

Risk factors for atopic dermatitis in New Zealand children at 3·5 years of age

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Summary

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Background The prevalence of atopic dermatitis (AD) is increasing in Western societies. The hygiene hypothesis proposes that this is due to reduced exposure to environmental allergens and infections during early life.

Objectives To examine factors associated with a diagnosis of AD at 3·5 years of age, especially those factors implicated by the hygiene hypothesis.

Methods The Auckland Birthweight Collaborative study is a case-control study of risk factors for small for gestational age babies. Cases were born at term with birthweight ≤ 10 th centile; controls were appropriate for gestational age, with birthweight > 10 th centile. The infants were assessed at birth, 1 year and 3·5 years of age. Data were collected by parental interview and examination of the child. AD was defined as the presence of an itchy rash in the past 12 months with three or more of the following: history of flexural involvement; history of generally dry skin; history of atopic disease in parents or siblings; and visible flexural dermatitis as per photographic protocol. Statistical analyses took into account the disproportionate sampling of the study population.

Results Analysis was restricted to European subjects. Eight hundred and seventy-one children were enrolled at birth, 744 (85·4%) participated at 1 year, and 550 (63·2%) at 3·5 years. AD was diagnosed in 87 (15·8%) children seen at 3·5 years. The prevalence of AD did not differ by birthweight. AD at 3·5 years was associated with raised serum IgE > 200 kU L⁻¹, and wheezing, asthma, rash or eczema at 1 year. In multivariate analysis, adjusted for parental atopy and breastfeeding, AD at 3·5 years was associated with atopic disease in the parents: maternal atopy only, adjusted odds ratio (OR) 3·83, 95% confidence interval (CI) 1·20–12·23; paternal atopy only, adjusted OR 3·59, 95% CI 1·09–11·75; both parents atopic, adjusted OR 6·12, 95% CI 2·02–18·50. There was a higher risk of AD with longer duration of breastfeeding: < 6 months, adjusted OR 6·13, 95% CI 1·45–25·86; ≥ 6 months, adjusted OR 9·70, 95% CI 2·47–38·15 compared with never breastfed. These findings remained significant after adjusting for environmental factors and a personal history of atopy. AD at 3·5 years was associated with owning a cat at 3·5 years (adjusted OR 0·45, 95% CI 0·21–0·97) but not with owning a dog at 3·5 years, pets at 1 year, nor with older siblings. Furthermore, AD at 3·5 years was not associated with gender, socioeconomic status, maternal smoking, parity, damp, mould, immunizations, body mass index or antibiotic use in first year of life.

Conclusions A personal and a parental history of atopic disease are risk factors for AD at 3·5 years. Duration of breastfeeding was associated with an increased risk of AD. No association was found with those factors implicated by the hygiene hypothesis. This study suggests that breastfeeding should not be recommended for the prevention of AD.

Atopic dermatitis (AD) is a chronic inflammatory dermatosis characterized by an erythematous papulovesicular eruption particularly affecting the flexural areas. There may be secondary changes of scaling, excoriation and lichenification. It occurs predominantly in childhood, with over half of cases presenting in the first year of life and subsequent clearance rates of around 60% by the age of 16 years. The prevalence of childhood AD in developed countries is 10–20%.^{1,2}

The prevalence of atopic diseases has increased in the last 30 years, although the reason for this is not well understood.^{3–5} Atopic disease is characterized by abnormal regulation of IgE production in response to environmental allergens: manifestations include asthma, hayfever and AD.¹ The cause of atopy is probably multifactorial, with influences from both genetic and environmental factors, although the rapid increase in prevalence suggests environmental precipitants. The hygiene hypothesis proposes that improved hygiene and reduced exposure to infections in developed countries are associated with the development of atopic disease. Supporting this, several studies have shown that exposure to older siblings, animals and infections in early life protects against atopy.^{6–9} It is postulated that failure to be exposed to infection in infancy somehow prevents the normal deviation of the immune system from a TH2-predominant (allergic) to a TH1-predominant (nonallergic) response.

