

Short communication

Health impacts of second-hand exposure to cat allergen Fel d 1 in infants

Background: Recent cross-sectional studies suggested that highest sensitization prevalences occur with moderate cat allergen exposures. We aimed to assess the impact of moderate levels of second-hand cat allergen exposure on the incidence of specific sensitization and wheezing in the framework of a birth cohort study. Therefore we restricted our analysis to infants without a cat at home since birth.

Methods: At infant's age 3 months, cat allergen levels were measured in the mattress dust of 1840 families without cats. At age 2 years, serum IgE specific to Fel d 1 was analyzed. Incidence of wheezing apart from respiratory infection was assessed by questionnaire. Logistic regression models were used to calculate adjusted odds ratios (OR) for the association between second-hand cat allergen exposure and health outcomes.

Results: Until age 2 years, 13 of 1301 infants (1%) were sensitized to cat allergen and 56 of 1492 infants (4%) had ever-wheezing without infection. Early exposure to second-hand cat allergen levels ≥ 1 $\mu\text{g/g}$ dust increased substantially the risk for specific sensitization to Fel d 1 (OR 10.9, 95% CI 3.4–35.0) and ever-wheeze without infection (OR 2.0, 95% CI 1.1–3.9) at age 2 years.

Conclusions: Second-hand exposure to cat allergen in homes without cats is detrimental in terms of allergy development in infants.

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Currently the linearity of the dose–response link between exposure and sensitization to cat allergen is questioned, and high cumulative exposure to cat allergen in early life is debated to induce tolerance, and to relatively reduce sensitization risk compared to moderate exposure (1–4). Several studies discussed a potential protective effect of pet-keeping during childhood on development of allergy; for instance, Roost et al. pointed out that childhood exposure to cats may be associated with a lower risk of

sensitization in adults (1). By demonstrating a modified Th2-helper cell response with increased IgG specific to Fel d 1 and decreased IgE sensitization in children exposed to high cat allergen levels, Platts-Mills and coworkers proposed that moderate exposure would be most detrimental (2). In accordance with this, in a study of adults the highest prevalence of specific sensitization to cats was observed in the exposure group with moderate cat allergen concentrations (3).

These cross-sectional studies consisted of study populations with and without cats, so the data do not allow differentiation regarding whether the exposure to high levels of cat allergen itself is related to the decreased risk of sensitization, or whether it is related to close contact with a cat and exposure to microbial factors such as endotoxin play a role. Endotoxin levels in settled house dust have been shown to be associated with cat-keeping (5).

In an attempt to disentangle the issues, we focused our analysis on infants living without a cat in the home. For this purpose, we selected from the ongoing birth cohort study LISA all those families who had not kept a cat since the infant's birth. Our study aimed to assess the health impacts of second-hand exposure to mostly low or moderate cat allergen levels during the first months of life in infants without concomitant exposure to other cat-related factors at home. As health effects, we analyzed the

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incidence of specific sensitization to cat allergen and wheezing among infants until the age of 2 years. Furthermore, we wanted to define which factors contributed to the indoor cat allergen levels found in homes without a cat.

Material and methods

Study subjects

The birth cohort study LISA (Influences of life-style related factors on the immune system and the development of allergies in childhood) enrolled 2443 healthy term newborns in Munich and Leipzig during 1998. At infant's age 3 months, samples of settled house dust were collected from the mother's mattress as surrogate for early cumulative exposure in homes of 2110 families (86% of the cohort). From birth until age 2 years, parents completed at regular time intervals questionnaires on living conditions and the infant's health. For analyzing the effect of second-hand cat allergen exposure, we only included families ($n = 1840$) that had not kept a cat since the infant's birth, and that had data on cat allergen levels in their house dust.

Dust collection and allergen analysis

Samples of settled house dust were obtained by vacuuming a 1 m² surface of mothers' mattresses for 2 min. Details of the dust extraction method are given elsewhere (6). Cat allergen Fel d 1 concentrations and levels of the house-dust mite allergens *Dermatophagoides pteronyssinus* (Der p 1) and *Dermatophagoides farinae* (Der f 1) were analyzed with a two-site monoclonal enzyme-linked immunosorbent assay (ELISA) as described before (6). Values below the detection limit (15 ng Fel d 1/g dust and 10 ng/g Der p 1 or Der f 1, respectively) were assigned a value of one half of the detection limit.

Characterization of second-hand cat allergen exposure

For the analysis of determinants of indoor cat allergen exposure in households without a cat, we used questionnaire data for passive potential transport of allergen into the homes. We asked the parents whether their infants had frequent or regular contact with a cat outside their homes during the first 3 months of life and whether a cat had been kept in their home before the infant's birth.

Outcome assessment

Questionnaire data were used to assess incidence of wheezing apart from respiratory infections. At age 2 years, specific sensitization to cat allergen was determined by analyzing specific serum IgE to Fel d 1 with the RAST FEIA CAP system (Pharmacia, Freiburg, Germany).

