

Short communication

Etiologic role of unapparent exposure in cat allergy

Brasó-Aznar JV, Pelaez-Hernandez A, Rochina-Puchades A, Morales-Rubio C, Burches-Baixaui E. Etiologic role of unapparent exposure in cat allergy.

Allergy 1995; 50: 447–450. © Munksgaard 1995.

To determine the importance of unnoticed exposure to cat, we studied 20 patients with a history of respiratory allergy. All the patients had a positive prick test to cat dander extract, and none of them kept cats as pets. The prick test was carried out with a dander extract from cat at a concentration of 100 BU/ml. The specific IgE was determined by the commercially available Pharmacia CAP System. We carried out a conjunctival challenge test. The concentration of *Fel d 1* was quantified in dust samples from the patients' homes by a commercially available method. The patients were reassessed in order to establish a relation between exposure and symptoms, and concealed allergen sources. Sixteen patients showed significant levels of *Fel d 1* in their homes (mean of 3.35 µg/g of dust). The conjunctival challenge test was positive in 15 patients. These patients showed an exposure mean of 0.4 µg/g of dust. The mean levels of specific serum IgE were higher in those patients with a positive challenge than in those with a negative challenge ($P = 0.0145$). In nine reassessed patients, a relation was established between natural exposure and the onset of the symptoms. A possible hidden allergen source was established in 11 patients. Hidden exposure to cat allergen may play a role in the symptomatology of many atopic patients, and investigation of sensitization to *Fel d 1* should be included in the routine allergologic evaluation of all patients with asthma or perennial rhinitis.

J. V. Brasó-Aznar, A. Pelaez-Hernandez, A. Rochina-Puchades, C. Morales-Rubio, E. Burches-Baixaui

Unidad de Alergia, Hospital Clinic Universitario, Avda. Blasco Ibáñez n° 17, 46010 Valencia, Spain

Key words: allergen exposure; cat allergy; *Fel d 1* allergen; respiratory allergy.

Dr José V. Brasó-Aznar
Unidad de Alergia, Hospital Clinic Universitario
Avda. Blasco Ibáñez n° 17
46010 Valencia
Spain

Accepted for publication 17 January 1995

During the last few years, we have observed the existence of patients with perennial respiratory allergy whose clinical evolution could not be satisfactorily explained by the results of allergologic evaluation with the series of pneumoallergens commonly used. The possible existence of one or various hidden allergens was then considered. These allergens must be potent, ubiquitous, and difficult to detect by clinical history. A candidate that fulfils these requirements is the major cat allergen.

The major cat allergen, *Fel d 1*, is actually considered a ubiquitous allergen, present in significant levels in dust samples from homes where the animal has never been kept (5, 12, 14, 22), and various authors have demonstrated that the levels can remain significantly high in dust for a long time (18, 21) and that the allergen is very stable.

On the other hand, sensitization to *Fel d 1* seems quite high in the allergic population of the Occidental

countries. In different studies, it has been placed at 20–30% of asthmatic patients (3, 9), and some studies carried out in Spain give figures of around 2.5% for atopic patients (4).

The great prevalence, ubiquity, and stability of the allergen and its sensitization potency point to the possibility of hidden exposure, which is difficult to detect by clinical history, but which could be responsible for the symptoms of some patients with asthma or rhinitis.

To validate this hypothesis, we carried out a study in 20 patients with skin sensitivity to *Fel d 1*; none of them referred in the first anamnesis to a relation between their symptoms and exposure to cat, and no cat was present in their usual environment. Our main objectives were to: 1) evaluate the etiologic responsibility of *Fel d 1* sensitivity in patients with respiratory allergy and for whom the clinical history showed no relation with a cat environment, 2) determine the

unnoticed exposure level in the home, and 3) determine the relationship between the distinct parameters studied.

Material and methods

Patients

For 2 months, we carried out skin tests (prick test) on all our patients with respiratory symptoms who had no known relation with cats, and whose clinical evolution did not agree with the results of the allergologic evaluation with the series of pneumoallergens that we used.

Twenty patients with positive skin tests to cat allergen, and with a history of asthma, or perennial rhinitis, or both, were selected. The ages ranged between 13 and 56 years with a mean of 24 years. There were 11 females and nine males. All but two of them showed sensitization to pneumoallergens other than *Fel d 1*.

Diagnostic methods

The prick test was done by the puncture method with Dome-Hollister lancets. Cat dander extract was used at a concentration of 100 BU/ml (BU = biological units used by the laboratory supplier for the biological standardization of the cat dander extract: 100 BU/ml is equivalent to 10 BU/ml by the Brighton method), as supplied by Alergia e Inmunología Abelló SA. Physiologic saline solution and hydrochloride histamine at a concentration of 10 mg/ml were used as controls. The reading was carried out after 20 min, and the test was considered positive if the wheal obtained was the same size as or greater than that of histamine, in agreement with the Scandinavian method (1), and its minimum diameter was at least 3 mm in length.

