
The effect of reducing levels of cat allergen (Fel d 1) on clinical symptoms in patients with cat allergy

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Background: Treatment of cat allergy normally entails removal of the cat from the household, but cat owners are often unwilling to part with their pets, despite clinically relevant allergies.

Objective: To determine whether levels of Fel d 1 can be reduced without removal of the cat and whether this will affect symptoms of cat allergy.

Methods: Cat-allergic patients underwent randomization to either a group instructed in environmental control (EC) and a group with unchanged environment (UE). Dust samples were obtained and settled Fel d 1 measured by enzyme-linked immunosorbent assay. Patients recorded daily nasal inspiratory flow rates. At baseline, 3 months, and 8 months, patients underwent symptom evaluation.

Results: Eighteen patients were randomized to the EC group and 22 to the UE group; the final number completing the study was 31, 15 in the EC group, and 16 in the UE group. At 8 months, home Fel d 1 levels had diminished to 6.8% of baseline levels in the EC group, whereas no reduction in levels was noted in the UE group. In the EC group, significant improvements were found in nasal inspiratory flow rate and symptoms compared with the UE group. Patients did not have difficulties adhering to EC measures.

Conclusion: A decrease in the allergen load was found in the EC group, which had a significant effect on symptoms of nasal allergy.

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INTRODUCTION

High levels of indoor allergens are associated with an increased degree of sensitization and morbidity from allergic rhinoconjunctivitis and asthma.^{1,2} Allergens from pets, such as the cat allergen Fel d 1, can be important sensitizers.^{1,2} Although the best way to reduce home allergen levels is to remove the pet, this is often difficult to achieve. Furthermore, even when the pet is removed, allergens may still persist for up to 5 months.³

Previous studies have examined the effect of environmental control (EC) measures on allergen load with the cat in situ.⁴ In these studies, upholstered furniture and carpeting were replaced with wipeable furnishings and uncarpeted floors. Room ventilation was increased and the cat washed, resulting in a significant reduction in the amount of Fel d 1 recovered. Wood et al⁵ examined the clinical effect of reducing levels of cat allergen in homes. This study was conducted for 3 months, and reservoirs such as carpeting were not removed from the bedrooms. Although airborne Fel d 1 levels

decreased, no effect on disease activity was detected. However, in a similar study, van der Heide et al⁶ examined the effect of an air filter on clinical measures in children with pet allergy and asthma. They found that application of the air filter decreased airway hyperresponsiveness and peak flow amplitude. The purpose of this study was 3-fold: to evaluate the effect of EC measures on levels of Fel d 1, without removing the cat from the home; to examine the effect of reducing these levels on nasal symptoms; and to evaluate the patients' ability to comply with these detailed measures.

METHODS

Patient Characteristics

Cat owners with symptoms suggestive of allergy and unwilling to part with their pets were recruited by advertisement. To qualify for participation, patients needed to be allergic to cats on the basis of clinical history and positive skin test results (ALK, Copenhagen, Denmark), with reactions to cat allergen of more than 3 mm in diameter or half the response to a histamine control. Additionally, patients had a positive response to radioallergen sorbent tests of grade 2 or greater by the Pharmacia system (Uppsala, Sweden). In addition, a nasal challenge to cat allergen, Fel d 1 (Aquagen extract, 0.3 to 1,000 BAU/mL), was performed, and only patients responding with nasal symptoms and a reduction in nasal peak flow rate were included. Skin prick testing was additionally performed to timothy grass, birch, *Cladosporium*, dog, horse,

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Dermatophagoides pteronyssinus, and *Dermatophagoides farinae* (ALK). The allergic status of enrollees is seen in Table 1. If patients showed positive responses to other pets (dog or horse allergens) and owned the respective pet, they were excluded from the study.

Study Design

The study was a controlled, single-blind trial. Patients were randomized to 2 groups. The first group received detailed instruction on EC measures (Table 2). The second received no instructions. In this second group, cats received a placebo EC pill once a week to create the impression that an intervention was being made. The principal investigators were blinded with regard to this randomization, and all instructions were reinforced every 2 months throughout the study by a nurse or public health specialist. Outcome measures were nasal symptoms and inspiratory peak flow rate.