The nomenclature for allergy as recommended by the EAACI was applied (7).

Statistical analysis

Allergen concentrations were log-transformed to normalize the distribution. Mean concentrations were expressed as geometric means with 95% confidence intervals. Multiple linear regression models were applied to analyze determinants of indoor cat allergen levels. Associations between Fel d 1 levels and explanatory factors

such as contact to cats outside the home were expressed as means ratios with 95% confidence intervals (CI). The means ratio is the ratio of the geometric mean (GM) in the respective category vs the reference category. The means ratios were calculated from the coefficients β of the linear regression model as $\exp(\beta)$.

The association between second-hand cat allergen exposure and health outcome was analyzed by logistic regression. Odds ratios with 95% CI were adjusted for sex, study region, parental atopy, and parental education. In case of wheezing as outcome variable, odds ratios were additionally adjusted for the sum of levels of mite allergen Der p 1 and Der f 1. Complete data on exposures and potential confounders were available for 1301 infants in terms of IgE sensitization and for 1492 infants in terms of wheezing. The SAS software package, version 8.2, was used for all calculations.

Results

In the LISA birth cohort, data on allergen levels in house dust and housing characteristics at infant's age 3 months were available for 2098 infants. In 208 homes a cat was kept since the infant's birth, whereas in 1840 homes there was no cat present. Data on cat-keeping were missing for 50 families.

As expected, in homes without cats ($n = 1840$) measured Fel d 1 levels in settled house dust were low (geometric mean 0.17 $\mu\text{g/g}$ dust, 95% CI 0.16–0.18) with 12.8% of the samples below the detection limit (i.e. 0.015 μg Fel d 1/g dust), 85.3% of the samples below 1 $\mu\text{g/g}$ and only 3.8% above 8 $\mu\text{g/g}$. In contrast, cat-keeping families in our birth cohort ($n = 208$) had much higher Fel d 1 exposure levels (GM 70.60 $\mu\text{g/g}$, 95% CI 50.13–99.43) with only 1.4% of the samples below the detection limit, 5.8% below 1 $\mu\text{g/g}$, and most of the samples (84.6%) above 8 $\mu\text{g/g}$.

For assessing the effect of second-hand cat allergen exposure on infant health we restricted our analysis to those families who had not kept a cat since the infant's birth ($n = 1840$). This study population comprised 904 girls and 936 boys. Parental atopy was reported for 55% of the infants.

We assumed that regular contact of the infant with a cat outside the home, and keeping a cat in the home before the infant's birth, could be determinants of Fel d 1 concentrations in house dust. Infants without contact to cats outside the house, and with no cat kept in the home previously were exposed to significantly lower cat allergen levels compared to infants living in a home where a cat had been kept before birth and/or with contact to cats outside during the first 3 months of life (Table 1).

We used multiple linear regression to analyze the relationship between Fel d 1 levels and potential determinants of second-hand exposure. Former cat-keeping in the home and cat contact outside the home were found to be the main factors influencing actual Fel d 1 levels in settled house dust (Table 1). Considering these two factors as questionnaire-based exposure definition, 12.3% infants were exposed due to contact with a cat

Table 1. Effect of second-hand cat allergen exposure defined by questionnaire data on actually measured cat allergen levels in settled house dust in homes without a cat since infant's birth ($n = 1840$)

Exposure	<i>n</i>	GM	95% CI	Means ratio	95% CI	<i>P</i> value
Never cat-keeping in home nor contact to cats outside the house	1482	0.12	0.11–0.14	1.00	(reference)	
Cat keeping in home before infant's birth	102	0.47	0.31–0.73	4.11	2.88–5.86	0.002
Contact with cats outside home during first 3 months of life	227	0.58	0.46–0.73	5.02	3.92–6.43	0.001
Contact with cats outside home and former cat-keeping in home	29	2.34	1.13–4.86	20.03	10.46–38.34	0.001

Means ratios were calculated by multiple linear regression. For explanation see Material and methods.

GM, geometric mean (μg Fel d 1/g dust); CI, confidence interval.

Table 2. Differences in incidence and risk (adjusted odds ratio with 95% confidence interval) of specific sensitization to cat allergen and wheezing at age 2 years according to early exposure to moderate cat allergen levels

	Specific sensitization*			Wheezing ever†		
	% incidence	<i>n</i> / <i>N</i>	Odds ratio (95% CI)	% incidence	<i>n</i> / <i>N</i>	Odds ratio (95% CI)
Reported exposure‡						
No	0.5	5/1058	1.0 (reference)	3.3	40/1214	1.0 (reference)
Yes	3.3	8/243	8.12 (2.54–25.96)	5.8	16/278	1.86 (1.01–3.44)
Measured Fel d 1 concentrations¶						
<1 $\mu\text{g/g}$ dust	0.4	5/1125	1.0 (reference)	3.3	43/1288	1.0 (reference)
$\geq 1 \mu\text{g/g}$ dust	4.5	8/176	10.91 (3.40–34.98)	6.4	13/204	2.03 (1.05–3.91)

Odds ratios (OR) were adjusted for sex, study region, parental atopy, and parental education.

