

Original article

Exposure to pets and atopy-related diseases in the first 4 years of life

Background: It is still unclear how early-life exposure to pets is related to children's risk of developing atopy-related diseases. We estimated associations between early-life exposure to pets and atopy-related diseases at 0–4 years of life in a cohort of Norwegian children.

Methods: A population-based cohort of 2531 children born in Oslo, Norway, was followed from birth to the age of 4 years. Information on early-life exposure to pets, a number of possible confounders, and atopy-related diseases was mainly collected by questionnaire.

Results: In logistic regression analysis adjusting for potential confounders, the odds ratio for being exposed to pets in early life (reference category: not exposed) was, for bronchial obstruction at 0–2 years of life, 1.2 (95% confidence interval 0.9, 1.8); for asthma at the age of 4 years, 0.7 (0.5, 1.1); for allergic rhinitis at the age of 4 years, 0.6 (0.4, 1.0); and for atopic eczema at 0–6 months of life, 0.7 (0.5, 0.9).

Conclusions: The results indicate that early-life exposure to pets or lifestyle factors associated with exposure to pets reduce the risk of developing atopy-related diseases in early childhood. However, these findings might also be explained by selection for keeping pets.

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Studies have shown that exposure to furred pets can increase the occurrence of atopy-related diseases and conditions (1–9). Whether early exposure to pets could increase the risk of developing atopic diseases is more uncertain (1, 10–11). Even so, it has been common to advise families disposed to allergic diseases to avoid keeping pets. Results from recent studies have challenged this practice, as they show negative associations between early-life exposure to domestic pets and the occurrence of atopy-related conditions (6, 12, 13). This is further supported by the findings of reduced risks of developing atopy among children raised on farms with livestock (14–16). It seems that early exposure to pet allergens could be favorable or that growing up in an environment with pets or other animals could change children's exposure to other factors in a protective direction. So far, most of these studies have collected information on exposure to pets retrospectively, and the time from exposure to the assessment of the health outcomes has been long. We used data from the Oslo Birth Cohort Study (17–19) to estimate associations between early-life exposure to pets and atopy-related diseases during the first 4 years of life.

Material and methods

Study population

The study population comprised a cohort of 3754 children born in Oslo in 1992/93 (17). The inclusion criteria and data collection

procedure for the children's first 4 years of life are described in detail elsewhere (17–19). Briefly, the population included children born at the two main birth clinics in Oslo during a 15-month period in 1992–3. The eligibility criteria were as follows: permanent address within the city of Oslo, no plans of moving from Oslo in the near future, birth weight greater than 2000 g, no serious illness which might impair respiration, no assisted ventilation or oxygen therapy after 6 h of life, at least one family member able to speak and write Norwegian, at least one biologic parent living with the child, and no known drug abuse in the family. Information on the child's health and environmental exposures was collected by self-administered questionnaires at birth and when the child was 6 months, 12 months, 18 months, and 24 months old. The follow-up rate was 81% ($n=3048$) at the age of 2 years.

We conducted a follow-up by mailing self-administered questionnaires at the end of 1996 to all 4-year-old children living in Oslo and children of the cohort living outside Oslo (19, 20). Only the 3048 children with complete information on respiratory health during the first 2 years of their life were included in the present study. A correct mailing address was obtained for 2985 of these children, and a completed questionnaire was received from families of 2594 children (87% of the 2-year cohort and 67% of the baseline study population). Children with incomplete information on atopic diseases at the age of 4 years were excluded ($n=63$), leaving 2531 children for the present analysis.

A subsample (251 cases and controls) of the cohort was included in a matched case-control study on early-life environmental exposure and the risk of bronchial obstruction in the first 2 years of life (21). Children in this subsample received home visits to assess environmental exposures, including collection of house-dust samples, which were analyzed for house-dust mites, and cat and dog allergens. This information was mainly used to estimate the agreement between the questionnaire information on keeping pets and allergen concentrations in house dust.

Atopy-related conditions at 0–4 years of age

Bronchial obstruction at 0–2 years of life. Bronchial obstruction was defined as two or more episodes with symptoms and signs of obstruction or one episode lasting more than 1 month during the first 2 years of life (18). At least one of the episodes had to be diagnosed by a physician, and the guidelines were that at least three out of five symptoms or signs (wheezing, chest recession, rhonchi during auscultation, forced expiration, and rapid breathing) should be observed.

