Indoor environmental risk factors in young asthmatics: a case-control study

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Abstract

One hundred and ninety three children with asthma and 318 controls aged 1–4 years were evaluated for atopic heredity and exposure to possible indoor risk factors for asthma – for example exposure to furred pets, tobacco smoke, and home dampness. A subgroup of cases were classified as cat and/or dog allergic on the basis of skin prick tests.

Heredity for asthma was a significant risk factor (odds ratio (OR) 3.0, confidence interval (CI) 2.1 to 4.6). Environmental tobacco smoke was associated with an excess risk for asthma (OR 1.7, CI 1.1 to 2.3) and signs of home dampness tended to increase this risk (OR 1.3, CI 0.9 to 2.0). High dose exposure to cat and/or dog resulted in an increased risk only in asthma cases sensitised to cat and/or dog (OR 2.7, CI 1.0 to 7.3). A combination of high dose exposure to cat and/or dog, environmental tobacco smoke and damp housing was associated with an OR of 8.0 (CI 1.9 to 34.1). Raised indoor humidity has been shown to reflect low air exchange, which may also lead to increased doses of inhaled aeroallergens and tobacco smoke, and contribute to the interaction between the three risk factors.

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In the last decades a considerable increase in the prevalence of atopic disease in childhood and adolescence has been reported in the western world.^{1–5} Considerable environmental changes have also taken place during this period. For instance, pollution from motor vehicle has increased outdoors and energy saving measures, undertaken particularly in temperate areas, may have changed the indoor climate. A large number of studies confirm environmental influences on the development of atopic disease,^{6–13} but interactions between risk factors have only been investigated to a limited extent.¹²

Exposure to inhalant allergens and pollutants influence the development and prognosis of wheezing and asthma in childhood^{14–16} and allergen exposure during the first few years of life appears particularly important for atopic sensitisation and induction of atopic disease.^{17–21} It has even been claimed that increased sensitisation to inhaled allergens is the most probable explanation for the increased prevalence of asthma.²² Among air pollutants environmental

tobacco smoke seems especially detrimental during this first vulnerable period of life.^{23 24}

The aim of the present study was to analyse the importance of exposure in early childhood to various indoor environmental risk factors for the development of bronchial asthma in young children. Particular emphasis was put on exposure to furred pets and interactions between risk factors.

Patients and methods

STUDY SUBJECTS

A case-control study in children 1 to 4 years of age was conducted in the catchment areas of three of four major Stockholm hospitals, Danderyd, Huddinge, and St Görans. The areas are mainly urban and suburban. All the hospitals have paediatric departments with wards and emergency units as well as an out-patient allergy clinic, which serves as a referral unit for children with atopic disorders. Admissions of children due to acute asthma in the catchment areas occur almost exclusively to the paediatric wards of these hospitals.

The case group included 193 children 12–48 months old who had been referred to the specialist allergy clinics of the three hospitals for evaluation of bronchial asthma between May 1990 and March 1992. On the basis of the result of skin prick tests (see below) the cases were subclassified either as cat and/or dog allergen positive (CDP, n=34) or negative (CDN, n=159). Sixty nine per cent of the children were below 30 months of age at inclusion. Only children with three or more episodes of airway obstruction with asthmatic symptoms such as wheezing, cough, etc, were included, but the symptoms were generally more severe than indicated by this minimal inclusion criterion. The main reason for referral was one or several hospital admissions (n=122) or emergency visits (n=58) for asthma symptoms. Another 13 children had been referred from other physicians after repeated acute episodes of wheezing.

