

The Role of Furry Pets in Eczema

A Systematic Review

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Objective: To systematically search, summarize, and critically appraise the literature to examine whether pet exposure in early life is associated with an increased risk of eczema.

Data Sources and Study Selection: We searched MEDLINE (1950 to June 2006) supplemented by citation lists in retrieved articles and contact with researchers. No language restrictions were imposed.

Data Extraction: Cohort studies were sufficiently similar to allow pooled analysis. Meta-analysis was not possible for cross-sectional studies owing to differences in methods and populations.

Main Outcome Measures: Incidence or prevalence of eczema.

Results: Evidence from longitudinal studies showed that previous exposure to cats (pooled odds ratio [OR], 0.76; 95% confidence interval [CI], 0.62-0.92), dogs

(pooled OR, 0.68; 95% CI, 0.53-0.87), or "any furry pet" (pooled OR, 0.79; 95% CI, 0.74-0.84) is associated with a lower risk of eczema. However, in the only cohort study adjusted for avoidance behavior, this "protective effect" disappeared (for cats: OR, 0.80; 95% CI, 0.33-1.97). Stratified analysis by family history in 2 birth cohort studies showed that dog exposure was protective in patients with atopic families. For cats, 1 study showed reduced risk in atopic families only; the other study showed no effect. Eight cross-sectional studies evaluated past pet exposure; a protective effect was seen in 3 studies for cat, dog, or any pet; no study demonstrated an increased risk.

Conclusions: There was no clear evidence that early pet exposure is associated with increased risks of subsequent eczema. We found some evidence of a possible protective effect of early pet exposure, but this might be explained by avoidance behavior in high-risk families.

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SEVERAL RESEARCHERS HAVE suggested that early exposure to animal allergens contributes to the development of eczema.¹ Such assertions have mainly been based on the finding of high serum IgE levels to purified animal allergen in children with eczema.² Making inferences about disease causation using allergic sensitization is potentially misleading; specific serum IgE levels to cat or dog allergens cannot distinguish between past or current pet exposure, and the presence of such antibodies may simply be an epiphenomenon of the atopic state. Pet allergens, especially for cat, have been shown to be ubiquitous in public places, in schools, and in families that never owned a pet.³⁻⁵ The presence of a cat or dog in the house does not necessarily lead to allergic sensitization of the owners, and their direct contact with the animal may vary considerably.⁶

The possible role of domestic animals in eczema development remains unclear,

resulting in widely conflicting advice being given to parents. Some researchers^{7,8} recommend prophylactic avoidance of pets in the perinatal period and early childhood, whereas others advocate the removal of pets from households after the development of eczema in offspring. The opposite view has also been suggested by proponents of the hygiene hypothesis, that is, pet keeping in early life may increase exposure to endotoxins that provide a protective benefit against later development of eczema.⁹ To inform this lack of clarity of clinical advice to parents, we conducted a systematic review of the literature to determine whether keeping domestic furry pets is associated with an increased risk of eczema.

METHODS

MEDLINE was searched for articles published between its inception in 1950 and June 30, 2006, using the following search terms: *domestic ani-*

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imals, cats, dogs, horses, and pets combined with the following Cochrane Skin Group search terms for atopic eczema¹⁰:

1. exp Dermatitis, Atopic/
2. atopic dermatitis.mp.
3. atopic eczema.mp.
4. exp NEURODERMATITIS/
5. neurodermatitis.mp.
6. infantile eczema.mp.
7. childhood eczema.mp.
8. Besniers' Prurigo.mp.
9. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8
10. domestic animals.mp. or exp Animals, Domestic/
11. exp CATS/ or cats.mp.
12. exp DOGS/ or dogs.mp.
13. horses.mp. or exp HORSES/
14. pets.mp.
15. 10 or 11 or 12 or 13 or 14
16. 9 and 15

The online search was supplemented by an extensive hand search of citations in the retrieved articles, and researchers were contacted for additional data as appropriate. We included longitudinal and cross-sectional studies. We imposed no restrictions on participant age or study language. Each relevant article underwent standardized data extraction by one of us (S.M.L.), and all of the data were then assessed by the author panel.

Studies were described in 2 categories: those that prospectively followed cohorts of children from birth or before (in utero) and all other designs. More weight was given to cohort than cross-sectional studies because of their ability to better separate the chronological relationship between exposure (pets) and disease (eczema). Meta-analysis using a random-effects model (a technique described by DerSimonian and Laird¹¹) (RevMan; The Cochrane Collaboration, Oxfordshire, England) was planned if studies were deemed to be sufficiently similar in terms of design, participants, and age. We also looked carefully for adjusted analyses whereby the effects of avoidance behavior by atopic parents can be taken into account. Throughout this article, we use the new World Allergy Association nomenclature for eczema.¹²

RESULTS

The initial search retrieved 458 articles, of which 319 were related to eczema in animals and, therefore, were excluded, leaving 139 articles. In the final analysis, 30 articles^{6,9,13-40} were identified that specifically included data on the association between eczema and domestic animals. No previous systematic reviews or randomized controlled trials were identified. Results of cohort and cross-sectional studies according to type of pet are summarized herein.

