Genetic risk for asthma, allergic rhinitis, and atopic dermatitis

Sigrid Dold, Matthias Wjst, Erika von Mutius, Peter Reitmeir, Eva Stiepel

Abstract
In order to explore the genetic risk of a child with a family history of allergies developing asthma, allergic rhinitis, or atopic dermatitis, questionnaires filled in by 6665 families were analysed. The data were collected in a population based cross sectional survey of 9-11 year old schoolchildren living in Munich and southern Bavaria. The relation between asthma, allergic rhinitis, and atopic dermatitis and the number of allergic first degree relatives, and the type of allergic disease was examined. Analyses were done separately for families with single or multiple allergic diseases. In families with one allergic parent the risk of the child developing asthma was increased by asthma in a parent, with an odds ratio (OR) of 2.6 (95% confidence interval 1.7 to 4.0) but not by parental allergic rhinitis with OR 1.0 (0.7 to 1.5) or atopic dermatitis, OR 1.0 (0.6 to 1.6). For allergic rhinitis the highest risk with OR 3.6 (2.9 to 4.6) was observed with allergic rhinitis of one parent, apparently lower for asthma of one parent, OR 2.5 (1.6 to 4.0) or atopic dermatitis, OR 1.7 (1.1 to 2.5). Children with parental atopic dermatitis had a high risk for atopic dermatitis, OR 3.4 (2.6 to 4.4), compared with children with parental asthma, OR 1.5 (1.0 to 2.2), or parental allergic rhinitis, OR 1.4 (1.1 to 1.8). Risk factors in families with combined allergies of two relatives (parents and siblings) were analysed separately for the different combinations. These results support the hypothesis that asthma, allergic rhinitis, and atopic dermatitis are multifactorial diseases brought about by various familial and environmental influences.

Environmental and hereditary factors are the most important causes of allergies. Little is known about the interaction between genetics and environment and how they influence the manifestation and severity of allergies. In 1923, Coca and Cooke introduced the concept of atopy to describe allergies of a familial or hereditary nature, which included asthma, allergic rhinitis, atopic dermatitis, urticaria, and food allergies.1 Whereas in the past recessive and dominant models were discussed,2,3 the results of studies in the last 30 years implicate a multifactorial determination.4 The variability of manifestation and severity, the polymorbidity, and the different organ systems involved make it difficult to locate the hereditary base and its molecular genetic mechanisms.8

Because of the small number of cases involved in many of the studies and the fact that overlapping effects of multiple diseases in the families were not taken into consideration,5-13 it has not to date been possible to determine clearly the risk factors for different atopic family situations.

A population based epidemiological survey with a high number of cases should permit a more differentiated examination of the risk due to heredity. The selection of subgroups with a homogeneous allergic family situation allows the estimation of individual risk factors.

The Munich Asthma and Allergy Study is a cross sectional study to determine the prevalence of allergic and asthmatic diseases in schoolchildren in Bavaria. The relationship between atopic diseases of the parents and siblings and the risk of the investigated child developing an allergic disease such as asthma, allergic rhinitis, or atopic dermatitis is analysed with the data from questionnaires completed by 6665 families.

Methods
The data reported in this paper were collected as part of the Munich Asthma and Allergy Study from October 1989 to July 1990. This survey comprised 9349 schoolchildren aged 9 to 11 years, including all fourth grade children in 118 primary schools in Munich and 65 schools in southern Bavaria. The schools in the rural districts were selected for lower air pollution. Questionnaires were sent home from school with the children, answered by their parents, returned to school, and collected by the investigators. The response rate was 88% (8204 questionnaires). This was an informed consent study approved by the ethics commission of the ‘Bayerische Landesärztekammer’.

QUESTIONNAIRE
Both current and previous allergic diseases of the child and its relatives were evaluated using a total of 58 questions. The questionnaire was standardised according to the recommendation of the American Thoracic Society and supplemented by some of our own questions.

Information given by the parents that a physician had diagnosed asthma at least once or there had been multiple episodes of wheezy bronchitis ('spastische, asthmoide Bronchitis') was taken as representing asthma. Allergic rhinitis was used synonymously with hay fever. Eczema, neurodermatitis, or itching skin lesions in typical locations were interpreted as atopic dermatitis.
The question ‘Did you or a family member ever suffer from one of the following diseases?’ was answered separately for the parents, siblings, and grandparents by means of a chart which was divided into sections for bronchial asthma, allergic rhinitis, and atopic dermatitis. Familial allergy was taken to exist when it was stated that at least one family member had at some time asthma, allergic rhinitis, or atopic dermatitis. To estimate the risk of developing asthma, allergic rhinitis, or atopic dermatitis only the data of first degree relatives, parents and siblings, were included.

Because of possible language difficulties and ethnic differences, only questionnaires from German children were considered for evaluation. The response rate of the German children could be estimated only indirectly. In all the primary schools in Munich (from first grade to fourth grade) 24% of children and in southern Bavaria less than 5% are non-German. Considering these figures the response rate for German children was about 89%. The child’s sex, nationality, place of residence (Munich/southern Bavaria), parents’ education, the number of cigarettes smoked at home, and the person who filled in the questionnaire were analysed as possible confounding variables.

STATISTICS

Only data of first degree family members were included, the grandparents’ allergies were not taken into consideration. In analysing the effect of an allergic disease of a sibling or of more than two allergic first degree relatives, children who had no siblings were excluded. To avoid the overlapping effects of multiple genetic disposition, we analysed the genetic risk of different family histories in successive steps. Firstly, additional allergic diseases of other first degree relatives were excluded and the prevalence of the different diseases in children with a positive family history involving one family member was compared with children whose first degree relatives had no atopic disease. Secondly, only single allergic diseases in one parent were evaluated. Thirdly, the effect of different combinations of two allergic diseases in two first degree relatives was estimated.

