

Worsening of Asthma in Children Allergic to Cats, after Indirect Exposure to Cat at School

CATARINA ALMQVIST, MAGNUS WICKMAN, LUCA PERFETTI, NIKLAS BERGLIND, ANNE RENSTRÖM, MARIE HEDRÉN, KJELL LARSSON, GUNILLA HEDLIN, and PER MALMBERG

Department of Environmental Health, Karolinska Hospital, Stockholm, Sweden; Astrid Lindgren Children's Hospital, Department of Woman and Child Health, Karolinska Institutet, Stockholm, Sweden; Sachs Children's Hospital, Karolinska Institutet, Stockholm, Sweden; Institute of Environmental Medicine, Karolinska Institutet, Stockholm, Sweden; National Institute for Working Life, Stockholm, Sweden; and Fondazione Salvatore Maugeri, Clinica del Lavoro e della Riabilitazione, IRCCS, Istituto Scientifico di Pavia, Pavia, Italy

Exposure to cat allergen at school might exacerbate symptoms in asthmatic children with cat allergy. To study this, we identified 410 children, 6–12 yr of age, who were being treated for asthma (inhaled steroids and β -agonists), were allergic to cats, and had no cat at home. Peak expiratory flow (PEF), asthma symptoms, medication, fever and/or sore throat, and contact with furred pets were recorded twice daily during the last week of summer holidays and the second and third weeks of school. The number of cat owners in each class was recorded. Ninety-two children with asthma reported no contact with furred pets. Among these, children who attended classes with $> 18\%$ (median value) cat owners reported significantly decreased PEF, more days with asthma symptoms, and increased use of medication after school started. Those in classes with $\leq 18\%$ cat owners reported no change. Children in classes with many cat owners ran a 9-fold increased risk of exacerbated asthma after school start compared with children in classes with few cat owners, after adjusting for age, sex, and fever and/or sore throat. Thus, asthma symptoms, PEF, and the use of asthma medication in children with cat allergy may be affected by indirect cat exposure at school.

Individuals with asthma who are allergic to cats and are exposed to cat at home show signs of bronchial hyperresponsiveness and have more asthma symptoms than cat-sensitized individuals with asthma without cats at home (1). This indicates that direct exposure to allergen from cats and possibly all furred pets is a health hazard to individuals sensitized to pets. The effect of indirect pet exposure on children with asthma has not been studied previously. However, the clinical impression is that asthma grows worse in children allergic to furred pets when they return to school after summer holidays.

Pet allergens are the allergens most closely correlated with asthma in Sweden and parts of the United States (2–4). Even small doses of allergen may elicit an inflammatory response in the airways of an allergic person (5, 6). Cat allergen is ubiquitous in schools and day care centers where children spend their days (4, 7–11). Cat allergen is transported to school in the clothing of cat owners, and is subsequently dispersed in the air (12–14). We have previously shown that there is a 5-fold difference in the median levels of airborne cat allergen *Fel d 1* in classes with many and few cat owners, and that the levels are significantly higher than the airborne levels found in homes without a cat (12). It can therefore be assumed that the respiratory health of children allergic to cats relates to the percentage of cat owners in the class.

The aim of this study was to examine whether children with asthma and verified cat allergy suffer a worsening of their disease when they return to school after the summer holidays. The study focused on the children who reported no direct contact with furred pets, in order to examine whether asthma symptoms and use of medication were related to indirect exposure to cat in class.

METHODS

Study Design and Population

All children aged 6–12 yr with diagnosed asthma, asthma medication, and cat sensitization (skin prick test ≥ 3 mm [15] or positive RAST class ≥ 0.7 kU/ml) were identified from patient records at five pediatric allergy outpatient clinics in Stockholm. Children receiving continuous asthma medication (inhalation steroids and β -agonists) and without furred pets at home were asked to participate in the study (Figure 1). In August 1997, 410 children and their families received diary forms (modified Pollution Effects on Asthmatic Children in Europe [PEACE] study [16]) to fill in twice daily for 3 wk: the last week of the summer holidays and the second and third weeks of school. The children were instructed to practice using a peak flow meter before the start of the study period.

