

Early pet exposure: friend or foe?

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Purpose of review

Sensitization to pets is a risk factor for asthma and it was assumed that pet ownership was a risk factor for sensitization. Epidemiological studies failed to confirm this, some even suggesting that keeping pets decreased the risk of sensitization and asthma. In the last year, 10 studies have been published which have, at least in part, attempted to address the question. The results, however, are heterogeneous and it is still not clear how we should advise our patients on this issue of pet ownership.

Recent findings

Results of studies of the association between exposure to cat or cat allergen and the development of sensitization are such that almost any view on the relationship could be supported by evidence from the literature. For dogs, there are fewer data, but there is little to suggest that keeping a dog increases the risk of sensitization to dog. The majority of studies reviewed find either no association or a reduced risk of asthma amongst pet owners, but only one of these selectively excludes those who deliberately avoid pets from the analysis. There is evidence to suggest that amongst non-pet owners, the risk of sensitization and of asthma increases in areas with a high proportion of pet owners. There is evidence emerging that the effect of exposure to pets may be different in different relative risk groups, based on parental allergy. There is also evidence that asthma is more severe amongst pet sensitized pet owners.

Summary

There are several large birth cohort studies being conducted around the world designed to measure the development of asthma and allergies in children with prospective and objective measures of environmental exposures. The results of such studies are required before the association between pets and asthma can be determined.

Keywords

cats, dogs, pets, allergies, asthma

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Introduction

Why do people keep cats and dogs? In a straw poll of friends and colleagues, not a single one answered 'to reduce the risk of me/my children developing asthma', but is this a beneficial 'side effect' of keeping such pets? Many studies have published results on the association between exposure to pets, sensitization and asthma, 10 of them in the last year. As we shall see, not all studies were designed to address the issue, but this has not stopped the authors from making speculations based on their results.

Much of the work on pet allergen exposure comes from Scandinavia where mite allergen levels tend to be low and cat ownership rates are very high [1]. Cat allergen is passively transferred from the homes of cat owners, on clothing, to public places. Passive exposure to pet allergen is likely therefore to be higher in areas where pet ownership is more common, and results of studies conducted in Scandinavia may not apply to other areas with fewer cats and dogs.

So why do some of us not keep pets? For some this is because exposure to pets causes a clear exacerbation of asthma symptoms, and there is evidence to suggest that pet sensitized pet owners have more severe asthma than pet sensitized non-pet owners [2]. Others will add that they are afraid that their children will develop asthma if they keep pets.

Are pets relevant in asthma? There are extensive data to suggest that sensitization to cats is a major risk factor for asthma [1–3,4••] and there are some data to suggest that early sensitization is associated with more severe asthma [5]. There are fewer data for dogs [3] and one cannot assume that the effects of exposure to dogs are the same as for cats. Also, the findings of these studies conducted in the western world may not be relevant to Africa [6].

So how do we advise our patients when they ask about pet ownership? In short, we don't know, but in the following review we will break down the question of pet ownership, exposure and sensitization into component parts and use the evidence in the literature to provide answers when possible. The review is not exhaustive, but focuses on relevant studies and those published most recently. The studies reviewed are summarized in Table 1. They are heterogeneous both in design and in results; some include exposure to birds and rodents, some are of high-risk children only, some look at early life exposure and many have not measured allergic

Table 1. Summarizing studies of the effect of exposure to cats and dogs on the development of allergies and asthma