EC Measures

Before embarking on EC measures, a baseline dust sample was collected. The EC measures are listed in Table 2. Patients received written instructions to vacuum and wet mop all floors and vacuum furniture. Walls and surfaces were wiped and wet mopped. Bedding was washed at 60° C (130° F), and patients and their spouses were supplied with polyester-filled (Du Pont, Wilmington, DE) duvets and pillows (Ajungilak, Oslo, Sweden). Mattress and pillows were covered with impermeable covers (Acb covers; Allergy Control Products, Ridgefield, CT). Once a week, EC was maintained by repeating these procedures. The cat was washed every 2 weeks. To standardize the method, participants were given 3 options: to soak the cat for at least 2 minutes with a shower head, to soak the cat for at least 2 minutes in a tub, or to soak the cat for at least 2 minutes using a supplied water-spray can. The cat was restricted to an area away from the patients' bedrooms. Patients in the EC group were encouraged to remove bedroom and living room carpeting. To increase ventilation in the bedrooms, we encouraged opening of bedroom windows at night. No mechanical ventilation was used in any home. The unchanged environment (UE) group was instructed to continue all household tasks as they had and not to remove or replace carpeting during the study.

Table 1. Allergic Status of the Study Subjects

Allergy	No. of subjects with positive skin test results	
	Environmental control (n = 15)	Unchanged environment (n = 16)
Cat	15	16
Dog	6	6
Horse	3	4
House-dust mite	1	2
Molds	0	2
Grass	8	7
Trees	2	2

Table 2. Environmental Control Measures

Wash all wall and floors at study entry.
Remove carpeting from bedrooms.
Remove upholstered furniture from bedrooms.
Close closets at all times when not in use.
Vacuum floors, carpets, and furniture weekly.
Apply tannic acid (3%) to carpeting and upholstered furniture every 2 months.
Wash bedding at 60° C (130° F) weekly.
Replace old duvets and pillows with polyester-filled duvets and pillows for both patient and spouse.
Cover mattresses and pillows with impermeable covers, mop floor, and wet-wipe surfaces weekly.
Wash cat every 2 weeks.
Keep cat out of bedroom.
Sleep with bedroom windows open.

Collection of Dust and Measurement of Fel d 1

Patients were initially encouraged to pursue EC and dust sampling during an entire 12-month period; only 9 of 15 patients in the EC group and 12 of 16 in the UE group complied with sample collection after 9 months. Dust samples presented were obtained from participants' homes at the start of the study and after 1, 3, and 8 months

Samples were obtained by means of a vacuum cleaner attached to a special suction device (ALK) containing a 6-mm Millipore filter (Allergy Laboratories, Copenhagen, Denmark). The sampling device was cleaned and a new filter fitted before each sample was obtained. Samples were obtained by vacuuming a designated 1-m² area for 5 minutes using the method of Wood et al.³ Two areas were selected and samples combined: from the patient's bedroom mattress and from the living room area. The same areas were vacuumed each time.

The total dust collected was weighed and extracted in 1:5 (wt/vol) buffer (0.125M ammonium-hydrogen-carbonate and 0.1% NaN₃) for 2 hours at room temperature. The suspension was filtered through filter paper and diluted 1:10, 1:100, and 1:1,000 for analysis. Fel d 1 concentrations in dust were measured by sandwich enzyme-linked immunosorbent assay (Allergy Laboratories).⁷

Evaluation of Nasal Response

The primary outcome measures were nasal symptom scores and nasal peak flow rate. These were recorded for a period of 2 weeks at baseline and for 4 weeks at 3 and 8 months. Symptom scoring included nasal congestion, rhinorrhea, and itching. Patients recorded these symptoms on a scale of 0 to 10. If 0 symptoms were recorded, this meant that the individual had remained entirely asymptomatic, and 10 correlated with the worst symptoms the patients had experienced.

Inspiratory nasal peak flow rate was measured daily by means of a Youtlen peak flow rate meter.⁸ This gave measurements of nasal peak inspiratory flow in milliliters.

Evaluation of Compliance

Patients randomized to the EC group underwent two 1-hour instruction sessions 2 to 4 days apart; they also received detailed written instructions on each EC measure. In addition, instructions were verbally reinforced every 2 months. After 3 and 8 months, patients were asked to answer a detailed written questionnaire on compliance.

Statistical Analysis

For analysis of Fel d 1 in dust samples, independent sample *t* tests were used. The between-group comparisons of nasal peak flow and symptom scores involved *t* tests whenever the distribution of the data made it possible and the Mann-Whitney test for nonnormally distributed data. In all comparisons, 2-sided probability tests were used. $P < 0.05$ was considered statistically significant.