CATS

Cohort Studies

Eight cohort studies^{6,9,13-18} examined the relationship between cat exposure and eczema (**Figure 1** and **Table 1** and **Table 2**). In a large cohort study, Nafstad et al⁶ followed up 2531 Norwegian children to age 4 years and found a 50% reduction in eczema risk with cat exposure at birth (adjusted odds ratio [OR], 0.50; 95% confidence interval [CI], 0.30-0.90). Stratified analysis showed that the reduced eczema risk was strongest in atopic families (OR, 0.3; 95% CI, 0.1-0.9) compared with those with-

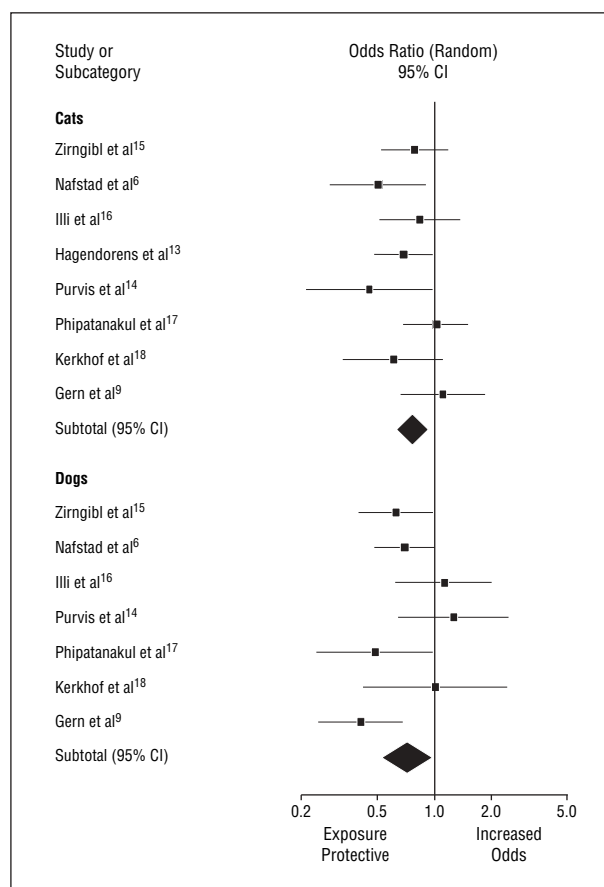


Figure 1. Forest plot of cohort studies arranged by sample size for cats and dogs separately. CI indicates confidence interval; diamonds, the overall summary estimate for the analysis (width of the diamond represents the 95% CI).

out an atopic family history (OR, 0.6; 95% CI, 0.3-1.2). Another study of 1128 Belgian children by Hagendorens et al¹³ showed a 32% reduction in eczema with postnatal cat exposure (adjusted OR, 0.68; 95% CI, 0.47-0.97). However, 6 additional longitudinal studies, 2 conducted in the United States,^{9,17} 1 in New Zealand,¹⁴ 1 in the Netherlands,¹⁸ and 2 in Germany,^{15,16} could not confirm these results. For example, Zirngibl et al¹⁵ studied 4578 children up to age 2 years. At that age, cat exposure was not significantly associated with subsequent eczema risk (adjusted OR, 1.03; 95% CI, 0.70-1.51). Stratified analysis by family history of atopy showed no significant association with the outcome (positive family history: OR, 0.92; 95% CI, 0.58-1.47; and negative family history: OR, 1.32; 95% CI, 0.65-2.68) (Joachim Heinrich, PhD, written communication, June 2006).¹⁵ Illi et al¹⁶ followed up 1314 children from birth to age 7 years. Eczema was determined by parental reporting of symptoms, by a physician's diagnosis, and by a dermatologist on physical examination. There was no association between exposure to cats in early life and eczema at age 2 years (adjusted OR, 0.83; 95% CI, 0.50-1.39) (Sabina Illi, MPH, written communication, October 2005).¹⁶ Pooled analysis for all cohort studies showed an overall statistically significant protective association between previous cat exposure and subsequent eczema (OR, 0.76; 95% CI, 0.62-0.92).^{6,9,13-18}

Table 1. Summary of Data From Birth Cohort Studies Arranged by Sample Size

Source and Country	Participants, No.	Age at Follow-up	Diagnostic (D) and Exposure (E) Criteria	Outcome Measures: OR (95% CI)	Confounders Adjusted for in Analysis
Benn et al, ¹⁹ 2004, Denmark	24 341	18 mo	Questionnaire and subgroup examination (D), questionnaire (E)	Any pet during pregnancy or first 6 mo: adj OR, 0.87 (0.79-0.96)	Parental history of allergy, siblings, sex, maternal age and education, and infections
Zirngibl et al, ¹⁵ 2002, Germany	4578	2 y	Questionnaire (D), questionnaire (E)	Any pet at 2 y: adj OR, 0.74 (0.57-0.97); family history of atopy: adj OR, 0.74 (0.55-1.01); no family history of atopy: adj OR, 0.72 (0.43-1.20); cat at 2 y: adj OR, 1.03 (0.70-1.51); family history of atopy: adj OR, 0.92 (0.58-1.47); no family history of atopy: adj OR, 1.32 (0.65-2.68); dog at 2 y: adj OR, 0.63 (0.40-0.98); family history of atopy: adj OR, 0.53 (0.30-0.93); no family history of atopy: adj OR, 0.88 (0.43-1.83); small furry pets at 1 and 2 y: adj OR, 0.57 (0.24-1.32)	Parental history of allergy, siblings, sex, maternal age, smoke exposure, study area and group, and parental nationality
Nafstad et al, ⁶ 2001, Norway	2531	4 y	Questionnaire (D), questionnaire (E)	Any pet at birth: adj OR, 0.70 (0.50-0.90); atopic parents: adj OR, 0.60 (0.40-0.90); nonatopic parents: adj OR, 0.80 (0.60-1.20); cat at birth: adj OR, 0.50 (0.30-0.90); atopic parents: adj OR, 0.30 (0.10-0.90); nonatopic parents: adj OR, 0.60 (0.30-1.20); dog at birth: adj OR, 0.70 (0.40-1.00); atopic parents: adj OR, 0.50 (0.20-1.00); nonatopic parents: adj OR, 0.80 (0.50-1.40)	Parental history of allergy, siblings, sex, maternal age and education, infections, birth order and weight, income, smoke exposure, duration of breastfeeding, and respiratory tract infections
Illi et al, ¹⁶ 2004, Germany	1314	7 y	Questionnaire and physical examination (D), questionnaire and cat allergen concentration at 6 mo (E)	Cat at 3 mo: adj OR, 2.33 (0.85-6.38); cat allergen concentration at 6 mo: adj OR, 1.23 (0.44-3.39); dog at 3 mo: adj OR, 1.11 (0.62-2.00)	≥2 Atopic family members, increased cord blood IgE level, and early wheezing
Tariq et al, ²⁰ 1998, United Kingdom	1218	4 y	Physical examination (D), questionnaire (E)	Any pet at birth: OR, 0.77 (0.55-1.09)	None
Arshad et al, ²¹ 1993, United Kingdom	1215	2 y	Physical examination (D), questionnaire (E)	Any pet at birth: OR, 1.03 (0.71-1.51)	None
Hagendorens et al, ¹³ 2005, Belgium	1128	1 y	Questionnaire (D), questionnaire (E)	Prenatal cat: adj OR, 0.90 (0.60-1.30); cat postnatally: adj OR, 0.68 (0.47-0.97); prenatal dog: adj OR, 0.60 (0.40-0.90); dog postnatally: adj OR, 0.70 (0.50-1.10)	Sex, mode of delivery, birth weight, breastfeeding, siblings, day care, smoke exposure, parental education, parental atopy, and carpet in bedroom
Purvis et al, ¹⁴ 2005, New Zealand	871	3½ y	Questionnaire (D), questionnaire (E)	Cat at 1 y: OR, 0.81 (0.44-1.49); cat at 3½ y: adj OR, 0.45 (0.21-0.97); dog at 1 y: adj OR, 1.31 (0.66-2.62); dog at 3½ y: adj OR, 1.25 (0.63-2.46)	Parental history of allergy, siblings, smoke exposure, duration of breastfeeding, early wheezing, antibiotic use in first year of life, and damp/mold
Phipatanakul et al, ¹⁷ 2004, United States	498	1 y	Questionnaire (D), dust sampling for pet allergen exposure (E)	Cat at 2-3 mo: adj OR, 1.01 (0.70-1.50); dog at 2-3 mo: adj OR, 0.48 (0.24-0.97)	Sex and income
Kerkhof et al, ¹⁸ 2003, the Netherlands	76 patients with eczema; 228 controls	1 y	Physical examination (D), questionnaire (E)	Cat at 3 or 12 mo: adj OR, 0.60 (0.30-1.10); dog at 3 or 12 mo: adj OR, 1.00 (0.40-2.40)	Sex, birth weight, gestational age, maternal age, duration of breastfeeding, siblings, day care, and smoke exposure; borderline negative association for cat disappeared after adjusting for avoidance behavior
Gern et al, ⁹ 2004, United States	285	1 y	Questionnaire (D), questionnaire (E)	Cat at birth and 1 y: OR, 1.10 (0.66-1.84); dog at birth and 1 y: OR, 0.40 (0.24-0.68); adj OR not given (although P values for confounders given)	None