Study	Design, age, numbers	Definition of exposure	Outcome measures	Association between exposure and specific sensitization to C or D	Association between exposure to C or D and atopy	Association between exposure to C or D and asthma	Comments, ownership rates if given
Remes (2001) [7•], USA	UBC, 13 years, <i>n</i> = 1076	C, D indoors in infancy	spt (but not to D), Q	NA for C, NR for D	NA	D owners in infancy had decreased frequent wheeze if no history of parental asthma. NA for C	Lowest risk of frequent wheeze at 13 was in persistent D owners, highest risk in never D owners. 32% had D, 22% C
Arshad (2001) [8•], UK	UBC, 4 years, <i>n</i> = 1218	Current C, D owner	spt, Q	NA	NR	NR	Only 44% of those children with asthma were atopic; 39% had C, 30% D
Ownby (2002) [9••], USA	UBC, 6–7 years, <i>n</i> = 474	C, D, current infancy	spt, IgE, BHR	D in infancy associated with decreased sensitization to D by spt but not IgE. NA for C	D or C in infancy associated with decreased risk of atopy	NA with asthma diagnosis, but less BHR for boys with increasing C and D exposure in infancy. NA for current C or D owners	45% had D, 32% C in infancy. No difference in parents of pet owners and non-pet owners
Nafstad (2001) [10], Norway	UBC, 4 years, <i>n</i> = 2531	C, D, any pet at birth	Q	NR	NR	NA	9% had D, 8% C
Wahn (1997) [11], Germany; Lau (2000) [12]	SBC, 3 and 7 years, <i>n</i> = 939	C, Fel d 1	IgE to cat, BHR, Q	Higher Fel d 1 levels associated with increased risk of sensitivity to C at 3 and 7 years. NR for C owners	NR	NA at 7 years for ownership or Fel d 1 levels	Levels of Fel d 1 generally low
Custovic (2001) [13•], UK	SBC, 1 year, <i>n</i> = 517	C, D ownership	spt, IgE, Q	In HR group, C owners had increased risk of sensitivity to C. NA for D	NR	NR (but NA for respiratory symptoms, too young to diagnose asthma)	1-year-old children only
Celedon (2002) [14••], USA	HRBC, 5 years, <i>n</i> = 448	C, D owners, Fel d 1, Can f 1	Q	NR	NR	For C, risk of wheezing decreased if mother did not have asthma, increased if mother had asthma. NA for D	21% had D, 16% had C
Munir (1997) [15], Sweden	HRBC, 5 years, <i>n</i> = 86	Current C, D ownership, peak Fel d 1, Can f 1	spt	NA for Fel d 1 or C owners. Too few sensitive to D to comment	NR	NR	Sensitivity to C or D can occur at low allergen levels; 9% had D, 8% had C
Burr (1997) [16], UK	HRBC, 7 years, <i>n</i> = 440	C, D ownership	spt, IgE, Q	NR	Reduced atopy by IgE in C or D in infancy. NA for spt	NA	Conclude strong FH atopy operates against the keeping of pets
Rhodes (2001) [17], UK	HRBC, 22 years, <i>n</i> = 63	C, D before 5 years	spt, IgE, Q, BHR	NR	NR	NA	24% had asthma, 29% had D, 21% C
Smedje (2001) [18•], Sweden	CS, 7–17 years, <i>n</i> = 1347	C, D, current, Fel d 1, Can f 1 in school	Q	NR	NR	Incident asthma less likely in current C owners, NA for D	High Fel d 1 in school associated with increased risk incident asthma, regardless of C owners

(continued overleaf)

Table 1. (continued)

