Association of parental eczema, hayfever, and asthma with atopic dermatitis in infancy: birth cohort study

N Wadonda-Kabondo, J A C Sterne, J Golding, C T C Kennedy, C B Archer, M G S Dunnill, the ALSPAC Study Team

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Objective: To evaluate the association of parental history of atopic disease with childhood atopic dermatitis, and to examine the relative strength of associations with maternal and paternal disease.

Design: Mothers were recruited to the Avon longitudinal study of parents and children (ALSPAC) from the eighth week of pregnancy. Before parturition, both parents were asked, separately, to report their lifetime history of eczema, asthma, and hayfever. Parents reported symptoms of atopic dermatitis in their children at ages 6, 18, 30, and 42 months.

Results: Of 8530 children with complete information on rash at ages 6, 18, 30, and 42 months, 7969 had complete information on maternal atopic disease and 5658 on maternal and paternal atopic disease. There was a strong association between parental eczema and childhood atopic dermatitis: odds ratio 1.69 (95% confidence interval, 1.47 to 1.95) for maternal eczema only, 1.74 (1.44 to 2.09) for paternal eczema only, and 2.72 (2.09 to 3.53) for eczema in both parents. Associations with parental asthma or hayfever were attenuated after controlling for parental eczema. There was no evidence that associations with parental atopy were stronger than with paternal.

Conclusions: Associations between parents’ atopic disease and the risk of atopic dermatitis in offspring vary according to the type of atopic disease in the parents, but not according to parental sex. These results are at variance with previous studies reporting stronger associations with maternal than paternal atopy, and suggest that there is no “parent-of-origin” effect in atopic dermatitis. Parental eczema may be a better marker than parental asthma/hayfever in predisposing to childhood eczema.

METHODS

ALSPAC is an ongoing prospective birth cohort study that enrolled 14 541 mothers from the eighth week of pregnancy. These mothers were resident in the county of Avon, with expected date of delivery between 1 April 1991 and 31 December 1992. Of a total of 14 062 children born alive, 12 411 were followed up at least once between the ages of 6 and 42 months. Data are collected through self-completed questionnaires, biological samples, and clinical assessments. Before the birth of their children, fathers and mothers were asked, separately, to report their lifetime history of eczema, asthma, and hayfever as part of a large booklet questionnaire. Before embarking on the study, the social characteristics of Avon were checked against those of Britain as a whole, using data from the 1970 British birth cohort. It was found that characteristics such as living in a single room or flat, race, parental education, being a single mother, and prevalence of smoking were similar to those of the country as a whole. The distribution of atopic diseases such as eczema, wheezing, and hayfever was also similar. However, children from the county of Avon were less likely to live in rented accommodation and were also less likely to have a father in manual occupation.

Abbreviation: ALSPAC, Avon longitudinal study of parents and children
than children in the rest of Britain. Details of the study design and selection of participants can be found on the ALSPAC website.16

Details of the ascertainment and definition of childhood atopic dermatitis are given elsewhere.17 Briefly, questions about current rash and rash during the previous six months were sent to the mothers when the children were aged 6, 18, 30, and 42 months. These questions, which were modified from Hanifin and Rajka,17–19 focused on itchy rash in joints and creases. At six months, mothers were also asked to report oozing and crusted rash on the face, shins, or forearms. Those children whose mothers reported such rashes in at least two follow up questionnaires were defined as having atopic dermatitis.17 Presence or absence of a family history was therefore not included in our definition.

**Data analysis**

Analyses were done using Stata version 7.0 (Stata Corporation, College Station, Texas, USA). We employed logistic regression to estimate odds ratios for the association between childhood atopic dermatitis and parental atopic diseases before and after controlling for parental social class, parental education level, parity, breast feeding, and birth weight. Missing information on social class variables was coded as a separate category when these variables were included in the regression models.

**RESULTS**

Complete information on rash at 6, 18, 30, and 42 months was available for 8530 children, of whom 7969 had complete information on maternal atopic disease and 5658 had complete information on maternal and paternal atopic disease. Among these 5658 families, 36.7% of the fathers and 15.7% of the mothers had manual jobs, while 57.3% of the mothers and 41.5% of the fathers had educational qualifications below A level (advanced level qualification obtained at the end of secondary education and a prerequisite for university entry in most universities in the United Kingdom). Most of the mothers (82.1%) had parity of 2 or less at the time of the study pregnancy. Median maternal age was 28 years (range 14 to 45 years, interquartile range 26 to 32 years).

