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Can the presence of cat/dog at home be considered the only criterion of exposure to cat/dog allergens? A likely underestimated bias in clinical practice and in large epidemiological studies

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Key words
Allergen exposure; allergic rhinitis; allergic sensitization; bronchial asthma; cat, dog, cat/dog allergy, hypersensitivity; pet

Summary
An important aspect of allergic sensitization to furry animals is the association of dog and cat exposure in early childhood with the incidence of respective allergies later in life. This topic is very controversial, because some authors have found a “facilitating” effect, while others have noticed a “protective” or even no significant effect in individuals living in urban areas. It is likely that some biases could be responsible of these contradictory findings. Cat/dog ownership or their presence in indoor environments are considered usually the main criteria to assess the exposure to these pets in studies’ questionnaires. Even in clinical practice “are there animals at home?” is the common query usually done when collecting anamnestic data. In our opinion, these commonly used questions should not be considered the main index of exposure to pet allergens, because they can lead to erroneous interpretation of the clinical significance of positive skin prick tests for pet allergens as well as of the real risk of exposure to allergens of dog/cat in epidemiological studies. Consequently, we suggest a new, more realistic, classification of modalities of exposure to pet allergens in “real life” based on five possible conditions.

Although domestic animals have been kept in our homes for thousands of years, the last one hundred years have seen two major developments: firstly, the combination of clean water, shoes, separation from animals, and helminth eradication that we refer to as hygiene, and secondly, the lifestyle changes associated with overheated, airtight homes and indoor sedentary entertainment. The result has been a dramatic increase in immediate hypersensitivity to indoor allergens including those of common pets (1).

Exposure to animal allergens constitutes a relevant risk factor for the development of allergic sensitization and respiratory allergic diseases, such as asthma and rhino-conjunctivitis in susceptible individuals (2,3). Cats and dogs are the most common pets living indoor environments and the frequency of their ownership is highly variable in Europe ranging from 7.2 to 35% for the cats and from 5.4 to 35% for the dogs (4). The prevalence of allergic sensitization to cats/dogs varies in different countries according to cultural differences, environmental factors and rate of pet ownership.

An important aspect of allergic sensitization to furry animals is the association of dog and cat exposure in early childhood with the incidence of respective allergies later in life. This topic is very controversial because some authors have found a “facilitating” while others have noticed a “protective” or even no significant effect in individuals living in urban areas (5-16). On the contrary, it is widely recognized that early exposure to animals,
especially cattle, in the farms may induce a “protective” effect on development of respiratory allergy later in life (17,18). It is likely that some biases could be responsible of these contradictory findings. Recent studies suggested that the seemingly protective effect of pet exposure might be a result of a “healthy pet keeping effect” or a “selective avoidance” because parents with asthmatic diseases tend to keep their child from being exposed to cats/dogs to avoid a possible allergic sensitization (19,20).

In our opinion, a serious and underestimated limitation to the conclusions of these particular studies should be acknowledged. Cat/dog ownership or their presence in indoor environments is usually considered the main criteria to assess the exposure to these pets in study questionnaires. Even in clinical practice, “are there animals at home?” is the common query usually done when collecting anamnestic data.

These commonly used questions should not be considered the main index of exposure to pet allergens and, consequently, the main risk factor for allergic sensitization either in clinical practice or in large epidemiological studies.

Dynamic distribution of the main pet allergens indoors is complex, depending on production, aero-dispersion, sedimentation and passive transport through clothes and other items. These variables determine a diffuse presence of pet allergens (indirect exposure) also in indoor environments without pets and in those where pets are no longer present for a long time (e.g. voluntary removal or re-location, natural death etc.) (21). The higher is the frequency of pet ownership in a given community the higher will be the degree of pet allergen contamination of pet-free private homes (22). In this context, also in some public places (schools, day care centres, means of transport etc.), passive transfer constitutes the exclusive modality of common pet or other animal allergens contamination (23-25). Finally, several studies have shown that amounts of pet allergens passively transferred in pet-free environments are of sufficient magnitude to induce

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**Figure 1 - Suggested modalities of exposure to pet allergens and possible consequences in “real-life”**

- **Possible modalities of exposure to pet allergens at home**
  - Direct domestic contact (b)
  - Direct contact elsewhere (c)
  - Indirect contact (d)
  - No apparent contact (e)