Study	Design, age, numbers	Definition of exposure	Outcome measures	Association between exposure and specific sensitization to C or D	Association between exposure to C or D and atopy	Association between exposure to C or D and asthma	Comments, ownership rates if given
Anyo (2002) [19*], Holland	CS, 7–12 years, <i>n</i> = 2729	Pet (C, D, rodents, birds), owner early C/D	spt and/or IgE, BHR, Q	NR (as C/D were taken together, NA)	NR	NA with early C/D. NA with current PO. Increased risk of asthma in past PO	36% had C/D in infancy
Ritz (2002) [4**], Germany	CS, 5–14 years, <i>n</i> = 1893	Regular contact with C	IgE, Q	NA	NR	NA	High C exposure in class increases risk of sensitivity in those without regular direct contact. 36% had regular C contact
ECRHS, Svanes (1999) [20]; Roost (1999) [21]	CS, adults 20–44 years, <i>n</i> = 18 097 (blood on 13 509)	C, D ownership, current, childhood	IgE, Q	Childhood C associated with decreased sensitivity to C in adulthood if FH of atopy. Current C indoors associated with increased sensitivity to C in asymptomatic but not symptomatic group. NR for D	D ownership in childhood was associated with less atopy in adulthood. NA for C	Community prevalence of asthma in non-C owners proportional to community prevalence of C (no stats given). NR for D	Community C ownership proportional to community prevalence of C sensitivity amongst non-C owners. C ownership ranged from 4% in Spain to 69% in New Zealand
Ronmark (1999) [22], Sweden	CS, 7–8 years, <i>n</i> = 3525	C, D ownership	Q, spt on 2/3	Reduced sensitivity to C or D in those who had C or D (but no stats given)	NA	Atopic asthma decreased in current or past C or D ownership	72% had animals at home
Brunekreef (1992) [23], Holland	CS, 6–12 years, <i>n</i> = 3344	Pets (C, D, birds, rodents)	Q	NR	NR	Trend higher in previous C owners (but no stats given). Decreased asthma in current pet owners	31% had D, 14% C. 14% avoided or removed pets because of allergy
Noertjojo (1999) [24], Canada	CS, 20–44 years, <i>n</i> = 2999	C, D, pets, current, previous	Q, spt on 504 to C	NA in subgroup between C ownership (past or present) and sensitivity. NR for D	NR	NA between ownership of C or D in childhood and asthma. Current pet owners had increased risk of asthma diagnosis	10% had D, 21% had C
Hesselmar (1999) [25], Sweden	CS, 7 then 12 years	C, D inside in infancy	spt, Q	C in infancy associated with decreased risk of sensitivity to C at 12 years, but effect lost when avoiders excluded. NA for D	NA	C or D in infancy associated with decreased risk of asthma at 12 years, even when avoiders excluded	Excluded those who avoided pets because of symptoms (avoiders). 24% had C or D in infancy
Linneberg (2001) [26*], Denmark	CC, adults, <i>n</i> = 1112	C, D owners, never, past, current	spt, IgE, Q	NR	Past D associated with decreased atopy (spt). NA for C	NR	Association still seen when those who got rid of D because of symptoms were excluded
Addo-Yobo (2001) [6], Ghana	CC, 8–17 years, <i>n</i> = 100	Current C, D owners, Fel d 1, Can f 1	spt, IgE, Q	NR	NR	NA in multivariate analysis	Sensitivity to C or D was rare despite 50% of homes owning pets. Poor correlation between spt and IgE

(continued overleaf)

Table 1. (continued)

Study	Design, age, numbers	Definition of exposure	Outcome measures	Association between exposure and specific sensitization to C or D	Association between exposure to C or D and atopy	Association between exposure to C or D and asthma	Comments, ownership rates if given
Ingram (1995) [27]; Sporik (1999) [28], USA	CC, 12–14 years, <i>n</i> = 332	Current C, D ownership, Fel d 1, Can f 1 levels	spt and IgE, BHR, Q	NA for allergen levels. NR for pet ownership	NR	NA for allergen levels. NR for pet ownership	Huge range of allergen levels. C or D ownership rates not given
Ichikawa (1999) [29], Japan	AC, 1–34 years, <i>n</i> = 504	C, D ownership	IgE	Sensitivity to C higher amongst C owners (no stats given). NA for D	NR	NR	13% had D, 10% C
Lindfors (1999) [30]; Melen (2001) [5], Sweden	AC, 4 years, <i>n</i> = 181	C, D, no/low/high exposure, Fel d 1	IgE, spt, Q	Exposure to C before age 2 associated with sensitivity to C. High Fel d 1 exposure associated with increased sensitivity to C. NA for D or Can f 1	NR	NA for C or D exposure. High Fel d 1 associated with increased risk of severe asthma	8% had D, 14% had C at 2 years, but half got rid of pets by 4 years
Warner (1991) [31], UK	AC, 2–14 years, <i>n</i> = 68	C, Fel d 1 in dust and air	spt, IgE	Increased risk of sensitivity to C if had C at birth, or if detectable Fel d 1 in air	NR	NR	31% had C
Chan–Yeung (1999) [32], Tristan da Cunha	Whole population of island, <i>n</i> = 282 (102 have asthma)	C were eliminated from island in 1974	spt	NR	NR	NR	20% sensitive to C, six of whom were born 1 or more years after extermination of C. Fel d 1 in only one home. Sensitivity occurs with no direct C contact. Sensitivity to D low at 8.8% despite lots of D

C, cat; D, dog; UBC, unselected birth cohort; spt, skin prick test; NA, no association; NR, not reported; BHR, bronchial hyperresponsiveness; SBC, selected birth cohort; HR, high risk; HRBC, high-risk birth cohort; FH, family history; CS, cross-sectional study; PO, pet owners; CC, case control study; AC, asthma cases.

sensitization, all of which makes it difficult to draw out common themes.

