

Does early exposure to cat or dog protect against later allergy development?

B. HESSELMAR, N. ÅBERG, B. ÅBERG, B. ERIKSSON* and B. BJÖRKSTÉN†

Department of Paediatrics, University of Göteborg, Göteborg, *Nordic School of Public Health, Göteborg and †Division of Health and Environment, University Hospital Linköping, Sweden

Summary

Background It is unknown which factors in modern western society that have caused the current increase in prevalence of allergic diseases. Improved hygiene, smaller families, altered exposure to allergens have been suggested.

Objectives To assess the relationship between exposure to pets in early life, family size, allergic manifestations and allergic sensitization at 7–9 and 12–13 years of age.

Methods The prevalence of allergic diseases and various background factors were assessed in 1991 and 1996 by questionnaire studies. In 1991, the study comprised representative samples of children from the Göteborg area on the Swedish west coast (7 years old, $n=1649$) and the inland town Kiruna in northern Sweden (7–9 years old, $n=832$). In 1992, a validation interview and skin prick test (SPT) were performed in a stratified sub-sample of 412 children. In 1996, this subgroup was followed up with identical questions about clinical symptoms as in 1991, detailed questions about early pet exposure were added and SPT performed.

Results Children exposed to pets during the first year of life had a lower frequency of allergic rhinitis at 7–9 years of age and of asthma at 12–13 years. Children exposed to cat during the first year of life were less often SPT positive to cat at 12–13 years. The results were similar when those children were excluded, whose parents had actively decided against pet keeping during infancy because of allergy in the family. There was a negative correlation between the number of siblings and development of asthma and allergic rhinitis.

Conclusion Pet exposure during the first year of life and increasing number of siblings were both associated with a lower prevalence of allergic rhinitis and asthma in school children.

Keywords: exposure, infancy, pets, sensitization, tolerance

Clinical and Experimental Allergy, Vol. 29, pp. 611–617. Submitted 22 April 1998; revised 11 June 1998; accepted 23 October 1998.

Introduction

The prevalence of allergic diseases in childhood has increased over the last decades and at least one third of Swedish school children have reported recent symptoms of either asthma, allergic rhinitis or atopic eczema [1]. The cause(s) of this increase is unknown [2]. Recent studies indicate, however, that lifestyle factors might be of importance, since the prevalence of allergic diseases are lower in

the eastern Europe, as compared with Sweden and the former West Germany [3–5]. These geographical differences may be relevant for an understanding of the increasing trend over time in Sweden, since the lifestyle in countries like Estonia and Poland in many ways resembles that of Sweden some 30–40 years ago. Several studies have reported a negative correlation between family size, overcrowding and allergy [4,6–8]. Changes in allergen exposure, the pattern of infections and hygiene standard in childhood may be contributing factors. During the analysis of data from a prevalence study on allergic diseases in 7–9-year-old children from different parts of Sweden [1], we

Correspondence: B. Hesselmar, Department of Paediatrics, Sahlgrenska University Hospital, 416 85 Göteborg, Sweden.

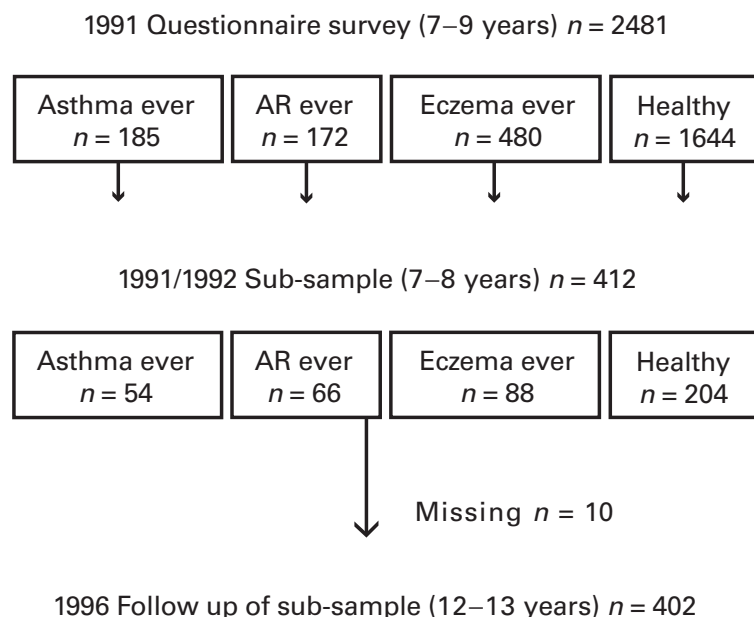


Fig. 1. Flow sheet of the population studied 1991–1996.

found indications of a negative correlation relationship between early pet exposure and allergy. The objective of this study was to assess the relationship between exposure to pets early in life, family size and allergic manifestations later during childhood. In the present follow up study we have taken selection mechanisms behind pet keeping into consideration when investigating the relationship between early pet exposure and allergy development.