To be included, $> 50\%$ of the peak expiratory flow (PEF) recordings were required each week, and the child must have attended school $> 50\%$ of the week. Missing data on symptoms, medication, fever and/or sore throat, and contact with furred pets was interpreted as a negative answer. Twenty-seven children who used bronchodilators before the PEF recording more than two mornings a week were excluded.

Information about the number of cat owners and children in each class was obtained through questionnaires to the teacher.

Respiratory Status and Medication

Four main indices of respiratory status and medication were calculated for the last week of summer holidays (Week 0, baseline week) and for the second and third weeks of school: (1) weekly mean morning PEF (Tuesday through Saturday), (2) number of days per week with asthma symptoms (Monday through Friday), (3) weekly average of the number of puffs of β -agonist per day, and (4) weekly average of dose of inhaled steroids per day (Monday through Friday). The highest of the three PEF recordings was used, unless it was $> 20\%$ higher than the second highest PEF, in which case the latter was used.

Statistical Analysis

The effect of indirect cat exposure on week-specific individual average PEF, days with asthma symptoms, puffs of β -agonist, and dose of steroids, was computed using a linear regression model including indicator variables for indirect cat exposure groups, time period (weeks), and interaction terms. The difference in the changes from baselines for exposure groups was derived from the parameter estimates for the interaction terms. Standard errors are corrected for within-subject correlation by clustering observations within subjects and using the robust Huber and White estimator of variance (17).

Because there is an interaction between lung function, symptoms, and medication, an outcome variable called “decreased respiratory health” (DRH) was defined as at least three of the following: lower

(Received in original form June 22, 2000 and in revised form December 7, 2000)

Supported by the Vardal Foundation and Samariten.

Correspondence and requests for reprints should be addressed to Catarina Almqvist, M.D., Department of Environmental Health, Norrbacka Building, 3rd floor, Karolinska Hospital, S-171 76 Stockholm, Sweden. E-mail: catarina.almqvist@kbh.ki.se

Am J Respir Crit Care Med Vol 163, pp 694–698, 2001

Internet address: www.atsjournals.org

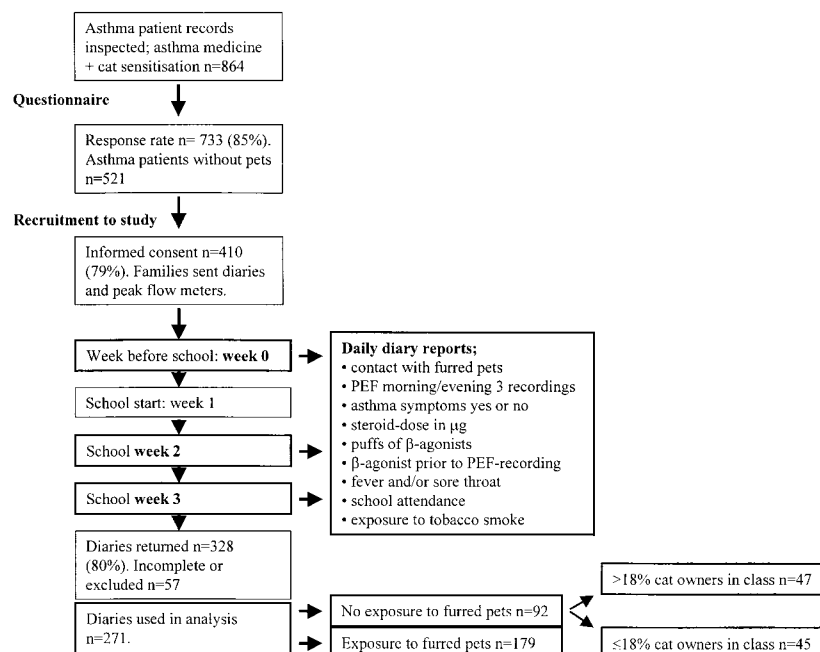


Figure 1. Study design.