Current asthma and allergic rhinitis (allergy from the nose or eyes including hay fever). These outcomes were defined on the basis of answers to the 4-year follow-up questionnaire. Both outcomes had to be diagnosed by a physician, and current disease meant that the child had to have experienced symptoms of the disease during the previous 12 months.

Atopic eczema at 0–6 months of age. This outcome was defined on the basis of answers to the 6-month follow-up questionnaire. (Has your child experienced infant eczema [atopic eczema]?). A similar question was asked about the experience of eczema related to the use of diapers (diaper eczema).

Child and family characteristics, and environmental exposures

We obtained information on covariates and potential confounders from the questionnaires and hospital records. This includes parental atopy, child's sex, birth weight, birth order, maternal age at delivery, maternal education (number of years), family income per year (Norwegian kroner [NOK]), environmental tobacco smoke exposure, length of breast-feeding, and one or more episodes of lower respiratory tract infections during the first year of life (17). Their categorization and distribution according to whether or not the children had pets at home at birth are presented in Table 1.

Parental atopy was based on information on parental asthma and hay fever from the birth questionnaire. We considered children living with one or more persons who smoked when they had been born, as being exposed to environmental tobacco smoke. According to the length of breast-feeding reported in both the 6- and 12-month questionnaires, children were categorized according to whether or not they were breast-fed for more than 6 months.

Concentration of cat and dog allergen in house dust

A subsample of 502 children (251 one-to-one matched case-control pairs) received a home visit during their first 2 years of life, and an area on the floor in the living room was vacuum cleaned for 2 min with a nozzle containing a cellular filter. The procedure for the data collection and the analyses of house-dust-mite allergens are described elsewhere (21). Cat allergen (Fel d 1) concentrations were determined by capture ELISA using Dynatech Immulon II M129B polystyrene microtiter plates and monoclonal antibodies (purchased from Dr Martin Chapman and Indoor Biotechnologies, Clewyd, UK), mainly according to the manufacturer's instructions (22). Dog allergen (Can f 1) was measured on similar plates with a monoclonal capture antibody (Indoor Biotechnologies), and polyclonal rabbit anti-Can f 1 (kindly provided by Dr C. Schou, ALK, Hørsholm, Denmark) and alkaline phosphatase-labeled donkey antirabbit IgG (Jackson ImmunoResearch Laboratories, West Grove, PA, USA) as second and third antibodies, respectively. A series of dilutions of reference cat dander preparation CBER Cat E3 (FDA, Bethesda, MD, USA) or dog hair and dander extract 84/685 (NIBSC, Hertfordshire, UK) were induced on every plate to provide a standard curve. Results were given as ng or µg allergens per g sieved dust. The assay sensitivity was 0.3 ng/ml for cat allergens and 1.6 ng/ml for dog allergens, corresponding to 12 and 64 ng/g of sieved dust,

Table 1. Prevalences of keeping pets at home when child was born compared with child and family characteristics, and environmental exposures

		Any pet (n = 563) (22.4%)	Cat (n = 178) (7.1%)	Dog (n = 228) (9.1%)
	n	%	%	%
Parental hay fever and/or asthma				
Mother – /father –	1640	23.2	7.8	9.6
Mother + /father –	346	24.3	5.5	8.4
Mother – /father +	404	18.6	6.2	8.2
Mother + /father +	118	19.5	5.1	6.8
Child's sex				
F	1218	22.4	7.8	9.4
M	1290	22.5	6.4	8.8
Birth weight				
<2500 g	299	22.1	6.0	9.7
2500–3499 g	787	24.1	7.9	8.4
+3500 g	1409	21.5	6.9	9.4
Birth order				
First	1320	23.5	7.5	9.0
Second	885	20.6	6.7	8.5
Third or later	293	23.5	6.5	11.3
Maternal age at delivery				
<25 years	238	34.9	8.4	10.1
25–39 years	890	21.5	7.1	7.5
+30 years	1380	20.9	6.9	9.9
Maternal education				
<12 years	117	27.4	6.0	12.0
12–15 years	905	27.6	7.5	10.6
>15 years	1467	19.0	7.0	7.8
Family income per year				
<200 000 NOK	323	24.8	7.1	9.9
200–500 000 NOK	1655	22.9	7.7	8.5
>500 000 NOK	496	19.4	4.8	10.9
Environmental tobacco smoke exposure in early life				
No	1503	19.4	5.3	8.4
Yes	997	27.0	9.7	10.2
Length of breast-feeding				
≤6 months	703	25.5	7.7	10.2
>6 months	1730	21.2	6.9	8.8
One or more lower respiratory infection first year of life				
No	2100	22.5	7.3	8.7
Yes	408	22.1	6.1	11.0

Subjects missing information on pets at home: 23.

