effect on disease activity for any parameter. Indeed, we cannot simply compare these reported findings with our results here, but we believe that removal of pets from homes should be recommended as the first choice to reduce symptoms.

The changes in airway hyperresponsiveness we observed in the keeping group were small (a 2.3-fold

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Table 3—*Changes in Pulmonary Function and Posttreatment Status

Parameters	Removal Group (n = 10)	Keeping Group (n = 10)	p Value
FEV_1, % predicted			
Pretreatment	90.7 (15.9)	87.8 (19.6)	NS
Posttreatment	100.1 (14.0)†	96.2 (20.6)	NS
PC_{20}, mg/mL			
Pretreatment	1.4 (1.4)	0.9 (1.4)	NS
Posttreatment	8.3 (8.1)†	2.1 (6.3)	< 0.05
PEF variability, %			
Pretreatment	22.5 (13.8)	19.2 (8.6)	NS
Posttreatment	11.3 (7.1)	10.6 (9.5)	NS
Posttreatment status			
Induced sputum eosinophils, %	3.6 (4.9)	16.3 (26.1)	NS
Peripheral blood eosinophils, 1/μL	248 (179)	374 (204)	NS
Serum ECP, μg/L	14.0 (6.2)	18.2 (13.0)	NS

*Data are shown as mean (SD). NS = not significant.
†$p < 0.05$ for difference between pretreatment and posttreatment in the removal group.

increase) but significant in comparison with the pretreatment values. Our findings are in agreement with previous studies[16,17] concerning allergic asthma without allergen avoidance, in which improvement in airway responsiveness ranged from 1.4- to fourfold after 1 year of treatment with inhaled corticosteroids. This suggests that adequate treatment with inhaled corticosteroids may mask the worsening of asthmatic symptoms induced by domestic animals.

In a cross-sectional epidemiologic study of pet allergic asthma, Plaschke et al[18] found that more subjects with cats or dogs had symptoms, inhaled or oral steroids, abnormal PEF records, higher eosinophil counts, and a higher degree of airway hyperresponsiveness than subjects without pets. Piacentini et al[19] reported that a 3-month period of house dust mite avoidance could significantly reduce the eosinophil percentage in the sputum, along with bronchial hyperresponsiveness, in patients with asthma. We found no differences in the posttreatment PEF values and parameters of airway inflammation, including sputum and peripheral blood eosinophils or serum ECP between the removal and the keeping groups. Possible explanations for these discrepancies may be the diversity of the population studied or a difference in the severity of the disease. However, our results suggest that airway inflammation might be controlled by optimal pharmacotherapy, even in pet allergic patients exposed to substantial amounts of allergens.

There was a high rate of house dust mite sensitization within each group, which was not significant between the groups. Since no avoidance measure for house dust mites was applied, ongoing exposure to mite allergens might have influenced the airway hyperresponsiveness in this study. However, there was a marked improvement in FEV_1 and medication requirements in the removal group. Pet removal could be a potent stimulus for a change in behavior resulting in increased cleaning, removal of mite habitats, and a reduction in allergen levels. Another explanation is that the causative allergens for the development of asthma might be the removed pets rather than house dust mites.

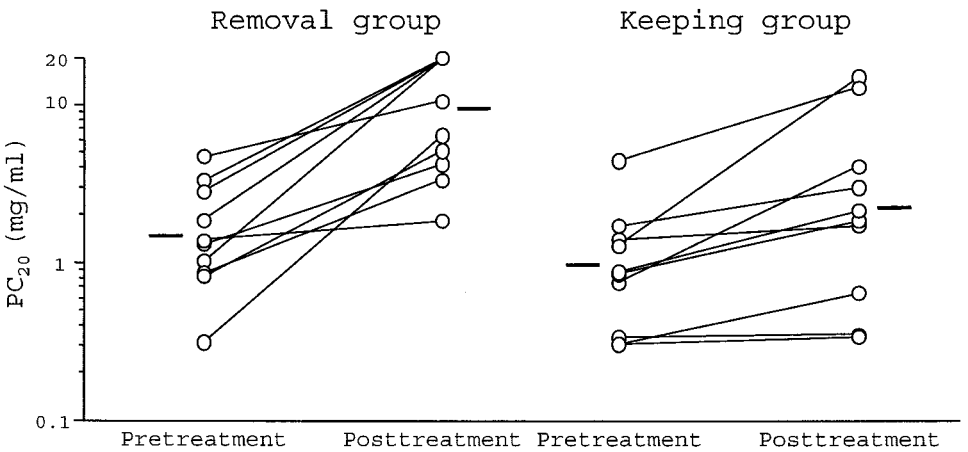

FIGURE 1. Changes in airway responsiveness to methacholine (PC_{20}) in patients with pet allergic asthma in the removal group and the keeping group. Overall, a 5.9-fold increase in the PC_{20} was observed in the removal group (from 1.4 ± 1.4 to 8.3 ± 8.1 mg/mL) in comparison with a 2.3-fold increase in the keeping group (from 0.9 ± 1.4 to 2.1 ± 6.3 mg/mL), which was statistically significant ($p < 0.05$, two-way ANOVA). Pretreatment and posttreatment values of PC_{20} refer to the data that were measured at the second visit and on the day of the final methacholine challenge, respectively. Horizontal bars represent geometric means.

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We did not measure the allergen levels in the air or dust samples in this study. If we had done so, it would have improved our study and confirmed the allergen levels in the removal group. However, at the time of the study, we did not have the necessary resources to determine this.

Pet allergens are ubiquitous in society, and even if pets are removed the allergen may stay in the house for several weeks or months.[19] Likewise, the patients are still exposed to allergens in public places (schools, shops, offices, etc).[20] However, Wood et al[21] found reduced allergen levels (100- to 1,000-fold) after the removal of cats. In addition, a study[22] of allergen levels has shown the highest levels in homes with pets. In three patients in the removal group who were sensitized to cats, airway responsiveness to methacholine improved 2 months after removal and kept on improving subsequently. This suggests that airway responsiveness may improve earlier than expected after pet removal. It is unknown how long it will take for the environmental allergen levels of rodents to decrease after removal. It is certain, however, that reduction of exposure to pets can be attained by their removal from the home.

The lack of information on cleaning and air purification, use of hypoallergenic products, and cessation of smoking is a major limitation of this study. Other limitations may be in the diversity of the number and type of pets and the treatment or follow-up period. Further, conclusions only apply to adults with recent-onset asthma, and with mild intermittent or persistent asthma. No measure of airway sensitivity to the suspected pet allergen was made. Considering these limitations, this study must be considered a preliminary study. Further studies with more complete control of variables and bias, and uniformity of allergens tested are needed for convincing evidence. In conclusion, removal of pets from homes reduces airway responsiveness in patients with pet allergic asthma more than optimal pharmacotherapy, thereby enabling a decrease in inhaled corticosteroid doses.

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