Materials and methods

In 1991, a questionnaire study of allergic diseases was conducted in the Göteborg area (Göteborg and Mölndal) on the south-west coast of Sweden, and in Kiruna, a mining town in the northern inland mountains, north of the Arctic Circle. In Göteborg, a sample of schools with 7 year olds was chosen to represent all parts of the city, covering the variations in socio-economic differences and environmental pollution. There were 1115 complete answers from the parents (response rate 83%). In addition, all 7 year olds in Mölndal, a smaller town adjacent to Göteborg, were included, yielding 534 complete answers (response rate 93%). In Kiruna, all 7–9 year olds were included to get a sufficient number for geographical comparisons. There were 832 complete answers (response rate 91%). The questions about disease and symptoms included: 'Has your child ever had asthma/wheezy bronchitis, allergic rhinitis/conjunctivitis (AR), eczema or urticaria/allergic congestion? Have there been any symptoms last year?' The same questions about disease ever were also asked for the parents. Questions were asked about both pet exposure (cat/dog, not specified) and the number of respiratory tract infections

during the first year of life. More than five colds during the first year of life was labelled 'frequent colds'.

A subsample was selected in 1992 from the main study population for a more detailed interview and skin prick tests (SPT). The children in the main study population were stratified into four groups: asthma ever, AR ever, eczema ever and healthy controls. Each stratum was given a weighting according to its relative size, i.e. 0.0746, 0.0694, 0.1935 and 0.6625, respectively. Equal numbers of cases (children with a history of asthma ever, AR ever or eczema ever) and controls were randomly selected (Fig. 1). In the Göteborg area, 203 children were interviewed. Eleven of them refused SPT. In Kiruna, 209 children were interviewed and four refused SPT.

The 412 children who underwent the validation interview and SPT in 1992 were contacted once again in the winter 1996 for a follow up study (Fig. 1). The children in the Göteborg area were now 12 years old and in Kiruna 12–13 years old. Two-hundred and one parents in the Göteborg area and 201 in Kiruna completed a questionnaire. The questions about disease and symptoms were the same as in 1991. Exposure to animals during the first year of life were further analysed in 1996 by detailed questions about type and duration of animal exposure or if anyone in the family had been horse back riding. A child was considered as 'pet exposed' only if the family had kept a cat or a dog inside their house. Families who had decided not to have furred pets during the child's first year of life were asked about the reasons for their decision. A statement that the presence of allergy in the family (among older siblings, parents or other relatives) was the reason for not having pets was assumed to indicate a high risk for allergy development. The children

Table 1. Reported asthma, allergic rhinitis, pet-keeping during first year of life and frequent colds (>5) during first year of life in relation to the number of siblings

	No. of siblings					
	0	1	2	≥ 3		
<i>n</i>	179	1146	770	359	<i>P</i> -value*	OR**
<i>Asthma</i>						
Cum. incidence	17 (9.6)	94 (8.2)	52 (6.8)	20 (5.6)	0.034	0.74 (0.60–0.83)
Prevalence	11 (6.2)	73 (6.4)	41 (5.3)	15 (4.2)	0.12	0.91 (0.49–1.46)
<i>Allergic rhinitis</i>						
Cum. incidence	24 (13.4)	115 (10.1)	86 (11.2)	17 (4.8)	0.007	0.77 (0.64–0.91)
Prevalence	17 (9.5)	95 (8.3)	73 (9.5)	13 (3.6)	0.035	0.80 (0.66–0.96)
<i>n</i>	179	1143	768	359		
<i>Pet keeping</i>						
First year of life	39 (21.8)	246 (21.5)	189 (24.6)	100 (27.9)	0.012	
<i>n</i>	157	1051	710	320		
<i>Freq. colds</i>						
First year of life	11 (7.0)	70 (6.7)	69 (9.7)	35 (10.9)	0.006	

Percentage values within brackets. * Chi-square for trends. ** Multiple logistic regression with pet keeping during first year of life, parental history of allergy and frequent colds during first year of life and siblings as independent variables. 95% CL within brackets. Questionnaire data at 7–9 years of age.

were invited for an interview and SPT during early spring and autumn, i.e. outside the main pollen season. In the Göteborg area, 200 children underwent interview and 188 SPT. In Kiruna the corresponding numbers were 196 and 183, respectively.

