

Focus on Cat Allergen (Fel d 1): Immunological and Aerodynamic Characteristics, Modality of Airway Sensitization and Avoidance Strategies

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Key Words

Cat allergen · Fel d 1 · Bronchial asthma · Indoor environment · Prevention · Respiratory allergy · Pet

Abstract

The increasing frequency of pet ownership (especially cats) in many industrialized countries has raised the level of exposure to the allergens produced by these animals. Moreover, it is likely that modern energy-saving systems and the wide use of upholstered furniture has resulted in closer contact between cats (and their allergens) and humans. Many different methods have been developed to quantify the main cat allergen (Fel d 1) in settled dust and in ambient air. The threshold levels of cat allergen inducing sensitization or triggering respiratory symptoms in sensitized patients have been calculated in settled dust, but airborne amounts of Fel d 1 probably represent a more reliable index of allergen exposure. Noticeably, the amount of Fel d 1 may be relatively high also in confined environments where cats have never been kept. It has been demonstrated that clothes of cat owners are the main source for dispersal of allergens in cat-free environments. This fact may be of relevance, because recent studies have shown that allergic sensitization to

cats is more likely to develop in children exposed to moderate levels of this allergen than in children exposed to high amounts of Fel d 1. The ubiquity of cat allergen may justify the common observation that allergen avoidance is often insufficient to reduce the risk of developing allergic sensitization and/or symptom exacerbation in highly susceptible patients. Further efforts are needed to improve the efficacy of Fel d 1 avoidance strategies to try to reduce the risk of allergic sensitization to this allergen.

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Introduction

It is generally accepted that changes induced by human activities in indoor environments and the 'Western life-style' play a role in the increasing rate of exposure to indoor allergens and/or pollutants [1–3]. In fact, most modern indoor environments are built with insulated windows and doors, which may cause an increase in indoor humidity and temperature and a dramatic reduction of the natural outdoor-indoor air exchange [4–6]. In these conditions, allergens and pollutants which are produced or are present indoors cannot be adequately re-

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1018–2438/03/1321–0001\$19.50/0

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moved or diluted by natural air circulation, with a consequent increase of the degree of exposure of susceptible populations [7–9].

Sensitization to animal allergens is a common occupational hazard in laboratory workers [10]. However, the increasing presence of furred pets (especially cats) indoors has raised the level of exposure to the allergens produced by these animals [11]. For instance, in northern Europe, it has been estimated that 23–34% of schoolchildren own a dog and/or cat [12, 13]. In some areas, 50–70% of children with bronchial asthma are sensitized to domestic animals [14]. A high rate of allergic sensitization to pet allergens has also been found in some cold geographical areas with low humidity [15], where the climate does not favour the growth of mites and cockroaches.

Humans have kept domestic animals for thousands of years, but the level of contact between humans and domestic animals is quite different in urban and rural areas. In urban areas, pets frequently live in small apartments with insulated windows and doors and the frequent presence of upholstered furniture, carpets and/or moquettes. In these conditions, the level of exposure to pet allergens is very high. In contrast, in rural areas, pets usually live outdoors and, consequently, the degree of indoor contamination is less significant. However, in rural communities, the contact between humans and animals and animal products is usually relevant, and children growing up in these environments usually live in close contact with domestic animals from the time of birth. Despite this fact, recent studies carried out in farming communities have shown a decreased prevalence of allergic sensitization to common aeroallergens, including those produced by domestic animals [16–20].

In the last few years, the availability of specific monoclonal antibodies against Fel d 1 has made it possible to study the environmental levels of the allergen in different geographical areas and under different conditions [21].

The determination of sources, aerodynamic characteristics of allergen-carrying particles and particle size distribution of cat allergen in indoor environments (such as private homes, offices, public and working places) is an important help in understanding the mechanism of sensitization and the clinical presentation of asthma in allergic patients. These characteristics are also important to optimize avoidance strategies in order to reduce personal exposure to allergens and the severity of symptoms [22–25].

Characteristics of Cat Allergens

Although the cat produces 7–8 different proteins, only Fel d 1 is able to induce specific IgE production in a high percentage of cat-sensitized patients (about 85–95%) [26]. The physiological function of Fel d 1 is unknown. Some studies suggest that this protein may play a role in the protection of epithelia, in pheromonal regulation or in inter-cat communication [27]. In fact, Carayol et al. [27] demonstrated that the cat face is the main area of Fel d 1 production (about 10 times greater than the chest). A Fel d 1-like molecule has been identified in big cats such as the Siberian tiger, lion, puma and jaguar, suggesting that this molecule may have biological significance [28]. Fel d 1 is a 17-kD heterodimer with two disulphide-linked peptide chains: chain 1 with 70 amino acids and chain 2 with 90–92 amino acids. Under native conditions, two of these heterodimers associate together to form a 33- to 39-kD glycoprotein.

Chain 1 of the Fel d 1 molecule has been suggested as a member of the lipocalin family of proteins, which are characterized by a low molecular weight (about 17–20 kD) [29]. Moreover, one Fel d 1 chain shows approximately 25% homology with rabbit uteroglobin, a mouse salivary protein and human Clara cell protein [30].

Patients sensitized to pets (particularly cats and dogs) frequently display IgE reactivity against allergenic proteins derived from different animals. This finding suggests the possibility of cross-reactions between the common allergenic determinants [31].

Shared IgE epitopes of the major cat and dog allergens may provide an explanation for the frequent clinical observation that respiratory allergies to these two species of animals are often associated [31]. Studies with immunoblotting and RAST inhibition techniques have shown that albumins (66 kD) and proteins of other molecular weights are relevant cross-reactive allergens [26].

Recently, it was demonstrated that the 18-kD form of Fel d 1 is associated with slight enzymatic activity [32].

The main cat allergen is secreted in high amounts since a single animal is able to produce 3–7 µg/day. The quantitatively most important sources of the allergen are the sebaceous, salivary and perianal glands, whereas the skin and the fur are the principal reservoirs [33, 34]. Since Fel d 1 production is under testosterone control, males produce higher quantities than females [35]. However, castration does not induce any change in Fel d 1 concentration on the fur of female cats, and castrated male cats produce Fel d 1 in amounts sufficient to induce respiratory symptoms in sensitized patients [36].

Fel d 1 is characterized by great heat stability; in fact, exposure at 140°C for 60 min resulted in only 30% denaturation of the molecule [37]. Both the cDNA and genomic sequences of Fel d 1 have been determined [29, 38], and studies have been carried out to engineer recombinant Fel d 1 with IgE and IgG antibody binding comparable with that of the natural allergen that could be targeted to antigen-presenting cells. It has been shown that recombinant Fel d 1 can be targeted to antigen-presenting cells through CD64 and that these constructs will facilitate structural studies of Fel d 1 and the development of improved allergy diagnostics and therapeutics [39]. Moreover, certain domains of the molecule might preferentially induce IL-5 rather than IFN-gamma, and as a result, could be more important in respiratory allergy pathogenesis [40].

It has been demonstrated that cat albumin may determine IgE responses in about 20% of subjects sensitized to cat, but only a few patients are sensitive only to this allergen [41].

Recently, a new allergen was identified; it is called cystatin (Fel d 3) and is a member of the cysteine protease inhibitory family [42, 43]. Fel d 3 is able to induce IgE responses in about 10% of patients with cat allergy [42].

Evaluating and Monitoring Cat Allergens in Indoor Environments

The collection of materials containing cat allergens can be carried out by using environmental dust collectors on given surface areas (usually 2 m²) or by using person-carried pumps with filters [44].

In order to simplify the measurement of airborne Fel d 1, Karlsson et al. [45] used the petri dish sampling method to collect the allergen. A comparison between petri dish sampling and personal air sampling was carried out in classrooms with many or few cat owners and pet-free homes. The authors concluded that petri dishes can be considered a useful and reliable sampling method for the assessment of cat allergen exposure.

Recently, O'Meara et al. [46], Graham et al. [47] and Renstrom et al. [48] developed a new method to capture inhaled allergens in domestic or occupational environments. Their intranasal air sampler (Inhalix) collects inhaled particles by impaction on adhesive strips within the samplers [46–48].

