

The natural history of eczema from birth to adult life: a cohort study

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Summary

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Conflicts of interest

None declared.

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Background Eczema is common in infancy; however, there is little evidence about its natural history to adulthood.

Objectives To study the natural history of eczema from birth to young adult life with particular reference to its relation to atopy.

Methods A birth cohort of children with atopic family histories was followed for 23 years. Clinical examinations were conducted until the age of 7 years, skin-prick tests and serum total IgE were recorded in infancy and at ages 7 and 23 years, and questionnaires about eczema symptoms were completed at 15 and 23 years.

Results Information was obtained on 497 subjects at birth, 482 at 1 year, 440 at 7 years, 363 at 15 years and 304 at 23 years. Eczema usually remitted from age 1 to 7 years but became more persistent from the age of 15 years, especially in those who were atopic. The prevalence of eczema rose in women from age 15 to 23 years but declined in men. Adults with eczema had higher IgE than those without at 3 months (geometric mean 3.0 vs. 1.7 kU L⁻¹; $P = 0.01$), 7 years (107.9 vs. 45.2 kU L⁻¹; $P = 0.01$) and 23 years (123.4 vs. 42.3 kU L⁻¹; $P = 0.01$), and were more likely to have had positive skin-prick tests at 1 year of age. Current eczema was associated with raised IgE in infancy and adulthood but not in childhood.

Conclusions Predisposed infants and children with eczema usually grow out of the disease, but in adolescence it is more likely to persist. Adult eczema is related to atopy from the age of 3 months.

Eczema is a common disease in childhood. It is often associated with atopy (hence the term 'atopic dermatitis'), and also asthma and rhinoconjunctivitis.^{1–3} The incidence is highest in infancy; there is some expectation that affected children will grow out of the disease, but in a recent British cohort study the prevalence remained fairly constant from birth to 18 years.⁴ The association with atopy, defined usually by skin-prick tests or IgE measurements, varies widely between different countries.⁵ To know whether it also varies with age and to understand the natural history of the disease, a longitudinal study is required in which eczema and atopic markers are recorded at intervals from infancy to adulthood.

This study presents the findings of a birth cohort of infants with a family history of atopic disease, followed up for 23 years to see to what extent eczema tends to remit or persist

during different intervals and to examine its relationship with atopy from infancy to adult life.

Patients and methods

A birth cohort study was set up in 1982–1984 to monitor the natural history of allergic diseases.^{6,7} Infants with a family history of asthma, eczema or hay fever, whose parents gave consent, were recruited antenatally into a randomized trial that compared soya milk with cow's milk protein for the first 4 months of life. No difference was found in the incidence of atopic disease after 7 years.⁸

When the children were 3, 6 months, 1 and 7 years old they were examined by a doctor. Rashes were classified as a noneczematous rash, a history of eczema, inactive eczema and

active eczema. Blood was taken from the umbilical cord at birth, and from the child at 3 months and at 7 years for measurement of serum total IgE. At the ages of 6 months, 1 and 7 years skin-prick tests (SPTs) were also performed.^{6–8}

At age 15 years the subjects were sent a short questionnaire including questions about eczema and rhinoconjunctivitis from the International Study of Asthma and Allergies in Childhood (ISAAC).⁹ At 23 years of age they were invited to attend a clinic and complete a questionnaire that contained the same questions as before; blood was taken for serum IgE measurement using UniCAP (Thermo Scientific, Waltham, MA, U.S.A.), and SPTs were performed. Nonattenders were asked to complete the questionnaire.

Because of the skewed distribution of serum IgE concentrations, these data were summarized using geometric means. In many cases, serum IgE in cord blood and during infancy was undetectable. For descriptive purposes, to accommodate zero values, the mean $\pm$ SD of $\log(\text{IgE} + 1)$ was calculated, transformed back into the original units, and one subtracted from each value. Where a negative value for geometric mean $-$ SD ensued, it was replaced by zero. For significance testing, *t*-tests were performed on the $\log(\text{IgE} + 1)$ variables, except for cord blood, where a Mann–Whitney *U*-test was used because of the non-normal distribution even after logarithmic transformation.