In 1992, a nurse and a research assistant carried out the SPTs according to the standards from the subcommittee on skin tests of the European Academy of Allergology and Clinical Immunology [9]. Forty-nine SPTs on the same seven persons yielded similar results between the two investigators, confirming the reproducibility. One of the nurses who carried out the SPTs in 1992 also performed all the tests in 1996 in the Göteborg area and almost all in Kiruna. A few SPTs in Kiruna were carried out by a trained nurse at the local paediatric department.

Allergen extracts from the same manufacturer were used in 1992 and 1996, i.e. birch, timothy grass, dog, cat, horse and *Dermatophagoides pteronyssinus* (Soluprick SQ 10 HEP, ALK, Horsholm, Denmark). In 1996 *Dermatophagoides farinae* was added to the panel. Soluprick in dilution 1:20 represented the airborne mould spore, *Cladosporium herbarum*. Histamine 10 mg/mL Soluprick was employed as positive control. A positive SPT corresponds to a weal with a diameter exceeding the negative control (NaCl 9 mg/mL) by at least 3 mm.

The statistical analyses were made using the statistical packages PC-SAS (SAS Institute, Cary NC, USA) and Epi-Info (WHO, Geneva, Switzerland). In the questionnaire study 1991, the estimated prevalences were compared using large sample normal approximation test. In the sub-sample (1992 and 1996) the estimates of prevalences were calculated as weighted proportions using the estimates in the individual strata and the weights from the original 1991 sample. The statistical significance of differences between groups was assessed with Chi-squared and multiple logistic regression models to adjust for differences in background variables. Chi-squared for trends was used for the trend analysis. The study was approved by Ethics Committee of Gothenburg University.

Results

Main questionnaire study in 1991, age 7–9 years

The cumulative incidence and the prevalence of AR, as well as the cumulative incidence of asthma decreased significantly with increasing number of siblings (Table 1). There was a similar, non-significant trend for the prevalence of asthma. The trends were independent of whether the siblings were older than the index child or not. A multiple

	Pet-keeping first year		Diff.
	No	Yes	
	% (SE)	% (SE)	P-value
<i>Cum. Incidence, 7–8 years</i>			
Asthma	7.9 (0.43)	7.5 (0.0)	0.31
Rhinitis	9.7 (0.74)	9.2 (1.08)	0.74
Eczema	27.3 (0.94)	24.9 (1.39)	0.15
<i>Cum. Incidence, 12–13 years</i>			
Asthma	13.3 (1.44)	8.6 (1.68)	0.03
Rhinitis	23.9 (2.24)	17.0 (3.08)	0.068
Eczema	39.0 (2.26)	34.8 (4.82)	0.43
<i>Prevalence, 7–8 years</i>			
Asthma	6.4 (0.64)	5.2 (1.08)	0.35
Rhinitis	9.5 (0.89)	5.9 (1.22)	0.016
Eczema	21.8 (1.12)	20.7 (1.67)	0.60
SPT total	20.7 (2.14)	20.0 (3.76)	0.87
SPT pollens	12.8 (1.69)	12.1 (2.99)	0.83
SPT dog	8.6 (1.40)	5.6 (1.83)	0.18
SPT cat	11.1 (1.67)	8.0 (2.30)	0.27
<i>Prevalence, 12–13 years</i>			
Asthma	10.0 (1.36)	3.3 (1.21)	<0.001
Rhinitis	18.1 (1.96)	15.2 (3.12)	0.42
Eczema	23.3 (2.11)	23.1 (4.41)	0.96
SPT total	32.5 (2.75)	29.9 (4.57)	0.60
SPT pollens	23.4 (2.44)	19.4 (4.09)	0.39
SPT dog	10.1 (1.62)	10.6 (3.22)	0.88
SPT cat	14.4 (1.93)	11.9 (3.06)	0.49
	Dog-keeping first year		
	No	Yes	
SPT dog, 7–8 years	8.3 (1.32)	6.4 (2.51)	0.50
SPT dog, 12–13 years	9.5 (1.52)	12.9 (4.06)	0.43
	Cat-keeping first year		
	No	Yes	
SPT cat, 7–8 years	10.6 (1.47)	5.5 (2.41)	0.067
SPT cat, 12–13 years	14.3 (1.75)	6.0 (2.96)	0.016

Table 2. The relation between pet-keeping during first year of life, allergy symptoms and skin prick tests at 7–8 and 12–13 years of age. Weighted proportions from stratified subsample.

logistic regression model with symptoms as dependent variables was used. The independent variables were frequent colds during the first year of life, pet exposure during the first year of life, number of siblings and parental history of allergy, confirmed the results from the bivariate analyses.

