

Associations between cat keeping, allergen exposure, allergic sensitization and atopic diseases: Results from the Children of Lübeck Allergy and Environment Study (KLAUS)

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The role of cat keeping on the promotion of allergies is discussed controversially. We investigated the associations between cat keeping, allergen exposure, allergic sensitization and atopic diseases in pre-school children. A total of 606 children (5- to 6-yr old) were studied in the course of the mandatory school entrance examination. Information on doctor diagnosed asthma and allergic rhinitis, pet keeping and confounders was obtained by questionnaire. The prevalence of atopic eczema was determined by dermatological examination, allergic sensitization was assessed by skin prick test, and the allergen exposure to cat allergen Fel d 1 was measured by a commercial wipe test. Cats were present in 16% of the households and results of the exposure categories (0–III) on cat allergen were 47.2%, 25.5%, 24.3% and 3.0% respectively. The prevalence of cat keeping increased significantly with exposure categories from 0.5% to 61.5% ($p_{\text{trend}} < 0.001$). Children (6.3%) were sensitized to cat allergen and sensitization rates increased also significantly with exposure categories from 3.0% to 15.4% ($p_{\text{trend}} < 0.001$). Children (9.3%) were diagnosed with atopic eczema and a positive history of asthma/rhinitis was given in 3.6% and 3.9% respectively. Sensitization to cat was associated with atopic eczema (23.3% vs. 7.4%; $OR_{\text{adj.}} = 3.8$, CI: 1.4–10.8), asthma (12.5% vs. 3.7%; $OR_{\text{adj.}} = 4.9$, CI: 1.1–21.2), allergic rhinitis (6.9% vs. 2.7%; $OR_{\text{adj.}} = 3.1$, CI: 0.7–15.2) and any atopic disease (43.5% vs. 16.3%; $OR_{\text{adj.}} = 3.8$, CI: 1.5–9.5). The data suggest a promoting effect of cat keeping for atopic diseases.

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The prevalence of atopic diseases has increased in the past decades, especially in Western industrialized countries (1). Beside a genetic pre-disposition, several environmental conditions may play a role as contributing cause for the development, and possibly the increase of allergic diseases. The contribution of pet keeping and especially the role of cats in the development and prevention of atopic diseases are discussed controversially. Some studies identified cat keeping

as risk factor for atopic diseases, whereas others showed a preventive or no effect. Interestingly, a preventive effect was mostly shown in subgroups of genetically pre-disposed subjects. Persons without an increased risk for allergies seem not to profit (2). Recent studies indicated links between cat keeping and corresponding allergen exposure, allergen exposure and allergic sensitization, and allergic sensitization and signs of asthma (3–5). Others, however, were not able to

confirm the association of allergen exposure and allergic symptoms (6). Attempts to follow an associative chain from cat keeping over allergen exposure measurements to allergic sensitization and clinical manifestations of atopy within one study group have barely been made. Furthermore studies have a focus on bronchial symptoms rather than other outcomes of atopy including allergic rhinitis and atopic eczema. We aimed to fill in these gaps by conducting a population-based study in pre-school children and analysing the associations between cat keeping, allergen exposure, allergic sensitization and atopic diseases.

Methods

This cross-sectional study (KLAUS – Kinder von Lübeck Allergie- und UmweltStudie) was conducted in the framework of the compulsory school entrance examinations in Lübeck, Germany, in 2003 (7). The entire group of school beginners in the City of Lübeck, which were 2071, received an informative letter explaining the study and asking for participation as well as a questionnaire and a ready-to-use test for allergen exposure. We asked to return the written consent, the questionnaire and the allergen test at the date of the school entrance examination, which took place at the public health department of Lübeck for all children. The ethical committee of the Medical Faculty of the University of Lübeck has approved the study protocol.

A total of 606 children with a balanced gender ratio participated, which corresponds to a response of 30.3%. A non-responder analysis was performed during a 4-wk time period in a random subgroup ($n = 518$), and parents who were not willing to agree to the participation of their children were asked for their motivation and whether their child has a doctor's diagnosed atopic disease.