Ethical Considerations

The study was reviewed and approved by the ethical committee of the National University Hospital of Iceland. All patients provided written informed consent before enrollment in the study.

RESULTS

Characteristics of the Study Groups

Of 215 individuals who volunteered to participate in the study, 40 met study criteria and were willing to participate. Eighteen patients were randomized to the EC group and 22 to the UE group; the final number completing the study was 31, 15 in the EC group and 16 in the UE group. Two patients failed to return for their scheduled visits, and 3 did not collect dust samples as directed. The study was designed to last 11 months. However, 6 patients from the EC group and 4 from the UE group failed to collect dust samples after the 8-month period. Therefore, data are presented for the first 8 months of the study. The patients' ages ranged from 15 to 60 years, with a mean age of 26.3 years in the EC group and 25.8 years in the UE group. There were 19 females and 12 males. All patients had a history of cat-induced rhinitis (by history and nasal allergen provocation). Twenty-eight homes had a single cat, and 3 homes had 2 cats. Eleven patients had positive skin test results to cat alone, and 20 had at least one other positive skin test result (Table 1).

No carpets were in the bedrooms in the EC group (3 homes had bedroom carpets but were removed). Living room carpets were in 2 households. In the UE group, only 1 home had bedroom carpeting and 1 had living room carpeting at study start. The same number of carpets was present at the completion of the study.

All patients in both groups slept with open windows, and other areas of the home were ventilated in this fashion as well. All but 2 patients in the EC group worked away from home. Patients had abstained from nasal corticosteroids and antihistamines for 2 months before study initiation (March) and the 8-month evaluation (November).

Fel d 1 Concentrations in Homes

At each time point after baseline, concentrations of Fel d 1 in homes where EC measures were practiced were lower than in those with an UE and significantly lower after the 2-month dust collection (Fig 1). Levels obtained before initiation of EC were not significantly different between the EC and UE groups ($P = 0.72$). Fel d 1 concentrations in the EC group had decreased sharply after 1 month of EC initiation, from 39,440 ng/g of dust to 17,599 ng/g (UE vs EC, $P = 0.42$). Levels continued to decrease to a mean of 9,258 ng/g at 2 months (UE vs EC, $P = 0.05$) and to a mean of 4,077 ng/g at 3 months (UE vs EC, $P = 0.002$) and reached a mean of 2,707 ng/g (6.8% of baseline levels) at 8 months (UE vs EC, $P < 0.001$). In the UE group, concentrations of Fel d 1 did not change throughout the study period (29,561 ng/g at baseline, 28,964 ng/g after 1 month, 24,734 ng/g at 3 months, and 33,810 ng/g at 8 months).

Nasal Inspiratory Peak Flow and Symptom Scores

Eight months after institution of EC, significant differences were found in peak nasal inspiratory flow rate between the EC and UE groups (Table 3). In the EC group, mean nasal flows increased from 154.9 mL at baseline to 216.7 mL at 8 months. In the UE group, these values were 177.6 mL at baseline and 168.8 at 8 months. Furthermore, at 8 months, a significant improvement in nasal symptoms was found with regard to congestion, rhinorrhea, and itching. An improvement in mean nasal congestion scoring was found (3.4 at baseline to 0.9 at 8 months in the EC group; $P = 0.05$), but a worsening in symptom scores by -0.2 was found in the UE

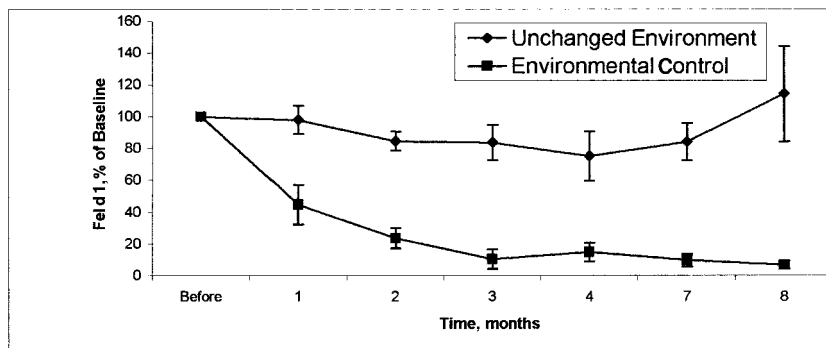


Figure 1. Mean Fel d 1 concentrations in dust from environmental control vs unchanged environment homes. Results are presented as mean $\pm$ SEM percentage decrease from baseline Fel d 1 values. Baseline Fel d 1 equals 100%. After 2, 3, and 8 months, there was a significant difference between the environmental control and unchanged environment groups.