Twenty-three per cent of the children were exposed to pets (cat or dog) during their first year of life, 32% ($n = 264$) in Kiruna and 20% ($n = 321$) in the Göteborg area. Frequent colds during the first year of life was reported in 8.3% of the children. Both pet keeping and frequent colds during the first year of life increased with the number of siblings (Table 1). There was no association between early pet

exposure and frequent colds during first year of life (OR 0.95, 95% CL 0.66–1.36). In Kiruna, pet-exposed children with a parental history of allergy had a lower frequency of allergic rhinitis (OR 0.55, 95% CL 0.29–0.90), multiple logistic regression with pet exposure during first year of life, colds during first year of life and number of siblings as independent variables), whereas no difference was seen in children without a parental history. In Göteborg, pet exposure during the first year of life did not affect the cumulative incidence or the prevalence of asthma, allergic rhinitis or eczema at 7–9 years of age. There was a significant difference in reported allergy between the two areas. At

Table 3. The relation between pet-keeping during first year of life, allergy symptoms and skin prick tests at 7–8 and 12–13 years of age after excluding children who had retrained from pets because of allergy in the family. Weighted proportions from stratified sub sample

	Pet-keeping first year		Diff. <i>P</i> -value
	No % (SE)	Yes % (SE)	
Asthma Cum. Incidence, 12–13 years	11.2 (1.49)	8.6 (1.68)	0.25
Asthma prevalence, 12–13 years	8.5 (1.53)	3.3 (1.21)	0.008
Rhinitis prevalence, 7–8 years	8.8 (1.22)	5.9 (1.29)	0.08
Cat keeping first year and pos SPT to cat at 12–13 years	11.1 (1.85)	6.0 (2.96)	0.14

7–9 years of age, children in Kiruna with allergic rhinitis reported allergy to animals more often than children from Göteborg (OR 2.8, 95% CL 1.79–4.45), whereas there was no difference in reported allergy to pollens (OR 0.94, 95% CL 0.57–1.52).

Sub-sample study in 1991/1992 and 1996, age 7–8 and 12–13 years

All analyses were performed using detailed information about pet exposure obtained in 1996.

Keeping of pets (cat or dog) inside the house during the first year of life of the child was reported in 23.8% (97) of the children, and in this group the frequency of a parental history of allergy was 56%. The group of children who did not have a pet consisted of 305 children and the corresponding figure for parental history was 55%. When excluding the children in the unexposed group whose parents had decided against pet keeping because of allergy in the family, the number decreased from 305 to 214, and the frequency of parental history decreased from 55% to 47%.

Pet exposure during first year of life was associated with a lower prevalence of allergic rhinitis at 7–8 years of age, a lower cumulative incidence of asthma and a lower prevalence of asthma at 12–13 years of age. The difference in asthma prevalence at 12–13 years of age was mainly due to a high incidence in the unexposed group during the follow up period. A lower prevalence of cat sensitization (positive SPT to cat) at 12–13 years of age was seen in children exposed to cat in their home during their first year of life. Eczema as well as sensitization, i.e. to at least one of the antigens tested (SPT total), were not associated by pet exposure during the first year of life (Table 2).

To evaluate the influence of selection mechanisms behind early pet keeping as an explanation for the observed associations, the data was further analysed after excluding the children whose parents had decided against pet keeping during early childhood because of allergy in the family (Table 3). The analysis was based on 91 children less, and showed similar results but remained statistically significant only for the prevalence of asthma at 12–13 years of age.

The lower prevalence of asthma at 12–13 years of age in children exposed to pets in their home during their first year of life, was not explained by differences in parental history of allergy, the number of siblings, frequent infections during first year of life or by gender of the child (OR 0.34 95% CL 0.07–0.77 multiple logistic regression).