Approval was obtained from the local ethics committee for each stage of the study. Informed consent was obtained from mothers or (at 23 years) participants.

Results

Of the 497 infants who entered the study at birth, 99% were examined at 3 months, 97% at 1 year and 89% at 7 years. Questionnaires were completed by 73% of the original cohort at 15 years and by 61% at 23 years. At each stage, similar proportions participated among those who did and did not have eczema on the previous occasion. Figure 1 shows the prevalence of eczema up to the age of 23 years. The prevalence of active or symptomatic eczema in male subjects declined after the age of 12 months, whereas in female subjects it rose markedly after 7 years.

Associations between active and symptomatic eczema at different ages are shown in Table 1. Female sex was independently associated with eczema at 15 years [odds ratio (OR)

Table 1 Associations between active and symptomatic eczema at different ages

Earlier age	Later age	Total number	Odds ratio (95% CI)
1 year	7 years	427	2.52 (1.11–5.71)
	15 years	349	3.61 (1.62–8.05)
	23 years	295	1.95 (0.76–5.01)
7 years	15 years	342	2.03 (0.77–5.37)
	23 years	292	5.45 (2.05–14.48)
15 years	23 years	262	6.04 (2.50–14.56)

CI, confidence interval. Odds ratios, calculated using logistic regression, have been adjusted for sex and randomization group.

1.93; 95% confidence interval (CI) 0.99–3.95] and 23 years (OR 3.65; 95% CI 1.67–7.99), but there was no association with randomization group at any age. Eczema at 1 year was associated with eczema at 7 and 15 years, at 7 years it was associated with eczema at 23 years, and at 15 years it was strongly associated with eczema at 23 years.

Table 2 shows the geometric mean total IgE concentrations in serum taken at various ages in subjects with and without eczema, at those ages and subsequently. Eczema at 3 months was related to IgE at that age; at 1, 7 and 15 years eczema was not significantly associated with IgE at any age, but at 23 years it was related to IgE at 3 months, 7 and 23 years. There were no significant associations with cord IgE.

An analysis was performed to determine whether positive SPTs occurred before, at or after the age when eczema was detected. At 1 year, eczema was associated with a positive SPT at 1 and 7 years, and wheeze at 7 years. There was also a strong relationship with a positive SPT to egg at 1 year (OR 7.57; 95% CI 3.57–16.05). At 15 years, symptoms of eczema were associated with wheeze at 1 and 15 years, and rhinoconjunctivitis at 15 years. Eczema at age 23 years was associated with positive SPTs at 1 and 7 years, wheeze at 7, 15 and 23 years, and rhinoconjunctivitis at 15 and 23 years. Those with eczema at 6 months and negative SPTs were more likely than infants without eczema to be sensitized at 7 years (adjusted OR 1.95; 95% CI 1.03–3.69) but were not different at 7 or 23 years in terms of skin sensitivity or IgE. In contrast, those with eczema and a positive SPT at 6 months consistently

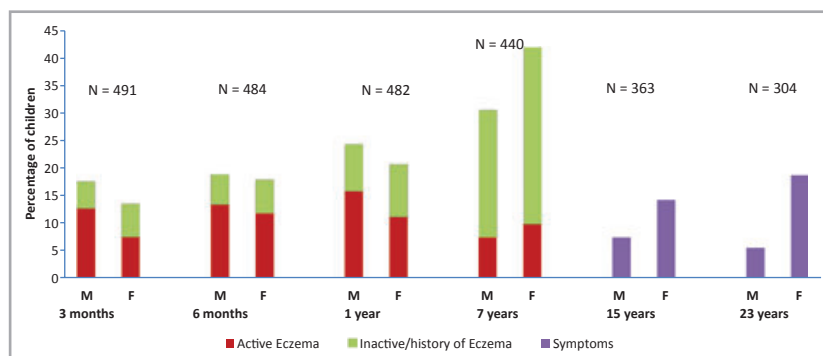


Fig 1. Prevalence of eczema in male and female subjects at different ages. Active eczema: inflamed, itchy eczematous rash. Inactive eczema: eczematous rash not currently inflamed or itchy. History: eczema present since the last examination, or (at 7 years) in the past year but not currently. Symptoms: as defined in the ISAAC questionnaire.⁹