The aim of this study is to examine factors associated with having a diagnosis of AD at 3.5 years in a group of appropriate for gestational age (AGA) and small for gestational age (SGA) infants. Particular attention is paid to those factors implicated by the hygiene hypothesis.

Materials and methods

The Auckland Birthweight Collaborative (ABC) study was designed to look at differences between appropriate for gestational age (AGA) and small for gestational age (SGA) infants, with similar numbers recruited into each group. Data were collected on a number of variables. For the purposes of this report, we have focused on the main demographic variables, factors related to the presence of atopic disease, and those environmental factors implicated by the hygiene hypothesis.

Subjects

Initial recruitment is described in detail elsewhere.¹⁰ Briefly, babies born at 37 weeks' completed gestation were eligible for inclusion. SGA was defined as equal to or below the sex-specific 10th percentile for gestational age in the New Zealand population. AGA babies weighed greater than the 10th percentile. Between 16 October 1995 and 12 August 1996 all SGA babies born and resident in the Waitemata Health or Auckland Healthcare regions were eligible for inclusion. From 12 August 1996 to 30 November 1997 only babies born in the Auckland Healthcare region were eligible. A random sample of all AGA infants was also included. Infants were excluded from the study if they were from multiple births or had

congenital anomalies likely to affect birthweight and later growth. Babies delivered at home (< 1%) were not included. Ethical approval was obtained from the North Health Research Ethics Committee.

Data collection

Phase 1 (birth data)

A trained interviewer interviewed women in the week following delivery. Data collected included pregnancy history, obstetric history, family history and sociodemographic variables.

Phase 2 (12-month data)

The parents were posted a questionnaire when the infant was 1 year old. Data collected included growth, development, social/family/home environment, respiratory symptoms and atopic symptoms. Nonresponders were followed up by telephone and at previously supplied alternative addresses.

Phase 3 (3.5-year data)

Children were invited to attend the Children's Research Centre at Starship Children's Hospital at age 3.5–4 years for assessment of growth, development, home environment, respiratory symptoms and atopic symptoms. A trained investigator examined the child for evidence of dermatitis. Blood was taken for full blood count, ferritin and total IgE. Skin prick testing was performed against aeroallergens *Dermatophagoides pteronyssinus*, cockroach, cat, *Alternaria tenuis*, mixed grasses and mixed trees, as well as a positive control (histamine 10 mg mL⁻¹) and negative control (diluent). A weal > 3 mm at 15 min was considered a positive response. Ebos Group (Christchurch, New Zealand) supplied extracts.

Definition of atopic dermatitis

AD was defined according to a modified version of the U.K. diagnostic criteria as the presence of an itchy skin rash in the last 12 months plus three or more of the following: history of flexural involvement; history of generally dry skin; history of atopic disease in parents or siblings; and visible flexural dermatitis as per photographic protocol.^{11,12}

Statistical analysis

The ABC study was designed as a case-control study of SGA infants, with SGA and AGA infants being sampled with different probabilities of selection. The analyses in this study in which the outcome of interest is the diagnosis of AD at 3.5 years have taken the disproportionate sampling design into account.

Logistic regression was used to investigate associations between potential risk factors and AD. For the multivariate analysis variables we fitted three models. The first included

variables at the univariate level with $P < 0.05$, except those related to a personal history of atopy. A second model included the addition of variables related to the hygiene hypothesis: older siblings, cat ownership in the first year of life or at present, dog ownership in the first year of life or at present, damp or mould on the ceilings or walls, antibiotic use in the first year of life and maternal smoking during pregnancy. A third model added variables related to symptoms of a personal history of atopy at 1 year to the first model. The analyses were also stratified by SGA/AGA.

SAS v8 and v9 (SAS Institute, Cary, NC, U.S.A.) were used in analyses: in particular, the procedure surveylogistic that was developed for data from surveys with complex sampling designs.