Table 1 shows the reported prevalence of atopic diseases in the parents. The prevalence of maternal atopic diseases for 7969 mothers who provided complete information was similar to that in the 5658 mothers for whom there was also complete information on paternal atopic disease. The most commonly reported disease was hayfever, and the least commonly reported was asthma. The proportion of fathers reporting eczema (14%) was notably smaller than the proportion of mothers (24%). The prevalence of reported asthma and hayfever was, however, similar for fathers and mothers.

Table 2 shows the association between different maternal atopic diseases and atopic dermatitis in children. Controlling for potential confounding factors made little difference to the magnitude of estimated associations, which were similar in the 7969 mother–child pairs with complete maternal and child information and in the 5698 pairs for which there was also complete paternal information. The strongest association was with maternal eczema, adjusted odds ratio 1.63 (95% confidence interval (CI), 1.47 to 1.82). The adjusted odds ratios for maternal asthma (1.30 (1.12 to 1.50)) and maternal hayfever (1.28 (1.16 to 1.42)) were similar. The adjusted odds ratio for the association between any maternal atopic disease and childhood atopic dermatitis was 1.43 (1.30 to 1.57). Table 3 shows associations between paternal atopic diseases and atopic dermatitis in the 5658 children with complete information on both maternal and paternal eczema (this number was similar to the total number of children with information on paternal eczema). Again, the strongest association was with paternal eczema. Associations with paternal atopic disease were slightly stronger than the corresponding associations with maternal atopic disease (shown in table 2).

Table 4 examines the association between a history of maternal disease, paternal disease, or both, for the three atopic diseases and for any parental atopic disease. Associations were again strongest for parental eczema, and similar for parental asthma and hayfever. Table 5 shows that associations between parental atopic disease and childhood atopic dermatitis were generally similar to or stronger than the corresponding associations for maternal atopic disease. Controlling for atopic disease in the spouse made little difference to these findings.

**DISCUSSION**

It is important to establish the nature of inheritance of childhood atopic dermatitis, to facilitate the search for the genes that cause this disease.12 14 20–24 Patterns of inheritance will influence both the design and the analysis of genetic linkage and association studies. Dissection of individual genetic influence will rely on a clear understanding of mode...
of inheritance and the relation of one atopic disease to another. The results of this study suggest that associations between parents’ atopic disease and the risk of atopic dermatitis in their children vary according to the type of atopic disease in the parents, but not by sex of the parent manifesting that disease. A parental history of eczema is the strongest predictor of atopic dermatitis in their children, while parental histories of asthma alone or hayfever alone had substantial associations with childhood atopic dermatitis only if both of the parents manifested the disease. Furthermore, associations with parental asthma or hayfever were markedly attenuated after controlling for parental eczema.

Two important strengths of this study are the large number of families included, and that information was collected prospectively. In particular, information on parental atopic disease was collected in questionnaires sent separately to both mothers and fathers before the birth of their child. This should minimise differences in the accuracy of reporting of parental atopic disease between mothers and fathers, and avoid recall bias. Complete information on childhood atopic dermatitis and parental atopic disease was available for 5658 families. Although this represents only 45.6% of the children who were followed at least once between 0 and 42 months, we think it is unlikely that selection biases have affected our results. First, associations with maternal atopy were little changed when we considered the 7979 (93.5%) of mother–child pairs with complete information on childhood atopic dermatitis and maternal atopic disease. Second, although the prevalence of childhood atopic dermatitis is likely to be somewhat lower in families with missing information,17 the magnitude of the association between parental atopic disease and childhood atopic dermatitis is unlikely to be very different.

It is notable that although, as previously reported, there were no sex differences in the incidence of childhood atopic dermatitis,17 the reported prevalence of maternal eczema was substantially higher than that of paternal eczema. Although this could reflect differences in the propensity to report the condition, no such differences were seen for asthma or hayfever and the differences did not lead to changes in the magnitude of associations between maternal and paternal eczema.