Abbreviations: adj, adjusted; CI, confidence interval; OR, odds ratio.

Cross-sectional Studies

Four cross-sectional studies¹⁹⁻²² evaluated the association be-

tween current eczema and a history of cat exposure (**Figure 2** and Table 2 and **Table 3**). One study²² demonstrated a reduced risk with past cat exposure during the first year of life

Table 2. Summary of Cohort and Cross-sectional Study Results

Exposure	Studies, No.		
	Reduced Eczema Risk	No Association	Increased Eczema Risk
Cohort studies			
Cat	2	6	0
Dog	4	3	0
"Any pet"	3	2	0
Cross-sectional studies			
Past cat	1	3	0
Past dog	1	3	0
Past any pet	1	4	0

(adjusted OR, 0.40; 95% CI, 0.20-0.80); the other 3 studies²³⁻²⁵ showed no significant association.

DOGS

Cohort Studies

Four of 8 cohort studies^{6,9,13-18} demonstrated a protective effect of dog exposure with risk reductions of 30% to 60% (Figure 1 and Tables 1 and 2). Overall, pooled analysis for all cohort studies for past exposure to dogs showed a 36% reduction in eczema risk (OR, 0.68; 95% CI, 0.53-0.87). One of these studies¹⁷ reported that ownership of a dog as early as age 2 to 3 months provided significant protection against eczema until 1 year of age (adjusted OR, 0.48; 95% CI, 0.24-0.97). These results were echoed by Gern et al,⁹ who found a 60% reduction in eczema risk at age 1 year if children had been exposed to a dog at the time of birth (adjusted OR, 0.40; 95% CI, 0.24-0.68). Zirngibl et al¹⁵ and Nafstad et al⁶ also demonstrated significant risk reductions at 2 and 4 years of age with dog exposure in German and Norwegian children (adjusted OR, 0.63; 95% CI, 0.40-0.98; and adjusted OR, 0.70; 95% CI, 0.40-1.00, respectively). In the study by Zirngibl et al,¹⁵ the beneficial effect was seen only in patients with a family history of atopy (OR, 0.53; 95% CI, 0.30-0.93) compared with children without a positive family history (OR, 0.88; 95% CI, 0.43-1.83) (Joachim Heinrich, PhD, written communication, June 2006). Similarly, in the study by Nafstad et al,⁶ a significant protective effect of dog exposure was seen only in atopic families (atopic families: OR, 0.5; 95% CI, 0.2-1.0 vs no family history: OR, 0.8; 95% CI, 0.5-1.4). Purvis et al¹⁴ did not find an association between past and current dog exposure and eczema. A similar lack of association was reported by Illi et al¹⁶ at 7 years (adjusted OR, 1.11; 95% CI, 0.62-2.00).

Cross-sectional Studies

Four cross-sectional studies²²⁻²⁵ evaluated parent-reported past dog exposure and current eczema. One large survey²³ of 5360 German children showed a significant inverse association between eczema at ages 5 to 14 years and dog exposure in the first year of life (OR, 0.65; 95% CI, 0.48-0.87). Three other studies^{22,24,25} revealed no significant association (Tables 2 and 3 and Figure 2).