Results

Participants

Participation rates by non-European ethnic groups were poor at phases 2 (41·3%) and 3 (18·9%), so for this report the analysis has included data on New Zealand European subjects only. Eight hundred and seventy-one children participated at birth, 744 (85·4%) at 1 year, and 550 (63·2%) at 3·5 years. The reasons for nonparticipation at phase 3 were: refusal for this follow-up ($n = 68$), moved overseas ($n = 45$), booked appointments but did not attend ($n = 42$), unable to find despite having collected several parental contact points, e.g. parents, siblings ($n = 40$), earlier refusal for further follow-up ($n = 39$), unable to be seen before 4 years of age ($n = 38$), moved within New Zealand ($n = 35$), and death of mother or child ($n = 2$). Birthweight and gender did not differ between participants and nonparticipants. Participants were more likely to have high socioeconomic status ($P < 0.001$) and no exposure to maternal smoking ($P = 0.008$).

Prevalence

Eighty-seven children met the U.K. diagnostic criteria for AD, giving a 1-year period prevalence of 15·8%. The prevalence was not significantly different ($P = 0.52$) between AGA infants (16·7%) and SGA infants (14·7%).

Sociodemographic, obstetric, postnatal and environmental factors

AD at 3·5 years of age showed no association with gender, socioeconomic status, maternal smoking in pregnancy or maternal parity (Table 1).

Only 26 (4·7%) mothers reported never having breastfed their child, and 355 (64·5%) breastfed for 6 months or more. Having breastfed for more than 6 months was a significant risk factor for AD [odds ratio (OR) 9·95, 95% confidence interval (CI) 2·66–37·14] when compared with never breastfeeding. Although there was a suggestion of a dose–response effect with increasing risk of AD with increasing duration of

breastfeeding, this trend was not significant ($\chi^2 = 0.69$, $P = 0.87$). The findings for exclusive breastfeeding showed a similar pattern. Further analysis showed no association between the parents being atopic and the duration for which the child was breastfed ($P = 0.85$).

Data were collected at 3·5 years regarding whether the family had a cat or dog currently or when the child was in the first year of life. Owning a cat or dog showed no association with AD. Other factors including the number of older siblings, damp and mould in the bedroom, antibiotic use in the first year of life, immunization, haemoglobin level and body mass index were not significantly associated with AD at 3·5 years.

Atopic disease

The results of analysis of the association of AD with personal and family histories of atopic disease are presented in Table 2. Those with AD were more likely to have total IgE $> 200 \text{ kU L}^{-1}$ (normal 0–100) and a positive skin prick test to one or more aeroallergen, supporting the diagnosis of atopy in these children.

A personal history of atopy at 1 year of age (wheeze, asthma, rash, eczema) was associated with having AD at 3·5 years. Atopic disease was commonly reported by parents, with 56·5% of mothers and 44·9% of fathers having asthma, AD and/or hayfever. A history of atopy in a parent was associated with the diagnosis of AD at 3·5 years (mother atopic, OR 2·35, 95% CI 1·25–4·42; father atopic, OR 2·05, 95% CI 1·10–3·81). If both parents were atopic the odds of the child having AD were much greater (OR 5·99, 95% CI 1·97–18·2).

Multivariate analysis

A history of atopy in the parents and the duration of breastfeeding remained significant risk factors for AD at 3·5 years in all three models used for multivariate analysis (Table 3). Apart from cat ownership at 3·5 years (adjusted OR 0·45, 95% CI 0·21–0·97) and presence of a rash at 1 year (adjusted OR 4·06, 95% CI 2·07–7·96), environmental factors associated with the hygiene hypothesis and a personal history of atopy at 1 year showed no association with AD at 3·5 years.

Discussion

This study found that a diagnosis of AD at 3·5 years was associated with a history of atopic disease in the parents and duration of breastfeeding. These associations persisted after controlling for socioeconomic status, gender and maternal smoking. The risk was similar for both paternal and maternal atopy. Having been breastfed was a significant risk factor for AD. There was a nonsignificant trend to increasing risk of AD with increasing duration of breastfeeding (exclusive or nonexclusive). Having symptoms or a diagnosis of asthma or eczema at 1 year, a raised serum IgE and a positive skin prick test to aeroallergens were also associated with AD at 3·5 years.

