

The prevalence of and risk factors for atopy in early childhood: A whole population birth cohort study

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Objectives: A birth cohort was followed-up to age 4 years to record the development of allergic disorders and to study the influence of genetic and environmental factors.

Methods: Information on family history and environmental factors was obtained at birth, and serum cord IgE was measured. At age 4 years, 1218 children were reviewed.

Results: By age 4 years, 27% of the children had symptoms of allergic disease. Period prevalence of asthma increased from 8.7% in infancy to 14.9% at 4 years. Family history of atopy was the single most important risk factor for atopy in children. Sibling atopy was a stronger predictor of clinical disease than maternal or paternal atopy, whereas paternal atopy, male sex, and high cord IgE were significant for the development of allergen sensitization. Children of asthmatic mothers were three times more likely to have asthma (odds ratio [OR]: 3.0, 95% confidence interval [CI]: 1.6-5.8) and rhinitis (OR: 2.9, CI: 1.1-7.4). Formula feeding before 3 months of age predisposed to asthma at age 4 years (OR: 1.8, CI: 1.2-2.6). The effect of maternal smoking on childhood wheeze seen at 1 and 2 years was lost by age 4, except for a subgroup with negative skin test responses (nonatopic asthma). Less than half (46%) of the infantile wheezers were still wheezing at 4 years of age.

Conclusion: Family history of atopy remains the most important risk factor for atopy in children, but other markers can be identified with a potential for intervention at an early age. (*J Allergy Clin Immunol* 1998;101:587-93.)

Key words: Atopy, family history, cord IgE, asthma, eczema, allergic rhinitis, birth cohort, skin prick test

Over the past 25 years, the prevalence of atopic disorders has shown an alarming increase.^{1,2} A number of genetic and environmental factors have been implicated. Family history of atopy predisposes to allergic disorders,³⁻⁵ childhood asthma could affect more boys than girls,^{4,6} and studies suggest that high cord serum IgE predicts the development of atopy.^{7,8} Although maternal influence is generally accepted as greater than paternal influence,^{4,9} the relative contributions of he-

Abbreviation used

S-E: Socioeconomic

redity and maternal environment are not known. A search for reliable genetic markers of atopy has so far been inconclusive.¹⁰ Studies of environmental factors remain critical because they help in the determination of effective intervention measures. The influence of environmental factors such as month of birth,^{11,12} method of feeding,^{4,8,13,14} passive smoking,^{15,16} and exposure to household pets^{4,17} has been studied in some detail. However, the complex interplay of these and other factors requires further research.

In 1989, a whole population birth cohort was recruited on the Isle of Wight to assess the impact of heredity and environment on the development of allergic disorders and allergen sensitization. A review of these children at age 4 years describes the prevalence of and risk factors for atopy in early childhood, and provides information on the predictive value of infantile eczema and allergy to food (e.g. egg and cow's milk) during the first 2 years of life. It also helps clarify the outcome of infantile wheeze.

METHODS

Study population

Fifteen hundred thirty six children born consecutively on the Isle of Wight between January 1989 and February 1990 were included prenatally in a prospective cohort study. After excluding perinatal deaths, adoptions, and refusals, 1456 babies were available for follow-up. The findings at age 1 and 2 years have been reported.^{4,18,19} At birth, cord serum total IgE was measured in a majority by using an enzyme immunoassay (EIA ULTRA; Pharmacia Diagnostics AB, Uppsala, Sweden).⁴ At age 4 years, 1218 children were reviewed. Cord serum IgE levels were available in 1064 of them.

Details of environmental factors (e.g., parental smoking, exposure to pets, housing conditions, and intercurrent illness) were updated. Seasons of birth were defined as winter (December to February), spring (March to May), summer (June to August), and autumn (September to November). Socioeconomic (S-E) groups were assigned on the basis of the criteria used previously.⁴ Data on social class was available for 723 children from the recruitment records.