Should assessment of exposure be based on pet ownership or allergen levels?

Collecting dust samples from the home and analysing them for content of allergens Fel d 1 and Can f 1 is much more expensive than asking about pet ownership, and neither of these methods give details of contact with pets outside the home. We have found that in UK homes with cats, Fel d 1 levels are more than 50-fold higher than in homes without cats [33] and a similar situation is seen for Can f 1 and dogs [34]. In Ghana, however, where rates of pet ownership appear to be similar to the UK (~50%), there is no difference in Fel d 1 levels between homes with and without cats, and for homes with dogs, Can f 1 levels

are only threefold higher than in homes without dogs [35]. Furthermore, homes without pets in the UK contain higher levels of pet allergen than homes with pets in Ghana, as in Ghana pets are kept outdoors to control rodents and ward off intruders. We have also identified homes in the UK with cats with very low levels of Fel d 1 and homes without cats with very high levels [36]. Recording pet ownership alone may be misleading as an index of allergen exposure. Living in a house with a pet may bring other environmental exposures, independent of allergen exposures, such as microbiologic exposures and endotoxin. That is, pet ownership and allergen assays do not measure precisely the same thing and so both should be recorded in prospective studies when possible. Other significant exposure to pets, such as at a childminder's house, should also be recorded.

Is there a dose–response relationship between exposure to pet allergen (Fel d 1 and Can f 1) and specific allergen sensitization?

Six studies have addressed this question for Fel d 1 [5,11,12,15,27,28,31] and two for Can f 1 [15,27]. From Germany an enriched birth cohort study of approximately 1000 children found a clear dose–response relationship between sensitization to cat and Fel d 1 level in the carpets at age 3 years [11], which was still present at age 7 years [12]. The range of Fel d 1 levels was small, however, the 75th centile level being 0.22 µg/g of Fel d 1. A study from Sweden of children with asthma at age 4 years found that those who were sensitized to cat had been exposed to higher levels of Fel d at age 2 years [5]. In the UK, children who had Fel d 1 detectable in the air of their home were more likely to be sensitized to cat [31].

In contrast, in the USA, a case control study of 12-year-old children found a wide range of allergen levels, but no association between current Fel d 1 exposures and cat sensitization [28] or current Can f 1 levels and dog sensitization [27]. In a high-risk birth cohort study from Sweden, there was no association between peak Fel d 1 exposure and sensitization to cat at age 5 years, but too few children were sensitized to dog to comment. It was clear from this study that high-risk children can become sensitized to cat with very low peak domestic exposure to cat allergen [15].

These results are difficult to summarize; all that is clear is that some children become sensitized to cat with very low levels of domestic exposure to Fel d 1, and there are too few data on Can f 1 exposures to comment.

Is there an association between cat or dog ownership and sensitization to cat or dog, or to atopic status?

Recent publications on the effects of pets on the development of allergy have more commonly used pet ownership as a marker of pet exposure.

Seven studies present results on the association between cat or dog ownership and atopy (i.e. sensitization to any allergen, by skin prick test or IgE, without necessarily implying disease). Three found no association [7•,22,25] and two found that atopy was reduced if pets were kept in infancy [9•,16]. Keeping a dog during childhood or ‘previously’ (undefined) was associated with reduced atopy in adulthood in two large studies [20,26•], and in one study this effect persisted when those who avoided dogs because of symptoms were excluded [26•]. No effect was seen for cat ownership in these two studies.

Thirteen studies address the question of specific sensitization to cats and to dogs amongst pet owners.