The parents were given written information about the study and an appointment for an initial visit to a nurse was given. Participation was refused for five children. Skin prick tests were performed at the visit with aqueous extracts of egg white, *Dermatophagoides pteronyssinus*, cat, dog, rabbit, horse, birch, and timothy (Soluprick 10 HEP, ALK, Hørsholm, Denmark). Extracts of the same batch were used in all three hospitals. Histamine hydrochloride 10 mg/ml and saline were used as positive and negative controls. The control tests and those with cat and dog allergen extracts were performed in duplicate. The test

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Table 1 Hereditary risk factors in children with asthma not sensitised to cat and/or dog (CDN group) or with such sensitisation (CDP group)

	Control group (n=318)	CDN group (n=159)	CDP group (n=34)	CDN group v control group		CDP group v control group	
				OR	CI	OR	CI
Asthma							
Maternal	25	34	6	3.2	1.8 to 5.5	2.5	1.0 to 6.5
Paternal	28	30	8	2.4	1.4 to 4.2	3.2	1.3 to 7.6
Parental	51	60	11	3.2	2.0 to 4.9	2.5	1.2 to 5.4
Rhinoconjunctivitis							
Maternal	87	60	11	1.6	1.1 to 2.4	1.3	0.6 to 2.7
Paternal	71	65	15	2.4	1.6 to 3.6	2.7	1.3 to 5.6
Parental	135	101	19	2.4	1.6 to 3.5	1.7	0.9 to 3.5
Atopic eczema							
Maternal	70	44	11	1.4	0.9 to 2.1	1.7	0.8 to 3.6
Paternal	40	25	8	1.3	0.8 to 2.2	2.1	0.9 to 5.0
Parental	95	64	16	1.6	1.1 to 2.4	2.1	1.0 to 4.3

was considered positive if the weal diameter was at least 3 mm in a single or one of the duplicate tests. At a later visit to a paediatric allergologist a structured clinical evaluation was performed, which included a final evaluation of compliance with the inclusion criteria. At this visit the treatment and medical handling of the patient was revised and a standardised written instruction about allergen avoidance measures was handed out.

Four hundred children were randomly selected from the population of the hospital catchment areas to serve as controls, after matching with the cases for time of birth in intervals of half a year. The parents of nine children could not be located and one control had fulfilled the case criteria before the time of the study and was excluded.

The controls were selected in the later part of the study period, after identification of the cases, and their age was about nine months higher in average, at the time of inclusion. The response rate was 82% (n=318) and 99 (31%) were below 30 months of age.

QUESTIONNAIRE

A questionnaire was sent to the parents of the children under study. It focused on heredity, atopic symptoms, and on various indoor environmental conditions on the children's homes. Heredity for atopic diseases was defined by the occurrence of atopic disease in one or both of the parents.

Questionnaire information was also obtained about parental tobacco smoking during pregnancy and after the child's birth. Exposure to environmental tobacco smoke was defined as any period of regular parental smoking in the

home during the child's first two years of life. Window pane condensation in the bedroom or living room during the winter was used as a marker of home dampness.^{25 26}

Special emphasis was put on direct and indirect exposure to fur coated animals, particularly to cat and dog. Using the questionnaire data, exposure to cat and/or dog during the first two years of life was classified into three different categories: 'High dose exposure': cat and/or dog in the current and/or previous home or nursery of the child, or any other home where the child had lived for more than three days monthly; 'low dose exposure': direct contact up to three days a month or indirect exposure to such animals, for example in the homes of friends, neighbours, summer-house, or other locations regularly visited by family members; and 'no exposure': no obvious direct or regular indirect contacts with cat and/or dog.

STATISTICAL ANALYSES

Risks associated with various exposures were expressed as the odds ratio (OR) calculated using the Mantel-Haenszel procedure with maximum likelihood method estimates of the 95% confidence interval (CI).²⁷ Tests for trend were performed according to the method proposed by Mantel, using two tailed p values.²⁸ In some analyses adjustments were made for age (more or less than 30 months), sex and parental asthma, which were significant risk factors for asthma. However, this did not have a marked effect on the results, indicating that there was no confounding, and the data are presented without adjustments.

This study was approved by the ethical committee of the Karolinska Institute, Stockholm, Sweden.

Results

There were significantly more boys in the case group (75%) (OR 3.0, CI 2.0 to 4.4) and parental divorce was more common among cases than among controls (OR 1.9, CI 1.0 to 3.6).