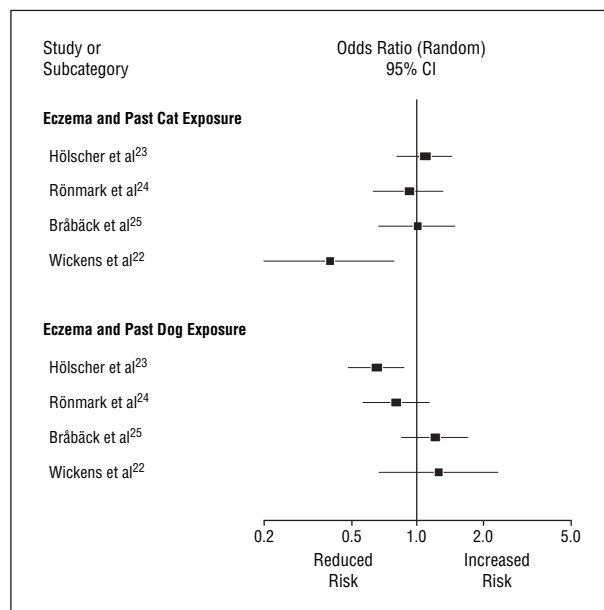


Figure 2. Forest plot of cross-sectional studies of pet exposure in the past arranged by sample size for cats and dogs separately. CI indicates confidence interval.

SMALL FURRY PETS (HAMSTERS, RABBITS, AND GUINEA PIGS)

The only cohort study¹⁵ that examined past exposure to small furry pets other than cats or dogs found no significant association with eczema (adjusted OR, 0.57; 95% CI, 0.24-1.32). No cross-sectional studies have systematically examined the role of small furry pets in eczema.

PETS UNSPECIFIED

Cohort Studies

Three of 5 cohort studies^{6,15,19-21} reported a significant reduction in eczema risk, one of which was of borderline significance, with "any pet exposure" ranging from 13% to 30% (Tables 1 and 2). The largest of these was a Danish national birth cohort study with 24 341 infant-mother pairs that used a questionnaire to measure pet exposure before age 6 months. A randomly selected subgroup was also physically examined for eczema using clearly defined diagnostic criteria. Pet exposure remained in the final logistic regression model, suggesting that individuals exposed to a pet before age 6 months had 13% less eczema until age 18 months (adjusted OR, 0.87; 95% CI, 0.79-0.96).¹⁹ The only other study that used physical examination to determine eczema found a 23% risk reduction with pet exposure during the study period, but the results were not significant (adjusted OR, 0.77; 95% CI, 0.55-1.09).²⁰ No association was seen between eczema and any pet in another study by the Isle of Wight group,²¹ with follow-up of 2 years and diagnosis by questionnaire in relation to pet exposure at birth (univariate OR, 1.03; 95% CI, 0.71-1.51). Pooled analysis combining the 5 cohort studies that included any pet exposure showed an overall protective effect (OR, 0.79; 95% CI, 0.74-0.84).

Table 3. Summary of Data From Cross-sectional Studies Arranged by Sample Size

Source and Country	Participants, No.	Age, y	Diagnostic (D) and Exposure (E) Criteria	Outcome Measures: OR (95% CI)	Confounders Adjusted for in Analysis
Bornehag et al, ²⁶ 2003, Sweden	14 077	1-6	Questionnaire (D), questionnaire (E)	Any pet at time of birth: adj OR, 0.73 (0.66-0.81); avoidance behavior: adj OR, 0.87 (0.78-0.97)	Age, sex, smoke exposure, familial allergy, breastfeeding, type of building, and avoidance behavior
Zutavern et al, ²⁷ 2005, Germany	12 601	5-7; 9-11	Physician examination (D), questionnaire (E)	Authors report no increase in eczema with pet exposure in first year of life; unable to calculate OR from data	Age, sex, grade, parental allergy, parental education, antibiotic use, onset of antipyretic medication, breastfeeding duration, dampness, and drafty rooms
Hölscher et al, ²³ 2002, Germany	5360	5-14	Questionnaire (D), questionnaire (E)	Cat first year of life: adj OR, 1.08 (0.81-1.45); dog first year of life: adj OR, 0.65 (0.48-0.87)	Age, sex, region, survey, parental education, parental atopy, breastfeeding, day care, sharing bedroom, smoke exposure, and contact with rodents and birds
Morales Suárez-Varela et al, ²⁸ 2005, Spain	4387	8-15	Questionnaire (D), questionnaire (E)	Any pet (past): OR, 0.90 (0.70-1.10)	None
Rönmark et al, ²⁴ 1998, Sweden	3431	7-8	Questionnaire (D), questionnaire (E)	Cat (past): adj OR, 0.91 (0.63-1.33); cat (current): adj OR, 0.73 (0.46-1.18); dog (past): adj OR, 0.80 (0.56-1.15); dog (current): adj OR, 0.58 (0.38-0.87); SPT+ to cat: OR, 2.59 (2.10-3.19); SPT+ to dog: OR, 2.75 (2.20-3.44)	SPT+, family history of asthma, sex, damp at home, breastfeeding < 3 mo, smoking mother, urban living, and birth order
Anyo et al, ²⁹ 2002, the Netherlands	2729	7-12	Questionnaire (D), questionnaire (E)	Any pet (past): adj OR, 1.16 (0.86-1.56); any pet first 2 y: adj OR, 0.95 (0.79-1.15); any cat/dog first 2 y: adj OR, 1.01 (0.83-1.22)	Age, sex, parental nationality, parental allergy, parental education, siblings, smoke exposure, day care, and area of residence
Hesselmar et al, ³⁰ 1999, Sweden	2481 in 1991; 412 in subgroup	7-9; 12-13	Questionnaire (D), questionnaire (E)	Any pet in first year: adj OR, 0.91 (0.54-1.52)	Parental allergy, siblings, and frequent colds; adjustment for avoidance behavior showed similar results
Bråbäck et al, ²⁵ 2001, Sweden	2108	10-11	Questionnaire (D), questionnaire (E)	Cat (past): OR, 1.00 (0.70-1.50); dog (past): OR, 1.20 (0.80-1.70); adj data not given	None
Wickens et al, ²² 2002, New Zealand	293	7-10	Questionnaire (D), questionnaire (E)	Cat first year of life: adj OR, 0.40 (0.20-0.80); dog first year of life: adj OR, 0.80 (0.40-1.50)	Farm abode, exposure to poultry or pigs, sex, ethnicity, maternal education, family history of allergy, siblings, antibiotic use in first year, maternal smoking, fires, infections, and dairy food consumption

Abbreviations: adj, adjusted; CI, confidence interval; OR, odds ratio; SPT+, positive skin prick test.