Table 1 Obstetric, sociodemographic, postnatal and environmental factors, and atopic dermatitis at 3.5 years

		Atopic dermatitis at 3.5 years			
		Yes (n = 87)	No (n = 463)	Univariate odds ratio (95% CI)	P-value
Obstetric and sociodemographic factors					
Gender	Male	37	224	1.00	
	Female	50	239	1.28 (0.71–2.30)	0.42
Socioeconomic status ^a	High	64	322	1.00	
	Middle	17	122	1.07 (0.51–2.26)	
	Low	6	19	2.45 (0.61–9.78)	0.45
Maternal smoking in pregnancy	No	68	365	1.00	
	Yes	19	98	0.65 (0.28–1.51)	0.31
Maternal parity	Multiparous	37	188	1.00	
	Primiparous	50	275	0.86 (0.47–1.59)	0.63
Postnatal factors					
Duration of breastfeeding	Never	3	23	1.00	0.002
	< 6 months	26	142	6.53 (1.62–26.28)	
	≥ 6 months	58	297	9.95 (2.66–37.14)	
Duration of exclusive breastfeeding (no other foods)	Never	3	23	1.00	0.012
	< 2 months	12	67	8.00 (1.77–39.20)	
	2–4 months	42	204	9.59 (2.50–36.83)	
	> 4 months	30	167	8.58 (2.70–33.48)	
Immunizations:					
6-week	No	1	17	1.00	
	Yes	80	419	1.73 (0.22–13.7)	0.60
3-month	No	2	19	1.00	
	Yes	79	417	1.34 (0.28–6.56)	0.72
5-month	No	4	26	1.00	
	Yes	77	410	0.89 (0.27–2.87)	0.84
15-month	No	5	27	1.00	
	Yes	82	431	1.21 (0.34–4.26)	0.77
Antibiotics used in 1st year of life (Missing = 24)	No	24	133	1.00	
	Yes	57	312	1.18 (0.61–2.26)	0.62
Body mass index (kg m ⁻²) (Missing = 20)	< 15	15	83	1.00	
	15	27	142	0.77 (0.29–2.08)	0.36
	16	28	121	0.88 (0.33–2.36)	
	17	10	61	0.53 (0.17–1.69)	
	> 18	4	39	0.28 (0.07–1.16)	
Haemoglobin (g dL ⁻¹) (Missing = 118)	< 11.9	16	92	1.00	
	12.0–12.9	40	193	1.49 (0.65–3.41)	0.27
	> 13.0	17	74	2.20 (0.85–5.71)	
Environmental factors					
Older siblings (Missing = 2)	No	47	250	1.00	
	Yes	40	213	1.24 (0.69–2.24)	0.48
Dog at 1 year	No	68	352	1.00	
	Yes	19	111	1.31 (0.66–2.62)	0.44
Dog at 3.5 years	No	64	337	1.00	
	Yes	22	123	1.25 (0.63–2.46)	0.52
Cat at 1 year	No	51	262	1.00	
	Yes	36	201	0.81 (0.44–1.49)	0.50
Cat at 3.5 years	No	51	236	1.00	
	Yes	36	225	0.61 (0.33–1.12)	0.11
Damp	No	71	364	1.00	
	Yes	16	99	0.84 (0.39–1.83)	0.66
Mould	No	65	335	1.00	
	Yes	22	128	1.25 (0.65–2.38)	0.51

CI, confidence interval. ^aSocial class was defined using the subject's occupation, or that of her partner if that was higher, using the Elly Irving classification of occupation. Social classes I and II; III and IV; and V, VI and other were combined and are described as high, middle and low, respectively.