The serum specific IgE was quantified by the commercially available Pharmacia CAP System. All tests were carried out simultaneously and duplicated in order to avoid intra- and intertest variations. Levels of ≥ 0.7 kU/ml were considered significant.

In the conjunctival challenge test, the same extract as in the prick test was used. Three dilutions were prepared with lyophilized extract of 30 BU, using sterile physiologic saline solution at 10, 2, and 0.4 BU/ml, respectively. These dilutions were not used 72 h after their preparation. Before the test, we ensured that the patients were asymptomatic and that the conjunctival mucosa was whole. A drop of sterile physiologic saline solution was administered as a negative control. Afterwards, the administration of the different allergen concentrations was carried out at intervals of 30 min, beginning with the most dilute. The unequivocal presence of signs and symptoms of conjunctivitis (hyperemia, pruritus, and epi-

phora) was considered positive. Previously, the irritation capacity of the preparation had been tested in five controls with negative skin tests. The test was considered negative if no response was obtained at a concentration of 10 BU/ml.

To evaluate the level of exposure to the allergen, we quantified the concentration of *Fel d 1* in dust samples from the patients' homes. Material supplied by a commercial company (Dea-Test, Alergia e Inmunología Abelló SA) was used, the patients were previously instructed on the method of collecting the samples (with a vacuum cleaner during 3 alternate days in a week), and samples from the most convenient places were collected then. The samples were sent to the reference laboratory, where the concentration of the allergen was quantified by solid-phase ELISA with monoclonal antibodies. The method has a high specificity and sensitivity, as previously reported (2, 10, 20). As a comparison, the level of *Fel d 1* was determined by the same method in six homes where cats were kept. Levels lower than 0.05 $\mu\text{g/g}$ of dust were considered nonsignificant. Higher levels of exposure were considered as mild (0.05–0.2 $\mu\text{g/g}$), moderate (0.2–2 $\mu\text{g/g}$), high (2–10 $\mu\text{g/g}$), or very high ($> 10 \mu\text{g/g}$).

All patients were reassessed at a follow-up visit, by means of a directed anamnesis, to establish any unnoticed relation between natural exposure to cat environments and clinical worsening, and to discover unnoticed allergen sources in their homes.

The statistical treatment of the data was carried out with the Wilcoxon nonparametric test (Wilcoxon rank sum test) and the Pearson test for correlations.

Results

The results of the Dea-Test showed that 16 patients (80%) had significant levels of *Fel d 1* in their homes. Nine patients (45%) showed moderate levels, and three patients (15%) high or very high levels (Table 1). The results obtained from home with domestic cats were significantly higher, with a mean of 235.3 $\mu\text{g/g}$ ($P < 0.001$).

The determination of specific IgE showed that all but two patients had significantly high levels. The average level was higher in patients with a positive challenge test than in those with a negative one. These differences were statistically significant ($P = 0.01$).

The conjunctival challenge test was positive in 15 patients (75%), showing that sensitization had a clinical explanation.

No significant relation was found between exposure levels and specific IgE levels ($P = 0.40$), or between exposure levels and results of the conjunctival challenge ($P = 0.44$).

A relation between evident natural exposure to

Table 1. Results of quantification of *Fel d 1* in dust samples from the patients' homes, specific IgE, and conjunctival challenge in 20 patients with positive skin prick test to cat dander extract, and without apparent cat exposure

Patient no.	Levels of <i>Fel d 1</i> ($\mu\text{g/g}$ of dust)	Specific IgE (Cap) kU/l	Conjunctival challenge
1	0.06	33	+
2	0.08	0.7	-
3	<0.05*	0.7	-
4	0.40	92	+
5	0.2	44	+
6	0.1	1.6	+
7	0.1	14	+
8	<0.05*	4	+
9	28	2.7	-
10	0.23	5.4	+
11	0.3	2.7	-
12	<0.05*	9.4	+
13	1.27	3	+
14	1.82	3.27	+
15	0.26	7.7	+
16	2.20	0.3	-
17	0.39	100	+
18	<0.05*	2	+
19	18	0.4	+
20	0.3	1.14	+
Mean $\pm$ SD	3.35 $\pm$ 7.9	16.4 $\pm$ 29.5	

* Levels lower than 0.05 $\mu\text{g/g}$ of dust were considered nonsignificant.
SD: standard deviation.

cats and symptomatic worsening could be established in nine of the 15 patients with positive conjunctival challenge reassessed in a follow-up visit (60%). In the rest, no evident exposure was established. None of the patients with a negative conjunctival challenge noted a relation between natural exposure to cats and the symptoms.