Table 3. Nasal Scores for the Environmental Control (EC) and Unchanged Environment (UE) Groups*

Symptom	Mean (SEM) nasal score		P value†
	0 mo	8 mo	
Nasal flow			
EC	154.9 (10.5)	216.7 (10.8)	0.01
UE	177.6 (11.2)	168.8 (12.8)	
Congestion			
EC	3.4 (0.5)	0.9 (0.2)	0.05
UE	2.7 (0.4)	2.9 (0.4)	
Rhinorrhea			
EC	3.6 (0.6)	1.1 (0.2)	0.005
UE	2.6 (0.3)	2.4 (0.4)	
Itching			
EC	1.1 (0.4)	0.1 (0.06)	<0.001
UE	0.9 (0.4)	1.7 (0.6)	

* The primary outcome measures were nasal symptom scores and nasal peak flow rate. These are presented as mean symptom scores and mean nasal inspiratory flow rates. Mean values were calculated at baseline from a diary recording daily symptoms (scale 0–10) and Youten (nasal flow) measurements during a 2-week period at baseline and throughout a 4-week period at 3 and 8 months.

† P values between the EC and UE groups.

group. Similarly, mean symptom scores of rhinorrhea improved in the EC group from 3.6 at baseline to 1.1 at 8 months ($P = 0.005$) compared with 2.6 to 2.4 in the UE group. Mean symptom scores for itching improved in the EC group from 1.1 to 0.1 ($P < 0.001$), but worsened in the UE group by 0.8.

Compliance With EC Measures

Compliance with all EC measures was good. The major laxity was with cat washing; all but one patient washed the cat at 8 months (Table 4).

DISCUSSION

In the practice of allergy, most physicians recommend that cat-allergic individuals remove the cat from the home. If the patient is unwilling to do so, EC measures are recommended

Table 4. Compliance with Instructions on Environmental Control (n = 15)

Instruction	No. of patients	
	3 mo	8 mo
Keep cat out of bedroom	14/15	14/15
Remove carpeting from bedroom	15/15	15/15
Use pillow and mattress covers	15/15	15/15
Use supplied duvet	15/15	15/15
Wash supplied duvet every 2 weeks	15/15	14/15
Wash cat every 2 weeks	14/15	14/15
Wash bedding weekly	15/15	15/15
Wet mop floors and surfaces	15/15	15/15
Vacuum weekly	15/15	15/15
Wash walls at study entry	15/15	

along with appropriate pharmacotherapy. Despite this general consensus in clinical practice, the evidence supporting the efficacy of EC measures for cat allergy is scant.

Previous studies have documented that EC measures can effectively reduce cat allergen.^{3,4} However, as Wood et al³ have demonstrated, it may take months after removal of the cat from a home for significant reductions in levels of Fel d 1 to be apparent: allergen concentrations decrease steadily throughout 6 months to 100- to 1,000-fold lower levels.

Two published studies^{5,6} have examined the clinical effect of reducing cat allergen. In the first,⁵ the combination of HEPA room air cleaner, mattress, and pillow covers along with cat exclusion from the bedroom was found to reduce airborne cat-allergen levels throughout 3 months. However, no effect on disease activity, evaluated by nasal symptoms and methacholine challenge, was detected. The study was performed for 3 months, and carpeting was present in all but one bedroom. The second study⁶ was also performed for 3 months, and carpeting was present in half of the bedrooms. In contrast to the previous study, a significant reduction in bronchial hyperresponsiveness and peak flow rate amplitude was found. Furthermore, the investigators observed changes in airborne animal allergen levels but no decrease of levels in floor dust.

The aim of our study was to examine the effect of stringent EC on levels of Fel d 1 in homes with a resident cat throughout 11 months. We postulated that allergen load would not have fallen to low enough levels to affect disease expression until after 3 months or even longer. High concentrations of Fel d 1 were present in the homes of patients at the start of the study, but EC measures resulted in significant and immediate (occurring after 1 month) reductions in allergen load. Comparable changes were not observed in homes with UE. The immediate reduction in allergen load could be due to the method of EC. Patients were instructed to perform all EC measures within the first study day and remove all reservoirs. Almqvist et al⁹ demonstrated that cat allergen is transferred by cat owners' clothes from room to room. By performing all EC measures at once, transference of allergen among rooms within the household may have been decreased. Initial measures were involved and included washing all walls and cupboards and vacuuming and washing floors and bedding. Our final dust analysis in this study was performed at 8 months.