During the compulsory school entrance examinations, the physicians of the public health department recorded three allergy-related items (asthma, eczema and allergy/rhinitis). This information was used for an additional non-responder analysis.

The standardized questionnaire of this study assessed the lifetime prevalence of doctor's diagnosed hay fever and asthma, the family history of atopic diseases, pet keeping or selective avoiding, socio-demographic parameters and relevant risk factors in part for several time periods from birth to the time of examination.

An additional clinical examination was performed by a resident of the Department of

Dermatology and Allergy of the Medical University Luebeck (AK). Thereby the entire skin of the child except the region of the underpants was examined. Atopic eczema was diagnosed on a clinical basis and the severity was assessed using the SCORing Atopic Dermatitis (SCORAD) index. An allergic sensitization to cat allergen was determined by conventional skin prick test (ALK Scherax, Hamburg, Germany). Histamine and saline were used as controls. Test reactions with a wheal diameter of at least 3 mm were regarded as positive.

The exposure to cat allergen at home was measured on the carpet or a chair in the child's room using the semi-quantitative rapid test Bio-Check Allergen Control (Dräger Lübeck, Germany). For that purpose the sampling pin was wiped manually over the surface area for 1 min. Ten minutes after applying five drops of buffer solution the results were read. The test utilizes allergen-specific antibodies to cat allergen Fel d 1 and allows a semi-quantitative assessment of the allergen exposure by comparing the intensity of the test stripe with a control stripe. The resulting four categories (0–3) represent a mean (first to third quartile) allergen exposure of 263 (90–685), 844 (192–3699), 5.670 (3564–29,376) and 56.800 (20,114–158,534) ng Fel d 1 per gram dust respectively (8).

In the bivariate statistical analyses of categorical exposure variables, the Chi-squared-trend-test was used. Logistic regression models were implemented to investigate associations between cat allergen exposure and allergic sensitization or cat keeping as well as associations between allergic sensitization to cat and various atopic diseases. Sex, parental history of atopic diseases and maternal school education were taken as dependent variables. We did not include variables such as smoking, number of siblings and worm infestation, which did not show significant associations in bivariate or multivariate analyses. Adjusted odds ratios (OR) and corresponding 95% confidence intervals (CI) were reported as measures of association and stability. The statistical software package SPSS 14.0 (SPSS Inc., Chicago, Illinois, USA) was used for analyses.

Results

Non-responder analysis

The main reasons for non-participation were time reasons (32.0%), low interest (16, 6%), other reasons such as difficulties to fill in the questionnaire (15.3%) and having no allergy (14.7%). The Table 1 gives details on the main

outcomes of the KLAUS study population ($n = 606$), those who did not participate ($n = 1465$) and the subgroup of those who were interviewed for a specific non-responder analysis ($n = 518$). In the group of non-responders, a history of an ever doctor's diagnosed atopic eczema was given in less frequently than in the actual study group. No significant differences between responder and non-responder were seen for doctor's diagnosed hay fever and asthma. The physicians who performed the compulsory school entrance examination diagnosed eczema almost equally frequent in the KLAUS study population and in the non-participating children. Similar, no significant difference was observed for asthma. A significant difference was observed for the item allergy which was also assessed by the physicians of the public health department and which mainly reflected an allergic rhinitis.