Table 2 Personal and family history of atopy and atopic dermatitis

		Atopic dermatitis at 3.5 years			
		Yes (n = 87)	No (n = 463)	Univariate odds ratio (95% CI)	P-value
Wheezing at 1 year	No	58	327	1.00	
(Missing = 32)	Yes	23	110	2.09 (1.08–4.07)	0.03
Asthma at 1 year	No	73	412	1.00	
(Missing = 34)	Yes	8	23	3.67 (1.38–9.79)	0.009
Rash at 1 year	No	39	346	1.00	
(Missing = 34)	Yes	41	90	4.32 (2.27–8.20)	< 0.0001
Eczema at 1 year	No	39	368	1.00	
(Missing = 33)	Yes	42	68	5.90 (3.07–11.3)	< 0.0001
Runny nose without cold	No	69	391	1.00	
at 1 year (Missing = 34)	Yes	12	44	2.19 (0.87–5.49)	0.09
IgE at 3.5 years (kU L ⁻¹)	< 100	43	273	1.00	
(Missing = 128)	100–200	6	43	0.45 (0.13–1.60)	
	> 200	23	3	3.54 (1.60–7.81)	< 0.0001
Skin prick to aeroallergens	0 positive	43	351	1.00	
(Missing = 80)	> 1 positive	31	45	5.62 (3.22–9.81)	< 0.0001
Mother atopic	No	24	215	1.00	
	Yes	63	248	2.35 (1.25–4.42)	0.008
Mother:					
Asthma (Missing = 1)	No	61	365	1.00	
	Yes	26	98	1.66 (0.85–3.24)	0.14
Hayfever (Missing = 1)	No	48	304	1.00	
	Yes	39	158	1.94 (1.07–3.54)	0.03
Atopic dermatitis	No	43	352	1.00	
(Missing = 2)	Yes	43	110	2.69 (1.45–4.98)	0.002
Father atopic	No	30	273	1.00	
	Yes	57	190	2.05 (1.10–3.81)	0.02
Father:					
Asthma (Missing = 6)	No	60	382	1.00	
	Yes	27	75	2.60 (1.37–4.93)	0.004
Hayfever (Missing = 8)	No	48	334	1.00	
	Yes	38	122	2.31 (1.27–4.24)	0.007
Atopic dermatitis	No	55	398	1.00	
(Missing = 11)	Yes	28	58	3.28 (1.67–6.44)	0.0006
Parental history of atopy	Neither	7	131	1.00	
	Father only	23	142	3.68 (1.13–12.0)	0.02
	Mother only	17	84	3.99 (1.25–12.7)	
	Both	40	106	5.99 (1.97–18.2)	

CI, confidence interval.

There was no association between AD and birthweight, number of older siblings, pet dogs, use of antibiotics in the first year of life, immunization or damp and mould in the home.

Limitations of this study must be recognized. Due to small numbers from other ethnic groups continuing to participate in the ABC study by phase 3, we could include data only on New Zealand European infants. Those with low socioeconomic status or maternal smoking were less likely to remain involved and this affects the power of our estimates of the association of AD with those variables, if anything making them more conservative. The strengths of this study include the large sample size and prospective collection of data on many of the risk factors studied.

The prevalence of AD found in this study is comparable with that found in studies in other Western nations. The

International Study of Asthma and Allergies in Childhood looked at the worldwide burden of AD symptoms by questionnaire and found rates of 2–16% among 6–7-year-olds, and 1–17% among 13–14-year-olds. Rates were significantly higher in Scandinavia, the U.K., Japan and Australasia than in China, central Asia and Eastern Europe.² Estimates of prevalence of AD in New Zealand schoolage children and adolescents were 13–15%.¹³ The Christchurch Child Development study found the prevalence of reported eczema in 2-year-old New Zealand children to be 16.6%.¹⁴ One of the limitations of these studies was that the diagnosis of AD was based on report, with no confirmatory objective examination.