Cross-sectional Studies

Five cross-sectional studies²⁶⁻³⁰ evaluated past pet exposure and current eczema. A large Swedish postal survey,²⁶ which recruited 14 077 children, found a protective effect with exposure to furry pets at the time of birth (adjusted OR, 0.73; 95% CI, 0.66-0.81). The protective effect of early life exposure remained significant even after adjustment for avoidance behavior (adjusted OR, 0.87; 95% CI, 0.78-0.97).²⁶ Four additional studies²⁷⁻³⁰ showed no significant association between past exposure and eczema risk (Tables 2 and 3).

OTHER EFFECTS

Overall, there seemed to be no systematic effect of age to follow-up or timing of pet exposure measurement (past

or present) on study results (eTable; available at <http://www.archdermatol.com>). Most cohort and cross-sectional studies used multiple logistic regression analysis to control for potential confounding factors, but only 3 studies^{18,26,30} directly adjusted for avoidance behavior (1 cohort study and 2 cross-sectional studies). Two cohort studies^{6,15} indirectly assessed avoidance behavior by using stratified analysis of a family history of atopic disease.

Where avoidance behavior (ie, parents stating that familial atopy was the reason for not having pets) was directly taken into account, the protective effect of pet exposure on eczema risk was either reduced or rendered insignificant.^{18,26,30} In the study by Kerkhof et al,¹⁸ after exclusion of babies where avoidance behavior was present, the borderline protective effect of cat exposure disappeared (including avoidance behavior: OR, 0.6; 95% CI, 0.3-1.1; and excluding avoidance behavior: OR, 0.8;

95% CI, 0.3-2.0) (Marjan Kerkhof, MD, written communication, September 2006). In the cohort studies by Zirnigbl et al¹⁵ and Nafstad et al,⁶ data were stratified by familial atopic disease. In the former study, the protective effect was retained only for dog exposure in individuals from atopic families (at 2 years only) and was no longer seen with cat exposure in either atopic or nonatopic families after stratification. In the latter study, the protective effect of cat and dog exposure was preserved only in the stratum with atopic parents and was no longer seen in those with no family history. In the 2 cross-sectional studies that directly assessed avoidance behavior, 1 study³⁰ did not show any significant association between pet exposure and eczema, and stratification for avoidance behavior did not alter this (avoidance behavior included: OR, 0.91; 95% CI, 0.54-1.52; and avoidance behavior excluded: OR, 0.93; 95% CI, 0.53-1.6). In the other cross-sectional study, Bornehag et al²⁶ asked parents if they avoided or got rid of pets because of allergy. The OR when avoidance behavior was present was 0.99 (95% CI, 0.81-1.21) and when this behavior was not present was 0.80 (95% CI, 0.70-0.91). Formal adjustment for avoidance behavior did not significantly change the study results, with the overall protective effect seen with pet exposure still being present (adjusted OR, 0.87; 95% CI, 0.78-0.97).

COMMENT

This systematic review did not find any convincing evidence of a positive association between past and current pet exposure and eczema risk. The results of some well-conducted prospective studies suggest that exposure to a pet, especially to a dog, may be protective against childhood eczema.

AVOIDANCE BEHAVIOR

Although longitudinal studies are generally seen as being methodologically superior to cross-sectional studies, it was disappointing that most of the birth cohorts included in this review did not adjust for potential avoidance behavior. Such parents may also opt to get rid of an existing pet if their child develops eczema, illustrating the importance of evaluating cohort studies that separate early exposure and subsequent disease.^{26,30} The 3 cohort studies^{18,26,30} that recognized avoidance behavior as an important confounding factor noted either a weakened or a nonsignificant association between pet exposure and eczema after adjustment.

In the Prevention and Incidence of Asthma and Mite Allergy study of high-risk births,¹⁸ parents were asked at a 3-month visit whether allergy was the reason for not having a cat; excluding these participants removed a borderline nonsignificant protective effect. However, no study has been performed in a birth cohort of high-risk families stratifying by parental previous belief at birth to determine whether prospectively recorded avoidance behavior is the true explanation for the association between pet exposure and eczema. At the same time, we found a similar negative association for dogs vs cats and ec-

zema, despite dog allergy being less prevalent than cat allergy and, therefore, less likely to trigger avoidance behavior. This finding suggests that avoidance behavior alone is unlikely to be a full explanation for these negative associations. An alternative explanation for the stronger inverse association between pets and eczema in children with a family history of allergic disease (Nafstad et al⁶) is that any such effect is more likely to be detected in high-risk groups with high disease incidence than in low-risk groups.

LIMITATIONS OF THIS REVIEW

Some of the differences in results seen between cross-sectional and birth cohort studies could well be explained by methodological differences. For example, cross-sectional studies that ask about antecedent events, such as pet exposure at birth, are prone to recall bias, and this may lead to a positive or negative association between eczema and pet exposure, depending on whether a parent believes that pets are harmful or otherwise. Parents with children who have eczema may be less likely to admit to pet exposure than parents of other children because of feelings of guilt. Studies used different ways of defining eczema. Some used the UK Working Party refinement of the Hanifin and Rajka criteria,⁴¹ others used physician diagnosis, and many of the questionnaire studies used the International Study of Asthma and Allergies in Childhood questionnaire.⁴² The variety of definitions used is a source of heterogeneity between studies. Using clinical history rather than skin prick test results or specific IgE levels to define atopy is another possible source of heterogeneity among studies.