Other subjects missing information: birth weight (n = 13), environmental tobacco smoke exposure in early life (n = 8), maternal education (n = 19), family income (n = 34), and length of breast-feeding (n = 75).

respectively. However, some beds had very low dust levels, leading to more diluted samples and consequently poorer sensitivity when expressed as ng/g.

Statistical methods

Agreement between methods for measuring exposure to pets was compared by estimating the Kappa coefficient of children with/without pets at home and having high/low concentrations of cat or dog allergens in house dust. We defined cutoff levels to obtain prevalences of high allergen concentrations of similar size as the prevalence of keeping pets. We estimated the agreements between pet allergen concentrations and reports of having pets at home at birth and having pets according to the questionnaire filled in nearest in time to the home visits.

We estimated the relation between the early-life determinants/exposure and the atopic diseases by calculating crude odds ratios. These were adjusted for confounding factors in logistic regression analysis. Some children had missing information for some of the variables, and a category for missing was made for these variables. Results of logistic regression analyses with and without the missing category gave similar results. Only the results of the first approach are presented.

Results

Exposure

Pets at home at birth were equally common among children included in the cohort, children followed for 2 years and children followed for both 2 and 4 years (any pet: 22.9%, 22.5%, and 22.4%; cat: 7.6%, 7.2%, and 7.1%; and dog: 9.3%, 9.2%, and 9.1%). The homes of well-educated and older mothers less often had pets than those of less educated and younger mothers, respectively (Table 1). Children exposed to environmental tobacco smoke at home were also more exposed to pets.

According to when the information on domestic pets were collected, low levels of cat ($\leq 1 \mu\text{g/g}$ dust) and dog ($\leq 10 \mu\text{g/g}$ dust) allergen concentrations were found in 93–97% of the homes without and high levels in 64–82% of homes with cats or dogs (Table 2). Corresponding agreements between cat ownership and high/low cat allergen concentrations, as measured by the Kappa coefficient, were 0.57 and 0.63; for dog ownership and high/low dog allergen concentrations, they were 0.58 and 0.58. The agreement was similar among children with and without bronchial obstruction during the first 2 years of life (figures not given).

Relations between pet exposure and atopic diseases

Conditional logistic regression analyses did not show any significant association between high and low levels

Table 2. Agreement between questionnaire information on children's exposure to cats and dogs in early life and concentrations of cat and dog allergen in house dust from children's homes*

			Allergens in house dust	
Cats at home		<i>n</i>	≤1 µg/g	> 1 µg/g
Having cat**	No	432	93%	7%
	Yes	39	18%	82%
Having cat at home at birth	No	419	93%	7%
	Yes	40	20%	80%

			Allergens in house dust	
Dogs at home		<i>n</i>	≤10 µg/g	> 10 µg/g
Having dog**	No	434	96%	4%
	Yes	33	33%	67%
Having dog at home at birth	No	413	97%	3%
	Yes	42	36%	64%

* Allergen concentrations in house dust from living room measured once during children's first 2 years of life.

** Information extracted from questionnaire filled in nearest in time to collection of house dust.

Missing information from 31–47 cases in each analysis.

of cat and dog allergen and bronchial obstruction during the first 2 years of life; odds ratio (OR): 0.9 (95% confidence interval [CI] 0.5, 1.6) and 1.5 (0.7, 3.0). Among children followed for 4 years, keeping dogs at home at birth was positively associated with the risk of bronchial obstruction during the first 2 years; OR: 1.6 (95% CI 1.0, 2.6) (Table 3). Table 3 also shows that the associations between early-life exposure to pets and asthma and allergic rhinitis at the age of 4 years were mainly negative. The odds ratio for having allergic rhinitis if the child had been exposed to pets at birth was 0.6 (95% CI 0.4, 1.0); for exposure to cats, it was 0.5 (95% CI 0.2, 1.4). Including exposure to cats and dogs in the same model did not change the estimated effects of these exposures. The risks of having both asthma and allergic rhinitis ($n=44$) among children exposed