Karlsson et al. [49] compared the efficacy of four allergen-sampling methods to assess the level of personal or indirect exposure to cat allergen in homes, schools and

other public buildings and working environments. They showed a lack of correlation between sampling methods used simultaneously, demonstrating the difficulty in assessing allergen levels in these environments. Moreover, the levels of cat allergens may vary according to the sampling season [50]. For instance, it was demonstrated in a north-western US city (Boston) that Fel d 1 peaks in winter and spring. The influence of housing type and cat ownership could explain the seasonal variation of these indoor allergens.

Some important aspects remain to be clarified. For instance, it has yet to be established whether cat allergen concentrations in indoor environments should be more appropriately expressed as micrograms per gram of dust or micrograms per square metre of floor surface [51–53]. Moreover, it has to be established if allergens produced by domestic animals, such as Fel d 1 and Can f 1, should be evaluated/monitored by sampling airborne or settled components, considering the aerodynamic characteristics of allergen-carrying particles [22, 23, 54, 55].

The levels of indoor allergens, in particular those produced by cats, should be periodically monitored to assess the efficacy of avoidance measures; therefore, the devices used for sampling should be simple, effective and cheap in order to encourage patient compliance [44].

The levels of cat allergen (Fel d 1) in domestic and public indoor environments may be determined in dust samples by using specific monoclonal antibodies [56, 57]. Recently, a new strip assay (Dustscreen™, Heska AG, Freiburg, Switzerland) has allowed easy measurement (semiquantitatively or quantitatively) of the concentration of Fel d 1 and other indoor allergens such as those of mite (Der p 1, Der f 1 or Der group 2) and cockroach (Bla g 2) [58]. This new assay is simple to perform under clinical practice conditions and provides the results within 4 h. In contrast, quantitative ELISA assays require specific laboratory tools and expertise and the procedures usually require up to 24 h. Lau et al. [59] demonstrated that quantitative ELISA and semiquantitative Dustscreen™ produced comparable results in evaluating the levels of indoor allergens, including cat allergens.

Another integrated analytical system has recently been developed for easy collection and analysis of dust-associated indoor allergens (wipe test) [60]. The wipe test includes a self-contained immunochemical test and a microporous sampling pin, both packed in a plastic container. The wipe test provides semiquantitative results for dust mite and cat allergens. The wipe test, as compared to the ELISA method, has a sensitivity of 79% and a specificity of 92% for cat allergens [60].

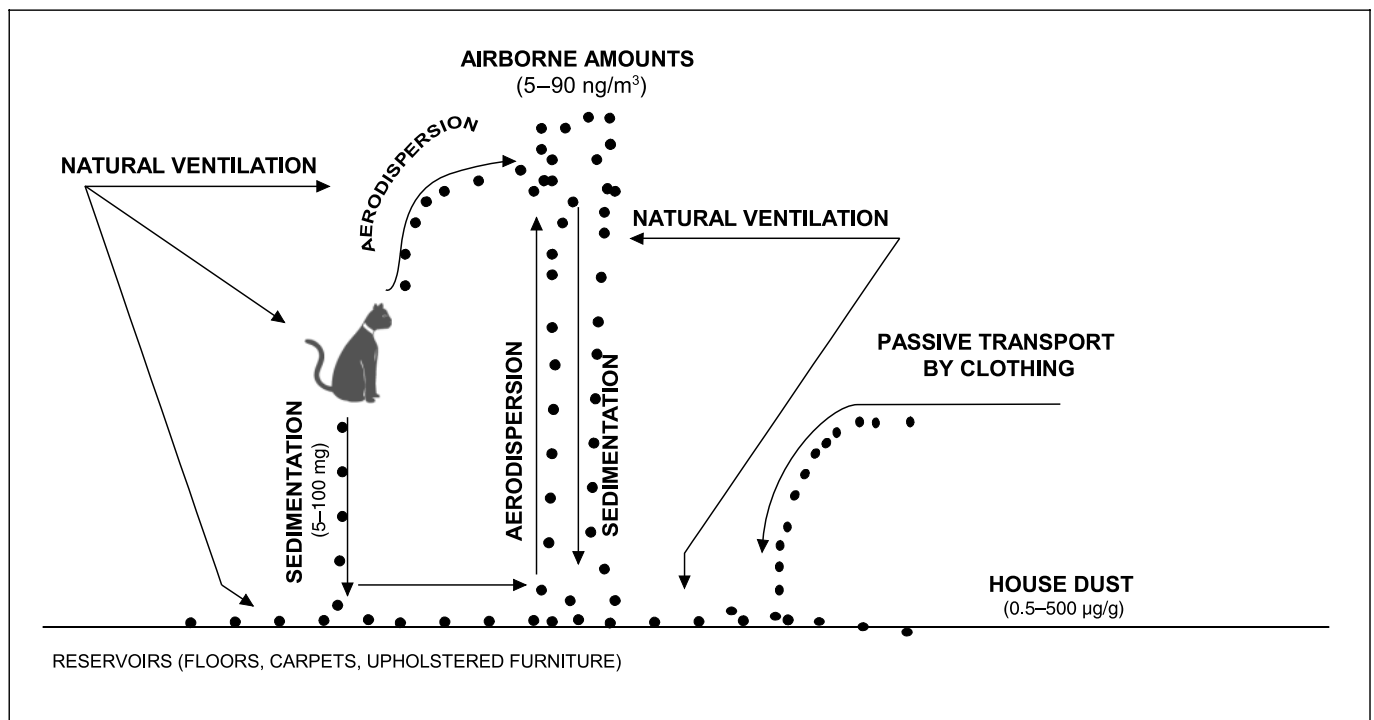


Fig. 1. Dynamic behaviour of cat allergens indoors.

Another method for quantification of airborne cat allergens is the direct sampling on filters in solution method [61]. In this technique, allergens firmly adsorbed to a porous polytetrafluoroethylene filter are reacted with specific antibodies conjugated to alkaline phosphatase complex. The treated filter is subsequently floated on a commercially available chemiluminescent phosphatase substrate solution. This method confirmed the particulate nature of airborne cat allergen.

Recently, Parvaneh et al. [62] compared the efficacy of two low- and high-volume stationary pumps and an ionizer in collecting airborne cat allergen (Fel d 1). Levels of allergens collected by pumps are often below the detection limit of the conventional ELISA [62]; for this reason, many studies have used an amplified ELISA to measure the amount of allergen in the air of indoor environments [63, 64]. Collection with the ionizer device resulted in a more concentrated sample, which could be assayed with an ordinary ELISA [62]. A drawback of the ionizer, as compared to pumps, is that the amount of allergen collected cannot be calculated as nanograms per cubic metre of air, but must be expressed as the total amount per sampling period [62].

Characteristics of Particles Carrying Cat Allergens

Knowledge of the aerodynamic characteristics of the major cat allergen is critical to understand the modality of sensitization to this protein and to design adequate avoidance measures (fig. 1).

Allergens produced by domestic animals such as the cat (Fel d 1) and dog (Can f 1) are carried by large particles of about 10 µm or more in diameter (75% of the total amount) and by small particles <5 µm in diameter (approximately 25%) [65, 66]. These small allergen-carrying particles are light and are thus readily airborne for long periods after minimal disturbance of the indoor environment [65, 66].

Several studies have shown that cat (and dog allergen) levels range between less than 1 µg and more than 3,000 µg/g of dust [41, 65, 66]. In some particular conditions, such as during animal shows, in facilities used for these events, the dog allergen (Can f 1) content can be exceptionally high, up to 2,100,000 ng/g of dust, but it can be reduced by proper cleaning [67].

Analyses carried out on airborne or settled dust have shown that the levels of cat allergens are very high in

homes housing these animals, but significant amounts of these allergens have also been found in the majority of houses where cats have never been kept. The presence of pet allergens indoors also strongly depends upon the geographical area and characteristics of housing and pet ownership. Woodcock et al. [68] studied the levels of cat allergens in houses in Ghana and in the United Kingdom. In the United Kingdom, homes with cats contained much higher allergen levels than did homes with cats in Ghana (mean difference in Fel d 1: 275-fold). In the United Kingdom, houses with cats contained 77 times more Fel d 1 than did houses without cats; there was no difference in cat allergen levels between houses with and without cats in Ghana.