Discussion

The main findings in the present study were a lower prevalence of allergy in the respiratory tract in school children who were exposed to pets during the first year of life and a lower prevalence of these diseases in children with increasing number of siblings. The results of the questionnaire survey were supported by the lower prevalence of a positive SPT to cat in children exposed to cat during the first year of life.

Several previous studies have shown a negative correlation between the number of siblings and allergy [6,8,10], but the impact of early pet exposure on allergy development is less clear. Several studies have shown that sensitization to furred pets is common in children with asthma [11–15] but these studies did not address the question whether pet exposure is a risk factor for asthma development. Even in studies directly focusing on risk factors for allergy development, only limited conclusions can be drawn regarding early pet exposure as a risk factor for sensitization or allergy development since an increased risk was seen only in the subgroups of children who were already sensitized [16,17].

As in many other studies, especially among younger children [18–22], our questionnaire study from 1991 did not show any major association between pet exposure during early childhood and allergy at 7–9 years of age. However, there were some observations of interest. Children with many siblings were less often allergic, even if they were more often exposed to pets during their first year of life. In Kiruna, children with a parental history of allergy had as a lower cumulative incidence of allergic rhinitis. There are other studies indicating a negative association between early pet keeping and later allergy [4,23,24], but as

in our study from 1991, the results are often difficult to interpret because of possible selection mechanisms behind pet keeping. Therefore, the follow up study in 1996 focused on the children's first year of life. With the improved questions about exposure, we were able to identify those who had kept their pet inside the house, i.e. those with a high or direct exposure. With specific questions about selection mechanisms, we were also able to identify those who had decided against pet keeping because of allergy in the family. When these children were excluded from the analysis, the number of children in the unexposed group decreased with about 30%, resulting in a higher proportion of parental history in the pet-exposed group than in the unexposed group, which would tend to weaken our results.

In the main questionnaire study of children at 7–9 years of age, a lower cumulative incidence of allergic rhinitis was seen only in a subgroup of children, whereas there was a significant difference in the prevalence of allergic rhinitis in the sub-sample. This discrepancy between the results is probably explained by the more specific questions from the follow up used in the latter analysis. At 12–13 years of age, pet-exposed children were less often asthmatic and children exposed to cats were less often sensitized to cat. Despite the exclusion of the 91 children who had decided against pet keeping because of allergy in the family, the differences remained. The figures were still lower for the pet-exposed children even if most of them lost their statistical significance, partly because of the reduced number of children in the unexposed group. For the prevalence of asthma, however, the difference remained statistically significant, and was not explained by gender of the child, parental history, the number of siblings or by colds during first year of life.

The results indicate that exposure to pets during infancy might have a protective effect on later allergy development, as supported by less sensitization to cat in cat-exposed children. It was interesting to note that it was asthma that was influenced by early pet exposure, since childhood asthma is often associated with allergy to animals [11–15]. In another Swedish study, children were followed from birth to 12–15 years of age and those born during the tree pollen season were less likely to develop allergic rhinoconjunctivitis, IgE antibodies to pollen, or a positive screening test for IgE antibodies [25]. These findings indicate a specificity in the development of tolerance, and such a mechanism might explain why there was a negative association in the present study between early pet exposure and allergic rhinitis only in Kiruna at 7–9 years of age and not in Göteborg, or at 12–13 years of age. In Kiruna, 7–9-year-old children with allergic rhinitis more often reported allergy to animals than children in Göteborg did. At 12–13 years of age, allergic rhinitis was predominantly associated with allergy to pollens. It may be speculated that early pet

exposure induces tolerance to 'animal-associated diseases' and early pollen exposure to 'pollen-associated diseases'.

In conclusion, our study indicates that pet exposure during the first year of life is associated with less allergic rhinitis and asthma in school age. Decreasing number of children in the families and a changing pattern of animal exposure may have contributed to the current increase of allergic diseases in the western society, alternatively they are all consequences of other changes in life style.

Acknowledgements

The authors want to express their gratitude to the nurses at the paediatric clinic, Kiruna hospital. The study was supported by grants from the Vardal Foundation and the Swedish Association against Asthma and Allergy.