Thirty four cases were skin prick test positive to cat and/or dog and constituted the CDP group; of these children 29 were skin prick test positive to cat and 20 to dog. The remaining 159 cases constituted the CDN group. Fifteen children were skin prick test positive to horse and 11 to rabbit; all but six of these children

Table 2 Housing conditions in children with asthma not sensitised to cat and/or dog (CDN group) or with such sensitisation (CDP group)

	Control group (n=318)	CDN group (n=159)	CDP group (n=34)	CDN group v control group		CDP group v control group	
				OR	CI	OR	CI
Apartment house	139	81	18	1.3	0.9 to 2.0	1.4	0.7 to 2.9
Residence area <21 m ² /inhabitant	58	37	6	1.4	0.9 to 2.2	1.0	0.4 to 2.4
Window pane condensation	70	41	12	1.3	0.8 to 2.0	1.9	0.9 to 4.3
Damage due to dampness	54	33	5	1.3	0.8 to 2.0	0.8	0.3 to 2.4
Visible mould	44	27	4	1.3	0.7 to 2.2	0.8	0.2 to 2.6
Fitted carpets >10 m ²	67	19	3	0.6	0.3 to 1.1	0.4	0.1 to 1.5
Allergen avoidance measures*	27	52	15	5.2	3.1 to 8.6	8.5	6.3 to 11.5
Vacuum cleaning >3 times/week	74	52	11	1.6	1.1 to 2.4	1.6	0.8 to 3.3

*Removal of fitted carpets, unsuitable bedding, flowers and/or pets, measures to handle dampness problems and/or avoidance of indoor smoking.

Table 3 Exposure to cat and dog during the first two years of life in children with asthma not sensitised to cat and/or dog (CDN group) or with such sensitisation (CDP group)

	Control group (n=318)	CDN group (n=159)	CDP group (n=34)	CDN group v control group		CDP group v control group	
				OR	CI	OR	CI
Cat							
High dose	71	30	14	0.7	0.4 to 1.2	3.0	1.3 to 7.2
Low dose	108	49	11	0.8	0.5 to 1.2	1.6	0.6 to 3.8
No dose	139	80	9				
			Trend	p=0.20		p=0.02	
Dog							
High dose	51	20	8	0.8	0.4 to 1.4	2.0	0.8 to 4.9
Low dose	117	61	14	1.0	0.7 to 1.5	1.5	0.7 to 3.3
No dose	150	78	12				
			Trend	p=0.49		p=0.18	
Cat/dog							
High dose	105	46	18	0.7	0.4 to 1.2	2.7	1.0 to 7.3
Low dose	134	64	11	0.8	0.5 to 1.2	1.3	0.5 to 3.7
No dose	79	49	5				
			Trend	p=0.20		p=0.04	

were positive to cat and/or dog. Eight children were positive to mite, 20 to birch, and four to timothy, while 20 cases were skin prick test positive to egg white.

Heredity for atopic diseases was more prevalent among cases than controls (table 1). The difference was found for all diseases under study, but appeared more prominent for parental airway disease than dermatitis. The influence of parental asthma was particularly strong. Thus, more than 20% of the parents of the case group children reported bronchial asthma compared with 8% of those in the control group.

Duration of breast feeding and the age for introduction of common allergenic foods in the children's diet did not differ markedly between cases and controls. Thus cows' milk had been introduced before 3 months' age in 44% of the case group children, compared with 38% of the controls. Dietary manipulations, that is reduction of maternal intake of allergenic foods during pregnancy, lactation, and/or delay of introduction of such food to the child during infancy, had been undertaken by similar proportions of cases (17%) and controls (15%).

Residential characteristics are given in table 2. No major differences were seen between cases and controls or between the two case groups in the occurrence of most residential factors. However, window pane condensation tended to be most frequent in the CDP group (OR 1.9, CI 0.9 to 4.3). Allergen avoidance measures during the last two years, that is removal of fitted carpets and unsuitable beddings, measures to control dampness problems, avoidance of indoor smoking, removal of pets and flowers, and frequent (>3 times/week) vacuum cleaning, were more common in the homes of the cases than of the controls.