The study was approved by the local research ethics committee and fully informed written parental consent was taken.

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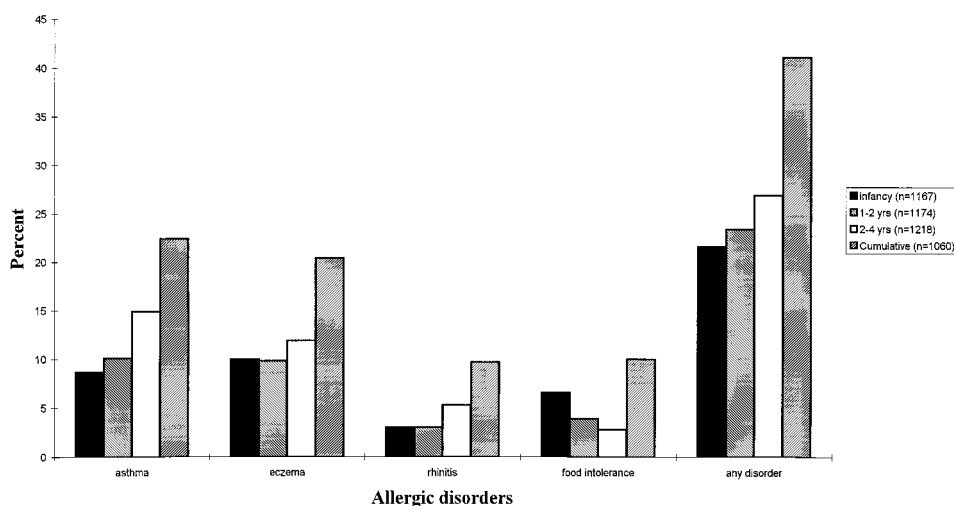


FIG. 1. Period and cumulative prevalence of atopic disorders in early childhood.

Diagnostic criteria for atopic disease

To maintain consistency, the diagnostic criteria were the same as those used in previous reviews.⁴ Briefly, a diagnosis of asthma required three or more separate episodes of wheeze, each lasting 3 days or more; eczema constituted recurrent, scaly, pruritic, erythematous rash in a typical distribution lasting more than 6 weeks; and rhinitis required at least two of three nasal symptoms of discharge, blockage, and recurrent sneezing accompanied by eye symptoms. For asthma, due consideration was given to the presence of typical diurnal variation and to the response to bronchodilator medication. A history of skin rash or respiratory or abdominal symptoms within 4 hours of ingestion of a particular food on two occasions was taken as food allergy. Food challenges were not performed, but confirmation of sensitization to the offending food was sought in every case.

Skin prick tests

Nine hundred eighty-one children underwent a skin prick test with a standard battery of aeroallergens (house dust mite [*D. pteronyssinus*], grass pollen mix, cat and dog epithelia, *Alternaria alternata*, or *Cladosporium herbarum*) and food allergens (milk, egg, soya, cod, wheat, and peanut), and, as indicated, other allergens were added. Histamine (0.1%) in phosphate-buffered saline and physiologic saline were used as positive and negative controls, respectively. All extracts were from Biodiagnostics (Germany). The test results were read after 15 minutes, and mean wheal diameter at least 3 mm greater than that with the negative control was taken as a positive result. Results of peanut and tree nut sensitization have been previously reported.²⁰

Statistical analysis

Data was entered into a computer file (SPSS PC⁺ V4, Chicago, Ill.). Chi-square analysis with Yate's correction was used to analyze the differences between proportions. For contingency tables with less than 10 cases in any cell, the Fisher's Exact test was used. Group differences in continuous variables were studied by the nonparametric Mann-Whitney U test. Multivariate analysis was performed by stepwise logistic regression. Adjusted odds ratios (ORs) and 95% confidence intervals (CIs) were calculated for an independent effect of risk factors on the development of atopy. The controls for logistic

regression analysis were female sex, birth weight less than 2.5 kg, winter birth, cord serum IgE less than 0.5 ku/L, infant feeding introduction to formula after age 3 months, higher S-E group (social classes 1 to 3), no family history of atopic disease among first degree relatives, no maternal smoking, and no cats or dogs in the house. Any other risk factor was studied by substituting it in the model for the relevant factor listed above. For example, the effect of maternal atopy was studied by replacing family history of atopy with maternal history.

