

Atopy among schoolchildren in northern and southern Sweden in relation to pet ownership and early life events

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Studies have suggested a higher prevalence of asthma and allergies in northern, as compared to southern, Scandinavia. The aim of this study was to evaluate regional differences in atopy in relation to pet ownership and certain early life events among schoolchildren ($n=2108$) aged 10–11 years from Linköping in southern Sweden and Östersund in northern Sweden. The parents completed a questionnaire, comprising questions on home environment, heredity, socio-economic conditions, and the core questions on symptoms from the International Study of Asthma and Allergies in Childhood. The children were skin-prick tested to eight common inhalant allergens. Information on maternal smoking habits, gestational age, and anthropometric measures were obtained from the Swedish Medical Birth Registry. The prevalence of atopic symptoms and sensitization to pollen were similar in Östersund and in Linköping. A higher prevalence of sensitization to animal dander among children in Östersund could be linked to a higher occurrence of pets in the community. Current cat ownership was related to less sensitivity to cat allergen but only in children with an atopic heredity. Ponderal index $>30 \text{ kg/m}^3$ was related to an increased risk of atopic sensitization, both in Linköping (adjusted odds ratio 2.1; 95% confidence interval 1.1–4.0) and in Östersund (adjusted odds ratio 2.0; 95% confidence interval 1.1–3.5). Maternal smoking during pregnancy was related to an increased risk of atopic sensitization among children in Linköping, whereas current smoking was associated with a decreased risk of sensitization in Östersund. In conclusion, we demonstrated that a high occurrence of pets in the community was associated with sensitization, whereas atopic symptoms were essentially unaffected. This study has also suggested an association between body size at birth and atopic sensitization at 10–11 years of age.

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Several studies have suggested a higher prevalence of asthma and atopic symptoms in northern Sweden, as compared to southern Sweden, both in schoolchildren and in male conscripts (1,2). However, studies on adults have been inconsistent (3,4), and a large cross-sectional study failed to find regional variations in atopic symptoms among schoolchildren in Finland (5). Recent findings suggest that atopy could be programmed very early in life (6). Therefore, environmental conditions during the initial encounters with an

allergen could be crucial for development of atopic disease in later life (7). The Swedish Medical Birth Registry provides rather unique opportunities for assessing the role of certain perinatal factors that could conceivably affect immune responses to allergens (8).

The aim of this study was to evaluate regional differences in atopy among schoolchildren in relation to pet ownership and early life events. The study involved 10–11-year-old schoolchildren from two study centres in northern and southern

Sweden. Skin prick test (SPT) results and questionnaire-reported information on symptoms and home environment were linked at an individual level to information from the Medical Birth Registry.

Material and methods

Study populations

In all, 2505 children in forms 4 and 5 (age 10–11 years), living in two cities in Sweden, were invited to participate in the study (i.e. 1115 children from a random sample of 15 schools in Linköping and 1390 children from all 25 schools in Östersund). The study was conducted between January and April 1997. Linköping, in southern Sweden (latitude 58°), is the fifth largest city in Sweden and is currently undergoing expansion, with a university and several large sites of industry. At the time of the study the population of Linköping was 132,089 (24% of whom were <20 years of age). The annual mean temperature is 6.1°C and the annual precipitation 517 mm (9). Östersund is an administrative center in northern Sweden (latitude 61°) with sparsely populated surroundings. In 1997, the total population in Östersund was 59,188 (23% of whom were <20 years of age). The annual mean temperature is 2.5°C and the annual precipitation 484 mm (9).

Questionnaire

The parents were asked to complete the standardized core questionnaire on wheezing, rhinitis, and eczema (10) from the International Study of Asthma and Allergies in Childhood (ISAAC) (10). Questions on home environment (type and size of dwelling, dampness, parental smoking, current or previous pets), atopic heredity, and socio-economic conditions, were also included. Many of these questions had been previously used in similar studies (11). The socio-economic position of the family was classified according to the occupation of both parents (12). The number of completed questionnaires in Linköping and Östersund was 911 (82%) and 1197 (86%), respectively.