Table 4 Interaction between parental smoking, window pane condensation and exposure to cat and/or dog in children with asthma not sensitised to cat and/or dog (CDN group) or with such sensitisation (CDP group)

No of risk factors	Control group (n=318)	CDN group (n=159)	CDP group (n=34)	CDN group v control group		CDP group v control group	
				OR	CI	OR	CI
None	105	35	6	—	—	—	—
One	127	77	11	1.8	1.1 to 3.3	1.5	0.5 to 4.7
Two	73	37	11	1.5	0.8 to 2.7	2.6	0.8 to 8.4
All three	13	7	6	1.6	0.5 to 4.8	8.0	1.9 to 34.1
			Trend			p<0.01	

Residential exposure to environmental tobacco smoke during the first two years of life was a significant risk factor for asthma. Thus, parental smoking was reported in 62% of the CDP group families (OR 2.1, CI 1.0 to 4.2), 55% of the CDN group families (OR 1.6, CI 1.1 to 2.3), and 44% of the control families. The greatest impact of tobacco smoke was found in the younger age group (below 30 months) both within the CDP group (OR 3.6, CI 1.0 to 13.3) and the CDN group (OR 2.1, CI 1.2 to 3.7). The CDN and CDP groups did not differ significantly in this respect.

High dose exposure to cat and/or dog during the first two years of life was significantly more prevalent in the CDP group children (OR 2.7, CI 1.0 to 7.3), but tended to be slightly less prevalent in the CDN group (OR 0.7, CI 0.4 to 1.2) in comparison with the control group (table 3). High dose exposure to cat alone was also found more often in the CDP group, compared with the controls (OR 3.0, CI 1.3 to 7.2), while the association to dog appeared less pronounced. Significantly more high dose exposure to cat and/or dog was reported for the CDP group when compared with the CDN group (OR 2.8, CI 1.3 to 5.8). This was also true for cat alone (OR 3.0, CI 1.4 to 6.6), and a tendency was seen for dog (OR 2.1, CI 0.9 to 5.3). The risk of asthma in the CDP group increased with the degree of exposure to cat (p trend=0.02). The youngest children (below 30 months of age) in the CDP group had been more exposed to cat and/or dog (OR 6.9, CI 2.1 to 22.2) as well as to cat (OR 4.5, CI 1.5 to 13.4), and dog (OR 6.2, CI 2.0 to 19.9) compared with controls of the same age. A dose related pattern was seen for exposure to cat (p trend=0.01) as well as for dog (p trend=0.01) in this young age group (not shown in table).

There was a combined effect between environmental tobacco smoke and damp housing in the CDP group and combined exposure to the two risk factors was associated with an OR of 4.0, CI 1.6 to 10.5. No such interaction was found in the CDN group. The combined effect in the CDP group was observed also for exposure to tobacco smoke and high dose of cat/dog (OR 3.8, CI 1.6 to 9.0) and to damp housing and high dose of cat/dog (OR 4.4, CI 1.6 to 12.0). In the CDP group the most pronounced effect (OR 8.0, CI 1.9 to 34.1) was observed when all the three risk factors coexisted (table 4). There was a significantly increased risk of asthma in the cat/dog sensitised group with increasing number of risk factors (test for trend p<0.001). The trend appeared strongest in the CDP group children below 30 months of age (not shown in table).

Discussion

A main finding in this study is that direct exposure to furred pets during the first few years of life favours the development of sensitisation to furred pets in asthmatic children. The influence of exposure to cat was particularly marked, which fits with several other studies.²⁹⁻³¹ This may have several reasons. Recent studies indicate that cat allergen may

remain airborne for long periods of time,³² possibly resulting in high inhaled doses of cat allergen. Another contributing factor may be that children's contact with cats are closer than with dogs.³³ Indirect exposure had little influence on the development of sensitisation to furred pets in asthmatic children in this study, which may be a consequence of the young age of the children. Indirect exposure in homes, at daycare centres and schools,^{34 35} may become more important later in life. A consequence of these results is that exposure to animal pets, cat in particular, should be at focus for primary intervention.