Six of these studies report results for cats only. Of the remaining seven which investigated the effects of dog ownership, five found no association between exposure and sensitization to dog [5,8•,13•,25,29]. One study from Sweden, where by the age of 7–8 years only 28% had never kept a pet, reports a slightly lower prevalence of sensitization to dog in dog owners (7.0 versus 9.6%), but no statistical test result is offered [22]. One study has found that dog ownership in infancy was associated with reduced sensitization to dog at age 6 or 7 years by skin prick test ($P=0.03$), but not by IgE ($P=0.06$) [9•].

For cat sensitization amongst cat owners, six studies found no association [4•,7•,8•,9•,15,24]. Three studies found cat ownership to be associated with a reduced risk of sensitization to cat. In one study, this effect was lost when those who avoided keeping cats because of symptoms were excluded [25]. A study from Sweden reported a reduction in sensitization to cat amongst owners (16.4 versus 8.6%), but presented no statistical analysis of this result [22]. The third was a huge questionnaire study of adults aged 20–44 years from 35 centres, who were asked to recall pet ownership from childhood [21]. It was found that keeping a cat in childhood was associated with a decreased risk of sensitization to cat as an adult in those who had a family history of atopy (OR 0.77, 95% CI 0.63–0.94). Interestingly, in the subgroup analysis, the authors found that for those without respiratory symptoms, current cat ownership was associated with an increase in the risk of sensitization to cat. Furthermore, amongst the non-cat owners, the community prevalence of sensitization to cats increased with increasing prevalence of cat ownership in the community.

Four studies found an increased risk of sensitization to cats amongst cat owners. Of these, one study reports at age 1 year, and this effect was for children with atopic parents only [13•]. The other three studies are of children recruited from asthma clinics. One small study from the UK found an increased risk of sensitization if a cat was living in the home at the time of birth [31]. A study of Japanese children and young adults with asthma found sensitization was twice as common amongst current or former cat owners compared with those who had never kept cats, but no statistical test was reported [29]. A study from Sweden of children aged 4 years found a significantly increased risk of sensitization to cat amongst those who had lived with cats during the first 2 years of life (OR 5.56, 95% CI 1.06–29) [5]. An interesting study reports from Tristan da Cunha, a small island where cats were eradicated in 1974 [32]. Despite this, 20% of the islanders are sensitized to cat, six of whom were born 1 year or more after the elimination of cats. Despite the presence of lots of dogs, the sensitization rate to dogs is less than 10%.

To summarize these results is again very difficult – almost any view on the relationship between cat ownership and sensitization could be supported by data from one or another study. For dogs there are fewer data available, but ownership in childhood seems to be associated with a reduced risk of atopy in adulthood, and there is little/no evidence to suggest that keeping a dog increases the risk of specific sensitization to dogs. The answers will become clearer when large birth cohort studies, designed to measure pet ownership prospectively, publish their results.

Is there an association between pet ownership and asthma diagnosis?

Studies have looked at the effects of both early exposure and current exposure to pets on asthma diagnosis, and so the two groups of studies will be considered separately.

Six studies found no significant association between keeping cats or dogs in the first few years of life and asthma diagnosis [5,9^{••},10,16,17,19[•]]. A large birth cohort study from the USA found that dog ownership in infancy was associated with a decreased risk of frequent wheeze at age 13 years, but no association was seen for cats [7[•]]. In Sweden, a large cross-sectional study found that cat or dog ownership in infancy was associated with a decrease in asthma diagnosis at age 12 years, and that this effect persisted when those who avoided pets because of symptoms were excluded [25]. A further large cross-sectional study from Sweden of children aged 7–8 years found that atopic asthma was less common in those with previous (or current) cat or dog ownership [22]. A high-risk birth cohort study from the USA has recently reported that the effect of exposure to cats or high levels of *Fel d 1* depends upon maternal asthma in children aged 5 years [14^{••}]; those whose mothers had asthma and had high cat exposure were at increased risk of wheeze, those whose mother did not have asthma were at significantly decreased risk of wheeze. No association was seen for dog.