RESULTS

Twelve hundred eighteen children (83.6% of the original cohort) were seen after their fourth birthday, and 981 (80.5%) underwent skin prick tests. There was no selective loss from follow-up because the prevalence of atopy in 169 children seen at age 2 but not at 4 years was similar to the prevalence for the whole cohort at 2 years (23% vs 23.4%). Fig. 1 gives the period prevalence of atopic disorders at 1, 2, and 4 years and the cumulative prevalence for those assessed at all three follow-up periods. Asthma increased markedly after infancy, whereas food allergy declined after the first birthday. At age 4 years, 327 (26.9%) children had one or more atopic disorders.

Risk factors for atopy

Family history. There was a history of atopic illness among first degree relatives of 713 (58.5%) children (Table I). Family history of atopy was the single most important risk factor for atopy in the children. Asthma was linked to family history of atopy, maternal atopy, and sibling atopy, with maternal asthma having the greatest effect (Table I). A dual family history nearly doubled the risk for asthma and rhinitis (Table I). Paternal or sibling history increased the risk of rhinitis, whereas family or paternal atopy predisposed to skin test reactivity. When atopic disorders were grouped together, family history of atopy, sibling atopy, and maternal asthma were significant for any atopic disorder at 4

TABLE I. The effect of genetic factors on atopic disease and skin prick test reactivity at age 4 years

	Asthma	Eczema	Rhinitis	Food allergy	Any	+SPT
Sex						
Male (<i>n</i> = 624)	15.9	13.0	6.6	3.7	29.0	22.5*
Female (<i>n</i> = 594)	13.8	10.8	4.0	1.9	24.6	16.5
Family history						
Negative (<i>n</i> = 505)	11.2	10.8	3.8	2.0	23.0	15.1
Positive (<i>n</i> = 713)	17.4†	12.6	6.5	3.4	29.5*	22.7†
Dual (<i>n</i> = 112)	21.1†	12.7	8.8*	3.5	31.6*	26.7†
Maternal atopy						
Yes (<i>n</i> = 411)	17.8*	12.4	6.6	2.7	28.7	22.3
No (<i>n</i> = 807)	13.3	11.6	4.7	2.9	25.8	18.2
Paternal atopy						
Yes (<i>n</i> = 311)	16.4	13.5	7.7*	3.9	29.3	28.7‡
No (<i>n</i> = 907)	14.2	11.3	4.5	2.4	25.9	16.4
Sibling atopy						
Yes (<i>n</i> = 250)	21.2†	12.0	8.4*	4.4	33.6†	20.3
No (<i>n</i> = 428)	12.9	10.3	4.2	2.8	23.6	18.5
Maternal asthma						
Yes (<i>n</i> = 127)	25.2‡	13.4	8.7	3.1	37.0†	26.0
No (<i>n</i> = 1091)	13.7	11.7	4.9	2.8	25.6	18.9
Cord IgE						
>0.5 ku/L (<i>n</i> = 139)	13.7	20.1†	2.9	5.0	30.2	23.2‡
0.5 ku/L (<i>n</i> = 925)	15.2	11.9	5.9	2.1	26.8	10.6

All figures are percentages.

Family history, Atopic disease in first degree relatives; *Dual*, atopic disease in both parents or one parent and at least one sibling; *Any*, any atopic disorder; *+SPT*, positive skin prick test response.

**p* < 0.05.

†*p* < 0.01.