When the patients were asked about the possibility of a hidden allergen source in their homes, nine denied it although they could not exclude the possibility, six confirmed the presence of cats in the neighborhood, and five confirmed that frequent visitors to their home kept cats.

Discussion

All our patients were sensitized to *Fel d 1*; however, none of them referred in the first anamnesis to having lived with cats or their connection to the onset of the symptoms. This suggests that the clinical history may not be sensitive enough in the detection of these cases. Data published by other authors indicate that only 54% of sensitized patients show a compatible history (4).

All but two patients showed significant levels of specific IgE in serum. These levels have no relation to the degree of exposure. This agrees with the fact that sensitization depends on the concurrence between exposure and individual factors.

The values of *Fel d 1* obtained in dust samples from the patients' homes agree with those previously published for homes without cats (5, 12, 18, 22). Eighty per cent of the patients showed significant levels; and 60% showed exposure levels considered moderate or high. These results confirm the possibility of unnoticed exposure and the utility of the determination of allergen levels in domestic dust samples, using the commercial methods available, to reveal hidden exposure. Previously, it has been reported that *Fel d 1* can be transported by people or objects (7). In 11 of our patients, we found evidence of a probable allergen brought into homes by frequent visitors who had regular contact with cats.

Pollart et al. suggested that doses of approximately 2 $\mu\text{g/g}$, commonly observed in homes without cats, could be a sensitization risk factor (15). Our patients had an exposure mean of 3.35 $\mu\text{g/g}$, which agrees with previous observations. But, if we exclude the patients with the highest mean levels (nos. 9 and 19), the mean exposure was substantially lower (0.55 $\mu\text{g/g} \pm 0.69$). Since no other exposure sources were identified, it is likely that many of our patients were sensitized by exposure to these levels over long periods. The importance of the length of exposure has been stated in other papers (6).

The conjunctival challenge test was positive in 75% of our patients. In nine of them, a relation was established between natural cat exposure and the onset of acute symptoms. None of them had mentioned this in the first anamnesis, probably because they also had symptoms in places where apparently there was no cat. These data suggest that at least some of the clinical manifestations were motivated by hypersensitivity to *Fel d 1* in our patients.

It is more difficult to demonstrate that the levels detected in the homes could trigger clinical symptoms. The symptomatology depends, above all, on the concentration of the allergen in the air, which is related to the amount present in dust, but this relation varies in each home, according to the grade of ventilation, accumulation of dust, and other factors (11, 16, 17). The mean concentration to which our patients, with significant levels and a positive conjunctival challenge test (if we exclude case no. 19, who showed unusually high levels), were exposed was about 0.4 $\mu\text{g/g}$ dust. For some authors, the concentration of *Fel d 1* that can be achieved with the figures in our study would probably be hardly relevant to the induction of acute symptoms (21, 23), but one must not forget that people spend 40% of their time at home; therefore, it can be estimated that the accumulated amount, inhaled after several days, may be important and may contribute to the worsening of the patients' symptoms.

Recently, Munir et al. suggested that the inhalation of 0.5 ng/h can produce clinical symptoms (12),

and Ihre & Zetterström (8) established that the inhalation during 1 week of 1% of the allergen that produces acute symptoms in the bronchial challenge test can induce bronchial hyperreactivity. It is probable that the accumulated amount inhaled by our patients was within the range of the different amounts described in the literature (13, 19). New studies are needed to determine whether such low concentrations, continually inhaled for hours, are capable of triggering symptoms; however, our data suggest the necessity of investigating hypersensitivity to *Fel d 1* and unnoticed exposure to cat allergen in all patients with symptoms of asthma, perennial rhinitis, or both disorders.

Acknowledgments

We wish to thank all our department staff, especially the nurses Mrs María Dolores Baixauli and Mrs Ana Alonso for their invaluable technical assistance.