PEF; more asthma days; increased β -agonist use; increased steroid use, all compared to the baseline week. The relation between DRH and the variable "indirect cat exposure" was examined by logistic regression adjusted for sex, age, and fever and/or sore throat. Analyses were performed with Stata 6.0 (Stata, College Station, TX) and SPSS 10.0 (SPSS, Chicago, IL). Point estimates are presented along with 95% confidence intervals (CI) and *p* values.

Permission for the study was obtained from the Ethics Committee of Karolinska Institutet (Stockholm, Sweden). Informed consent was obtained from the parents.

RESULTS

In the entire study population (*n* = 271), 179 children reported direct contact with furred pets during the study, and 92 children denied any pet contact (Table 1).

Children without Reported Direct Exposure to Furred Pets (*n* = 92)

The average age of children who were not directly exposed to pets was 9.7 yr (range, 6–13 yr), and 87% were boys. The median percentage of cat owners in the classes was 18%. Chil-

dren in classes with > 18% cat owners were on average 10.2 yr old and those in classes with few cat owners were on average 9.1 yr old.

Among the children in classes with many cat owners, lung function expressed as mean morning PEF decreased 3% from Week 0 to Week 2 (Table 2). Days with asthma symptoms were more than twice as frequent during Week 2 than during Week 0. The children reported a doubling of the average daily use of β -agonists in Week 2. Simultaneously, the average daily dose of steroids was 16% higher in Week 2 than in Week 0. Among children in classes with few cat owners, no significant change in PEF, symptoms, or medication was observed. For PEF and asthma there was a significant difference in change from baseline between the groups with many and few cat owners (Figure 2).

The risk of decreased respiratory health (DRH) in the group with many cat owners among their classmates was 9-fold increased by Week 2 compared with those in classes with few cat owners, after adjustment for sex, age, and fever and/or sore throat (Table 3). Exposure to environmental tobacco smoke was slightly higher in Week 0 than in Weeks 2–3. When exposure to environmental tobacco smoke was included in the logistic regression model the risk estimate increased slightly.

Fever and/or sore throat during Weeks 0 and 2 was reported in 36% (17 of 47) of the children in classes with many cat owners and in 16% (7 of 45) of the children in classes with few cat owners. Stratified analysis for reported fever and/or sore throat in Weeks 0 and 2 in the classes with many cat owners only slightly changed the point estimate for the outcome variables. In the group without reported fever and/or sore throat, the average PEF decrease was 6 L/min (compared with 9 L/min in the whole group), from 327 L/min at baseline to 321 L/min at Week 2. The average number of days with reported asthma symptoms changed by 0.5 (compared with 0.81), from 0.73 to 1.23 at Week 2, and the use of β -agonists increased by 0.11 (0.17 in the whole group), from 0.25 puffs at Week 0 to 0.34 at Week 2. The increase in steroid use was 40 μ g (33 μ g for the whole group), from 200 μ g at Week 0 to 240 μ g at Week 2. The results in Week 3 were similar (data not shown). With the exclusion of children who reported fever and/or sore

TABLE 1. DIRECT PET EXPOSURE AND INDIRECT CAT EXPOSURE IN THE STUDY POPULATION

	Total	Direct Pet Exposure	
		Any	None
No. of children	271	179	92
No. of schools	182	101	81
No. of classes	253	162	91
Indirect cat exposure			
Percent cat owners in class			
Mean	21.5	22.5	19.5
SD	12.2	13.0	10.2
Median	19.2	20.0	18.2
IQR (q1/q3)	13.3/26.9	14.3/29.2	12.0/26.3
Range (min/max)	0/78.3	0/78.3	0/52.0
No. of obs. > md	137	88	47
No. of obs. < md	134	91	45

Definition of abbreviations: IQR = interquartile range; max = maximum; md = median; min = minimum; obs. = observations.