‡*p* < 0.001.

years. Surprisingly, family history was not a significant risk factor for eczema at 4 years. Infantile eczema was more often associated with positive family history of atopy as compared with eczema after the first birthday (94 of 122 [77%] vs 52 of 89 [59%], *p* < 0.05). Logistic regression (Table II) showed that a positive family history doubled the risk of asthma (OR: 2.0, CI: 1.2-3.4, *p* < 0.01), quadrupled the risk of rhinitis (OR: 4.3, CI: 1.7-10.9, *p* < 0.01), and was significant for any atopic disorder. Maternal atopy significantly increased atopic disease in the children (Table II); those born to asthmatic mothers were three times more likely to develop asthma (OR: 3.0, CI: 1.6-5.8, *p* < 0.01) or rhinitis (OR: 2.9, CI: 1.1-7.4, *p* < 0.05) in early childhood. The contributions of sibling atopy mirrored those of maternal atopy, whereas paternal atopy was an independent risk factor for skin test reactivity (OR: 1.8, CI: 1.1-3.0, *p* < 0.05) (Table II).

Sex. Male sex was associated with increased skin test reactivity (OR: 1.7, CI: 1.1-2.8, *p* < 0.05) (Table II), and there was a trend for atopic disorders to affect more boys than girls (Table I).

Cord serum IgE. High serum IgE level (>0.5 ku/L) at birth was a risk factor for eczema and skin test reactivity (Table I). The risk of allergen sensitization was three-fold in children with both paternal atopy and high cord

IgE (43.8% vs 13.9%; *p* < 0.001). Although high cord IgE at birth increased the risk of allergen sensitization (OR: 2.3, CI: 1.2-4.4, *p* < 0.01) (Table II), it was a poor predictor for the development of atopic disease.

Passive smoking. By age 4 years, 307 (25.2%) of all children in the study had been exposed to maternal smoking since birth. The percentage of asthmatic children exposed to maternal tobacco smoke was similar (26.5%). A strong relation of asthma to maternal smoking was seen at age 1 and 2 years,^{4, 18} but this was lost by age 4 years (Table III). Children born to mothers who smoked during pregnancy had lower mean birth weight (3.29 ± 0.51 vs 3.5 ± 0.51 kg [geometric mean $\pm$ standard deviation], *p* < 0.001). By age 4 years, however, the mean height and weight of these children was similar to the mean height and weight of those born to non-smoking mothers (103.9 vs 103.5 cm and 17.5 vs 17.6 kg, respectively). Smoking mothers were more often from the lower S-E group (31.8% vs 16%, *p* < 0.001). They breastfed their babies for a shorter duration (8.5 ± 11.4 vs 16.6 ± 15.2 weeks, *p* < 0.001) and introduced formula milk at an earlier age (6.6 ± 9.1 vs 11.8 ± 11.5 weeks, *p* < 0.001). Parental smoking was equally prevalent among atopic and nonatopic families (36.7% vs 40%, not significant), and it neither increased asthma nor allergen sensitization among the children. There was, however, a

TABLE II. Risk factors for allergen sensitization and atopic disorders at age 4 years (logistic regression analysis)

	Skin prick test reactivity	Asthma	Rhinitis	Any
Male sex	1.7 (1.1-2.8)*	—	—	—
Cord IgE >0.5 ku/L	2.4 (1.5-3.7)†	—	—	—
Family history	—	2.0 (1.2-3.4)†	4.3 (1.7-10.9)†	1.6 (1.0-2.4)*
Maternal atopy	—	1.9 (1.1-3.1)*	2.9 (1.3-6.1)†	—
Maternal asthma	—	3.0 (1.6-5.8)†	2.9 (1.1-7.4)*	2.6 (1.5-4.7)†
Paternal atopy	1.8 (1.1-3.0)*	—	—	—
Sibling atopy	—	2.2 (1.2-4.0)*	3.6 (1.4-9.3)†	2.2 (1.2-3.7)†
Formula feeding‡	—	1.8 (1.2-2.6)†	—	—

Data are adjusted odds ratios (95% confidence limits).