References

1. AAS K, BELIN L. Suggestions for biological quantitative testing and standardization of allergen extracts. *Acta Allergol* 1974; 29: 238-40.
2. BARBER D, CHAMORRO MJ, CARPIZO JA, et al. Valoración de la presión alérgica ambiental. Interés de esta determinación en la prevención, diagnóstico y tratamiento de las enfermedades alérgicas. *Rev Esp Alergol Inmunol Clin* 1990; 5: 125-32.
3. BRYANT DH, BURNS MW. Skin-prick test reactions to inhalant allergens in asthmatic patients. *Med J Aust* 1976; 1: 918-24.
4. CISTERO BAHIMA A, BATISTA A, RAMÍREZ W, OLIVE A, CARREIRA J. Reactividad cruzada a epitelio de gato. XVI Congreso Nacional de la SEAIC, Murcia, 1988.
5. DE BLAY T, HEYMANN PW, CHAPMAN MD, PLATTS-MILLS TAE. Airborne dust mite allergens: comparison of group II allergens with group I mite allergen and cat-allergen *Fel d 1*. *J Allergy Clin Immunol* 1991; 88: 919-26.
6. DESJARDINS A, BENOIT C, GHEZZO H, et al. Exposure to domestic animals and risk of immunologic sensitization in subjects with asthma. *J Allergy Clin Immunol* 1993; 91: 979-86.
7. ENBERG RN, SHAMIE SM, McCULLOUGH J, OWNBY DR. Ubiquitous presence of cat allergen in cat-free buildings: probable dispersal from human clothing. *Ann Allergy* 1993; 70: 471-4.
8. IHRE E, ZETTERSTRÖM O. Increase in bronchial reactivity after inhalation of low doses of allergen [Abstract]. *Allergy Clin Immunol News* 1991; 3 (Suppl. 1): 227.
9. KURATA JH, GLOVSKY MM, NEWCOMB RL, EASTON JG. A multifactorial study of patients with asthma. II. Air pollution, animal dander and asthma symptoms. *Ann Allergy* 1976; 37: 398-409.
10. LOMBARDEO M, CARREIRA J, DUFFORT O. Monoclonal antibody based radioimmunoassay for the quantitation of the main cat allergen (*Fel d 1* or cat-1). *J Immunol Methods* 1988; 108: 71-6.
11. LUCZYNSKA CM, LY Y, CHAPMAN MD, PLATTS-MILLS TAE. Airborne concentrations and particle size distribution of allergen derived from domestic cats (*Felis domesticus*): measurements using cascade impactor, liquid impinger, and a two-site monoclonal antibody assay for *Fel d 1*. *Am Rev Respir Dis* 1990; 141: 361-7.
12. MUNIR AKM, EINARSON R, SCHOU C, DREBERG SKG. Allergens in school dust. I. The amount of the major cat (*Fel d 1*) and dog (*Can f 1*) allergens in dust from Swedish schools is high enough to probably cause perennial symptoms in most children with asthma who are sensitized to cat and dog. *J Allergy Clin Immunol* 1992; 91: 1067-74.
13. OHMAN JL, FINDLAY SR, LEITERMAN K. Immunotherapy in cat induced asthma. Double-blind trial with evaluation of *in vivo* and *in vitro* responses. *J Allergy Clin Immunol* 1984; 74: 230-9.
14. OHMAN JL, LORUSSO JL, LEWIS S. Cat allergen content of commercial house dust extracts: comparison with dust extracts from cat-containing environment. *J Allergy Clin Immunol* 1987; 76: 955-9.
15. POLLART SM, CHAPMAN MD, PLATTS-MILLS TAE. Allergen levels inside homes: risk factors for acute asthma attacks [Abstract]. *J Allergy Clin Immunol* 1988; 81: 242.
16. SWANSON MC, AGARWAL MK, REED CE. An immunochemical approach to indoor aeroallergen quantitation with a new volumetric air sampler: studies with mite, roach, cat, mouse and guinea pig antigens. *J Allergy Clin Immunol* 1985; 76: 724.
17. SWANSON MC, CAMPBELL AR, KLAUCK MJ, REED CE. Correlations between levels of mite and cat allergens in settled and airborne dust. *J Allergy Clin Immunol* 1989; 83: 776-83.
18. VAN DER BREMPST X, CHARPIN D, HADDI E, DA MATA P, VERVOLET D. Cat removal and *Fel d 1* levels in mattresses. *J Allergy Clin Immunol* 1991; 87: 595-6.
19. VAN METRE T, MARSH DJ, ADKINSON NF, et al. Dose of cat (*Felis domesticus*) allergen 1 (*Fel d 1*) that induces asthma. *J Allergy Clin Immunol* 1986; 78: 62-75.
20. VENTAS ALGUACIL P, LOMBARDEO M, DUFFORT O, CARREIRA J. Cuantificación de los alérgenos *Der p 1* y *Der f 1* de los ácaros del polvo doméstico y *Fel d 1* de gato mediante un ELISA en fase sólida. *Rev Esp Alergol Inmunol Clin* 1990; 5: 71-5.
21. WOOD RA, CHAPMAN MD, ADKINSON NF, EGGLESTON PA. The effect of cat removal on allergen content in household-dust samples. *J Allergy Clin Immunol* 1989; 83: 730-4.
22. WOOD RA, EGGLESTON PA, LIND P, et al. Antigenic analysis of household dust samples. *Am Rev Respir Dis* 1988; 137: 58.
23. WOODFOL JA, LUCZYNSKA CM, DE BLAY F, CHAPMAN MD, PLATTS-MILLS TAE. Cat allergy [Editorial]. *Ann Allergy* 1992; 69: 273-5.

This document is a scanned copy of a printed document. No warranty is given about the accuracy of the copy. Users should refer to the original published version of the material.