SPTs

SPTs were performed in duplicate on the volar aspects of the forearms and according to the standards of the European Academy of Allergy and Clinical Immunology (13). Standardized allergens (Solu-Prick SQTM; ALK, Hørsholm, Denmark) and lancets (ALK) were used. The potency of the extracts was 1:20 (w/v) (*Alter-*

naria) or 10 histamine-equivalent SPT units (HEP) (tree mix, grass mix, mugwort, horse, dog, cat, *Dermatophagoides pteronyssinus*, *D. farinae*). Two nurses in Östersund and four nurses in Linköping performed the SPTs. They all performed a number of series of SPTs with histamine before the onset of the study, until the coefficient of variation was less than 20%. The SPTs were conducted at the schools from January to April 1997. The mean histamine wheal size in children with negative SPTs was 5.1 mm in Linköping and 5.4 mm in Östersund (95% confidence interval [CI] for the difference was 0.1–0.5 mm). The number of children participating in the SPTs was 857 (77%) in Linköping and 991 (71%) in Östersund.

The Swedish Medical Birth Registry

The Swedish Medical Birth Registry continuously receives information from all Swedish antenatal clinics and delivery units on more than 99% of all births in Sweden. Data from each child and mother are linked to the personal identification code of the mother. The registry contains data on anthropometric measures at birth, gestational age, birth order, and perinatal complications. It also includes data on maternal smoking habits based on an interview by a midwife at the mother's first visit to the antenatal clinic (usually weeks 10–12 of gestation) (14). We received information from the Medical Birth Registry on 758 (68%) children in Linköping and 987 (71%) children in Östersund, after informed consent was given by the parents.

Statistics

All statistical calculations were performed using the spss package, version 10.0. Chi-square tests were used to compare rates between groups. Tests for trends were made using the Mantel–Haenszel statistics (15). Multi-variate logistic regression analyses were used to obtain estimates of odds ratios for sensitization and questionnaire-reported symptoms, with adjustments for significant covariables.

Ethics

The study was approved by the Ethics Committees at Umeå University and Linköping University.

Results

Data from the questionnaires and the Medical Birth Registry demonstrated that the educational

Table 1. Questionnaire-reported prevalence of wheezing and allergic rhinoconjunctivitis among schoolchildren in Linköping and Östersund

	Linköping n=911 %	Östersund n=1197 %	Relative risk* (95% CI)
Wheezing			
Lifetime prevalence	23.7	22.5	1.0 (0.8–1.1)
12-month prevalence	7.9	10.2	1.3 (1.0–1.7)
Asthma			
Lifetime prevalence	9.6	10.9	1.1 (0.9–1.5)
Allergic rhinoconjunctivitis			
12-month prevalence	14.1	12.3	0.9 (0.7–1.1)
Hay fever			
Lifetime prevalence	15.2	13.9	0.9 (0.7–1.1)
Eczema			
12-month prevalence	24.6	26.6	1.1 (0.9–1.3)

*Linköping reference area.

level of the parents was higher in Linköping: 28% of children in Linköping vs. 14% in Östersund ($p < 0.001$) had at least one parent with a profession requiring at least 6 years of vocational training. Pets were more common in Östersund, where past or present cat ownership was reported by 41% of families vs. 29% of the families in Linköping ($p < 0.001$); and dog ownership was reported by 41% of families in Östersund vs. 23% in Linköping ($p < 0.001$). A high gestational age (>41 weeks) was more common in Östersund (12.8%) than in Linköping (4.9%) ($p < 0.001$). The mean birth weight and the mean ponderal index were slightly higher in Östersund than in Linköping (95% CI for the differences were 21–124 g and 0.6–1.1 kg/m³, respectively). The prevalence rates of atopic heredity and passive smoking, as well as head circumference and length at birth, were similar in Östersund and Linköping.

The prevalence of questionnaire-reported symptoms indicating atopy was similar in the two study areas except for a slightly increased 12-month prevalence of wheezing in Östersund (Table 1). In contrast, positive SPTs to animal dander were more common in Östersund (Table 2). As the mean histamine wheal size was slightly larger in Östersund than in Linköping (5.4 mm vs. 5.1 mm, respectively; 95% CI for the difference was 0.1–0.5 mm), we also assessed the prevalence of a positive SPT defined as an allergen wheal of at least half of the histamine wheal. The prevalence rates of positive SPTs were unaffected by this definition (data not shown). Furthermore, the increased risk of sensitization to animal dander in Östersund persisted after multiple logistic regression analysis controlling for other significant variables (Table 2). The odds ratios were mainly unchanged in a logistic model including socio-economic position and gestational age (data not shown).