Other factors evaluated and found not significant were low birth weight, season of birth, parental smoking, exposure to pets, and low S-E group.

Any, Any atopic disorder.

* $p < 0.05$.

† $p < 0.01$.

‡Introduction to formula within 3 months of life (analyzed after excluding S-E group from the model).

link between a subgroup of nonatopic asthmatic subjects (those with a negative skin prick test response, $n = 90$) and maternal smoking (Table IV).

S-E group. There was more asthma among children from the lower S-E group, whereas eczema was more common in those from higher S-E group families (Table III). The lower S-E group had a significant independent association with nonatopic asthma (OR: 2.3, CI: 1.1-4.8, $p < 0.05$).

Method of feeding. Children introduced to formula before 3 months of age ($n = 667$, 54.8%) had significantly more asthma at age 4 years (Table III). Early introduction to formula increased the risk of any atopic disease. In the logistic regression model formula, feeding within 3 months was not significant for atopic disease. However, analysis after excluding S-E group from the model (which allowed the inclusion of 1064 cases) revealed that, apart from family history of atopy, introduction to formula within the first 3 months increased the risk of asthma (OR: 1.8, CI: 1.2-2.6, $p < 0.01$) (Table II).

Pets. There were cats, dogs, or both in the homes of 649 (53.3%) children. Other pets were less frequent. The presence of cats or dogs was not associated with atopic disorders or allergen sensitization (Table III). Furthermore, exposure to cats or dogs did not significantly increase skin test reactivity to these animals. There was no difference in cat and dog ownership among those with or without a family history of atopy (37% vs 37% for cat ownership and 28.5% vs 29.6% for dog ownership). Forty-seven percent of children were exposed to dogs, and 40% were exposed to cats elsewhere.

Other factors. Although no single season of birth was significant for the development of allergen sensitization or atopic disease, more children born during autumn and winter combined had eczema as compared with those born in spring and summer (90 of 644 [14%] vs 55 of 574 [9.6%], $p < 0.05$). The effect of position in sibship was studied by comparing allergic manifestations in the

firstborn ($n = 510$) with subsequent positions. There was more eczema among the firstborn as compared with other children (14.3% vs 10.2%, $p < 0.05$). Position in sibship, however, had no bearing on the development of asthma or rhinitis or on allergen sensitization. There was a weak inverse relation of the number of siblings with atopic illness (31.2% [no siblings] through 12.8% [four siblings], not significant) and skin test reactivity (20.9% [no siblings] through 12.9% [four siblings], not significant). Aeroallergen sensitivity ($n = 190$) was more common in boys than girls (22.5% vs 16.5%, $p < 0.05$), with increased skin test reactivity to house dust mite allergen (15.1% vs 8.7%, $p < 0.002$), grass pollen (10.3% vs 5.4%, $p < 0.005$), and dog epithelium (3.6% vs 1.2%, $p < 0.05$). Twenty-four of 61 children with positive skin prick test responses to *Alternaria alternata*, *Cladosporium herbarum*, or both were asymptomatic (latent atopy).²¹ Asymptomatic sensitization to house dust mite allergen (33 of 117, 28.2%) was also observed. Skin test reactivity to aeroallergens was not associated with season of birth, number of children in the house, reported damp, exposure to pets, or parental smoking.