Detailed studies on the distribution, aerodynamic properties and particle size of cat allergen-carrying particles in settled dust and in the air have been carried out by Custovic et al. [65]. In the United Kingdom, the concentrations of the major cat allergen Fel d 1 were much lower in houses without cats than in those with a cat (215- to 314-fold according to the site of sampling). In the homes with cats, the highest levels of Fel d 1 were found in upholstered furniture (range 7.1–6,000 µg/g) and living room carpets (range 2.8–3,000 µg/g). Bedrooms contained lower levels of Fel d 1 in carpets and mattresses [65].

In homes without cats, the highest levels of Fel d 1 were found in upholstered furniture in the living room (range 0.06–61.9 µg/g of dust). Airborne Fel d 1 was detected in all houses with cats; the levels varied from 0.7 to 38 ng/m³ of air. Low concentrations of airborne Fel d 1 (range 0.24–1.78 ng/m³ of air) were also found in 22 of 75 living rooms in houses without a cat [65].

The particle size distribution of airborne Fel d 1 on the stages of the Andersen sampler is similar to that demonstrated for Can f 1. Fel d 1 was mainly associated with large carrying particles (>9 µm in diameter) collected on the first stage of the Andersen sampler, the percentage being about 49% of the total allergen recovered. About 23% of the airborne Fel d 1 was carried on small particles (<4.7 µm in diameter) [65].

An important characteristic of cat dander particles is that these can 'stick' to all available surfaces such as walls, furniture and clothing, with consequent distribution of cat allergens in indoor environments which should be theoretically 'cat free' (houses, schools, means of transport and different public buildings) [63, 69–73]. This indirect exposure to cat allergens in cat-free environments may also be of sufficient magnitude to cause airway sensitization and/or triggering of asthma exacerbation in already sensitized patients [74]. Moreover, exposure to even low

doses of allergen (such as that inhaled during indirect exposure to pet allergen) might increase the degree of non-specific bronchial hyperreactivity [75].

Threshold Levels of Cat Allergens

Studies on the characteristics of cat allergen particles and the possibility of quantifying its amount indoors led to attempts to define the threshold level of allergen that causes airway sensitization and/or asthma exacerbation in susceptible individuals [41, 76, 77] (fig. 2). However, these suggested threshold amounts of cat allergens may vary according to the individual degree of bronchial hyperresponsiveness and the associated exposure, especially in adults, to other non-specific irritants such as tobacco smoke, professional agents and indoor/outdoor chemical pollutants [78]. This is the reason why a direct correlation between exposure to large amounts of indoor allergens, including those produced by domestic cats, and the resultant development of allergic sensitization is generally easy to demonstrate, especially in children. In contrast, a direct relationship between exposure to these allergens and the development of bronchial asthma is still debated [78–80].

A large body of evidence suggests that atopic asthma is more severe in sensitized patients exposed to higher levels of allergens, especially those produced from indoor environments [81–84]. Also, a familial background of atopy may be an important factor facilitating the sensitization process [85].

Studies have tried to determine if unsuspected cat allergen exposure may be of clinical significance [86, 87]. Bollinger et al. [87] challenged patients in an experimental cat exposure facility by using different amounts of cat allergen. It has been demonstrated that airborne levels of Fel d 1 of less than 100 ng/m³ were sufficient to induce nasal and bronchial symptoms and significant changes in lung function. Nevertheless, the suggested levels of cat allergen inducing allergic sensitization in susceptible individuals and asthma exacerbation in already sensitized patients ranged from 1 to 8 µg/g of dust (fig. 2) [11, 73].

'Paradoxical' Effect of Cat Ownership on Allergic Sensitization and Asthma [88]

Studies have consistently shown a direct relationship between exposure to mite allergens and development of allergic sensitization; a strong association has also been

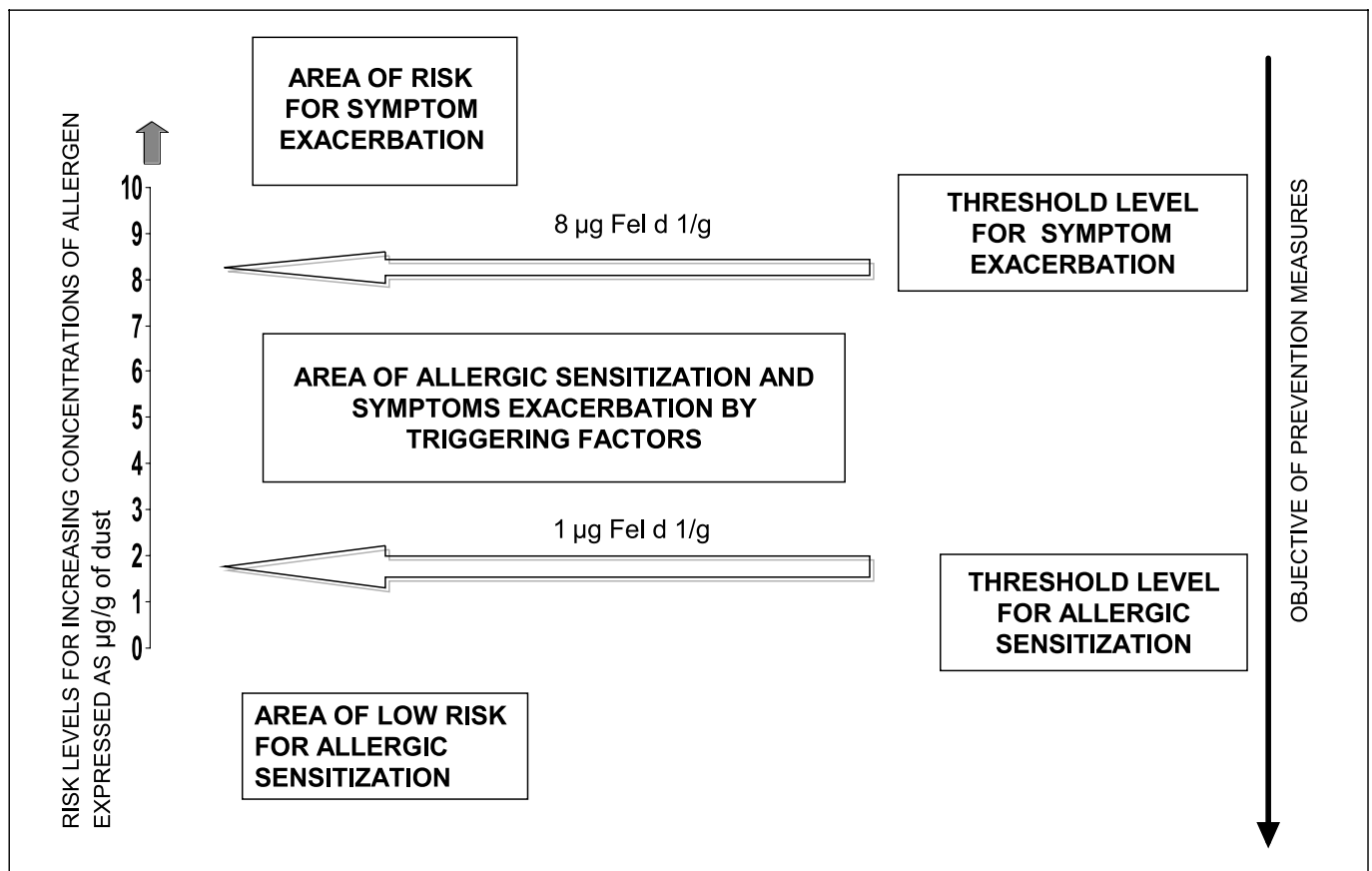


Fig. 2. Risk levels for allergic sensitization and/or symptoms, according to the degree of exposure.

demonstrated between sensitization and asthma [89–92]. In contrast, several reports on farming communities in Europe have shown that early contact with farm animals induces a protective effect on the development of allergic sensitization and bronchial asthma [93]. It has therefore been suggested that this protection might be mediated by high exposure to bacterial endotoxins [94, 95].