TABLE 2. CHANGES IN RESPIRATORY SYMPTOMS AND MEDICATION IN CHILDREN WHO DENY DIRECT EXPOSURE TO FURRED PETS AND ATTEND CLASSES WITH MANY OR FEW CAT OWNERS

	Week	High Indirect Cat Exposure* (n = 47)			Low Indirect Cat Exposure† (n = 45)			Difference in Change from Baseline: Change in High–Change in Low	
		Mean	Change from Baseline (95% CI)	p Value	Mean	Change from Baseline (95% CI)	p Value	Difference (95% CI)	p Value
Morning PEF, L/min	Baseline	334			300				
	2	325	–9 (–14, –3)	< 0.01	303	3 (–6, 12)	0.54	–12 (–22, –0.8)	0.04
	3	326	–8 (–14, –1)	0.02	305	5 (–5, 15)	0.34	–13 (–25, –0.5)	0.04
Asthma, d/wk	Baseline	0.66			0.96				
	2	1.47	0.81 (0.29, 1.32)	< 0.01	0.78	–0.18 (–0.49, 0.13)	0.26	0.99 (0.39, 1.59)	< 0.01
	3	1.09	0.43 (–0.05, 0.91)	0.08	0.84	–0.12 (–0.40, 0.17)	0.44	0.55 (–0.02, 1.10)	0.06
β-Agonist, daily doses	Baseline	0.18			0.40				
	2	0.35	0.17 (0.02, 0.31)	0.02	0.40	0.00 (–0.11, 0.11)	0.97	0.17 (–0.02, 0.35)	0.07
	3	0.29	0.11 (0.04, 0.17)	< 0.01	0.44	0.04 (–0.07, 0.15)	0.48	0.07 (–0.06, 0.20)	0.33
Steroids daily dose, μg	Baseline	205			206				
	2	238	33 (–4, 70)	0.08	200	–6 (–32, 20)	0.65	39 (–7, 84)	0.09
	3	240	35 (1, 69)	0.04	211	5 (–36, 47)	0.79	30 (–24, 83)	0.28

* High, > 18% cat owners in class.

† Low, ≤ 18% cat owners in class.

throat there were still 8 children with DRH of 47 in classes with many cat owners and 1 of 45 in classes with few cat owners.

Children with Reported Direct Exposure to Furred Pets (n = 179)

For the children who reported direct pet exposure during the study period, the morning PEF decreased 1% from Week 0 to Weeks 2 and 3 (Table 4). No significant change was seen in reported asthma symptoms or use of β-agonists. The average daily steroid dose increased 6% from Week 0 to Week 2. The median percentage of cat owners in these classes was 20%, and no difference in risk of DRH was seen between classes with many or few cat owners (Table 3).

DISCUSSION

The main finding of this study is that indirect exposure to cats at school may result in worsening of the asthma disease in children sensitized to cats.

In the group of children with asthma who denied any contact with furred pets outside school, those in classes with many cat owners reported decreased morning PEF, more days with asthma symptoms, and an increased use of β-agonists after school started. Their use of inhalation steroids increased over the whole study period. The children in classes with few cat owners reported no significant changes in lung function, symptoms, or medication.