Cat ownership was associated with a lower prevalence of sensitization to cat dander and allergic rhinoconjunctivitis (Table 3). However, current or previous cat ownership was related to a significantly reduced risk of sensitization only in children with a family history of asthma or allergic rhinitis. The odds ratios in children with and without a family history of asthma or allergic rhinitis were 0.4 (95% CI 0.3–0.6) and 0.7 (95% CI 0.4–1.2), respectively. Dog ownership had no relationship to sensitization. Thus, the proportion of positive SPTs to dog dander in children who had never had a dog at home was 7.4%, as compared to 7.1% in children with previous dog ownership and 6.1% in children with current dog ownership ($p = \text{NS}$).

Positive SPTs tended to be less common amongst children with a birth weight of <3500 g as compared to a higher birth weight (21.6% vs. 25.6%, $p = 0.06$). A ponderal index of at least 30 kg/m³ was associated with an increased risk of

Table 2. Prevalence of positive skin-prick tests (SPTs) (allergen wheal diameter ≥ 3 mm) among schoolchildren in Linköping and Östersund

	Linköping* n=857 %	Östersund n=991 %	Crude OR (95% CI)	Adjusted OR (95% CI)†
Tree	11.5	10.6	0.9 (0.7–1.2)	
Grass	11.8	14.5	1.2 (0.9–1.6)	
Cat	9.5	16.1	1.7 (1.3–2.2)	
Dog	4.0	9.1	2.3 (1.6–3.4)	
Horse	4.6	7.7	1.7 (1.2–2.5)	
<i>D. pteronyssinus</i>	1.6	1.0		
<i>D. farine</i>	0.8	0.6		
<i>Alternaria</i>	0.2	0.1		
Any pollen	16.4	18.7	1.1 (0.9–1.4)	1.3 (0.9–1.7)
Any animal	11.1	18.8	1.7 (1.4–2.1)	1.9 (1.4–2.6)
Any allergen	20.1	26.8	1.4 (1.1–1.6)	1.5 (1.2–2.0)

*Linköping reference group.

†Adjusted odds ratios (OR) after multiple logistic regression including other significant covariables: atopic heredity, gender, cat at home (now or previously), ponderal index at birth, and maternal smoking during pregnancy.

CI, confidence interval; *D. farine*, *Dermatophagoides farine*; *D. pteronyssinus*, *Dermatophagoides pteronyssinus*.

Table 3. Atopic sensitization to cat dander and allergic rhinitis (ever) in relation to cat ownership, prevalence (%), and crude odds ratios (OR) (95% confidence interval)

Cat at home	Atopic sensitization to cat dander n=1848	Allergic rhinitis: lifetime prevalence n=2108
Never	16.2, OR 1.0	25.9, OR 1.0
Past	10.6, OR 0.6 (0.4–1.0)	22.4, OR 0.9 (0.7–1.1)
Present	6.5, OR 0.4 (0.2–0.6)	17.3, OR 0.6 (0.5–0.8)
Chi-square (p-value) for trend	25.1 (p = 0.000)	13.6 (p = 0.000)

at least one positive SPT (Table 4), while length at birth and head circumference had no association with the outcome of the SPT. Furthermore, a high ponderal index was related to an increased prevalence of wheezing. Therefore, the lifetime prevalence of wheezing in children with a ponderal index of $\geq 30 \text{ kg/m}^3$ was 29.4% as compared to 23.3% and 21.5%, respectively, in children with a ponderal index of ≤ 26 –29 kg/m^3 (p-value for trend=0.02).