Notably, however, there was no increased overall risk of asthma with the keeping of a cat or dog. This may partly be due to a preponderance of non-atopic forms of asthma in the studied age group obscuring a relationship. Only a subgroup of the asthmatic children developed sensitisation to furred animals, and then particularly when directly exposed in early life. Thus to some extent, sensitisation to cat and/or dog in asthmatic children may be seen as a marker of exposure to these pets during the first years of life. We did not study sensitisation in children without asthma and the relative importance of environmental exposure versus host susceptibility for the observed association is not clear.

Damp housing is of importance for the development of sensitisation to mites,^{26 36 37} and living in a damp house has been associated with atopic disease and bronchial hyperreactivity.^{11 38} In a temperate climate, wintertime window pane condensation in bedrooms or living rooms is related to raised indoor humidity, and may be seen as a marker of poor ventilation.^{25 26} In spite of the fact that only few of the children were sensitised to mites, damp housing was associated with childhood asthma, particularly in children sensitised to furred pets. Possibly, the dose of inhaled allergen, cat in particular, may be increased with low indoor air exchange as allergenic particles are kept airborne for a longer period of time in a poorly ventilated dwelling.³² This hypothesis is supported by a recent study, where high concentrations of small airborne particles, suggested partly to consist of cat allergen, were found in damp homes.³⁹

In a many studies environmental tobacco smoke has been found to be related to development of asthmatic symptoms in children^{24 40 41} and our data confirm that the effect is strongest in young children. An effect of tobacco smoke was found both in children with and without sensitisation to cat and/or dog. Enhancement of the risk for atopic sensitisation, for example to animal domestic pets, could be one of the consequences of exposure to environmental tobacco smoke.⁴² Such an effect could explain the interaction between exposure to tobacco smoke and animal pets.

The use of a hospital based material for recruitment of cases involves a risk of selection bias. A bias would be introduced if the referral of cases to allergy specialists was related to some risk factor under study, such as exposure to furred pets. However, exposure to cat

and/or dog was of the same magnitude in the case group as in the control group. Only children who were skin test positive to cat and/or dog exhibited a higher reported exposure to these animals during their first two years of life. As no test results were available at the time of referral, it appears unlikely that selection bias could explain this result. Various kinds of recall bias of exposure also deserves attention. For example, there is a risk of underreporting of environmental tobacco smoke among the case group parents, which would rather lead to underestimation of its effects. Allergen avoidance measures particularly in the case families would have the same consequences.⁴³

Window pane condensation and occurrence of residential mould lesions could on the other hand be overreported by the parents of the asthmatic children due to increased awareness of the possible importance of such factors. There was, however, no difference in reported occurrence of mould lesions in the homes of the different groups of children, and over-reporting of window pane condensation in the homes of the cases also appears unlikely. Further, it cannot be excluded that there was a higher response rate among control families with atopic diseases, which would contribute to the high prevalence of reported atopy among the controls, and lead to an underestimation of the risk factors under study.

In the present study we found an influence of exposure to environmental tobacco smoke and damp housing on the development of asthma. In the subgroup of cases sensitised to cat and/or dog, exposure to furred pets seemed to be of importance. It was not possible to determine the type of interaction because of small numbers in this group. Allergy to furred domestic pets, cat and dog in particular, is of great importance in asthma all through childhood, and may indicate a poor prognosis of the disease when found in young children.⁴⁴⁻⁴⁶

Our findings stress that efforts should be made to help parents to refrain from smoking, improve the ventilation of their homes and reconsider the keeping of fur coated animals. This appears to apply in particular for families with young children and when there is a family history of atopy and asthma.

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