Several recent studies have suggested that early exposure of children to allergens derived from domestic animals (especially cats) might induce a lower degree of allergic sensitization to these proteins [96–98]. These results have recently been confirmed also among preteenage children [99]. Other studies have shown that children raised in a house with 2 or more dogs or cats in the first year of life have not only less allergic sensitization to the allergens of these animals but also less sensitization to other common allergens [100]. Anyo et al. [101] demonstrated that pet ownership in the first 2 years of life seemed to offer some protection against sensitization to pollen.

In particular, Platts-Mills et al. [102] demonstrated that a high level of exposure to cat allergens in children is associated with a lower risk of sensitization to cats. In contrast, increasing exposure to mites was associated with increased prevalence of sensitization to mite allergens.

An interpretation of these findings is that higher exposure to cat allergen can determine the production of an IgG and IgG4 antibody response without sensitization or risk of asthma. This modified T helper 2 cell response should be regarded as a form of induced tolerance. These results were confirmed by Custovic et al. [103, 104], who studied the relationship between current exposure to cat allergen and sensitization to cats in a large population of adults. Their results indicate that the prevalence of sensitization to cats was significantly decreased in patients exposed to the lowest and the highest levels of cat allergen. In contrast, the risk of sensitization to cats was significantly increased with medium-level exposure to Fel d 1.

Moreover, one of the studies from Custovic et al. [104] provided further evidence that the proportion of subjects

with skin test results positive to dust mite increases in parallel with the amount of mite allergens (a linear dose-response relationship). Similarly, studies performed in inner-city areas demonstrated that children are more likely to become sensitized to cockroach allergens [105] or to mouse allergens [106] if the exposure to these materials is very high.

This particular relationship between exposure to cat allergens and development of specific sensitization is also confirmed by data from some large epidemiological studies. It has been demonstrated that the prevalence of cat sensitization in countries with high levels of cat ownership (such as Australia and New Zealand) is about 10%; this value is relatively low when compared to the level of sensitization of about 30% for dust mites [107].

It is important to outline that the observed lower risk of wheezing among exposed than among unexposed young children is consistent with a protective effect; however, in large epidemiological studies it could be partially attributed to decisions made by allergic families to get rid of an animal or avoid having a cat or dog [108–110].

Avoidance of Cat Allergens

Conflicting opinions still exist in the literature about the efficacy of prevention strategies to avoid exposure to the allergens of domestic animals, particularly cats.

Although the removal of cats from the domestic environment is usually considered the first-line measure from a clinical point of view, there are no documented reports on the efficacy of cat removal in reducing clinical symptoms in highly sensitized patients. Moreover, many cat-sensitized patients, particularly children, refuse to give up their cats [112]. Other patients, despite the obvious source of their symptoms, are often unwilling to recognize the correlation between cat ownership and clinical symptoms and consequently refuse to remove the cat [113]. Finally, it has been shown that parents of cat-allergic children (about 55%) deny that their child's symptoms are worsened by the cat's presence [114].

These are the reasons why, in the majority of cases, removal of cat allergen must be carried out with the cat in situ. Moreover, even if the cat has been removed from the environment, it is unlikely that cat allergen exposure will be completely abolished. In fact, there is a large body of evidence suggesting that cat allergen may be found in many indoor environments where cats have been removed for long periods.

Intensive avoidance procedures (replacing furniture and blankets, vigorous vacuum cleaning, using air filtration systems) carried out after cat removal can significantly reduce the levels of Fel d 1. However, it is unlikely that cat allergens will be completely removed from a contaminated indoor environment.

Many studies have shown that the majority of domestic environments (and some public places) where a cat has never been kept may contain significant amounts of Fel d 1. Moreover, some clinical data have demonstrated that even the low levels of cat allergens which may be found in indoor environments without cats are able to induce respiratory symptoms in some highly sensitized patients. Data on the paradoxical effect [88] of pet ownership clearly demonstrated that moderate amounts of cat allergen are more likely to be responsible for allergic sensitization than high levels of this allergen. Our group and other colleagues have demonstrated that the clothes of cat owners represent the main source for the dispersal of cat allergens in cat-free environments [72]. These considerations suggest that the removal of cat proteins from the clothes of cat owners may be considered an important approach for the prevention of dispersal of these allergens in animal-free environments.

Against this background, we performed a study to evaluate the efficacy of different methods of cleaning (with and without the use of water) different materials passively contaminated by contact with cats (fig. 3). We demonstrated that Fel d 1 could be completely removed from contaminated cotton webs by simply washing them in water [115]. In this experiment, no detergent was used, to avoid possible chemical modifications of the allergen. Also, we recently evaluated the efficacy of commercial dry cleaning, which represents a very common cleaning modality in industrialized countries, by using the same study design and a different type of material (wool). Dry cleaning was able to remove large amounts of Fel d 1 from contaminated wool fabrics but did not completely abolish cat allergen contamination [116]. Further, Fel d 1 contamination of three control (previously nonexposed) wool rectangles after dry cleaning suggests the possibility that cat allergens can be transferred from other clothes during the dry cleaning process [116].

Further studies are currently in progress to evaluate alternative methods for cleaning pet-exposed materials in order to reach a good balance between efficacy, low costs and minimal damage to fabrics.

It has been suggested that washing cats may be an efficient procedure to remove allergens from their body surface [117]. Unfortunately, the amount of Fel d 1 rapidly

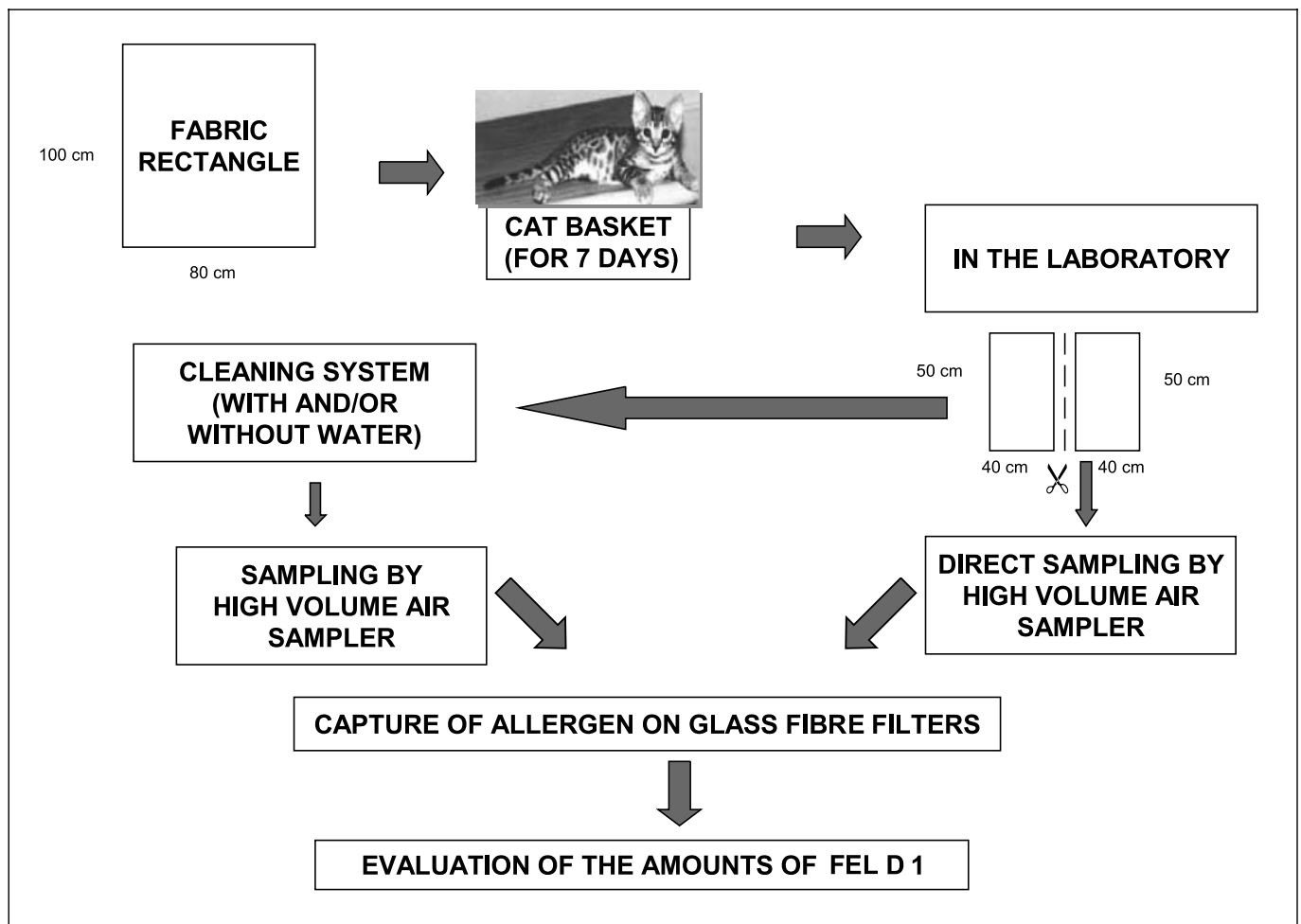


Fig. 3. Experimental model to assess the efficacy of different approaches for removing cat allergen from contaminated materials.