### Table 2
Relation between maternal atopy and the incidence of atopic dermatitis in 7969 children with complete information on maternal atopic disease, and 5658 children with complete information on maternal and paternal atopic disease

| Maternal eczema | No | 1798/6058 (29.7) | 1 | 1 | 1 |
| Maternal asthma | No | 2247/7076 (31.8) | 1 | 1 | 1 |
| Maternal hayfever | No | 1676/5474 (30.6) | 1 | 1 | 1 |
| Maternal atopic disease | No | 1224/4271 (28.7) | 1 | 1 | 1 |

### Table 3
Relation between paternal atopy and incidence of atopic dermatitis in 5658 children with complete information on maternal and paternal atopic disease

| Paternal atopic disease | No | 1566/4861 (30.8) | 1 | 1 | 1 |
| Paternal asthma | No | 1558/4922 (31.7) | 1 | 1 | 1 |
| Paternal hayfever | No | 1183/3911 (30.3) | 1 | 1 | 1 |

*Controlling for maternal and paternal social class, maternal and paternal education level, parity, breast feeding, and birth weight.

CI, confidence interval; OR, odds ratio.
eczema and childhood atopic dermatitis. Some misclassification of parental atopic disease is inevitable, as it was assessed using a single self report from a questionnaire. This implies first, that the associations reported here are underestimates of the true associations, and second, that we will not have controlled perfectly for the effect of each parental atopic disease in the multivariable analyses.

Another limitation of the study was that childhood atopic dermatitis was diagnosed using self reported questionnaires only. Clinical assessment by an experienced dermatologist is regarded as the best way to diagnose atopic dermatitis, although this is not practical in large epidemiological studies. In one epidemiological study there was good agreement between parental assessment of flexural dermatitis and assessment by a trained investigator. The magnitude of associations with parental atopy might vary between ethnic groups or between countries; we are not able to address this issue here.

The results of this study are not in agreement with various epidemiological studies reporting stronger associations of childhood atopic disease with maternal than with paternal atopy. Possible explanations for a greater associations with maternal than paternal atopy include paternal imprinting contributing to stronger maternal heritability, environmental factors more likely to be shared by mother and child than father and child, and maternal effects acting through foetal environment.

However, it is also possible that observation of a stronger maternal influence is artefactual. First, questionnaires used to assess parental atopy are usually completed by mothers and hence may misclassify paternal symptoms. This would imply that there is greater regression dilution bias in the estimated association with paternal atopy than maternal atopy. Second, reporting of paternal disease is usually less complete than reporting of maternal disease, as was the case in this study. In consequence, associations of similar