Table 2 Serum total IgE concentrations at different times in subjects with and without active or symptomatic eczema, then and subsequently

Age at IgE measurement	Age when eczema recorded	Numbers with/without eczema ^a	Geometric mean (95% confidence interval) IgE (kU L ⁻¹)		P-value
			Subjects with eczema	Subjects without eczema	
Birth (cord)	3 months	37/354	0.7 (0.0–2.2)	0.5 (0.0–1.4)	0.30
	6 months	44/334	0.7 (0.0–2.2)	0.5 (0.0–1.4)	0.85
	1 year	53/325	0.4 (0.0–1.1)	0.5 (0.0–1.5)	0.26
	7 years	26/316	0.4 (0.0–0.8)	0.5 (0.0–1.4)	0.64
	15 years	30/253	0.7 (0.0–2.5)	0.5 (0.0–1.3)	0.52
	23 years	33/208	0.3 (0.0–0.8)	0.5 (0.0–1.4)	0.11
3 months	3 months	50/410	3.1 (0.8–8.3)	1.9 (0.3–5.1)	0.01
	6 months	58/393	2.5 (0.4–7.6)	1.9 (0.4–5.1)	0.06
	1 year	60/386	2.1 (0.4–5.8)	1.9 (0.3–5.3)	0.55
	7 years	34/374	2.2 (0.5–5.9)	1.9 (0.3–5.5)	0.53
	15 years	37/300	2.4 (0.4–6.9)	1.8 (0.3–5.0)	0.17
	23 years	39/243	3.0 (0.7–8.6)	1.7 (0.3–4.5)	0.01
7 years	7 years	29/315	48.9 (7.8–282.6)	51.6 (9.9–251.6)	0.87
	15 years	32/242	74.9 (14.2–378.7)	47.7 (9.5–225.7)	0.13
	23 years	29/198	107.9 (20.3–555.7)	45.2 (9.0–213.1)	0.01
23 years	23 years	17/84	123.4 (29.5–506.6)	42.3 (9.6–176.6)	0.01

^aThe numbers in each cell are those respectively with and without eczema whose IgE was measured at the age shown.

showed more atopic features on subsequent occasions. Among those with no eczema at 6 months, individuals with a positive SPT were more likely to have active eczema at 1 year than those with negative SPTs (adjusted OR 4.87; 95% CI 1.81–13.09); this association was no longer present at 7 years.

Discussion

This study shows that adult eczema is associated with atopy (IgE and positive SPTs) from age 3 months. Infantile eczema is also associated with atopy, but in childhood the link is much weaker – indeed, total IgE at 7 years was more strongly associated with eczema at 23 years than when it was measured.

Follow-up of this cohort shows that eczema in infancy and childhood usually remits, but in adolescence it more often persists into adulthood, in line with Wüthrich's review.¹⁰ As in other studies, there was a male excess during infancy,¹¹ followed by a growing female preponderance.^{4,12} Possibly the later sex difference is, in part at least, attributable to differential self-reporting of eczema, as information at 15 and 23 years was obtained by questionnaire.

Weaknesses of the study include small numbers, restriction to high-risk families, and declining response rate, although reanalysis confined to those with data at 1, 7, 15 and 23 years made little difference. Another limitation of the study is that the 1-year period-prevalence data provided by the ISAAC questionnaire are not entirely equivalent to the point prevalence from clinical examination.¹³ However, the results of this study are broadly in agreement with findings of another recent British cohort study.⁴

In conclusion, this study shows the value of following up a birth cohort through to early adulthood in revealing long-term associations with eczema.

What's already known about this topic?

- Eczema is associated with atopy, asthma and rhinoconjunctivitis.
- Eczema in infancy usually remits but is more likely to persist if the child is atopic.
- After puberty eczema often persists to adult life.

What does this study add?

- Adult eczema is associated with atopy from the age of 3 months.
- Atopy increases the likelihood of persistence after adolescence.

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