Table 3. Risk, crude odds ratios (OR), and *adjusted odds ratios (aOR) and 95% confidence intervals (CI) of having bronchial obstruction at 0–2 years of life, and asthma and allergic rhinitis at age of 4 years by keeping pets at home when the child was born

	<i>n</i>	Bronchial obstruction at 0–2 years of life (<i>n</i> =224)				Asthma at age of 4 years (<i>n</i> =162)				Allergic rhinitis at age of 4 years (<i>n</i> =116)			
		Risk	OR	aOR	95% CI	Risk	OR	aOR	95% CI	Risk	OR	aOR	95% CI
Any pet													
No	1945	0.086				0.067				0.050			
Yes	563	0.101	1.2	1.2	0.9, 1.8	0.055	0.8	0.7	0.5, 1.1	0.034	0.7	0.6	0.4, 1.0
Cat													
No	2330	0.091				0.066				0.048			
Yes	178	0.067	0.7	0.7	0.4, 1.4	0.045	0.7	0.7	0.4, 1.5	0.022	0.5	0.5	0.2, 1.4
Dog													
No	2280	0.086				0.064				0.047			
Yes	228	0.127	1.6	1.6	1.0, 2.6	0.070	1.1	1.1	0.6, 1.9	0.039	0.8	0.8	0.4, 1.6

Subjects missing information on pets at home: 23.

* Adjusted for parental atopy, child's sex, birth weight, birth order, maternal age at delivery, maternal education, family income per year, environmental tobacco smoke exposure, length of breast-feeding, and one or more episodes of lower respiratory tract infections during first year of life.

Table 4. Risk, crude odds ratios (OR), and *adjusted odds ratios (aOR) and 95% confidence intervals for having atopic eczema at 0–6 months of age by keeping pets at home when child was born in total and different categories of parental atopy

	All children (n=2347)					Children of atopic parents (n=819)					Children of nonatopic parents (n=1528)				
	n	Risk	OR	aOR	95% CI	n	Risk	OR	aOR	95% CI	n	Risk	OR	aOR	95% CI
Pet exposure															
No	1818	0.169				647	0.215				1171	0.141			
Yes	529	0.125	0.7	0.7	0.5, 0.9	172	0.140	0.6	0.6	0.4, 0.9	357	0.118	0.8	0.8	0.6, 1.2
Cat exposure															
No	2178	0.164				770	0.206				1408	0.141			
Yes	169	0.089	0.5	0.5	0.3, 0.9	49	0.082	0.3	0.3	0.1, 0.9	120	0.092	0.6	0.6	0.3, 1.2
Dog exposure															
No	2135	0.163				756	0.206				1379	0.140			
Yes	212	0.113	0.7	0.7	0.4, 1.0	63	0.111	0.5	0.5	0.2, 1.0	149	0.114	0.8	0.8	0.5, 1.4

Information on pets (missing=23) and atopic eczema (missing=161) available for 2347 children.

* Adjusted for parental atopy, child's sex, birth weight, birth order, maternal age at delivery, maternal education, family income per year, and environmental tobacco smoke exposure.

and unexposed to pets at home were 0.006 and 0.023, respectively. The odds ratio for early-life exposure to pets for this group was 0.3 (95% CI 0.1, 0.8). Corresponding figures for exposure to cats were 0.000 vs 0.020 (OR not calculated), and for dogs 0.010 vs 0.020 (OR: 0.5 [95% CI 0.1, 2.0]).

Stratified analyses did not indicate that exposure to pets had a different effect in children with and without atopic predisposition (figures not given). The confidence limits grew larger due to reduced statistical power, especially among children of atopic parents.

Table 4 shows that exposure to pets at home at birth was significantly less common among children who experienced atopic eczema during the first 6 months of life than among children who did not. The adjusted odds ratio for exposure to any pet was 0.7 (95% CI 0.5, 0.9); for cats, it was 0.5 (95% CI 0.3, 0.9); and, for dogs, it was 0.7 (95% CI 0.4, 1.0). Stratified analysis showed that the associations were strongest in children of atopic parents. Diaper eczema at 0–6 months of life was about equally common among children with and without pets at home at birth (any pet: 16.7% vs 15.3%; cat: 15.6% vs 15.6%; dog: 13.2% vs 15.9%).