References

- 1 Åberg N, Hesselmar B, Åberg B, Eriksson B. Increase of asthma, allergic rhinitis and eczema in Swedish schoolchildren between 1979 and 1991. *Clin Exp Allergy* 1995; 25:815–9.
- 2 Strachan DP. Time trends in asthma and allergy: ten questions, fewer answers (editorial). *Clin Exp Allergy* 1995; 25: 791–4.
- 3 Bråbäck L, Breborowicz A, Dreborg S, Knutsson A, Pieklik H, Björkstén B. Atopic sensitization and respiratory symptoms among Polish and Swedish schoolchildren. *Clin Exp Allergy* 1994; 24:826–35.
- 4 Bråbäck L, Breborowicz A, Julge K et al. Risk factors for respiratory symptoms and atopic sensitisation in the Baltic area. *Arch Dis Child* 1995; 72:487–93.
- 5 Mutius E, Martinez F, Fritsch C, Nicolai T, Roell G, Thiemann HH. Prevalence of asthma and atopy in two areas of West and East Germany. *Am J Respir Crit Care Med* 1994; 149:358–64.
- 6 Strachan DP. Hay fever, hygiene, and household size. *BMJ* 1989; 299:1259–60.
- 7 Rona R, Duran-Tauleria E, Chinn S. Family size, atopic disorders in parents, asthma in children, and ethnicity. *J All Clin Immun* 1997; 99:454–60.
- 8 von Mutius E, Martinez FD, Fritsch C, Nicolai T, Reitmeir P, Thiemann HH. Skin test reactivity and number of siblings. *BMJ* 1994; 308:692–5.
- 9 Dreborg S. Skin tests used in type I allergy testing. Position paper. *Allergy* 1989; Suppl. 10:44.
- 10 Matricardi PM, Rosmini F, Ferrigno L et al. Cross sectional retrospective study of prevalence of atopy among Italian military students with antibodies against hepatitis A virus. *BMJ* 1997; 314:999–1003.
- 11 Croner S, Kjellman N-IM. Natural history of bronchial asthma in childhood. A prospective study from birth up to 12–14 years of age. *Allergy* 1992; 47:150–7.
- 12 Ingram JM, Sporik R, Rose G, Honsinger R, Chapman MD, Platts-Mills TA. 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; 96:449–56.

- 13 Kjellman B, Pettersson R. The problem of furred pets in childhood atopic disease. Failure of an information program. *Allergy* 1983; 38:65–73.
- 14 Platts-Mills TA, Sporik R, Ingram JM, Honsinger R. Dog and cat allergens and asthma among school children in Los Alamos, New Mexico, USA. altitude 7,200 feet. *Int Arch Allergy Immunol* 1995; 107:301–3.
- 15 Muljono IS, Voorhorst R. Atopy to dander from domestic animals. *Allerg Immunol Leipz* 1978; 24:50–60.
- 16 Suoniemi I, Björkstén F, Haahtela T. Dependence of immediate hypersensitivity in the adolescent period on factors encountered in infancy. *Allergy* 1981; 36:263–8.
- 17 Lindfors A, Wickman M, Hedlin G, Pershagen G, Rietz H, Nordvall SL. Indoor environmental risk factors in young asthmatics: a case-control study. *Arch Dis Child* 1995; 73:408–12.
- 18 Arshad SH. Pets and atopic disorders in infancy. *Br J Clin Pract* 1991; 45:88–9.
- 19 Arshad SH, Stevens M, Hide DW. The effect of genetic and environmental factors on the prevalence of allergic disorders at the age of two years. *Clin Exp Allergy* 1993; 23:504–11.
- 20 Austin JB, Russell G. Wheeze, cough, atopy, and indoor environment in the Scottish Highlands. *Arch Dis Child* 1997; 76:22–6.
- 21 Horwood LJ, Fergusson DM, Shannon FT. Social and familial factors in the development of early childhood asthma. *Pediatrics* 1985; 75:859–68.
- 22 Merrett TG, Burr ML, Butland BK, Merrett J, Miskelly FG, Vaughan-Williams E. Infant feeding and allergy: 12-month prospective study of 500 babies born into allergic families. *Ann Allergy* 1988; 61:13–20.
- 23 Sigurs N, Bjarnason R, Sigurbergsson F, Kjellman B, Björkstén B. Asthma and immunoglobulin E antibodies after respiratory syncytial virus bronchiolitis: a prospective cohort study with matched controls. *Pediatrics* 1995; 95:500–5.
- 24 Burr ML, Merret TG, Dunstan FDJ, Maguire MJ. The development of allergy in high-risk children. *Clin Exp Allergy* 1997; 27:1247–53.
- 25 Nilsson L, Björkstén B, Hattevig G, Kjellman B, Sigurs N, Kjellman N-IM. Season of birth as predictor of atopic manifestations. *Arch Dis Child* 1997; 76:341–4.