Table 4 summarizes the independent risk factors for sensitization. Maternal smoking during pregnancy was related to an increased risk of sensitization, but only among children in Linköping (p-value for trend=0.02). The association between maternal smoking during pregnancy and the lifetime prevalence of wheezing among children in Linköping was even stronger. Thus, the prevalence of ever wheezing was 21.4%, 24.5%, and 50%, respectively, in children exposed to 0, 1–9, or 10 or more cigarettes per day during fetal life (p-value for trend=0.001). The corresponding prevalence figures in Östersund were

23.8%, 19.8%, and 26.5%, respectively (p=NS). Current maternal smoking had no relationship with positive SPTs among children in Linköping (data not shown). By contrast, current maternal smoking was related to a decreased risk of positive SPTs among children in Östersund. The prevalence rates of positive SPTs were 29.6%, 19.9%, and 18.4%, respectively, in children currently exposed to 0, 1–9, or 10 or more cigarettes per day (p-value for trend=0.002). Comparison of data from the Medical Birth Registry and the questionnaires suggested that changes of maternal smoking habits had occurred after childbirth. Thus, 33% of the women who were reported as smokers in the registry had stopped smoking, and 8% of the women who did not smoke during early pregnancy were current smokers.

Discussion

Positive SPTs to animal dander, but not to pollen, were more common in Östersund in northern

Table 4. Prevalence and odds ratios (OR) for atopic sensitization (at least one positive skin-prick test) among schoolchildren in Östersund and Linköping

	Linköping			Östersund			All	
	Prevalence	Crude OR (95% CI)	Adjusted OR* (95% CI)	Prevalence	Crude OR (95% CI)	Adjusted OR* (95% CI)	Prevalence	Adjusted OR* (95% CI)
Ponderal index (kg/m^3)								
<26	36/185	1.0	1.0	31/133	1.0	1.0	67/318	1.0
26–29.9	82/330	1.0 (0.7–1.6)	1.1 (0.7–1.8)	132/530	1.1 (0.7–1.8)	1.3 (0.8–2.1)	215/944	1.2 (0.8–1.7)
≥ 30	23/83	1.6 (0.8–3.0)	2.1 (1.1–4.0)	60/187	1.6 (0.9–2.7)	2.0 (1.1–3.5)	83/270	2.0 (1.1–3.0)
Gender								
Female	69/390	1.0	1.0	123/495	1.0	1.0	193/887	1.0
Male	95/321	1.4 (1.0–1.9)	1.3 (1.0–1.9)	143/496	1.3 (0.9–1.6)	1.4 (1.1–1.7)	239/913	1.3 (1.0–1.7)
Maternal smoking during pregnancy (cigarettes/day)								
0	86/470	1.0	1.0	163/597	1.0	1.0	250/1069	1.0
1–9	21/97	1.2 (0.7–2.2)	1.3 (0.8–2.4)	34/155	0.8 (0.5–1.2)	1.0 (0.6–1.5)	55/252	1.1 (0.8–1.6)
≥ 10	20/62	2.1 (1.1–3.9)	2.7 (1.5–5.1)	15/63	0.8 (0.4–1.6)	1.0 (0.5–1.9)	35/125	1.6 (1.0–2.5)
Older siblings								
0	73/300	1.0	1.0	106/363	1.0	1.0	179/664	1.0
1	64/307	0.8 (0.6–1.2)	0.7 (0.4–1.1)	94/357	0.9 (0.6–1.2)	0.8 (0.6–1.2)	160/666	0.8 (0.6–1.0)
2 or more	27/199	0.5 (0.3–0.8)	0.5 (0.3–0.9)	65/270	0.8 (0.5–1.1)	0.8 (0.5–1.2)	92/469	0.6 (0.5–0.9)
Cat ownership								
Never	134/564	1.0	1.0	182/581	1.0	1.0	318/1147	1.0
Past	16/96	0.6 (0.4–1.2)	0.9 (0.4–1.6)	39/167	0.7 (0.4–1.0)	0.7 (0.4–1.1)	55/263	0.7 (0.5–1.0)
Present	14/141	0.4 (0.2–0.7)	0.4 (0.2–0.8)	44/241	0.5 (0.3–0.7)	0.6 (0.4–0.9)	58/383	0.5 (0.4–0.7)

*Adjusted OR after logistic regression also controlling for atopic heredity (number of family members with allergic rhinitis).

†Adjusted OR after logistic regression also controlling for atopic heredity (number of family members with allergic rhinitis) and study area.