Discussion

Pets were kept in 22.4% of the homes when the children were born (7.1% of homes had cats, and 9.1% dogs). The associations between early-life exposure to pets and atopy-related conditions at 4 years of age were mainly negative. This was also the case with atopic eczema at 0–6 months of life. The adjusted odds ratio for early-life atopic eczema if exposed to pets at home was 0.7 (95% CI 0.5, 0.9); if exposed to cats, it was 0.5 (95% CI 0.3, 0.9).

Unlike other researchers (6, 12–13), we were able to estimate associations between early-life exposure to pets and atopy-related diseases from prospectively collected information on pet keeping, as well as for a number of potential confounders. This approach reduced the

chance of recall bias. Keeping pets could have been associated with conditions that could confound the association between exposure to pets and atopic disorders. Environmental tobacco smoke exposure might have been such a confounder, as it was associated with keeping pets and was likely to influence some of the health outcomes. However, we found no convincing evidence of confounding factors. Due to a large study population, the health outcomes were mainly assessed by questionnaires. This could have led to some misclassification. A cohort study reduces the chance of systematic misclassification. However, it could be that parents who keep pets underreport diseases in general. This did not seem to be the case, as associations between diseases and exposure to pets varied, and negative associations seemed to be specific for the diseases we considered to be the most atopic. Nonsystematic misclassification may have weakened the associations, but could not have changed their direction.

Information on pet allergens and keeping pets was not collected at exactly the same time. Even so, the agreement between the results of two different methods for measuring exposure to dog and cat allergens was quite good. Few families kept pets (1, 2, 5–7). This could indicate that exposure to pet allergens in general was low, resulting in a larger difference in exposure between homes with and without pets than in populations with a higher prevalence of keeping pets. However, we also found that cat and dog allergens were present in homes without pets, demonstrating that it is difficult to establish a truly unexposed reference group (23, 24). For practical and economic reasons it is seldom feasible to monitor allergen levels on a large scale in house dust over time. Therefore, keeping pets is the most feasible way to assess exposure over time in large cohort studies. Due to this and to low statistical power, we have not focused on the associations between concentrations of pet allergens and the studied health outcomes.

The results of this study are generally in agreement

with earlier findings of negative associations between early-life exposure to pets and atopy-related conditions (6, 12, 13). The positive association between dog exposure and early-life bronchial obstruction could be explained by the fact that early-life bronchial obstruction is a more infectious and less atopic condition than asthma later in childhood, and that keeping dogs increases the risk of contracting infections. The negative associations could have several explanations. First, early exposure to pet allergens could have a general or specific protective effect, resulting in a reduced development of all or several types of allergic or atopy-related diseases/conditions later in life. Second, exposure to pets could indicate other exposures or lack of exposures of importance for the development of these diseases (25). Third, the associations could have been the result of selection for keeping pets both after and before childbirth, including previous generations. To single out the right explanation is difficult. Allergic reactions to pets in early life might lead to a reduction in children's exposure to pets that could reduce the occurrence of atopic disorders later in life. A lengthy period between the measurements of exposure and outcome would favor such an explanation. However, if the protective effect is of short duration, it could be overlooked. A follow-up of a birth cohort would not necessarily exclude these possibilities. The short periods between pet exposure and the occurrence of the

outcomes in this study (from 0–6 months to 4 years) support a true negative association. Furthermore, the association was specific for early-life atopic eczema, and not for diaper eczema. However, it is still possible that the tendency to keep pets has been under selection for prebirth experiences. The selection mechanism may not be captured by a simple control by parental atopy. It is likely that the decision to keep pets is often based on other conditions than a family history of asthma or hay fever. To reduce the chance of selection bias, one could try to control for reports of refraining from keeping pets (12), but the reasons for not keeping pets may not always be obvious and easy to report.

The effect of early-life exposure to pets on the development of atopic disorders is difficult to study. The negative associations shown in this study could have several explanations. They could indicate a protective effect of early-life exposure to pets, or that keeping pets is associated with a lifestyle that protects against the development of atopic diseases. However, they might also be explained by prebirth selection with regard to keeping pets.

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