increases after washing and returns to previous levels within a few days. Therefore, in order to achieve a satisfactory reduction of the allergen level, the cat should be washed once, or even better twice a week [118]. It is important to remember that such frequent washing is not feasible because it induces serious dangerous effects on the cat's fur by altering the lipidic film.

The aerodynamic properties of cat allergens justify the use of air filtration systems in indoor environments containing a cat [119–121]. Air cleaners or filters remove significant amounts of airborne Fel d 1, which represents the main risk factor for inducing clinical symptoms in cat-sensitized patients.

The use of a common furniture polish on either the dusty surfaces or the cleaning cloth during dusting was demonstrated to be useful in reducing the dispersal of

both dust mite and cat allergens (Der p 1 and Fel d 1) [122]. Fel d 1 allergen can be successfully removed from hard floors by using electrostatic cloth sweepers, which are now easy to find [123]. A summary of the possible strategies and procedures to reduce exposure to cat allergens is shown in table 1.

Conclusions

The problems associated with allergic sensitization to pet allergens, particularly those of the cat, represent an important field of research in respiratory allergy and have a non-negligible relevance, also from a socioeconomic viewpoint. It is true, in fact, that in principle, complete allergen avoidance should result in complete control of

Table 1. Measures to minimize exposure to cat allergen*Removal of cat(s) from the house*

After removal, it is necessary to vacuum clean and wash all surfaces (including walls) on which Fel d 1 may have accumulated
Carpets and upholstery must be cleaned and bedding must be washed

If patients choose to keep the cat at home

Use a vacuum cleaner equipped with a HEPA filter¹ and double-thickness bags in order to remove pet allergens from reservoirs
Remove carpeting from all environments and replace with linoleum or wood flooring
Wash bedding in water weekly
Cats should be washed twice weekly to obtain a significant reduction of Fel d 1 shedding
Cat beds must also be washed
Cat must be kept outdoors as much as possible and must not enter bedrooms and living rooms
The indoor environment must be naturally ventilated
Washing (water or dry cleaning) the clothes of cat owners and avoiding the use of allergen-contaminated clothes outdoors prevent the dispersal of Fel d 1²
The use of Allerpet/C® (Allerpet Inc., New York, USA) applied directly on the animal to remove allergens has provided controversial results

¹ Polyethylene filters may be used in alternative to high-efficiency particulate air (HEPA) ones [124].

² Detergent solutions at 25 °C for at least 5 min can extract most of the cat allergen from bedding [125].

symptoms, but it is also true that (for both practical and affective reasons) complete avoidance is seldom feasible. Therefore, it is important to define (1) what are the exposure risk levels, and (2) what are the most effective measures for controlling exposure.

Several questions are still unanswered, especially as far as characteristics of airway sensitization to cat allergens are concerned. This problem needs to be solved in particular during the first months of life. In contrast, we acknowledge an increasing awareness of the necessity to protect domestic animals in the general population worldwide with the increase in ownership of furred pets.

Unfortunately, the increasing presence of furred pets indoors in many industrialized countries is associated with an increasing rate of allergic sensitization to allergens, including those produced by domestic cats.

It is likely that keeping domestic animals in relatively small and insulated homes in urban areas increases the rate of exposure to their allergens in comparison with rural areas, where the animals usually live outdoors and only on some occasions enter indoors.

In the next few years, further studies are necessary to try to modulate the exposure to cat allergens so that pet ownership does not constitute, in general, a risk factor for public health.

References

- Duffy DL, Mitchell C, Martin C: Genetic and environmental factors for asthma. *Am J Respir Crit Care Med* 1998;157:840–845.
- Steenenbergh PA, Van Amsterdam JGC, Vandebriel BJ, Vos JG, Van Bree L, Van Loveren H: Environmental and lifestyle factors may act in concert to increase the prevalence of respiratory allergy including asthma. *Clin Exp Allergy* 1999;29:1304–1308.
- Platts-Mills TAE, Thomas WR, Aalberse RC, Chapman MD: Indoor allergens and asthma. Report of the Third International Workshop. *J Allergy Clin Immunol* 1997;100:S1–S24.
- Hirsch T, Hering M, Burkner K, Hirsch D, Leupold W, Kerkmann ML, Kuhlisch E, Jatzwauk L: House dust mite allergen concentrations (*Der f 1*) and mold spores in apartment bedrooms before and after installation of insulated windows and central heating systems. *Allergy* 2000;55:79–83.
- Harrison PTC: Creature comforts – living with mites and moulds. *Clin Exp Allergy* 1999;29:148–149.
- Hirsch T: Indoor allergen exposure in West and East Germany – a cause for different prevalences of asthma and atopy? *Rev Environ Health* 1999;14:159–168.
- Woods JE, Arora S: Indoor air quality. Engineering considerations. *Immunol Clin North Am* 1994;14:495–519.
- Schoenwetter WF: Building a healthy house. *Ann Allergy Asthma Immunol* 1997;79:1–4.
- Woods JE: Control of indoor air quality. An engineering perspective; in Bardana EJ, Montanaro A (eds): *Indoor-Air Pollution and health*. New York, Marcel Dekker, 1997, pp 285–301.
- Bush RK, Wood RA, Eggleston P: Laboratory animal allergy. *J Allergy Clin Immunol* 1998;102:99–112.
- Woodfolk JA, Luczynska CH, De Blay F, Chapman MD, Platts-Mills TAE: Cat allergen. *Ann Allergy* 1992;69:73–75.
- Aberg N, Hasselmar B, Aberg B, Eriksson B: Increase of asthma, allergic rhinitis, and eczema in Swedish schoolchildren between 1979–1991. *Clin Exp Allergy* 1995;25:815–819.
- Ronmark E, Lundback B, Jonsson E, Platts-Mills TAE: Asthma, type 1 allergy and related conditions in 7- and 8-year-old children in Northern Sweden: Prevalence rates and risk factor pattern. *Respir Med* 1998;92:316–324.
- Croner S, Kjellman NIM: Natural history of bronchial asthma in childhood – a prospective study from birth to 14 years of age. *Allergy* 1992;47:150–157.
- Ingram JM, Sporik R, Rose G, Honsinger R, Chapman MD, Platts-Mills TA: Quantitative assessment of exposure to dog (*Can f 1*) and cat (*Fel d 1*) allergens: Relation to sensitization and asthma among children living in Los Alamos, New Mexico. *J Allergy Clin Immunol* 1995;96:449–456.
- Braun-Fahrlander C, Gassner M, Grize L, Neu U, Sennhauser FH, Varonier HS, Vuille JC, Wuthrich B: Prevalence of hay fever and allergic sensitization in farmer's children and their peers living in the same rural community. SCARPOL team. Swiss Study on Childhood Allergy and Respiratory Symptoms with Respect to Air Pollution. *Clin Exp Allergy* 1999;29:28–34.
- Riedler J, Eder W, Oberfeld G, Schreiner M: Austrian children living on a farm have less hay fever, asthma and allergic sensitization. *Clin Exp Allergy* 2000;30:194–200.