The results also showed a 9-fold greater risk that asthma

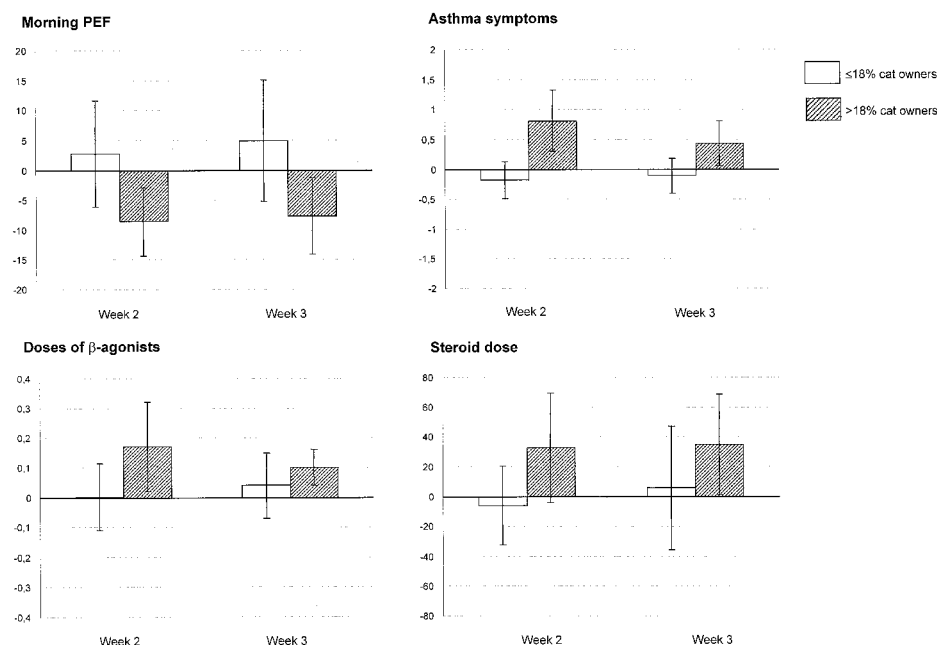


Figure 2. Changes from baseline to Weeks 2 and 3 for weekly average morning PEF (L/min); number of days with asthma symptoms; daily doses of β-agonist; and daily steroid dose (μg) for children in classes with many and few cat owners. Columns represent the point estimate and error bars the upper and lower limits of the 95% confidence interval.

TABLE 3. ADJUSTED ODDS RATIOS FOR INDIRECT CAT EXPOSURE ON DECREASED RESPIRATORY HEALTH* AFTER SCHOOL START (WEEKS 2 AND 3) COMPARED WITH BASELINE BEFORE SCHOOL START (WEEK 0)

DRH	Indirect Cat Exposure	Exposed Outside School (<i>n</i> = 179) [†]			Unexposed Outside School (<i>n</i> = 92) [‡]			Total (<i>n</i> = 271) [§]		
		n/Total	%	Adjusted OR (95% CI)	n/Total	%	Adjusted OR (95% CI)	n/Total	%	Adjusted OR (95% CI)
Baseline to Week 2	≤ median	13/88	15	0.9 (0.4, 2.1)	2/45	4.4	9.4 (1.9, 46.5)	16/137	12	1.8 (0.9, 3.6)
	> median	14/91	15		15/47	32		28/134	21	
Baseline to Week 3	≤ median	11/88	12	1.6 (0.7, 4.0)	2/45	4.4	6.4 (1.1, 35.4)	14/137	10	2.1 (1.0, 4.3)
	> median	18/91	20		10/47	21		27/134	20	

* DRH = Decreased respiratory health, defined as at least three of the following: lower PEF; more asthma days; more frequent β -agonist use; more frequent steroid use.

^{||} Adjusted for sex; age; and fever and/or sore throat (yes/no at baseline and comparison week).

[†] Median cat owners in class = 20.

[‡] Median cat owners in class = 18.

[§] Median cat owners in class = 19.

would grow worse after school started if a child attended a class with many cat owners than if the child attended a class with few cat owners. These data apply to those who denied direct contact with pets during the study period.

Approximately two of three children, however, reported direct contacts with pets during the study weeks. There was a trend toward exacerbated asthma also in this group, although no effects of indirect exposure to cat allergen at school were demonstrated. This finding raises the question of whether it is more dangerous to be indirectly exposed to cat than to actually encounter one (18). A more likely explanation is that children who reported contact with furred pets during the study weeks had also been exposed during summer holidays to such an extent that their condition did not deteriorate further when they were indirectly exposed to cat at school. There may also be a selection in which children who are highly allergic to cats and other furred pets make an effort not to encounter them (19). Such highly sensitive children might be more sensitive to the relatively low levels of allergen found in classrooms.

The health effects of indirect allergen exposure have, to our knowledge, not been studied previously. However, several studies demonstrate an association between decrease in PEF and exposure to furred animals, for instance, studies of occupational health following exposure to rats (20, 21).

It has been shown that the number of children admitted to hospital for asthma varies seasonally, with peaks in conjunctions with respiratory infections after school holidays (22, 23). In the PEACE diary form (16) the questions on fever and sore throat are posed separately, whereas we chose to combine the

question in the diary form and therefore cannot tell whether the children have had fever or sore throat or both.