Main outcome analysis

At the time of the examination a total of 9.3% showed an actual atopic eczema. Ever doctor's diagnosed hay fever was reported by 3.9% and asthma by 3.6%. At the time of examination a cat was kept in 16% of the households. Allergen exposure to cat allergen in the categories 0–3 were seen in 47.2%, 25.5%, 24.3% and 3.0% respectively. Thus, cat allergen was detectable in over 50% of the households, whereas cats were kept in only 16%. In homes where a cat was present at the time of examination, the measured allergen exposure resulted in categories >0 in all but one household. A positive prick test to cat allergen showed 6.3% of the children. We found a significant linear relationship between cat keeping and allergen exposure. The frequency of cat keeping increased from 0.5% in category 0 to 61.5% in the group with the highest allergen exposure ($p_{\text{trend}} < 0.001$; Fig. 1). The corresponding adjusted OR and CI comparing categories I, II and III to the baseline category (0) were OR = 24.5 (3.1–190.7), OR = 136.5 (18.3–1016.6) and OR = 574.7 (52.4–6304.1) respectively. With increasing allergen exposure, a significantly rising frequency of sensitization from 3.0% in the lowest to 15.4% in the highest exposure category was observed ($p_{\text{trend}} < 0.001$; Fig. 2). The corresponding adjusted OR and CI comparing categories I, II and III to the baseline category (0) were OR = 2.9 (0.9–9.3), OR = 2.6 (0.8–8.8) and OR = 6.7 (1.1–41.0) respectively. The exposure categories (0–III) correlated positively, but not significantly or in a linear way with the prevalence of any of the atopic diseases (22.1%, 21.1%, 25.0% and 15.4%). The highest

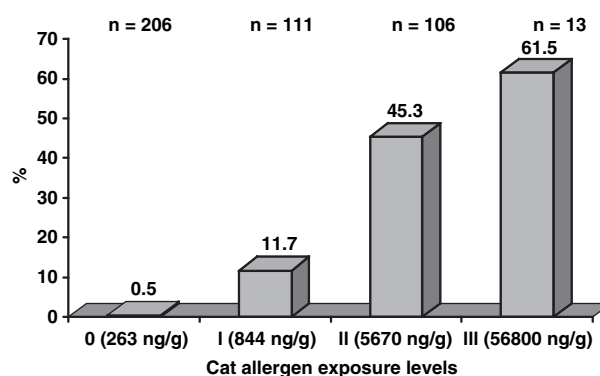


Fig. 1. Relationship between prevalence of cat keeping and measured cat allergen exposure levels (0–III and geometric means) in households of 606 school beginners.

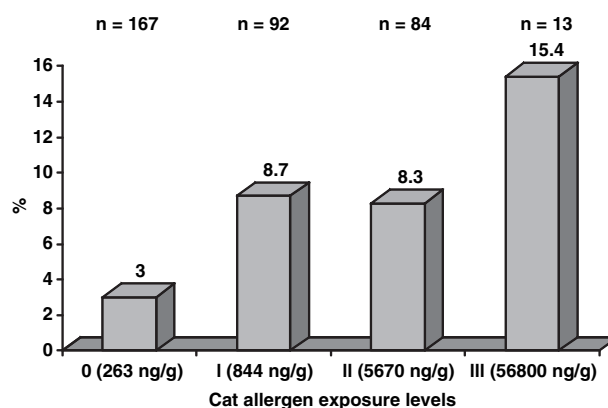


Fig. 2. Relationship between measured cat allergen exposure levels (0–III and geometric means) in households and prevalence of allergic sensitization in 606 school beginners.

prevalence of atopic diseases was observed in exposure category II, whereas the precision of the result for category III is reduced by the small sample size ($n = 13$). Associations between the measured exposure to cat allergen and sensitization or atopic disease were not altered by the actual presence of a cat. Eventually, sensitization to cat allergen was significantly associated with any of the atopic diseases (43.5% vs. 16.3%; $OR_{\text{adj.}} = 3.8$, CI: 1.5–9.5). For the single entities the association was significant for atopic eczema (23.3% vs. 7.4%; $OR_{\text{adj.}} = 3.8$, CI: 1.4–10.8) and for the lifetime prevalence of asthma (12.5% vs. 3.7%; $OR_{\text{adj.}} = 4.9$, CI: 1.1–21.2) and positive, but not significant, for hay fever (6.9% vs. 2.7%; $OR_{\text{adj.}} = 3.1$, CI: 0.7–15.2).