A further difference between the studies was the timing of pet exposure. Nine cohort studies^{6,9,13-19} examined pet exposure in the first year of life. In that group of studies, 5 studies^{6,9,16-18} concentrated on the period from birth to age 3 months. Two studies^{20,22} assessed pet exposure up to age 4 years. However, pooling only the data for studies evaluating pet exposure to 1 year^{6,9,13-19} resulted in a minimal change to the OR estimate (cat exposure: pooled OR, 0.75; 95% CI, 0.61-0.91; and dog exposure: pooled OR, 0.73; 95% CI, 0.58-0.93). The cross-sectional studies,²²⁻³⁰ in contrast, studied pet exposure either at birth or to the current age of the child.

Although we attempted to be as comprehensive as possible in the literature search, some relevant articles may have been missed, and some data could have been concealed in asthma or allergy articles that would not have been picked up by the eczema search terms. We also acknowledge that publication bias (selective reporting of studies with positive results) may contribute to these findings. Before formulation of the hygiene hypothesis, this may have made publication of negative associations between pets and eczema less likely.

It is also important to emphasize that this review addressed only the question of keeping household pets at or around the time of birth and the risk of subsequent eczema development. The question of whether a cat or dog in the home is responsible for disease flares in those who already have eczema is a separate one, and we did not find any high-quality studies that addressed such a notion.

CLINICAL AND RESEARCH IMPLICATIONS

Parents of children with eczema frequently ask whether keeping a cat or dog at home might increase the risk that another child might develop eczema. This review suggests that pet exposure is not associated with an increased risk of eczema, a finding that does not support advising families to avoid pets in early life in the hope of preventing subsequent eczema. A possible protective effect is shown in a variety of studies, which is likely, in part, to be due to avoidance behavior. Future cohort studies exploring the association between pet exposure and subsequent allergic disease need to record the timing and type of pet exposure and perform stratified analysis for atopic vs nonatopic families and according to previous beliefs. A systematic review of the role of pets in asthma has shown an increased risk in older children with pet exposure but a possible protective effect in young children; these findings need to be considered in the formulation of practical advice.⁴³ New research is needed to assess the roles of pets in disease flares in eczema. This evidence should ideally be obtained from direct experimental provocation or cohort studies with objective exposure and disease activity measurements.

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Author Contributions: Dr Langan had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. *Study concept and design:* Langan and Williams. *Acquisition of data:* Langan and Flohr. *Analysis and interpretation of data:* Langan and Flohr. *Drafting of the manuscript:* Langan. *Critical revision of the manuscript for important intellectual content:* Flohr and Williams. *Study supervision:* Williams.

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REFERENCES

1. Ruzicka T. Atopic eczema between rationality and irrationality. *Arch Dermatol*. 1998;134(11):1462-1469.

2. Bener A, Galadari I, Naser KA. Pets, allergy and respiratory symptoms in children living in a desert country. *Allergy Immunol (Paris)*. 1995;27(6):190-195.
3. Adinoff AD, Tellez P, Clark RA. Atopic dermatitis and aeroallergen contact sensitivity. *J Allergy Clin Immunol*. 1988;81(4):736-742.
4. Almquist C, Larsson PH, Egmar AC, Hedén M, Malmberg P, Wickman M. School as a risk environment for children allergic to cats and a site for transfer for cat allergen to homes. *J Allergy Clin Immunol*. 1999;103(6):1012-1017.
5. Custovic A, Green R, Taggart SC, et al. Domestic allergens in public places, II: dog (Can f1) and cockroach (Bla g 2) allergens in dust and mite, cat, dog, and cockroach allergens in the air in public buildings. *Clin Exp Allergy*. 1996;26(11):1246-1252.
6. 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(4):307-312.
7. Halken S, Høst A, Hansen LG, Osterballe O. Effect of an allergy prevention programme on incidence of atopic symptoms in infancy: a prospective study of 159 "high-risk" infants. *Allergy*. 1992;47(5):545-553.
8. Braun-Falco O, Ring J. Therapy of atopic eczema [in German]. *Hautarzt*. 1984;35(9):447-454.
9. Gern JE, Reardon CL, Hoffman S, et al. Effects of dog ownership and genotype on immune development and atopy in infancy. *J Allergy Clin Immunol*. 2004;113(2):307-314.
10. Hoare C, Li Wan Po A, Williams H. Systematic review of treatments for atopic eczema. *Health Technol Assess*. 2000;4(37):1-191.
11. DerSimonian R, Laird N. Meta-analysis in clinical trials. *Control Clin Trials*. 1986;7(3):177-188.
12. Johansson SG, Bieber T, Dahl R, et al. Revised nomenclature for allergy for global use: report of the Nomenclature Review Committee of the World Allergy Organization, October 2003. *J Allergy Clin Immunol*. 2004;113(5):832-836.
13. Hagendorens MM, Bridts CH, Lauwers K, et al. Perinatal risk factors for sensitization, atopic dermatitis and wheezing during the first year of life (PIPO study). *Clin Exp Allergy*. 2005;35(6):733-740.
14. Purvis DJ, Thompson JM, Clark PM, et al. Risk factors for atopic dermatitis in New Zealand children at 3.5 years of age. *Br J Dermatol*. 2005;152(4):742-749.
15. Zirngibl A, Franke K, Gehring U, et al; GINI Study Group. Exposure to pets and atopic dermatitis during the first two years of life: a cohort study. *Pediatr Allergy Immunol*. 2002;13(6):394-401.
16. Illi S, von Mutius E, Lau S, et al; Multicenter Allergy Study Group. The natural course of atopic dermatitis from birth to age 7 years and the association with asthma. *J Allergy Clin Immunol*. 2004;113(5):925-931.
17. Phipatanakul W, Celedón JC, Raby BA, et al. Endotoxin exposure and eczema in the first year of life. *Pediatrics*. 2004;114(1):13-18.
18. Kerkhof M, Koopman LP, van Strien RT, et al; PIAMA Study Group. Risk factors for atopic dermatitis in infants at high risk of allergy: the PIAMA study. *Clin Exp Allergy*. 2003;33(10):1336-1341.
19. Benn CS, Melbye M, Wohlfahrt J, Björkstén B, Aaby P. Cohort study of sibling effect, infectious diseases, and risk of atopic dermatitis during first 18 months of life. *BMJ*. 2004;328(7450):1223. doi:10.1136/bmj.38069.512245.FE.
20. Tariq SM, Matthews SM, Hakim EA, Stevens M, Arshad SH, Hide DW. The prevalence of and risk factors for atopy in early childhood: a whole population birth cohort study. *J Allergy Clin Immunol*. 1998;101(5):587-593.
21. Arshad SH, Stevens M, Hide DW. The effect of genetic and environmental factors on the prevalence of allergic disorders at the age of two years. *Clin Exp Allergy*. 1993;23(6):504-511.
22. Wickens K, Lane JM, Fitzharris P, et al. Farm residence and exposures and the risk of allergic diseases in New Zealand children. *Allergy*. 2002;57(12):1171-1179.
23. Höltscher B, Frye C, Wichmann HE, Heinrich J. Exposure to pets and allergies in children. *Pediatr Allergy Immunol*. 2002;13(5):334-341.
24. Rönmark E, Lundbäck B, Jönsson E, Platts-Mills T. 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(2):316-324.
25. Bråbäck L, Kjellman NI, Sandin A, Björkstén B. Atopy among schoolchildren in northern and southern Sweden in relation to pet ownership and early life events. *Pediatr Allergy Immunol*. 2001;12(1):4-10.
26. Bornehag CG, Sundell J, Hagerhed L, Janson S; DBH Study Group. Pet-keeping in early childhood and airway, nose and skin symptoms later in life. *Allergy*. 2003;58(9):939-944.
27. Zutavern A, Hirsch T, Leupold W, Weiland S, Keil U, von Mutius E. Atopic dermatitis, extrinsic atopic dermatitis and the hygiene hypothesis: results from a cross-sectional study. *Clin Exp Allergy*. 2005;35(10):1301-1308.
28. Morales Suárez-Varela MM, Jiménez-López MC, Llopis-González A, García-Marcos L. Study of the presence of domestic animals: cats and dogs and their role in asthma, allergic rhinitis and atopic dermatitis in children [in Spanish]. *Aten Primaria*. 2005;36(9):525.