Predictive value of eczema and wheeze during infancy. Eczema affected 122 children during infancy. In 68 (55.1%) children it cleared before their fourth birthday. Thirty-nine (32%) children with infantile eczema developed symptoms of asthma, and 19 (15.6%) had symptoms of rhinitis by age 4 years (both $p < 0.001$). Infantile eczema was also a predictor for skin test positivity (42.2%) and aeroallergen sensitization (46.6%) (both $p < 0.001$). Of all the children seen at 4 years, 105 (8.6%) had recurrent wheeze during infancy. In some the infantile wheeze improved (infantile wheeze, $n = 57$), whereas in others it persisted (persistent wheeze, $n = 48$). Another group had recurrent wheeze after infancy ($n = 133$). Table V compares the aforementioned subgroups with a control group who never wheezed. Family history of atopy, maternal smoking after birth, introduction to a formula milk within 3

TABLE III. Effect of environmental factors on the prevalence of atopic disorders at age 4 years

	Asthma	Eczema	Rhinitis	Food allergy	Any
Maternal smoking					
Yes (<i>n</i> = 307)	15.6	8.1	4.9	2.3	25.7
No (<i>n</i> = 911)	14.6	13.2*	5.5	3.0	27.2
Method of feeding					
Formula (<i>n</i> = 667)	17.1†	13.2	6.1	2.4	30.0†
Breast (<i>n</i> = 419)	10.3	10.7	4.5	3.4	21.5
S-E group					
Lower (<i>n</i> = 374)	18.7†	8.0	5.9	2.7	27.8
Higher (<i>n</i> = 349)	11.2	13.5*	5.7	2.6	23.8
Pets					
Yes (<i>n</i> = 649)	14.0	10.6	5.1	2.8	25.4
No (<i>n</i> = 569)	15.8	13.4	5.6	2.8	28.5

All figures are percentages.

Method of feeding: *formula*, introduction to formula within 3 months of life; *breast*, formula after age 3 months.

S-E group: *lower*, social class 4 or 5; *higher*, social class 1, 2, or 3.

Pets, presence of cat, dog, or both in the house.

**p* < 0.05.

†*p* < 0.01.

months, and lower S-E group were associated with persistent wheeze, and male sex, maternal smoking during pregnancy, and low birth weight (<2.5 kg) were significant for infantile wheeze. Children with persistent wheeze were four times more likely than those who "grew out of it" to react to aeroallergens by age 4 years (28.9% vs 6.7%, *p* < 0.02). For wheeze developing after infancy, aeroallergen sensitization was the most significant association (Table V). Wheeze during infancy, whether it improved or persisted, was related to maternal smoking during (40% vs 18.5%, *p* < 0.001) and after (34.9% vs 24.1%, *p* < 0.02) pregnancy and to low birth weight (<2.5 kg) (7.6% vs 3.1%, *p* < 0.05). A positive skin prick test response at age 1 year did not add to the predictive value of infantile wheeze because the wheeze became persistent in only 36.7% (11 of 30) of such cases. Overall, infantile wheeze had a poor predictive value for the development of atopic disease and allergen sensitization.

Milk and egg allergy. Allergy to cow's milk protein decreased from 4.4% in infancy to 0.4% by 4 years. Likewise, allergy to egg declined from 1.6% to 0.6%. Overall, 10% of children with any atopic illness at 4 years had had milk allergy, and 5.6% had had egg allergy before their second birthday (both *p* < 0.001). At 4 years of age, aeroallergen sensitization was more common in those who had allergy to milk (31.4% vs 18.6%, *p* < 0.05) or egg (59.3% vs 18.2%, *p* < 0.0001) before age 2 years. Egg allergy was an independent risk factor for sensitization to aeroallergens (OR: 4.6, CI: 1.2-17.8, *p* < 0.05). It was also associated with the development of peanut sensitization.²⁰ Logistic regression, however, failed to show an independent association between milk and egg allergy in early life and the development of atopic disease by age 4 years.

TABLE IV. Differences between atopic and nonatopic asthma at age 4 years

	Atopic asthma (<i>n</i> = 71)	Nonatopic asthma (<i>n</i> = 90)
Low S-E group	61.7	68.5
Low birth weight (<2.5 kg)	0	8.9†
High cord IgE (0.5 ku/L)	18.8	7.5
Family history of atopy	74.6	66.3
Maternal smoking		
In pregnancy	15.5	28.9
After birth	19.7	35.9*
Both	22.5	41.1
Formula feeding	68.8	3.1

All figures are percentages.