### Table 4

<table>
<thead>
<tr>
<th>Parental eczema</th>
<th>Children with atopic dermatitis (n (%))</th>
<th>Crude OR (95% CI)</th>
<th>Adjusted OR (95% CI)*</th>
<th>Adjusted OR (95% CI) controlling additionally for other parental atopic disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>1046/3729 (28.1)</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Mother only</td>
<td>453/1153 (40.0)</td>
<td>1.71 (1.49 to 1.96)</td>
<td>1.69 (1.47 to 1.95)</td>
<td>1.65 (1.43 to 1.91)</td>
</tr>
<tr>
<td>Father only</td>
<td>224/550 (40.7)</td>
<td>1.76 (1.47 to 2.12)</td>
<td>1.74 (1.44 to 2.09)</td>
<td>1.60 (1.32 to 1.94)</td>
</tr>
<tr>
<td>Both parents</td>
<td>128/246 (52.0)</td>
<td>2.78 (2.14 to 3.60)</td>
<td>2.72 (2.09 to 3.53)</td>
<td>2.40 (1.83 to 3.13)</td>
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<tr>
<td>Parental asthma</td>
<td>No</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Mother only</td>
<td>1366/4378 (31.2)</td>
<td>1.20 (0.99 to 1.45)</td>
<td>1.18 (0.98 to 1.43)</td>
<td>0.96 (0.79 to 1.18)</td>
</tr>
<tr>
<td>Father only</td>
<td>245/645 (38.0)</td>
<td>1.35 (1.14 to 1.60)</td>
<td>1.34 (1.12 to 1.59)</td>
<td>1.08 (0.89 to 1.30)</td>
</tr>
<tr>
<td>Both parents</td>
<td>43/91 (52.8)</td>
<td>2.46 (1.62 to 3.73)</td>
<td>2.46 (1.62 to 3.75)</td>
<td>2.13 (1.63 to 2.52)</td>
</tr>
<tr>
<td>Parental hayfever</td>
<td>No</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Mother only</td>
<td>790/2720 (29.0)</td>
<td>1.20 (1.04 to 1.39)</td>
<td>1.18 (1.02 to 1.37)</td>
<td>1.09 (0.94 to 1.28)</td>
</tr>
<tr>
<td>Father only</td>
<td>398/1144 (34.8)</td>
<td>1.30 (1.12 to 1.51)</td>
<td>1.26 (1.08 to 1.46)</td>
<td>1.17 (1.00 to 1.37)</td>
</tr>
<tr>
<td>Both parents</td>
<td>270/602 (44.9)</td>
<td>1.99 (1.66 to 2.38)</td>
<td>1.92 (1.60 to 2.31)</td>
<td>1.60 (1.32 to 1.94)</td>
</tr>
<tr>
<td>Parental atopic disease</td>
<td>No</td>
<td>477/1824 (26.2)</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Mother only</td>
<td>501/1510 (33.2)</td>
<td>1.40 (1.21 to 1.63)</td>
<td>1.37 (1.18 to 1.60)</td>
<td>NA</td>
</tr>
<tr>
<td>Father only</td>
<td>385/1183 (32.5)</td>
<td>1.36 (1.16 to 1.60)</td>
<td>1.32 (1.12 to 1.55)</td>
<td>NA</td>
</tr>
<tr>
<td>Both parents</td>
<td>488/1141 (42.8)</td>
<td>2.11 (1.80 to 2.47)</td>
<td>2.04 (1.74 to 2.40)</td>
<td>NA</td>
</tr>
</tbody>
</table>

*Controlling for maternal social class, paternal social class, maternal & paternal education level, parity, breast feeding; and birth weight.

### Table 5

<table>
<thead>
<tr>
<th>Parental atopic disease by sex</th>
<th>OR (95% CI)</th>
<th>OR (95% CI) after controlling for same disease in the spouse</th>
<th>OR (95% CI) after controlling for other atopic diseases in the spouse</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eczema</td>
<td>1.71 (1.50 to 1.94)</td>
<td>1.67 (1.47 to 1.90)</td>
<td>1.67 (1.47 to 1.90)</td>
</tr>
<tr>
<td>Asthma</td>
<td>1.27 (1.07 to 1.51)</td>
<td>1.27 (1.07 to 1.51)</td>
<td>1.27 (1.07 to 1.51)</td>
</tr>
<tr>
<td>Hayfever</td>
<td>1.30 (1.16 to 1.47)</td>
<td>1.29 (1.15 to 1.45)</td>
<td>1.28 (1.13 to 1.44)</td>
</tr>
<tr>
<td>Any atopic disease</td>
<td>1.46 (1.30 to 1.63)</td>
<td>1.45 (1.25 to 1.57)</td>
<td></td>
</tr>
<tr>
<td>Paternal</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eczema</td>
<td>1.75 (1.50 to 2.04)</td>
<td>1.70 (1.45 to 1.98)</td>
<td>1.69 (1.44 to 1.97)</td>
</tr>
<tr>
<td>Asthma</td>
<td>1.42 (1.21 to 1.66)</td>
<td>1.41 (1.20 to 1.66)</td>
<td>1.41 (1.20 to 1.65)</td>
</tr>
<tr>
<td>Hayfever</td>
<td>1.39 (1.23 to 1.56)</td>
<td>1.38 (1.22 to 1.55)</td>
<td>1.38 (1.22 to 1.55)</td>
</tr>
<tr>
<td>Any atopic disease</td>
<td>1.42 (1.26 to 1.59)</td>
<td>1.40 (1.25 to 1.57)</td>
<td></td>
</tr>
</tbody>
</table>

*Controlling for maternal and paternal social class, maternal and paternal education, parity, breast feeding; and birth weight.
Parental atopy in atopic dermatitis

J A C Sterne, Department of Social Medicine, University of Bristol
the A L S P A C Study Team, University of Bristol

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