A total of 47 parents reported that they decided not to have a cat or gave their cat away for reasons of general allergy prevention or a present allergy of the child or themselves. Including this variable in the regression models

Table 1. Results of non-responder analyses

	KLAUS (n = 606)	Non-responder (n = 1465)	Subgroup of non-responder (specific non- responder analysis; n = 518)	p-value (vs. KLAUS)
Outcomes of own study				
Atopic eczema (doctors diagnosed, lifetime prevalence)	18.1%		6.4%	<0.001
Hay fever (doctors diagnosed, lifetime prevalence)	5.0%		3.9%	n.s.
Asthma (doctors diagnosed, lifetime prevalence)	3.1%		3.6%	n.s.
Outcomes assessed by physicians of the school entrance examination				
Eczema	3.8%	2.5%		n.s.
Asthma	1.4%	2.4%		n.s.
Allergy (rhinitis)	5.3%	2.3%		<0.001

KLAUS, Kinder von Lübeck Allergie- und UmweltStudie; n.s., not significant.

did change the effect estimates only marginally and had no effect on the statistical significance of the results (data not shown).

Discussion

In this population-derived study, cat allergen was detectable in half of the households, whereas the prevalence of cat keeping was 16%. This is in accordance with other observations and confirms the fact that a cat allergen is distributed in the community and therefore detectable in households without cat keeping (9).

Cat allergen exposure at home is obviously associated with cat keeping and increases the chance of allergic sensitization. As allergic sensitization itself is associated with atopic diseases, at least on the basis of these cross-sectional data, cat keeping seems to be an allergy promoting factor. The temporal sequence of exposure and outcome, however, can not be demonstrated in this cross-sectional design. This includes, that exposure data from the early life period, which presumably have the highest impact on the development of allergic sensitization and allergies, have not been considered here. Cohort studies, however, showed that sensitization to aeroallergens and especially cat allergen increases the risk of asthma incidence. A Swedish cohort study followed more than 2000 first and second grade school children up for 3 yr and showed that the incidence of physician diag-

nosed asthma was associated with sensitization to cat (OR 7.4) (3). Similar, a cohort study from New Zealand found persistent wheeze to be associated with sensitization to house dust mites (10). Sensitization to pet allergens (cat or dog) was associated with the onset of asthma in young adults (20–44 yr) according to another Swedish study (4). Allergic sensitization to cat at school age obviously is a strong risk factor for incident asthma and hay fever in young adults (11). Recently published results of a German birth cohort study indicated that cat ownership and allergen exposure was associated with corresponding allergic sensitization. Associations with clinical outcomes, however, could not be confirmed (6). Similar results were obtained by a cohort study from the Netherlands, where early cat allergen exposure increased the risk of specific allergic sensitization significantly, whereas the risk of persistent wheeze was affected only marginally (12). Data from the German MAS birth cohort study showed that early sensitization to perennial allergens including cat, affects lung function test results negatively at school age (13). Furthermore, it was demonstrated by this study that cat ownership increases the allergen exposure and that allergic sensitization to cat is associated with asthma symptoms in children (5). In contrast to these findings on cat keeping, having a dog at home might even be protective with respect to allergic sensitization and disease (14–16).

Strengths of the study arise from objective allergen exposure measurement using allergen-specific antibodies and an assessment of atopic eczema by an actual dermatological examination. Selective allergen avoidance is crucial as it can introduce reverse causality. We have gathered information on that issue and could adjust our data accordingly.

The study is limited by an unsatisfying low-response rate. We were able, however, to perform an independent non-responder questioning and analysis in a large random subsample of non-responders (n = 518). Furthermore, there were allergy-related items in the compulsory school entrance examination which allowed a comparison between the KLAUS population and all non-responders (n = 1465). These analyses indicated that selection effects led to some overestimation of the eczema prevalence. It is hard to say, however, in how far the associations, which were described in the study were influenced by potential selection bias, which would be introduced by a differential participation with respect to exposure and outcome or exposure misclassification.