- 18 Leynaert B, Neukirch C, Jarvis D, Chinn S, Burney P, Neukirch F: Does living on a farm during childhood protect against asthma, allergic rhinitis, and atopy in adulthood? *Am J Respir Crit Care Med* 2001;164:1829–1834.
- 19 Kauffmann F, Oryszczyn MP, Maccario J: The protective role of country living on skin prick tests, immunoglobulin E and asthma in adults from the epidemiological study on the genetics and environment of asthma, bronchial hyper-responsiveness and atopy. *Clin Exp Allergy* 2002;32:379–386.
- 20 Portengen L, Sigsgaard T, Omland O, Hjort C, Heederik D, Doekes G: Low prevalence of atopy in young Danish farmers and farming students born and raised on a farm. *Clin Exp Allergy* 2002;32:247–253.
- 21 Chapman MD: Environmental allergen monitoring and control. *Allergy* 1998;53:48–53.
- 22 Custovic A, Simpson A, Chapman MD, Woodcock A: Allergen avoidance in the treatment of asthma and atopic disorders. *Thorax* 1998;53:63–72.
- 23 Custovic A, Simpson B, Simpson A, Hallam C, Craven M, Woodcock A: Relationship between mite, cat, and dog allergens in reservoir dust and ambient air. *Allergy* 1999;55:612–616.
- 24 Liccardi G, Custovic A, Cazzola M, Russo M, D'Amato G, D'Amato M: Avoidance of allergens and air pollutants in respiratory allergy. *Allergy* 2001;56:705–722.
- 25 Liccardi G, D'Amato G: Indoor prevention of respiratory allergy. *Eur Respir Monogr* 2002;21:226–240.
- 26 Ohman JL Jr, Lowell FC, Bloch KJ, Kendall S: Allergens of mammalian origin V. Properties of extracts derived from the domestic cat. *Clin Allergy* 1976;6:419–428.
- 27 Carayol N, Birnbaum J, Magnan A: *Fel d 1* production in the skin varies according to anatomical areas. *Allergy* 2000;55:570–573.
- 28 De Groot H, Van Swieten P, Aalberse RC: Evidence for a *Fel d 1*-like molecule in the 'big cats' (*Felidae* species). *J Allergy Clin Immunol* 1990;86:107–116.
- 29 Morgenstern JP, Griffith I, Brauer AW, Rogers BL, Bond JF, Chapman MD: Amino acid sequence of *Fel d 1*, the major allergen of the domestic cat: Protein sequence analysis and cDNA cloning. *Proc Natl Acad Sci USA* 1991;88:9690–9694.
- 30 Karn RC: The mouse salivary androgen-binding protein (ABP) alpha subunit closely resembles chain 1 of the cat allergen *Fel d 1*. *Biochem Genet* 1994;32:271–277.
- 31 Spitzauer S, Pandajaitan B, Muhl S, Ebner C, Kraft D, Valenta R, Rumpold H: Major cat and dog allergens share IgE epitopes. *J Allergy Clin Immunol* 1997;99:100–106.
- 32 Ring PC, Wan H, Schou C, Kroll Kristensen A, Roepstorff P, Robinson C: The 18 kDa form of cat allergen *Felis domesticus* 1 (*Fel d 1*) is associated with a gelatin-and-fibronectin-degrading activity. *Clin Exp Allergy* 2000;30:1985–1996.
- 33 Mata P, Charpin P, Charpin C, Luciani P, Vervloet D: *Fel d 1* allergen: Skin or saliva? *Ann Allergy* 1992;69:321–322.
- 34 Dornelas de Andrade A, Birnbaum J, Magalon C, Lauteaume A, Charpin D, Vervloet D: *Fel d 1* levels in cat anal glands. *Clin Exp Allergy* 1996;26:178–180.
- 35 Zielonka TM, Charpin D, Barbis P, Luciani P, Casanova D, Vervloet D: Effects of castration and testosterone on *Fel d 1* production by sebaceous glands of male cats. I. Immunological assessment. *Clin Exp Allergy* 1994;24:1169–1173.
- 36 Miller JD, Bell JB, Vaudernoot D: Castration of pets does not prevent allergy to pets. *Clin Exp Allergy* 1995;25:574–575.
- 37 Cain G, Elderfield AJ, Green R, Smillie FI, Chapman MD, Custovic A, Woodcock A: The effect of dry heat on mite, cat and dog allergens. *Allergy* 1998;53:1213–1215.
- 38 Griffith IJ, Craig S, Pollock J, Yu XB, Morgenstern JP, Rogers BL: Expression and genomic structure of the gene encoding Fd1, the major allergen from the domestic cat. *Gene* 1992;113:263–268.
- 39 Vailes LD, Sun AW, Ichikawa K, Wu Z, Sulahian TH, Chapman MD, Guyre PM: High-level expression of immunoreactive recombinant cat allergen (*Fel d 1*): Targeting to antigen-presenting cells. *J Allergy Clin Immunol* 2002;110:757–762.
- 40 Haselden BM, Syrigou E, Jones M, Huston D, Ichikawa K, Chapman MD, Kay AB, Larche M: Proliferation and release of IL-5 and IFN-gamma by peripheral blood mononuclear cells from cat-allergic asthmatics and rhinitics, non-cat-allergic asthmatics, and normal controls to peptides derived from *Fel d 1* chain 1. *J Allergy Clin Immunol* 2001;108:349–356.
- 41 Chapman MD, Wood RA: The role and remediation of animal allergens in allergic diseases. *J Allergy Clin Immunol* 2001;107:S414–S421.
- 42 Ichikawa K, Vailes LD, Pomes A, Chapman MD: Identification of a novel cat allergen – cystatin. *Int Arch Allergy Immunol* 2001;124:55–56.
- 43 Ichikawa K, Vailes LD, Pomes A, Chapman MD: Molecular cloning, expression and modeling of cat allergen, cystatin (*Fel d 3*), a cysteine protease inhibitor. *Clin Exp Allergy* 2001;31:1279–1286.
- 44 Liccardi G, Russo M, Barber D, Califano C, Parmiani S, D'Amato M, D'Amato G: Cat allergen sampling by a new personal collector (Partrap FA 52). *J Invest Allergol Clin Immunol* 2000;10:204–208.
- 45 Karlsson AS, Hedren M, Almqvist C, Larsson K, Renstrom A: Evaluation of petri dish sampling for assessment of cat allergen in airborne dust. *Allergy* 2002;57:164–168.
- 46 O'Meara T, De Lucca S, Sporik R, Graham A, Tovey ER: Detection of inhaled cat allergen. *Lancet* 1998;351:1488–1489.
- 47 Graham JA, Pavlicek PK, Sercombe JK, Xavier ML, Tovey ER: The nasal air sampler: A device for sampling inhaled aeroallergens. *Ann Allergy Asthma Immunol* 2000;84:599–604.
- 48 Renstrom A, Karlsson AS, Tovey ER: Nasal air sampling used for the assessment of occupational allergen exposure and the efficacy of respiratory protection. *Clin Exp Allergy* 2002;32:1769–1775.
- 49 Karlsson AS, Renstrom AS, Hedren M, Larsson K: Comparison of four allergen-sampling methods in conventional and allergy prevention classrooms. *Clin Exp Allergy* 2002;32:1776–1781.
- 50 Chen GL, Higgings KM, Gold DR, Muilenberg ML, Burge HA: Monthly measurements of indoor allergens and the influence of housing type in a northeastern US city. *Allergy* 1999;54:1058–1066.
- 51 Dreborg S, Einarsson R, Lau S, Munir AKM, Wahn U: Dust sampling for determination of allergen content. *Allergy* 1995;50:188–189.
- 52 Dreborg S: Mite allergens. Collections, determination, expression of results, and risk levels for sensitization and symptom induction. *Allergy* 1998;53(suppl 48):88–91.
- 53 Liccardi G, Cazzola M, D'Amato M, D'Amato G: Pets and cockroaches – two increasing causes of respiratory allergy in indoor environments. Characteristics of airways sensitization and prevention strategies. *Respir Med* 2000;94:1109–1118.
- 54 Liccardi G, Cazzola M, Russo M, Gilder JA, D'Amato M, D'Amato G: Mechanisms and characteristics of airway sensitization to indoor allergens. *Monaldi Arch Chest Dis* 2001;56:55–63.
- 55 Colloff MJ, Ayres J, Carswell F, Howarth PH, Merrett TG, Mitchell EB, Walshaw MJ, Warner JO, Warner JA, Woodcock AA: The control of allergens of dust mites and domestic pets: A position paper. *Clin Exp Allergy* 1992;22(suppl 2):1–28.
- 56 Bollinger ME, Wood RA, Chen P, Eggleston PA: Measurement of cat-allergen level in the home by use of an amplified ELISA. *J Allergy Clin Immunol* 1998;101:124–125.
- 57 Luczynska CM, Li Y, Chapman MD, Platts-Mills TAE: Airborne concentrations and particle size distribution of allergens 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;141:361–367.
- 58 de Weck AL, Derer M, Morrison-Smith G, Stadler BM, Walliser M: Dustscreen™. A new assay for simultaneous determination of multiple allergens in house dust. *Allergy Clin Immunol Int* 1998;10:133–140.
- 59 Lau S, Schulz G, Sommerfeld C, Wahn U: Comparison of quantitative ELISA and semi-quantitative Dustscreen™ for determination of *Der p 1*, *Der f 1* and *Fel d 1* in domestic dust samples. *Allergy* 2001;56:993–995.
- 60 Polzius R, Wuske T, Mahn J: Wipe test for the detection of indoor allergens. *Allergy* 2002;57:143–145.
- 61 Holmquist L, Vesterberg O: Direct on air sampling filter quantification of cat allergen. *J Biochem Biophys Methods* 2002;51:17–25.
- 62 Parvaneh S, Ahlf E, Elfman LHM, Nybom R, Elfman LH, van Hage-Hamsten M: A new method for collecting airborne allergens. *Allergy* 2000;55:1148–1154.