Sweden than in Linköping in southern Sweden, and this finding remained after adjustment for other significant variables. The prevalence of questionnaire-reported symptoms was similar in Linköping and Östersund, except for a slightly increased prevalence of current wheezing in Östersund. The differences in SPT sensitivity were not caused by differences in SPT technique, as the test procedure was carefully standardized by performing a number of SPT series with histamine, as recommended in the ISAAC phase 2 protocols (16).

Our study illustrates the complex relationship among pet ownership, atopic sensitization, and allergic disease. First, it is reasonable to suggest that the higher prevalence of sensitization to animal dander in Östersund was related to the greater occurrence of pets in the community (17). Second, the higher prevalence of atopic sensitization to animal dander in Östersund was only associated with a slight increase of current wheezing, but a similar prevalence of allergic rhinoconjunctivitis and eczema, as in Linköping. This supports previous population-based studies showing positive SPTs to be common in children without clinical symptoms (18,19). Third, cat ownership was related to a lower prevalence of sensitization to cat dander and allergic rhinoconjunctivitis. Several recent cross-sectional studies have now demonstrated an inverse relationship between pet keeping in early childhood and atopic disease in later life (11,17,20,21). As cat allergen is ubiquitous in many westernised countries (22), children may easily become sensitized without a cat at home (23,24). A similar relationship was not observed for exposure to dog, possibly because dog dander is a less potent allergen than cat dander (25). Environmental conditions during the initial encounters with an allergen could be more important than exposure to the allergen *per se*. Pet keeping has been related to a low prevalence of sensitization among children living in eastern Europe (26) and in farm environments (27).

It has been suggested that high levels of allergen exposure early in life may actually enhance immune deviation towards clinical tolerance (21). However, an inverse relationship between pet ownership and atopic disease in cross-sectional studies (17,20) could also be explained by avoidance measures and selection bias (28). Many families avoid pet keeping if animal contacts seem to provoke allergic symptoms in the child at an early age. Furthermore, selection bias could not be excluded either in this study or in the European Community Health Survey (17), as cat ownership was related to a

significantly reduced risk of sensitization only in children with an atopic heredity.

A rising prevalence of allergies is closely related to the increased standard of living in westernised countries (29), and socio-economic conditions at an early age seem to be crucial. Thus, atopic manifestations at 31 years of age have been associated with a high socio-economic status in early childhood (30). It has also been proposed that the rise of allergies could be linked to an enhanced fetal growth (31). Furthermore, large head circumference at birth has been linked to increased serum immunoglobulin E (IgE) levels in schoolchildren (32,33) and adults (34). Anthropometric measures at birth are markers of fetal nutrition and wellbeing. Some studies have demonstrated a positive relationship between birth weight and atopic eczema (35,36) and allergic rhinitis (8). We found an increased prevalence of positive SPTs and wheezing among children with a ponderal index $>30 \text{ kg/m}^3$. The association was similar in both study areas. Our findings are supported by a recent Finnish study showing a strong positive relationship between asthma and a high ponderal index (37). In contrast, however, there was no association between a ponderal index and asthma or allergic rhinitis among almost 150,000 Swedish conscripts (8). Such inconsistencies suggest that the relationship between ponderal index and atopy requires more detailed evaluation in further studies.

There was no clear relationship between maternal smoking and sensitization as the findings varied in the two study areas. Exposure to maternal smoking at the age of 10 had no association with atopic sensitization among schoolchildren in Linköping whereas an inverse relationship was demonstrated among schoolchildren in Östersund. Such observations suggest that some mothers had stopped smoking owing to allergic symptoms in their children. We also found that prenatal exposure to maternal smoking was related to an increased risk of sensitization, but only among children in Linköping. The evidence for a direct relationship between passive smoking and allergic sensitization is contradictory (38). It is possible that smoking in some societies is a marker for unknown risk factors.

In conclusion, our findings suggest that exposure to pets in the community may affect the prevalence of sensitization to animal dander (but only to some extent), the prevalence of current wheezing and not the prevalence of rhinoconjunctivitis or eczema. We also observed an intriguing association between body size at birth and sensitization. This might be consistent with the hypothesized link between increasing

allergies and enhanced fetal growth in industrialized countries with a market economy.

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