**What means in real-life?**
- a) Pets removed or deceased at least two years before
- b) Patients with pets at home because pet ownership
- c) Patients without pets at home but with close contact with pets outside the home (e.g. at home of others)
- d) Patients who deny any direct exposure to pets but who can be indirectly exposed to pet allergens because in contact with their owners (e.g. through clothes or other items)
- e) Patients who deny any known direct or indirect exposure to pets and pets allergens

**What appens in real-life?**
- a) Allergens at home for many years
- b) Higher levels of allergens indoors and direct exposure when patient is at home
- c) Direct exposure might be similar to that of pet at home and the levels of allergens indoors relatively high through passive transport.
- d) The levels of allergens indoors might be of sufficient magnitude to induce allergic sensitization
- e) The levels of allergens are likely to be very low or absent

**Misinterpretation of the results of skin prick tests in clinical practice and questionnaires in epidemiological studies**
Possible modalities of exposure to pets and allergy

Allergic sensitization in susceptible, atopic individuals, and to trigger respiratory symptoms in already and highly pet-sensitized subjects (26,27). In developed countries, the consequence of pet allergen ubiquity is a persistent stimulation of airways similar to that induced by dust mite, that would increase the risk of allergic sensitization either directly or by a cross-reaction mechanism involving albumins and lipocalins (28-30).

On the base of this background, we suggest a new, more realistic classification of possible modalities of exposure to pet allergens (figure 1).

Figure 1 clearly shows that only the condition “b” is reported usually in collecting anamnestic data during clinical consultations, and in the questionnaires utilized for large epidemiological studies on the relationship between early exposure to pet allergens and subsequent enhancing or protective effect on allergic sensitization to these allergens. In the conditions “a, c and d”, the presence of pets at home is considered “formally negative” in patients’ responses and in the questionnaires but the level of exposure (direct / indirect) to pet allergens could be outstanding. Only the condition “e” should be considered at the lower risk of pet allergen exposure after having certainly excluded any direct as well as “indirect contact”. It is evident that these biases can lead to erroneous interpretation of the clinical significance of positive skin prick tests for pet allergens as well as of the real risk of exposure to allergens of dog / cat in epidemiological studies. We have used this classification of exposure either for common / less common pets, pests or for a bigger animal such as horse, in this last case with some modifications. In these studies we have shown the role of these different modalities of exposure on the prevalence of allergic sensitization to several furry animals (31-38).

We think that our classification could be of particular importance to evaluate the modality of pet exposure at home in all countries characterized by a high frequency of pet ownership. It is likely that, in these countries, the “average amount” of pet allergens indoors could be high (or very high in some particular conditions) also in the absence of a pet at home. In conclusion, the magnitude of exposure to pet allergens at home is not related exclusively to pet ownership / presence of a pet indoors but it can be also relevant without a pet living with the inhabitants. These considerations should be taken into account during the planning of epidemiological studies on the relationship between exposure to pet and development of allergic sensitization to pet allergens. In clinical practice, a real assessment of the risk and clinical significance of allergic sensitization to pet allergens is crucial for the management of patients (pet-avoidance measures, allergen immunotherapy, pharmacological treatment of respiratory symptoms etc.).

We believe that the topic of animal allergy is very important not only for clinical but also for emotional implications in all pet-owner patients and especially in children. The love for animals in general and for pets in particular is increasing worldwide, so we wish to underline the necessity for an adequate assessment of risk factors for allergic sensitization and possible prevention strategies by using a more realistic evaluation of possible modalities of exposure.

References

14. Almqvist C, Gargen F, Kemp AS, Li Q, Crisafulli D, Tovey ER, Xuan W, Marks GB, CCAPS Investigators. Effects of early cat or dog ownership on sensitization and asthma in high-risk cohort without disease-related modification of exposure. Pediatr Perinatal Epidemiol. 2010;24:171-78.


23. Berge M, Munir AK, Dreborg S. Concentrations of cat (Fel d 1), dog (Can f 1) and mite (Der f 1 and Der p 1) allergens in the clothing and school environment of Swedish schoolchildren with and without pets at home. Pediatr Allergy Immunol. 1998;9:25-30.


27. Munir AKM, Einarsson R, Schou C, Dreborg SKG. Allergens in school dust.1. 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 asthm ma who are sensitized to cat and dog. J Allergy Clin Immunol. 1993;91:1067-74.