29. Anyo G, Brunekreef B, de Meer G, Aarts F, Janssen NA, 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(3):361-366.
30. Hesselmar B, Åberg N, Åberg B, Eriksson B, Björkstén B. Does early exposure to cat or dog protect against later allergy development? *Clin Exp Allergy*. 1999; 29(5):611-617.
31. Kurosaka F, Nakatani Y, Terada T, et al. Current cat ownership may be associated with the lower prevalence of atopic dermatitis, allergic rhinitis and Japanese cedar pollinosis in schoolchildren in Himeji, Japan. *Pediatr Allergy Immunol*. 2006;17(1):22-28.
32. Yemaneberhan H, Flohr C, Lewis SA, et al. Prevalence and associated factors of atopic dermatitis symptoms in rural and urban Ethiopia. *Clin Exp Allergy*. 2004; 34(5):779-785.
33. Miyake Y, Yura A, Iki M. Cross-sectional study of allergic disorders in relation to familial factors in Japanese adolescents. *Acta Paediatr*. 2004;93(3):380-385.
34. Schäfer T, Heinrich J, Wjst M, et al. Indoor risk factors for atopic eczema in school children from East Germany. *Environ Res*. 1999;81(2):151-158.
35. Austin JB, Russell G, Adam MG, Mackintosh D, Kelsey S, Peck DF. Prevalence of asthma and wheeze in the Highlands of Scotland. *Arch Dis Child*. 1994;71(3):211-216.
36. Austin JB, Russell G. Wheeze, cough, atopy, and indoor environment in the Scottish Highlands. *Arch Dis Child*. 1997;76(1):22-26.
37. Dotterud LK, Falk ES. Atopic disease among adults in Northern Russia, an area with heavy air pollution. *Acta Derm Venereol*. 1999;79(6):448-450.
38. Schäfer T, Vieluf D, Behrendt H, Krämer U, Ring J. Atopic eczema and other manifestations of atopy: results of a study in East and West Germany. *Allergy*. 1996; 51(8):532-539.
39. Kalyoncu AF, Selçuk ZT, Karakoca Y, et al. Prevalence of childhood asthma and allergic diseases in Ankara, Turkey. *Allergy*. 1994;49(6):485-488.
40. Sebök B, Schneider I, Harangi F; Primary Care Paediatricians in Baranya County. Familiar and environmental factors influencing atopic dermatitis in the childhood. *J Eur Acad Dermatol Venereol*. 2006;20(4):418-422.
41. Williams HC, Burney PG, Hay RJ, et al. The UK Working Party's Diagnostic Criteria for Atopic Dermatitis, I: derivation of a minimum set of discriminators for atopic dermatitis. *Br J Dermatol*. 1994;131(3):383-396.
42. Asher MI, Keil U, Anderson HR, et al. International Study of Asthma and Allergies in Childhood (ISAAC): rationale and methods. *Eur Respir J*. 1995;8(3): 483-491.
43. Apelberg BJ, Aoki Y, Jaakkola JJ. Systematic review: exposure to pets and risk of asthma and asthma-like symptoms. *J Allergy Clin Immunol*. 2001;107(3): 455-460.

Archives Web Quiz Winner

Congratulations to the winner of our September quiz, Mahmood Saeed Kalil, MD, Shaqra Hospital, Shaqra, Saudi Arabia. The correct answer to our September challenge was *lobomycosis*. For a complete discussion of this case, see the Off-Center Fold section in the October *Archives* (Chrusciak-Talhari A, Talhari C, Nunes de Souza Santos M, Ferreira LC, Talhari S. Nodular lesions on the arm. *Arch Dermatol*. 2007;143[10]: 1323-1328).