Atopic asthma, Asthma with a positive skin prick test response; *Non-atopic asthma*, asthma with a negative skin prick test response; *Low S-E group*, social classes 4 and 5; *Formula feeding*, introduction to formula milk before age 3 months.

**p* < 0.05.

†*p* < 0.02.

DISCUSSION

Studies recording the evolution of disease from birth over a prolonged period are often marred by a gradual loss of subjects.^{5, 7, 22} Over 80% of the Isle of Wight cohort was reviewed at the age of 4 years, and a majority underwent skin prick tests. Ambiguities over the definition of asthma, especially during infancy and early childhood, make the estimates of prevalence unreliable and render comparisons between studies difficult. In this study the cumulative prevalence of asthma by the age of 4 years (22.4%) is less than that of wheeze up to age 6 years (49.5%) as reported by Martinez et al.²² This is because in this cohort only those with recurrent wheeze were entertained. Episodic wheeze is common during early childhood, but recurrent or persistent wheeze is less frequent. One survey reported a cumulative prevalence of wheeze in 15.6% of preschool children.²³ Further follow-up of this cohort should elucidate the outcome of early childhood wheezing, particularly in relation to allergen sensitization.

Maternal smoking may increase early-life respiratory infections.²⁴ It has also been reported to increase allergen sensitization and asthma, especially in boys.²⁵ The effect of maternal smoking is, however, confounded by factors such as low birth weight, shorter breast feeding duration, and low social class.^{4, 18, 26} In this cohort maternal smoking was significantly associated with asthmatic wheeze and cough at age 1 and 2 years^{4, 18} but not at 4 years. Nevertheless, the effect of maternal smoking was discernible even at 4 years among the so-called nonatopic asthmatic subjects. Infantile wheeze is associated with diminished airway function and maternal smoking²² and may not necessarily lead to atopy in childhood. Thus it is possible that, just like the majority of infantile wheezers, the nonatopic asthmatic subjects may also "grow out of" their wheeze. Interestingly, infants whose wheeze persisted were more likely to

TABLE V. Risk factors for infantile wheeze, persistent wheeze, and new wheeze after infancy ($n = 1058$)

	No wheeze ($n = 820$)	Infantile wheeze ($n = 57$)	Persistent wheeze ($n = 48$)	New wheeze after infancy ($n = 133$)
Family history	57.6	51.7	79.2†	65.2
Male sex	49.0	67.2*	60.4	52.6
Maternal smoking				
In pregnancy	17.3	43.9	35.4†	20.3
After birth	23.4	32.8	37.5†	22.6
Aeroallergen sensitization	15.6	6.7	28.9*	50.0†
Birth weight <2.5 kg	2.5	8.8*	6.3	4.6
Formula within 3 months	58.4	69.6	84.4‡	67.9
Cord IgE 0.5 ku/L	13.0	14.6	7.3	13.4
Lower S-E group	48.2	65.7	68.8*	62.3*

All figures are percentages.

No wheeze group taken as control.

Infantile wheeze, recurrent wheeze during infancy; *Persistent wheeze*, wheeze starting in infancy and becoming persistent.

* $p < 0.05$.

† $p < 0.01$.

‡ $p < 0.001$.

develop atopy as evidenced by skin test reactivity at 4 years, and more often they had a family history of atopy. Similar findings have been reported in a group of children followed-up to the age of 6 years.²² The results of the Isle of Wight cohort suggest that maternal smoking could account for as much as half of the cases of infantile wheeze. However, viral respiratory infections and the onset of atopic asthma must always be considered.