In the present study, we attempted to observe the effect of EC in real life. We found that decreasing the load of Fel d 1 resulted in an improvement in nasal patency and symptoms of congestion, sneezing, and itching.

What could be the reasons for the discrepancy in clinical efficacy found in these 3 studies? First, the methods and duration of EC before evaluation of clinical symptoms differ, as does the mode of allergen sampling. Furthermore, a discrepancy in clinical response may possibly exist with regard to age. In our study, where we show a beneficial effect of EC, the duration of EC was 11 months, settled dust was sampled, and the age of the patients ranged from teenagers to adults,

with a mean age of 26.1 years. The EC measures were stringent and included thorough and regular washing of the cat and all surfaces and bedding and placement of impermeable mattress and pillow covers. Reservoirs such as carpeting were not present in the bedrooms during the study. However, the study did not involve the use of air cleaners of any kind. Ventilation was achieved through open windows. Furthermore, our patients had allergic rhinitis with variable involvement of the lower airway, and our primary outcome measure was nasal patency and symptoms. In the study by Wood et al,⁵ no beneficial effect of EC was found using nasal and chest symptom scores, peak flow rate measurements, medications, and methacholine challenge. The study lasted 3 months and airborne Fel d 1 was sampled. The EC measures included using bedroom HEPA air cleaners, using impermeable mattress covers, and shutting the bedroom door. No effort was made to remove potential reservoirs such as carpeting. The average age was somewhat older (36.3 years), and most patients had both asthma and allergic rhinitis (13 of 18 in the EC group had asthma).

In the study by van der Heide,⁶ the effects of EC were examined for 3 months with a crossover (total study duration, 6 months). EC was achieved by using air cleaners in both the bedroom and living room areas. Patients were asthmatic children with a mean age of 11.7 years. Outcome measures included adenosine challenge, peak flow rate, and medication use, and these were all significantly improved compared with baseline values.

Similar controversy exists with regard to beneficial effects of EC in patients with cat allergy as with house dust mite allergy.¹⁰⁻¹² This was reviewed in a recent Cochrane meta-analysis¹³ in which mite-allergen avoidance was highlighted. The reviewers concluded that "current physical and chemical methods aimed at reducing exposure to allergen from house dust mites seem to be ineffective and cannot be recommended as prophylactic treatment for asthma patients sensitive to mites." However, in the meta-analysis, only 6 of 23 studies reviewed reported a reduction in mite levels; furthermore, the asthmatic patients were of a heterogeneous phenotype, including both children and adults with varying degrees of disease severity.

In this study, we report a reduction in levels of settled Fel d 1, which associated with a benefit in both nasal symptoms and measures of nasal caliber. Our study population is homogeneous; all patients having allergic rhinitis, opposed to the previously published studies where asthmatic patients were targeted and symptoms from the lower airways examined. Further studies that examined patients with allergic rhinitis are needed to determine whether allergen ablation may be more effective in the upper rather than lower airways. Furthermore, we attempted to clear primarily the patients' bedrooms of the allergen by washing walls and removing all reservoirs and the cat from this area, where the patients spend at least 6 to 10 hours of their day.

Certainly, measuring settled rather than airborne Fel d 1 levels is a weakness of the study. Fel d 1 in settled dust may

not accurately reflect the decreases in allergen load that the patient inspires on a daily basis. A further drawback of all EC studies is the small number of participants. As in our study, of 219 patients volunteering for participation, only 31 completed the study. Reasons for this included patient perception of cat allergy at the time of initial enrollment and discontinuation once the study protocol was explained. We may have chosen a biased population, a very "hardy" group of individuals with stamina and endurance, and this may explain the reason for the positive response to compliance with otherwise complicated and time-consuming EC measures.

Most of our patients had no difficulties with compliance. Patients cleaned (vacuumed, wet mopped, wiped) weekly, washed bedding, and used their impermeable covers and duvets. All but one patient washed the cat every 2 weeks up to 8 months. We especially emphasized restricting the cat from the bedroom. Surprisingly, patients followed this advice. Patients even removed carpeting from the bedroom.

In conclusion, we have shown that stringent EC can decrease levels of Fel d 1 without removal of the cat from the home. This was associated with clinical improvement. Patients did not have difficulties complying with measures of EC.

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