A modified version of the U.K. diagnostic criteria for use in children under 4 years was used to diagnose AD.^{11,12} This included objective observer assessment of dermatitis. This was

Table 3 Logistic regression models for parental history of atopy and breastfeeding adjusted for sampling design

		Model 1 odds ratio (95% CI)	Model 2 odds ratio (95% CI)	Model 3 odds ratio (95% CI)
Parental history of atopy	Neither	1·00	1·00	1·00
	Father only	3·59 (1·09–11·75)	3·46 (1·07–11·18)	3·43 (1·03–11·4)
	Mother only	3·83 (1·20–12·23)	3·19 (0·98–10·39)	3·24 (1·00–10·5)
	Both	6·12 (2·02–18·50)	6·41 (2·11–19·52)	4·02 (1·32–12·2)
Duration of breastfeeding	Never	1·00	1·00	1·00
	< 6 months	6·13 (1·45–25·86)	7·05 (1·44–34·56)	6·12 (1·22–30·7)
	≥ 6 months	9·70 (2·47–38·15)	9·93 (2·18–45·36)	12·0 (2·62–54·8)

CI, confidence interval. Model 1, parental atopy and breastfeeding duration; model 2, parental atopy, breastfeeding duration, older siblings, cat and/or dog at 1 year and 3·5 years, damp, mould, maternal smoking, antibiotics used in first year of life; model 3, parental atopy, breastfeeding duration, history of wheeze, rash or runny nose at 1 year.

not used to diagnose AD at age 1 year, when information was collected by postal questionnaire. It is possible that other conditions, such as seborrhoeic dermatitis and napkin dermatitis, may have been mistaken for AD at 1 year. The diagnosis of atopic disease in family members was made by asking a caregiver (usually the mother) if she, the father or the siblings had asthma, eczema or hayfever. It is possible that rates of atopy in relatives were over- or under-reported.

The diagnostic criteria for AD that were used here included a history of atopy in the family. This potentially confounds any association found between AD in the child and family history of atopy. On repeat analysis excluding the criterion of family history from the diagnosis of AD, we found that although the association weakened, it was still present. In support of our findings, an association of AD with a history of atopy in first-degree relatives has been shown in other studies.^{7,15–18} This is perhaps due to a combination of genetic factors and similar environmental exposures.

Studies have found that a larger infant size at birth is associated with an increased risk of atopy in later life, particularly for the extremes of growth.^{19–21} Despite having a population with a large proportion of SGA infants, we did not find any association between low birthweight and AD at 3·5 years. It may be that this effect is seen only for some forms of atopic disease, or that it becomes evident only in later life.

Studies of the association between breastfeeding and atopic disease have produced conflicting results. Breastfeeding has been found to be associated with reduced, unchanged and increased rates of atopy.^{14,15,22–24} Breastfeeding is more likely to show a protective effect in those infants who come from an atopic family.²⁵ It is postulated that breastfeeding could protect against AD through reduced exposure of the gut to allergens, and the immunological properties of human breast milk. However, breast milk does contain small amounts of foreign proteins transferred from the mother and there are reports of AD improving in breastfed infants when their mothers started an exclusion diet or stopped breastfeeding.²⁶ We found a reduced risk of AD at 3·5 years in children who were never breastfed; however, there were only small numbers in this group. There was also a trend to an increased risk

of AD with increasing duration of breastfeeding. It is interesting that those studies finding breastfeeding to be protective have generally looked at atopy during the first few years of life, whereas those finding no protective effect have tended to look at AD and atopic disease later in childhood. It may be that the protective effect of breastfeeding is short-lived and does not prevent the expression of atopy in later childhood. Also the protective effect of breastfeeding may vary with maternal diet and allergy, and the timing of introduction of cow's milk formula and solids.^{27,28}

Bergmann *et al.* similarly found an increase in risk of AD with increased duration of breastfeeding.¹⁵ Rates of breastfeeding in their study were significantly higher when the mother had higher socioeconomic status, was older, did not smoke during pregnancy and if there was a history of AD in either parent: factors that were associated with increased risk of AD. One possibility is that mothers choose to breastfeed for longer if they believe their child to be at high risk of atopy. However, in our study there was no association between the presence of parental atopy and the duration of breastfeeding, thus making reverse causation a less likely explanation for our findings.