Five studies found no association between current pet ownership and asthma [4^{••},5,6,9^{••},12]. One study found the risk of developing asthma over a 4-year period was reduced amongst those who kept a cat, with no association for dog [18[•]]. One study, referred to in the previous paragraph, found decreased atopic asthma in children who currently kept a cat or dog [22]. A study from Holland found that although asthma was less common in current pet (cat, dog, bird, rodent) owners, there was a trend towards higher rates of asthma amongst those who had previously owned a cat [23]. A more recent study from Holland also found an increased risk in asthma amongst those who had previously owned a pet (cat, dog, bird or rodent), but no association with current pet ownership [19[•]]. Amongst a large cohort of adults from Canada,

current cat ownership was associated with an increase in the risk of asthma (OR 1.6, 95% CI 1.1–2.4) [24].

Only one study, however, specifically excluded those families who avoided keeping pets because of a family history of allergies [25]. They still found a higher rate of asthma amongst those who had not kept pets in the first year of life (8.5%) compared with those who had (3.3%).

It is possible that the lack of association between current pet ownership and asthma symptoms is seen because those who develop symptoms part with their pets, and this is supported by higher prevalences of asthma amongst former pet owners [19[•],23], but this again is not a consistent finding [7[•],22]. Equally, some parents with pet allergy may have offspring who are at high genetic risk of developing allergies and such children may have a lower threshold for sensitization, which occurs even though no pets are brought into the home.

Interestingly, the European Community Respiratory Health Survey found that those who did not keep cats were more likely to have a physician diagnosis of asthma if they lived in a community where cats were more common [21]. Taken together, these data do suggest that there may be some ‘protection’ from owning a pet yourself, but the effect of having more pets in the community increases the risk for those who do not keep pets.

Conclusion

Sensitization to pets is a risk factor for asthma. Sensitization can occur in children who live in homes with no pets and with low levels of pet allergen. Therefore, excluding pets from the home will not necessarily protect children from the development of sensitization to pets. The data on pet ownership and sensitization are heterogeneous – some studies suggest ownership increases the risk of sensitization, others suggest it decreases it. The effect is likely to be different in children with genetic predispositions, which at the moment at least, are estimated based on parental history. Certainly, there is not enough evidence in the literature to suggest that families should acquire pets to reduce the risk of their children developing allergies to pets. There is very little evidence that current pet ownership increases the risk of asthma, but such individuals are a self-selected group; those with symptoms may have already parted with their pets.

The most recently published studies [4^{••},6,8,7[•],9^{••},14^{••},17,18[•],19[•],26[•]], although providing a wealth of data, have also produced heterogeneous results. They have highlighted some important points, however. Passive exposure, particularly at school, is important amongst non-cat owners [4^{••},18[•]]. The effect of pet exposure in

the home may be markedly different for the different relative risk groups, based on parental history [14^{••}]. Atopy is an important outcome measure, as the effect of exposure to pets on the development of atopy may not be due to the development of specific sensitization to that pet [9^{••},26[•]]. The effects of cats may be different to the effects of dogs, and these should be recorded and analysed separately [7[•],14^{••},18[•]].

Passive exposure to pet allergens is clearly a problem, particularly in areas where pets are common. Why is such exposure as harmful if not more so than exposure to the pet itself? A pet is more than just its allergen and pet ownership may result in other exposures such as animal bites, scratches and fleas as well as higher levels of endotoxin [37]. It is plausible that the non-allergen exposures associated with pet ownership confer a benefit, protecting against the development of allergic disease, which is missing when the only exposure to pet allergen occurs in the absence of the pet. The results for the effects of cat and dog ownership are different in many studies and so if we are ever going to be able to offer specific advice, each type of pet must be recorded separately.

It has been reported that the association between exposure to cat allergen and sensitization follows a bell-shaped curve, with those at highest exposures less likely to be sensitized [38[•]]. Some individuals in the high exposure group who were not sensitized to cat had evidence of IgG and IgG4 to Fel d 1 but not IgE, suggesting a different immunological response to allergen, termed a 'modified Th2 response'. The presence of these antibodies was not associated with asthma. It is plausible, therefore, that the high dose exposures to cat allergen, which may be seen in the homes of some cat owners, are associated with immunological responses which are not associated with asthma.

We now require the results of the large birth cohort studies, in which children have been followed prospectively, with measurement of allergen levels and records of cat and dog ownership, together with parental allergic history, and in whom hard endpoints of asthma and its associated traits have been measured.

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- of special interest
- of outstanding interest

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