Be sure to visit the *Archives of Dermatology* Web site (<http://www.archdermatol.com>) to try your hand at the interactive quiz. We invite visitors to make a diagnosis based on selected information from a case report or other feature scheduled to be published in the following month's print edition of the *Archives*. The first visitor to e-mail our Web editors with the correct answer will be recognized in the print journal and on our Web site and will also receive a free copy of *The Art of JAMA II*.

eTable. Summary of Results of Cross-sectional Studies Assessing Current Pet Exposure Arranged by Sample Size

Source and Country	Participants, No.	Age, y	Diagnostic (D) and Exposure (E) Criteria	Outcome Measures: OR (95% CI)	Confounders Adjusted for in Analysis
Kurosaka et al, ³¹ 2006, Japan	35 242	6 and 7	Questionnaire (D); questionnaire (E)	Cat (current): OR, 0.79 (0.67-0.93); dog (current): OR, 1.04 (0.85-1.27); cat or dog (current): OR, 0.63 (0.30-1.32)	None
Bornehag et al, ²⁶ 2003, Sweden	14 077	1 to 6	Questionnaire (D); questionnaire (E)	Any pet (current): adj OR, 0.91 (0.72-1.14)	Age, sex, smoke exposure, familial allergy, breastfeeding, type of building, and avoidance behavior
Yemaneberhan et al, ³² 2004, Ethiopia	12 876	0 to $\geq$ 60	Questionnaire (D); questionnaire (E)	Any indoor pet (current): adj OR, 1.35 (0.97-1.88)	Age, sex, socioeconomic status, residence, and kerosene use
Miyake et al, ³³ 2004, Japan	5539	12 to 15	Questionnaire (D); questionnaire (E)	Any indoor pet (current): adj OR, 1.03 (0.85-1.25)	Age, sex, grade, siblings, maternal age, smoke exposure, and parental history of allergy
Hölscher et al, ²³ 2002, Germany	5360	5 to 14	Questionnaire (D); questionnaire (E)	Cat (current): adj OR, 0.93 (0.78-1.10); dog (current): adj OR, 0.92 (0.78-1.09)	Age, sex, region, survey, parental education, parental atopy, breastfeeding, day care, sharing bedroom, smoke exposure, and contact with rodents and birds
Morales Suárez-Varela et al, ²⁸ 2005, Spain	4387	8 to 15	Questionnaire (D); questionnaire (E)	Any pet (current): OR, 1.10 (0.90-1.30)	None
Rönmark et al, ²⁴ 1998, Sweden	3431	7 and 8	Questionnaire (D); questionnaire (E)	Cat (current): adj OR, 0.73 (0.46-1.18); dog (current): adj OR, 0.58 (0.38-0.87); SPT+ to cat: OR, 2.59 (2.10-3.19); SPT+ to dog: OR, 2.75 (2.20-3.44)	Positive skin test result, family history of asthma, sex, damp at home, breastfeeding < 3 mo, smoking mother, urban living, and birth order
Anyo et al, ²⁹ 2002, the Netherlands	2729	7 to 12	Questionnaire (D); questionnaire (E)	Any pet (current): adj OR, 0.96 (0.77-1.19)	Age, sex, parental nationality, parental allergy, parental education, siblings, smoke exposure, day care, and area of residence
Schäfer et al, ³⁴ 1999, Germany	2200 (Some from 1996 study)	5 to 14	Physician examination (D); questionnaire (E)	Cat (current): adj OR, 0.82 (0.38-1.76); dog (current): adj OR, 0.75 (0.33-1.70); guinea pig (current): adj OR, 3.56 (1.68-7.54); hamster (current): OR, 1.61 (0.45-5.72)	Age, bedroom sharing, smoke exposure, and automobile exhaust exposure
Bråbäck et al, ²⁵ 2001, Sweden	2108	10 and 11	Questionnaire (D); questionnaire (E)	Cat (current): OR, 0.80 (0.60-1.00)	None
Austin et al, ³⁵ 1994, United Kingdom	1919	12 and 13	Questionnaire (D); questionnaire (E)	Dog (current): OR, 0.90 (0.70-1.30); Dog (current): OR, 0.99 (0.76-1.30); cat (current): OR, 1.11 (0.84-1.47); other mammal (current): OR, 1.12 (0.81-1.56)	None
Austin and Russell, ³⁶ 1997, United Kingdom	1801	12 to 14	Questionnaire (D); questionnaire (E)	Dog (current): OR, 0.78 (0.60-1.03); cat (current): OR, 0.92 (0.70-1.20); other mammal (current): OR, 1.38 (1.02-1.88)	None
Dotterud and Falk, ³⁷ 1999, Norway	1800	8 to 17	Questionnaire (D); questionnaire (E)	Any pet (boys current): adj OR, 1.00 (0.70-1.30); any pet (girls current): adj OR, 1.00 (0.80-1.30)	Unclear what confounders were adjusted for
Schäfer et al, ³⁸ 1996, Germany	1274	5 to 7	Physician examination (D); questionnaire (E)	Small furry pets: rabbits (current): adj OR, 1.81 (0.96-3.41); fur in bedroom (current): adj OR, 2.17 (1.01-4.67)	Age, sex, location, and socioeconomic status
Kalyoncu et al, ³⁹ 1994, Turkey	1226	6 to 12	Questionnaire (D); questionnaire (E)	Any pet: authors describe increased risk of eczema in group with pets (current); insufficient data to calculate OR	None
Sebök et al, ⁴⁰ 2006, Hungary	461 Cases; 343 controls	0 to 12	Physician examination (D); questionnaire (E)	Any indoor pet: OR, 1.32 (1.20-2.58)	Age and sex
Wickens et al, ²² 2002, New Zealand	293	7 to 10	Questionnaire (D); questionnaire (E)	Cat (current): adj OR, 2.80 (1.30-6.10); dog (current): adj OR, 1.30 (0.60-2.70)	Farm abode, exposure to poultry or pigs, sex, ethnicity, maternal education, family history of allergy, siblings, antibiotic use in first year, maternal smoking, fires, infections, and dairy food consumption

Abbreviations: adj, adjusted; CI, confidence interval; OR, odds ratio; SPT+, positive skin prick test.