We found that among those who did not report direct pet contact, more children in the high-exposure group reported fever and/or sore throat (17 of 47) than in the low-exposure group (7 of 45). It may be that their allergy worsened because of cat exposure, and that they reported their symptoms of allergic inflammation in the mucous membranes as sore throat. It may also be pure coincidence that they had more respiratory tract infections than the low-exposed children. One fact speaks against this, namely that the 17 children attended 17 different classes in 16 different schools with a vast geographical spread: it is unlikely that there should have been a viral epidemic only in classes with many cat owners. Children with severe allergy may react to an infection more strongly than do children with a mild allergy. However, children in low-exposed classes had a tendency to have more asthma at baseline than children in high-exposed classes, which speaks against the reported fever and/or sore throat in the high-exposed group being due only to viral infections. Exclusion of children who reported fever and/or sore throat in the high-exposed group only slightly changed the point estimates of the main findings, and taking fever and/or sore throat into account in a logistic regression model did not change the final results.

The use of PEF monitoring and daily diaries has been recommended in the management of asthma patients (24–26). Our ambition was not to evaluate PEF variability, because it is difficult to accomplish PEF recordings more than twice daily in a group of children that attend school (26, 27). We chose to

TABLE 4. WEEKLY AVERAGES OF RESPIRATORY SYMPTOMS AND MEDICATION IN CHILDREN WITH AND WITHOUT DIRECT PET CONTACT

		Confirms Direct Pet Contact (<i>n</i> = 179)			Denies Direct Pet Contact (<i>n</i> = 92)			Total (<i>n</i> = 271)		
	Week	Mean	Change from Baseline (95% CI)	p Value	Mean	Change from Baseline (95% CI)	p Value	Mean	Change from Baseline (95% CI)	p Value
Morning PEF, L/min	Baseline	322			318			320		
	2	319	−3 (−7, 2)	0.24	314	−4 (−8, 2)	0.26	318	−2 (−6, 1)	0.11
	3	317	−5 (−9, −1)	< 0.01	316	−2 (−8, 4)	0.62	317	−3 (−7, −1)	0.02
Asthma, d/wk	Baseline	1.05			0.80			0.97		
	2	1.13	0.08 (−0.15, 0.31)	0.51	1.13	0.33 (0.01, 0.64)	0.04	1.13	0.16 (−0.03, 0.35)	0.09
	3	1.04	−0.01 (−0.22, 0.20)	0.92	0.97	0.17 (−0.12, 0.45)	0.26	1.01	0.04 (−0.12, 0.22)	0.58
β -Agonist, daily doses	Baseline	0.30			0.29			0.30		
	2	0.31	0.01 (−0.04, 0.06)	0.62	0.38	0.09 (0.00, 0.18)	0.06	0.33	0.03 (−0.01, 0.08)	0.10
	3	0.33	0.03 (−0.04, 0.08)	0.42	0.36	0.07 (0.01, 0.14)	0.03	0.34	0.04 (0.00, 0.09)	0.08
Steroids daily dose, μ g	Baseline	192			205			197		
	2	203	11 (−2, 24)	0.11	219	14 (−9, 37)	0.23	208	11 (0, 23)	0.05
	3	202	10 (−8, 27)	0.27	226	21 (−6, 47)	0.12	210	13 (−1, 28)	0.07

use morning PEF as an outcome variable because it was easier to standardize than evening PEF. Time since last medicine intake the evening before was fairly constant, and because morning PEF was checked within a short time range, the effect of the circadian rhythm on lung function was minimized (28, 29).

The children who did not respond to the questionnaire and were subsequently excluded from the study have most likely not affected the results, because each child constituted its own control. The study was blinded in that the families could not determine whether their child attended a class with many or few cat owners.

We have previously shown that cat allergen is transported in clothing and dispersed in air. The median levels of airborne cat allergen *Fel d 1* in classes with many (> 25%) cat owners are approximately 3 ng/m³, which is 5-fold higher than the levels found in classrooms with few (< 10%) cat owners (12). The findings in the present study indicate that the few nanograms of *Fel d 1* per cubic meter previously found in classes with many cat owners may be sufficient to worsen or maintain an allergic inflammation. On the other hand, they imply that the levels found in classes with few cat owners are not higher than in the community in general, and most likely do not constitute a risk to aggravate asthma in children allergic to cats. Thus, if the levels of cat allergen in school could be reduced to those in classes with few cat owners, the health of many asthmatic children with allergy to furred pets would improve.