These cross-sectional data must be interpreted with caution. However, considerable associations between cat keeping and allergen exposure, as well as between allergic sensitization and atopic diseases were observed.

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References

1. ASHER M, MONTEFORT S, BJÖRKSTÉN B, et al., Group IPTS. Worldwide time trends in the prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and eczema in childhood: ISAAC Phases One and Three repeat multicountry cross-sectional surveys. *Lancet* 2006; 368: 733–43.
2. MARKS G. What should we tell allergic families about pets? *J Allergy Clin Immunol* 2001; 108: 500–2.
3. PERZANOWSKI M, RONMARK E, PLATTS-MILLS T, LUNDBACK B. Effect of cat and dog ownership on sensitization and development of asthma among preteenage children. *Am J Respir Crit Care Med* 2002; 166: 696–702.
4. PLASCHKE P, JANSON C, NORRMAN E, BJÖRNSSON E, ELLBJAR S, JARVHOLM B. Onset and remission of allergic rhinitis and asthma and the relationship with atopic sensitization and smoking. *Am J Respir Crit Care Med* 2000; 162: 920–4.
5. LAU S, ILLI S, PLATTS-MILLS T, et al., Group MAS. Longitudinal study on the relationship between cat allergen and endotoxin exposure, sensitization, cat-specific IgG and development of asthma in childhood – report of the German Multicentre Allergy Study (MAS 90). *Allergy* 2005; 60: 766–73.
6. CHEN C, RZEHA P, ZUTAVERN A, et al. Longitudinal study on cat allergen exposure and the development of allergy in young children. *J Allergy Clin Immunol* 2007; 119: 1148–55.
7. SCHÄFER T, STIEGER B, POLZIUS R, KRAUSPE A. Atopic eczema and indoor climate: results from the children from Lübeck allergy and environment study (KLAUS). *Allergy* 2008; 63: 244–6.
8. POLZIUS R, WUSKE T, MAHN J. Wipe test for the detection of indoor allergens. *Allergy* 2002; 57: 143–5.
9. HEINRICH J, BEDADA G, ZOCK J, et al. Cat allergen level: its determinants and relationship to specific IgE to cat across European centers. *J Allergy Clin Immunol* 2006; 118: 674–81.
10. SEARS M, GREENE J, WILLAN A, et al. A longitudinal, population-based, cohort study of childhood asthma followed to adulthood. *N Engl J Med* 2003; 349: 1414–22.
11. SCHÄFER T, WÖLKE G, RING J, WICHMANN H, HEINRICH J. Allergic sensitization to cat in childhood as major predictor of incident respiratory allergy in young adults. *Allergy* 2007; 62: 1282–7.
12. BRUSSEE J, SMIT H, VAN STRIEN R, et al. Allergen exposure in infancy and the development of sensitization, wheeze, and asthma at 4 years. *J Allergy Clin Immunol* 2005; 115: 946–52.
13. ILLI S, VON MUTIUS E, LAU S, NIGGEMANN B, GRUBER C, WAHN U, Group MAS. Perennial allergen sensitization early in life and chronic asthma in children: a birth cohort study. *Lancet* 2006; 368: 763–70.
14. HÖLSCHER B, FRYE C, WICHMANN H, HEINRICH J. Exposure to pets and allergies in children. *Pediatr Allergy Immunol* 2002; 13: 334–41.
15. ZIRNGIBL A, FRANKE K, GEHRING U, et al. Exposure to pets and atopic dermatitis during the first two years of life. A cohort study. *Pediatr Allergy Immunol* 2002; 13: 394–401.
16. SANDIN A, BJÖRKSTÉN B, BRABÄCK L. Development of atopy and wheezing symptoms in relation to heredity and early pet keeping in a Swedish birth cohort. *Pediatr Allergy Immunol* 2004; 15: 316–22.