Several environmental factors have been suggested to have a role in the development of atopy. The hygiene hypothesis was initially proposed based on the finding of a protective effect against hayfever from older siblings, possibly through increased exposure to infections.²⁹ Various other studies have confirmed this effect,^{7,15,30} but results have not always been consistent for asthma or eczema.^{7,31} Use of antibiotics in the first year of life has been shown in retrospective studies to be associated with the development of atopic disease, although this has not been confirmed in prospective studies.^{17,32} Studies predominantly from northern Europe and America have suggested that early contact with pets (particularly cats and dogs) is protective against development of atopic sensitization and allergies.^{8,33,34} However, multiple potential sources of bias mean that this finding remains uncertain. We failed to find any association between the number of older siblings, use of antibiotics in the first year of life, dog ownership or other environmental factors, and AD at 3·5 years in our population.

Our only significant finding was that cat ownership at 3·5 years of life had a negative association with AD on multivariate analysis. It may be that other lifestyle factors in New Zealand make environmental factors less significant. Environmental causes for AD do not appear to have been important in this study.

Overall, the findings of this study do not support the hygiene hypothesis. Factors found to be associated with AD at 3·5 years in this population were parental history of atopy, personal history of atopy and duration of breastfeeding. There are many benefits of breastfeeding that warrant its recommendation, but on the basis of this study we cannot recommend it being advocated for the prevention of AD.