In conclusion, our findings suggest that asthmatic children allergic to cat suffer a worsening of their disease in relation to indirect exposure to cat at school start. This is most likely the result of significant exposure to allergens that give rise to airway inflammation after a period of nonexposure. It would be of considerable interest to look into possible intervening measures, preferably to take steps to minimize the amount of allergen brought to school in cat owners' clothing, a major source of cat allergen.

Acknowledgment: The authors thank the children and their families, without whose assistance this study would not have been possible. They are also indebted to the pediatric allergy outpatient clinics (St. Göran, Danderyd, Sachska, Huddinge, and Jakobsberg), and to Marie Ljungqvist for expert field work. Anne-Sophie Karlsson and Karl Magnusson have provided excellent data banking. Statistician Frédéric Lagarde is gratefully acknowledged for generously assisting them with data analysis, as is Professor Sven-Erik Dahlén for valuable advice. The study was supported by the Vårdal Foundation and Samariten. Dr. Luca Perfetti was at the time of this study a recipient of a scholarship from the Blanceflor Ludovisi Foundation.

References

- Plaschke P, Janson C, Norrman E, Björnsson E, Ellbjär S, Järholm B. Association between atopic sensitization and asthma and bronchial hyperresponsiveness in Swedish adults: pets, and not mites, are the most important allergens. *J Allergy Clin Immunol* 1999;103:58–65.
- Ingram JM, Sporik R, Rose G, Honsinger R, Chapman MD, Platts-Mills TAE. Quantitative assessment of exposure to dog (*Can f 1*) and cat (*Fel d 1*) allergens: relation to sensitization and asthma among children living in Los Alamos, New Mexico. *J Allergy Clin Immunol* 1995;96:449–456.
- Plaschke P, Janson C, Balder B, Löwhagen O, Järholm B. Adult asthmatics sensitized to cats and dogs: symptoms, severity, and bronchial hyperresponsiveness in patients with furred animals at home and patients without these animals. *Allergy* 1999;54:843–850.
- Perzanowski M, Rönmark E, Nold B, Lundbäck B, Platts-Mills TAE. Relevance of allergens from cats and dogs to asthma in the northernmost province of Sweden: schools as a major site of exposure. *J Allergy Clin Immunol* 1999;103:1018–1024.
- Ihre E, Zetterström O. Increase in non-specific bronchial responsiveness after repeated inhalation of low doses of allergen. *Clin Exp Allergy* 1993;23:298–305.
- Sulakvelidze I, Inman MD, Rerecich T, O'Byrne PM. Increases in airway eosinophils and interleukin-5 with minimal bronchoconstriction during repeated low-dose allergen challenge in atopic asthmatics. *Eur Respir J* 1998;11:821–827.
- Custovic A, Green R, Taggart SCO, Smith A, Pickering CAC, Chapman MD, Woodcock A. Domestic allergens in public places. II. Dog (*Can f 1*) 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;26:1246–1252.
- Munir AKM, Einarsson R, Dreborg SKG. Mite (*Der p 1*, *Der f 1*), cat (*Fel d 1*) and dog (*Can f 1*) allergens in dust from Swedish day-care centres. *Clin Exp Allergy* 1995;25:119–126.
- Smedje G, Norbäck D, Edling C. Asthma among secondary school children in relation to the school environment. *Clin Exp Allergy* 1997;27:1270–1278.
- Sporik R, Squillace SP, Ingram JM, Rakes G, Honsinger RW, Platts-Mills TAE. Mite, cat, and cockroach exposure, allergen sensitisation, and asthma in children: a case-control study of three schools. *Thorax* 1999;54:675–680.
- Wickman M, Egmar AC, Emenius G, Almqvist C, Berglund N, Larsson P, van Hage-Hamsten M. *Fel d 1* and *Can f 1* in settled dust and airborne *Fel d 1* in allergen avoidance day-care centres for atopic children in relation to number of pet-owners, ventilation and general cleaning. *Clin Exp Allergy* 1999;29:626–632.