* IgE specific for Fel d 1 ≥ 0.35 kU/l.

† OR additionally adjusted for mite allergen levels.

‡ Contact to cats outside home during first 3 months of life and/or cat-keeping in home before infant's birth.

¶ Dust samples from mother's mattress were collected at infant's age 3 months.

outside the home within the first 3 months of life, 5.5% due to cat keeping in the home before infant's birth, and 1.6% due to both modes of exposure.

Besides the questionnaire-based second-hand exposure to cat allergen, study region was the only variable significantly associated with Fel d 1 levels (Leipzig vs Munich: means ratio 1.73, 95% CI 1.46–2.05). Other factors investigated, such as parental atopy, were not associated with cat allergen levels in homes without a cat (data not shown).

To analyze the health impact of second-hand cat allergen exposure up until infant's age of 2 years we excluded infants living with a cat during the first 2 years of life, and those with missing data on health outcomes and covariates. Thus, 1492 infants remained for the analysis of wheezing and 1301 infants for the analysis of IgE sensitization. Multivariate logistic regression analysis gave a strong association between second-hand cat allergen exposure during the first months of life and specific sensitization to cat allergen, as well as lifetime prevalence of wheezing at age 2 years (Table 2). After adjusting for sex, study region, parental atopy, and parental education, Fel d 1 levels $\geq 1 \mu\text{g/g}$ were associated with 11-fold higher odds for cat allergen sensitization. Questionnaire-defined exposure gave a similar effect estimate of an 8-fold increase. Moreover, exposed infants (defined either by Fel d 1 $\geq 1 \mu\text{g/g}$ or by questionnaire

data) were two times more likely to ever having wheezed without concurrent respiratory infection.

Discussion

It is well-known that cat allergen can be found throughout the environment. Levels of second-hand cat allergen exposure in public transport vehicles or in schools have been found to be high enough to potentially induce sensitization or cause symptoms in people who are allergic to cats (8–10). Until now, no study exists on the effect of early second-hand exposure at home on allergy development in infants. Our study design of a prospective birth cohort enabled us to characterize exposure from birth prior to the first incidence of any health effect.

The cat allergen levels in homes without cats in our study (median 0.1 $\mu\text{g/g}$ settled mattress dust) were comparable to Almqvist et al. (10) who reported a median of 0.5 $\mu\text{g/g}$ mattress dust and to Bollinger et al. (11) who measured a median of 0.3 $\mu\text{g/g}$ carpet or upholstered furniture dust in homes without cats.

In accordance with other studies demonstrating cat allergen transfer into homes without cats (10), our results indicate that contact with cats and cat owners outside, respectively, increased cat allergen exposure at home. It is worth mentioning that in our study parental reports of

contact with cats outside the home were probably related to visiting cat owners, rather than the young infant playing directly with a cat. Moreover, cat-keeping in the home at least several months previously resulted in still detectable allergens in settled house dust.

Several studies have suggested that exposure to moderate cat allergen levels may induce relatively higher sensitization rates than exposure to high allergen levels (1–4). These studies did not differentiate between individuals living in homes with or without a cat. High cat allergen levels in house dust are mostly due to the presence of a cat in the home, which is also associated with increased endotoxin levels (5). Therefore it may be hypothesized that in homes with a cat there is concomitant exposure to cat allergen and to cat-related factors, such as endotoxin, which may modify the immune response. But the mechanism is not yet elucidated and several possible explanations for the effects of cat exposure are currently under discussion (4).

The only birth cohort study in Germany that reports a dose–response relationship between cat allergen levels in carpet dust and specific sensitization in infancy also did not differentiate between active exposure (cat-keeping) and second-hand exposure (12). Moreover, reported exposure levels were extremely low (median 0.06 µg/g) and in no way comparable to the range of exposure investigated by Platts-Mills et al. (2) (median 4.4 µg/g) or Custovic et al. (1.13 µg/g) (3), who proposed a

bell-shaped, or at least flattened, dose–response relationship.

Our results suggest that second-hand exposure to low cat allergen levels during the first months of life may have detrimental health effects during infancy. Since the proportion of affected infants until age 2 years was still low in our birth cohort (1% sensitized to cat allergen, 4% ever-wheezed without infection) further follow-up of the infants is needed to verify our results.

Taken together, the largely unavoidable passive transfer of cat allergen into the home, and the possibly unnoticed exposure from the previous presence of a cat, may result in moderate cat allergen levels in house dust that are capable of inducing allergic reactions. Platts-Mills et al. (4) recently pointed out that in communities with a high prevalence of cats, passive exposure may be the primary cause of allergic disease related to cat allergen. Thus, from a public health perspective cat avoidance at home as a single measure to prevent IgE sensitization to cat allergen seems to be questionable.

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