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References

- Harper J, Oranje AP, Prose N, eds. Atopic dermatitis. Chapters 3.1–3.11. In: *Textbook of Pediatric Dermatology*, 1st edn, Vol. 1. Oxford: Blackwell Science, 2000; 161–254.
- Williams HC, Robertson CF, Stewart A *et al.* Worldwide variations in the prevalence of symptoms of atopic eczema in the International Study of Asthma and Allergies in Childhood. *J Allergy Clin Immunol* 1999; **103**:125–38.
- Williams HC. Epidemiology of atopic dermatitis. *Clin Exp Dermatol* 2000; **25**:522–9.
- Oranje AP, de Waard-van der Spek FB. Atopic dermatitis: review 2000 to January 2001. *Curr Opin Pediatr* 2002; **14**:410–13.
- Butland BK, Strachan DP, Lewis S *et al.* Investigation into the increase in hay fever and eczema at age 16 observed between the 1958 and 1970 British birth cohorts. *BMJ* 1997; **315**:717–21.
- Sherriff A, Golding J, the ALSPAC Study Team. Hygiene levels in a contemporary population cohort are associated with wheezing and atopic eczema in preschool infants. *Arch Dis Child* 2002; **87**:26–9.
- McKeever TM, Lewis SA, Smith C *et al.* Siblings, multiple births, and the incidence of allergic disease: a birth cohort study using the West Midlands general practice research database. *Thorax* 2001; **56**:758–62.
- Nafstad P, Magnus P, Gaarder PI, Jaakkola JJK. Exposure to pets and atopy-related diseases in the first 4 years of life. *Allergy* 2001; **56**:307–12.
- Braun-Fahrlander C. Environmental exposure to endotoxin and other microbial products and the decreased risk of childhood atopy: evaluating developments since April 2002. *Curr Opin Allergy Clin Immunol* 2002; **3**:325–9.
- Thompson JMD, Clark PM, Robinson E *et al.* Risk factors for small-for-gestational-age babies: the Auckland Birthweight Collaborative Study. *J Paediatr Child Health* 2001; **37**:369–75.
- Williams HC, Burney PG, Pembroke AC, Hay RJ. The U.K. Working Party's diagnostic criteria for atopic dermatitis III. Independent hospital validation. *Br J Dermatol* 1994; **131**:406–16.
- Williams HC. How do I make the diagnosis of atopic eczema? A practical manual for researchers wishing to define atopic eczema (<http://www.nottingham.ac.uk/dermatology/eczema/contents.html>).
- Asher MI, Barry D, Clayton T *et al.* The burden of symptoms of asthma, allergic rhinoconjunctivitis and atopic eczema in children and adolescents in six New Zealand centres: ISAAC Phase One. *NZ Med J* 2001; **114**:114–20.
- Fergusson DM, Horwood LJ, Beutrais AL *et al.* Eczema and infant diet. *Clin Allergy* 1981; **11**:325–31.
- Bergmann RL, Diepgen TL, Kuss O *et al.* Breastfeeding duration is a risk factor for atopic eczema. *Clin Exp Allergy* 2002; **32**:205–9.
- Fergusson DM, Horwood LJ, Shannon FT. Risk factors in childhood eczema. *J Epidemiol Community Health* 1982; **36**:118–22.
- McKeever TM, Lewis SA, Smith C *et al.* Early exposure to infections and antibiotics and the incidence of allergic disease: a birth cohort study with the West Midlands General Practice Research Database. *J Allergy Clin Immunol* 2002; **109**:43–50.
- Harris JM, Cullinan P, Williams HC *et al.* Environmental associations with eczema in early life. *Br J Dermatol* 2001; **144**:795–802.
- Olesen AB, Ellingsen AR, Olesen H *et al.* Atopic dermatitis and birth factors: historical follow up by record linkage. *BMJ* 1997; **314**:1003–8.
- Leadbitter P, Pearce N, Cheng S *et al.* Relationship between fetal growth and the development of asthma and atopy in childhood. *Thorax* 1999; **54**:905–10.
- Braback L, Kjellman N-IM, Sandin A, Bjorksten B. Atopy among schoolchildren in northern and southern Sweden in relation to pet ownership and early life events. *Pediatr Allergy Immunol* 2001; **12**:4–10.
- Kull I, Wickman M, Lilja G *et al.* Breastfeeding and allergic diseases in infants—a prospective birth cohort study. *Arch Dis Child* 2002; **87**:478–81.
- Kramer MS, Chalmers B, Hodnett ED *et al.* Promotion of Breastfeeding Intervention Trial (PROBIT). *JAMA* 2001; **285**:413–20.
- Sears MR, Greene JM, Willan AR *et al.* Long-term relationship between breastfeeding and development of atopy and asthma in children and young adults: a longitudinal study. *Lancet* 2002; **360**:901–7.
- Gdalevich M, Mimouni D, David M, Mimouni M. Breast-feeding and the onset of atopic dermatitis in childhood: a systematic review and meta-analysis of prospective studies. *J Am Acad Dermatol* 2001; **45**:520–7.
- Isolauri E, Tahvanainen A, Peltola T, Arvola T. Breast-feeding of allergic infants. *J Pediatr* 1999; **134**:27–32.
- Fergusson DM, Horwood J, Shannon FT. Early solid feeding and recurrent childhood eczema: a 10-year longitudinal study. *Pediatrics* 1990; **86**:541–6.
- Bottcher MF, Jenmalm MC. Breastfeeding and the development of atopic disease during childhood. *Clin Exp Allergy* 2002; **32**:159–61.
- Strachan DP. Hayfever, hygiene, and household size. *BMJ* 1989; **299**:1259–60.
- Lewis SA, Britton JR. Consistent effects of high socio-economic status and low birth order and the modifying effect of maternal smoking on the risk of allergic disease during childhood. *Respir Med* 1998; **92**:1237–44.

- 31 Ponsonby AL, Couper D, Dwyer T *et al.* Cross-sectional study of the relation between sibling number and asthma, hay fever and eczema. *Arch Dis Child* 1998; **79**:328–33.
- 32 Farooqi IS, Hopkin JM. Early childhood infection and atopic disorder. *Thorax* 1998; **53**:927–32.
- 33 Holscher B, Frye C, Wichmann HE, Heinrich J. Exposure to pets and allergies in children. *Pediatr Allergy Immunol* 2002; **13**:334–41.
- 34 Ownby DR, Johnson CC. Does exposure to dogs and cats in the first year of life influence the development of allergic sensitization? *Curr Opin Allergy Clin Immunol* 2004; **3**:517–22.