- Almqvist C, Larsson PH, Egmar AC, Hedrén M, Malmberg P, Wickman M. School as a risk environment for children allergic to cats, and a site for transfer of cat allergen to homes. *J Allergy Clin Immunol* 1999;103:1012–1017.
- Enberg RN, Shamie SM, McCullough J, Ownby DR. Ubiquitous presence of cat allergen in cat-free buildings: probable dispersal from human clothing. *Ann Allergy* 1993;70:471–474.
- Patchett K, Lewis S, Crane J, Fitzharris P. Cat allergen (*Fel d 1*) levels on school children's clothing and in primary school classrooms in Wellington, New Zealand. *J Allergy Clin Immunol* 1997;100:755–759.
- Dreborg S, Backman A, Basomba A, Bousquet J, Dieges P, Malling HJ. Skin tests used in type I allergy testing. Position paper, prepared by the sub-committee on skin tests of the European Academy of Allergology and Clinical Immunology. *Allergy* 1989;44(Suppl 10):1–59.
- Roemer W, Hoek G, Brunekreef B, Schouten JP, Baldini G, Clench-Aas J, Englert N, Fischer P, Forsberg B, Haluszka J, et al. Effect of short-term changes in urban air pollution on the respiratory health of children with chronic respiratory symptoms: the PEACE project (introduction). *Eur Respir Rev* 1998;8:4–11.
- Stata user's guide, release 6. Collage Station, TX: Stata Press; 1999. p. 256–260.
- Noertjojo K, Dimich-Ward H, Obata H, Manfreda J, Chan-Yeung M. Exposure and sensitization to cat dander: asthma and asthma-like symptoms among adults. *J Allergy Clin Immunol* 1999;103:60–65.
- Brunekreef B, Groot B, Hoek G. Pets, allergy and respiratory symptoms in children. *Int J Epidemiol* 1992;21:338–342.
- Burge PS. Single and serial measurements of lung function in the diagnosis of occupational asthma. *Eur J Respir Dis Suppl* 1982;123:47–59.
- Hollander A, Heederik D, Brunekreef B. Work-related changes in peak expiratory flow among laboratory animal workers. *Eur Respir J* 1998;11:929–936.
- Storr J, Lenney W. School holidays and admissions with asthma. *Arch Dis Childhood* 1989;64:103–107.
- Johnston SL, Pattemore PK, Sanderson G, Smith S, Campbell MJ, Josephs LK, Cunningham A, Robinson BS, Myint SH, Ward ME, et al. The relationship between upper respiratory infections and hospital admissions for asthma: a time-trend analysis. *Am J Respir Crit Care Med* 1996;154:654–660.
- Warner JO, Naspitz CK, Cropp GJA. Third international pediatric consensus statement on the management of childhood asthma. *Pediatr Pulmonol* 1998;25:1–17.
- Sterk PJ, Buist SA, Woolcock AJ, Marks GB, Platts-Mills TAE, von Mutius E, Bousquet J, Frew AJ, Pauwels RA, Ait-Khaled N, et al. The message from the world asthma meeting. *Eur Respir J* 1999;14:1435–1453.
- Higgins BG, Britton JR, Chinn S, Cooper S, Burney PGJ, Tattersfield AE. Comparison of bronchial reactivity and peak expiratory flow variability measurements for epidemiological studies. *Am Rev Respir Dis* 1992;145:588–593.
- Quanjer PH, Lebowitz MD, Gregg I, Miller MR, Pedersen OF. Peak expiratory flow: conclusions and recommendations of a working party of the European Respiratory Society. *Eur Respir J* 1997;10(Suppl 24):2s–8s.
- Brand PLP, Duijverman EJ, Postma DS, Waalkens HJ, Kerrebijn KF, van Essen-Zandvliet EEM. Peak flow variation in childhood asthma: relationship to symptoms, atopy, airways obstruction and hyperresponsiveness. *Eur Respir J* 1997;10:1242–1247.
- Reddel HK, Ware SI, Salome CM, Marks GB, Jenkins CR, Woolcock AJ. Standardization of ambulatory peak flow monitoring: the importance of recent β_2 -agonist. *Eur Respir J* 1998;12:309–314.