- 63 Almqvist C, Larsson PH, Egmar AC, Hedren M, Malmberg P, Wickman M: School as a risk environment for children allergic to cats and a site for transfer of cat allergen to homes. *J Allergy Clin Immunol* 1999;103:1012–1017.
- 64 Wickman M, Egmar AC, Emenius G, Almqvist C, Berglund N, Larsson P, Van Hage-Hamsten M: *Fel d 1* and *Can f 1* in settled dust and airborne *Fel d 1* in allergen avoidance day-care centres for atopic children in relation to number of pet owners, ventilation and general cleaning. *Clin Exp Allergy* 1999;29:626–632.
- 65 Custovic A, Simpson A, Pahdi H, Green RM, Chapman MD, Woodcock A: Distribution, aerodynamic characteristics and removal of the major cat allergen *Fel d 1* in British homes. *Thorax* 1998;53:33–38.
- 66 Custovic A, Green R, Fletcher A: Aerodynamic properties of the major dog allergen *Can f 1* – distribution in homes, concentration and particle size of allergen in the air. *Am J Respir Crit Care Med* 1997;155:94–98.
- 67 Mussalo-Rauhamaa, Reijula K, Malmberg M, Makinen-Kiljunen S, Lapinlampi T: Dog allergen in indoor air and dust during dog shows. *Allergy* 2001;56: 878–882.
- 68 Woodcock A, Addo-Yobo EOD, Taggart SCO, Craven M, Custovic A: Pet allergen levels in homes in Ghana and the United Kingdom. *J Allergy Clin Immunol* 2001;108:463–465.
- 69 Wood RA, Laheri AN, Eggleston PA: The aerodynamic characteristics of cat allergen. *Clin Exp Allergy* 1993;23:733–739.
- 70 Wood RA, Mudd KE, Eggleston PA: The distribution of cat and dust mite allergens on wall surfaces. *J Allergy Clin Immunol* 1992;89:126–130.
- 71 De Lucca S, O'Meara TJ, Tovey ER: Exposure to mite and cat allergens on a range of clothing items at home and the transfer of cat allergen in the workplace. *J Allergy Clin Immunol* 2000;106:874–879.
- 72 D'Amato G, Liccardi G, Russo M, Barber D, D'Amato M, Carreira J: Clothing is a carrier of cat allergens. *J Allergy Clin Immunol* 1997;99: 577–578.
- 73 Neal JS, Arlian LG, Morgan MS: Relationship among house dust mites, *Der p 1*, *Fel d 1* and *Can f 1* on clothing and automobile seats with respect to densities in houses. *Ann Allergy Asthma Immunol* 2002;88:410–415.
- 74 Munir AKM, Einarsson R, Shou C, Dreborg S: 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* 1993;91: 1067–1074.
- 75 Ihre E, Zetterstrom O: Increase in non-specific bronchial responsiveness after repeated inhalation of low dose of allergen. *Clin Exp Allergy* 1993;23:298–305.
- 76 Platts-Mills TAE, Chapman MD: Dust mites: Immunology, allergic disease and environmental control. *J Allergy Clin Immunol* 1987;80: 755–775.
- 77 Platts-Mills TAE: Indoor allergens; in Middleton E Jr, Reed CE, Ellis EF, Adkinson NF Jr, Yunginger JW, Busse WW (eds): *Allergy: Principles and Practice*. St. Louis, Mosby Year Book 1998, pp 393–403.
- 78 Platts-Mills TAE, Sporik RB, Wheatley L, Heymann PW: Is there a dose-response relationship between exposure to indoor allergens and symptoms of asthma? *J Allergy Clin Immunol* 1995;96:435–440.
- 79 Sporik R, Squillace SP, Ingram JM, Rakes G, Honsinger RW, Platts-Mills TA: Mite, cat and cockroach exposure, allergen sensitization and asthma in children: A case-control study of three schools. *Thorax* 1999;55:675–680.
- 80 Lau S, Illi S, Sommerfeld C, Niggemann B, Bergmann R, von Mutius E, Wahn U: Early exposure to house dust mite and cat allergens and development of childhood asthma: A cohort study. Multicentre Allergy Study Group. *Lancet* 2000;356:1392–1397.
- 81 Custovic A, Taggart SCO, Francis HC, Chapman MD, Woodcock A: Exposure to house dust mite allergens and the clinical activity of asthma. *J Allergy Clin Immunol* 1996;98:64–72.
- 82 Peat JK, Tovey E, Mellis CN, Woolcock AJ: Asthma severity and morbidity in a population sample of Sydney schoolchildren. II. Importance of house dust mite allergens. *Aust NZ J Med* 1994;24:270–276.
- 83 Sporik R, Platts-Mills TAE, Cogswell JJ: Exposure to house dust mite allergen of children admitted to hospital with asthma. *Clin Exp Allergy* 1993;23:740–746.
- 84 Tunnicliffe W, Fletcher T, Hammond K, Roberts K, Custovic A, Simpson A, Woodcock A, Ayres JG: Sensitivity and exposure to indoor allergens in subjects with differing asthma severity. *Eur Respir J* 1999;13:654–659.
- 85 Von Mutius E: The environmental predictors of allergic disease. *J Allergy Clin Immunol* 2000;105:9–19.
- 86 Dreborg S: Impact of allergen exposure on bronchial hyperreactivity. *Pediatr Allergy Immunol* 1996;7(9 suppl):14–17.
- 87 Bollinger ME, Eggleston PA, Wood RA: Cat antigen in homes with and without cats may induce allergic symptoms. *J Allergy Clin Immunol* 1996;97:907–914.
- 88 Platts-Mills TAE: Paradoxical effect of domestic animals on asthma and allergic sensitization (editorial). *JAMA* 2002;288:1012–1014.
- 89 Sporik R, Holgate ST, Platts-Mills TAE, Cogswell JJ: Exposure to house dust mite allergen (*Der p 1*) and the development of asthma in childhood: A prospective study. *N Engl J Med* 1990;323:502–507.
- 90 Squillace SP, Sporik R, Rakes G, Couture N, Lawrence A, Merriam S, Zhang J, Platts-Mills AE: Sensitization to dust mites as a dominant risk factor for adolescent asthma among adolescents living in central Virginia: Multiple regression analysis of a population-based study. *Am J Respir Crit Care Med* 1997;156:1760–1764.
- 91 Peat JK, Tovey ER, Millis CM, Leeder SR, Woolcock AJ: Importance of house dust mite and *Alternaria* allergens in childhood asthma: An epidemiological study of two climatic regions of Australia. *Clin Exp Allergy* 1995;23: 812–820.
- 92 Peat JK, Tovey ER, Toelle BG, Haby MM, Gray EJ, Mahmic A, Woolcock AJ: House dust mite allergens. A major risk factor for childhood asthma in Australia. *Am J Respir Crit Care Med* 1996;153:141–144.
- 93 Riedler J, Braun-Fahrlander C, Eder W, Schreuer M, Waser M, Maisch S, Carr D, Schierl R, Nowak D, von Mutius E; ALEX Study Team: Exposure to farming in early life and development of asthma and allergy: A cross-sectional survey. *Lancet* 2001;358: 1129–1133.
- 94 Liu AH, Lerner DYM: Modulating the early allergic response with endotoxin. *Clin Exp Allergy* 2000;30:1538–1539.
- 95 Von Mutius E, Braun-Fahrlander C, Schierl R, Riedler J, Ehlermann S, Maisch S, Waser M, Nowak D: Exposure to endotoxin or other bacterial components might protect against the development of atopy. *Clin Exp Allergy* 2000;30:1230–1234.
- 96 Hasselmar B, Aberg N, Aberg B, Eriksson B, Bjorksten B: Does early exposure to cat and dog protect against later allergy development? *Clin Exp Allergy* 1999;29:611–617.
- 97 Svanes C, Jarvis D, Chinn S, Burney P: Childhood environment and adult atopy – results from the European Community Respiratory Health Survey. *J Allergy Clin Immunol* 1999; 103:415–420.
- 98 Nafstad P, Magnus P, Gaarder PI, Jaakkola JJ: Exposure to pets and atopy-related diseases in the first 4 years of life. *Allergy* 2001; 56:267–269.
- 99 Perzanowski MN, Ronmark E, Platts-Mills TAE, Lundback B: Effect of cat and dog ownership on sensitization and development of asthma among preteenage children. *Am J Respir Crit Care Med* 2002;166:696–702.
- 100 Ownby DR, Johnson CC, Peterson EL: Exposure to dogs and cats in the first year of life and risk of allergic sensitization at 6 to 7 years of age. *JAMA* 2002;288:963–972.
- 101 Anyo G, Brunekreef B, de Meer G, Aarts F, Janssen NAH, van Vliet P: Early, current and past pet ownership: Associations with sensitization, bronchial responsiveness and allergic symptoms in school children. *Clin Exp Allergy* 2002;32:361–366.
- 102 Platts-Mills T, Vaughan J, Squillace S, Woodfolk J, Sporik R: Sensitization, asthma, and a modified Th2 response in children exposed to cat allergen: A population-based cross-sectional study. *Lancet* 2001;357:752–756.
- 103 Custovic A, Hallam CL, Simpson BM, Craven M, Simpson A, Woodcock A: Decreased prevalence of sensitization to cats with high exposure to cat allergen. *J Allergy Clin Immunol* 2001;108:537–539.