In this cohort maternal smoking during pregnancy predisposed to a low birth weight. By age 4 years, however, the height and weight of those born with a low birth weight (<2.5 kg) were similar to the height and weight of other children, suggesting catch-up growth. This implies that maternal smoking-related early childhood wheeze could in part be due to small airway caliber linked to low birth weight.²⁷

Family history of atopy is a reliable risk factor. The effect of maternal atopy on the development of allergic disease in childhood is well described. In one study 48% of children born to atopic mothers and 33% of children with atopic fathers were affected.²⁸ In this study maternal atopy had a marked influence on the development of atopic disease, although it is possible that the maternal effect may have been exaggerated because in some cases family history was obtained from mothers alone. There are other studies that do not show a clear difference between the effect of maternal and paternal atopy.²⁹

The independent influence of maternal asthma on asthmatic wheeze in early childhood (OR: 3.0) is similar to that quoted previously.³⁰ Sigrid et al.²⁹ reported that the effect of one-sibling atopy was similar to that of one-parent atopy on the development of asthma, allergic rhinitis, and eczema. Apart from carrying similar genetic determinants, siblings share the same environment from an early age. Studies on sibship, however, suggest a diminished risk of atopy in younger siblings, presumably caused by a protective effect of early-life viral infec-

tions.^{31, 32} Interestingly, there was a lack of association between family history of atopy and eczema after infancy. A possible explanation is that eczema after infancy is less often atopic, as suggested by less frequent skin sensitization in these children (22 of 72) compared with those with infantile eczema (46 of 109). This led to an apparent lack of effect of heredity on eczema among the 4-year olds.

The Isle of Wight is a rural community, and household pets are common. No self-selection bias in pet ownership towards nonatopic families was noted. Furthermore, exposure of the children to pets elsewhere may have confounded the results.

As reported by others, male sex increased the risk of allergen sensitization. Ronchetti et al.³³ suggested that, at least in male children, exposure to tobacco smoke may augment allergen sensitization. Such an effect was not observed in this cohort. A study following a small group of children from atopic families showed that allergen sensitization increases throughout the first decade of life.³⁴ Follow-up of this large cohort may further elucidate this observation.

There are as yet no reliable objective tests to predict atopy. Studies have looked at the value of total cord IgE measured at birth.^{7, 8} Unfortunately, the sensitivity and specificity of raised cord IgE as a predictor of atopy during early childhood remain poor.³⁵ Although high cord IgE (>0.5 ku/L) emerged as a risk factor for allergen sensitization at age 4 years, it remained a poor predictor for the development of atopic disease. The link between cord serum IgE and the development of allergen sensitization suggests a common genetic predisposition. Because a large minority showed nonclinical (latent) allergen sensitization by age 4 years, the genetic risks for the development of atopic disease may not necessarily be the same as those for skin test reactivity.

Studies relating allergen sensitization to season of birth suggest that early exposure to allergen may in-

crease the risk of sensitization.^{11, 12} This study shows no clear effect of season of birth on the development of respiratory allergic disease or on sensitization to seasonal allergens. This may be due to a smaller number of subjects in this cohort compared with some studies. More eczema among children born during autumn and winter combined cannot be explained because there was no concomitant increase in sensitization to house dust mite, *Alternaria*, or *Cladosporium* allergens.

Recurrent wheeze is more prevalent among children of parents from lower S-E classes.^{4, 18, 26} The Registrar General's classification used in this study does not take into account assets and the distribution of wealth. Nevertheless, it remains an easy and reliable measure for determination of social class. On the basis of such a classification, an association between lower social classes and higher asthma morbidity has been shown.³⁶ Differences in parental smoking, infant feeding, and a number of other social factors across the social strata make the assessment of various risk factors for the development of disease very difficult indeed. Moreover, excluding those where information on social class was not available from the regression model reduced its power of detecting a difference. Only nonatopic asthma was predictably associated with lower S-E group.

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