- 104 Custovic A, Simpson BM, Simpson A, Hallam CL, Marolia H, Walsh D, Campbell J, Woodcock A; National Asthma Campaign Manchester Asthma and Allergy Study Group: Current mite, cat and dog allergen exposure, pet ownership, and sensitization to inhalant allergens in adults. *J Allergy Clin Immunol* 2003;111:402–407.
- 105 Huss K, Adkinson NF Jr, Eggleston PA, Dawson C, Van Matta ML, Hamilton RG: House dust mite and cockroach exposure are strong risk factors for positive allergy skin test responses in the Children Asthma Management Program. *J Allergy Clin Immunol* 2001;107:48–54.
- 106 Phipatanakul W, Eggleston PA, Wright EC, Wood RA: Mouse allergen. II. The relationship of mouse allergen exposure to mouse sensitization and asthma morbidity in inner-city children with asthma. *J Allergy Clin Immunol* 2000;106:1075–1080.
- 107 Roost HP, Kunzli N, Schindler C, Jarvis D, Chinn S, Perruchoud AP, Ackermann-Lieblich U, Burney P, Wuthrich B: Role of current and childhood exposure to cat and atopic sensitization. *J Allergy Clin Immunol* 1999;104:941–947.
- 108 Apelberg BJ, Aoki Y, Jaakkola JJK: Systematic review: Exposure to pets and risk of asthma-like symptoms. *J Allergy Clin Immunol* 2001;107:455–460.
- 109 Remes ST, Castro-Rodriguez JA, Holberg CJ, Martinez FD, Wright AL: Dog exposure in infancy decreases the subsequent risk of frequent wheeze but not of atopy. *J Allergy Clin Immunol* 2001;108:509–515.
- 110 Celedon JC, Litonjua AA, Ryan L, Platts-Mills TAE, Weiss ST, Gold DR: Exposure to cat allergen, maternal history of asthma, and wheezing in first 5 years of life. *Lancet* 2002;360:781–782.
- 111 Marks GB: What should we tell allergic families about pets? *J Allergy Clin Immunol* 2001;108:500–502.
- 112 Coren S: Allergic patients do not comply with doctor's advice to stop owning pets. *BMJ* 1997;314:517.
- 113 Purohit A, de Blay F: Cat allergen eviction with the cat in situ – is it worthwhile? *Allergy Clin Immunol Int* 1999;11:207–211.
- 114 Herring S, McGeady SJ, Jones JD, Mansmann HC Jr: The maintenance of pets in allergic families. I. A survey of health beliefs. *Ann Allergy* 1981;46:24–29.
- 115 Liccardi G, Russo M, Barber D, Carreira J, D'Amato M, D'Amato G: Washing the clothes of cat owners is a simple method to prevent cat allergen dispersal. *J Allergy Clin Immunol* 1998;102:143–144.
- 116 Liccardi G, Russo M, Barber D, Gilder JA, Di Penna F, Parmiani S, D'Amato M, D'Amato G: Efficacy of dry-cleaning in removing *Fel d 1* allergen from wool fabric exposed to cats. *Ann Allergy Asthma Immunol* 2002;88:301–305.
- 117 Avner DB, Perzanowski MS, Platts-Mills TAE, Woodfolk JA: Evaluation of different techniques for washing cats. Quantification of allergen removed from the cat and the effect on airborne *Fel d 1*. *J Allergy Clin Immunol* 1997;100:307–312.
- 118 Hodson T, Custovic A, Simpson A, Chapman M, Woodcock A, Green R: Washing the dog reduces dog allergen levels, but the dog needs to be washed twice a week. *J Allergy Clin Immunol* 1999;103:581–585.
- 119 Green R, Simpson A, Custovic A, Faragher B, Chapman M, Woodcock A: The effect of air filtration on airborne dog allergen. *Allergy* 1999;54:484–488.
- 120 Wood RA, Johnson EF, Van Natta ML, Chen PH, Eggleston P: A placebo-controlled trial of a HEPA air cleaner in treatment of cat allergy. *Am J Respir Crit Care Med* 1998;158:115–120.
- 121 Van Der Heide S, Van Aalderen WMC, Kauffman HF, Dubois AE, de Monchy JG: Clinical effects of air cleaners in homes of asthmatic children sensitized to pet allergens. *J Allergy Clin Immunol* 1999;104:447–451.
- 122 Jerrim KL, Whitmore LF, Hughes JF, McKechnie MT: Airborne dust and allergen generation during dusting with and without spray polish. *J Allergy Clin Immunol* 2002;109:63–67.
- 123 Taylor DJM, Battucci S, Brown LK, Counts JL, Tovey ER: Allergen removal from hard floors – assessment of a range of sweeping devices. *J Allergy Clin Immunol* 2002;109:716–717.
- 124 Vicentini L, Peroni D, Miraglia Del Giudice M Jr, Mazzi P, Bodini A, Piacentini GL: Comparison of vacuum cleaners. *Allergy* 2002;57:555.
- 125 Tovey ER, Taylor DJ, Mitakakis TZ, De Lucca S: Effectiveness of laundry washing agents and conditions in the removal of cat and dust mite allergen from bedding dust. *J Allergy Clin Immunol* 2001;108:369–374.