The risk of an allergic family history is given as an odds ratio (OR) with the corresponding 95% confidence interval (CI). Frequencies were compared for their statistic significance with the χ² test. All analyses were carried out with SAS 6.18.

RESULTS

The analysis was based on a total of 6665 questionnaires filled in by Germans, as defined by the nationality of the examined child. The 1539 foreign children were a heterogenous group, of whom 31% (470) were Turkish, 29% (443) Yugoslavian, and 41% (626) were from elsewhere. There were significant differences between German and non-German children in the prevalence of asthma, allergic rhinitis, and atopic dermatitis.14

A history of bronchial asthma, allergic rhinitis, and atopic dermatitis of at least one family member (parents, siblings, and grandparents, all with lifetime prevalence) was reported in 47% (3160) of the German families. Including only data from parents and siblings, 40% (2650) had a positive family history. In 15% (1024) of the families there was more than one allergic disease—that is, one or more first degree relatives suffered from one or more allergies. A total of 27% of the children (1776) had one parent suffering from one atopic disease. Allergy of both parents was reported in 4% (241) of the families and 3% (171) had more than two first degree relatives with atopic disease.

Children with atopic disease (asthma, allergic rhinitis, or atopic dermatitis) had a positive family history (first degree relatives) in 55% of cases compared with 35% in children without an atopic disease (p<0.001). The cumulative prevalence of allergies increased with the number of atopic first degree relatives. An allergy of both parents was associated with an allergy in the child in 56% of cases (77/137). There was no difference if the parents had the same type of allergic manifestation (55%, 45/82). In families with more than two allergic first degree relatives, 67% (109/163) of the children had an allergic disease.

The prevalence of asthma, allergic rhinitis, and atopic dermatitis was associated with the number of allergic family members (table 1). However, differentiation between the types of allergic disease in families with one allergic parent showed that the risk of asthma rose only if asthma was present in a parent, rather than allergic rhinitis or atopic dermatitis (table 2).

Allergic rhinitis was seen in 16% of the children with one allergic parent, in 25% if both parents had an allergy, and in 28% with more than two allergic family members (table 1). In families with one atopic parent, allergic rhinitis of the child was most frequent if a parent also had allergic rhinitis (table 2).

Atopic dermatitis similarly increased with the number of allergic family members, from 26% with one parent suffering from an allergy, to

---

**Table 1** Prevalence of asthma, allergic rhinitis, and atopic dermatitis in relation to the number of first degree relatives with an allergic disease. Results are number (%)

<table>
<thead>
<tr>
<th>Family history</th>
<th>Asthma</th>
<th>Allergic rhinitis</th>
<th>Atopic dermatitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>No allergic family history</td>
<td>257/3995 (6)</td>
<td>240/3984 (6)</td>
<td>553/3690 (15)</td>
</tr>
<tr>
<td>Allergic disease of:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>One sibling</td>
<td>47/555 (9)**</td>
<td>36/555 (10)**</td>
<td>118/520 (22)**</td>
</tr>
<tr>
<td>One parent</td>
<td>109/1279 (9)**</td>
<td>207/1280 (16)**</td>
<td>517/1219 (26)**</td>
</tr>
<tr>
<td>Both parents</td>
<td>23/146 (16)**</td>
<td>36/146 (25)**</td>
<td>55/137 (40)**</td>
</tr>
<tr>
<td>More than two first degree relatives</td>
<td>30/170 (18)**</td>
<td>47/170 (28)**</td>
<td>75/162 (46)**</td>
</tr>
</tbody>
</table>

Significance in relation to the group with no family history of allergies, *p<0.05; **p<0.01; ***p<0.001.

**Table 2** Prevalence of asthma, allergic rhinitis, and atopic dermatitis in relation to the type of allergy of one parent with an allergic disease. Results are number (%)

<table>
<thead>
<tr>
<th>Family history</th>
<th>Asthma</th>
<th>Allergic rhinitis</th>
<th>Atopic dermatitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>No allergic family history</td>
<td>257/3995 (6)</td>
<td>240/3984 (6)</td>
<td>553/3690 (15)</td>
</tr>
<tr>
<td>One parent with:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asthma</td>
<td>34/252 (13)**</td>
<td>38/251 (15)**</td>
<td>51/237 (22)**</td>
</tr>
<tr>
<td>Allergic rhinitis</td>
<td>63/783 (8)</td>
<td>152/786 (19)**</td>
<td>170/751 (23)**</td>
</tr>
<tr>
<td>Atopic dermatitis</td>
<td>35/402 (9)</td>
<td>49/401 (12)**</td>
<td>149/381 (39)**</td>
</tr>
</tbody>
</table>

Significance in relation to the group with no family history of allergies, *p<0.05; **p<0.01; ***p<0.001.
40% with both parents allergic, and 46% in families with more than two allergic subjects. With regard to the type of allergy, the highest risk for atopic dermatitis was observed when a parent also had atopic dermatitis (39%), while it was evidently lower for allergic rhinitis (23%) or asthma (22%) (table 2).

In comparing the prevalence of allergies associated with different types of parental exclusion of additional atopic diseases of first degree relatives. Results are number (%).

### Table 3: Child's asthma in relation to one allergic disease of one of the parents and exclusion of additional atopic diseases of first degree relatives. Results are number (%).

<table>
<thead>
<tr>
<th>Family history</th>
<th>Boys</th>
<th>Girls</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>No allergic family history</td>
<td>149/194 (8)</td>
<td>108/2080 (5)</td>
<td>257/994 (6)</td>
</tr>
<tr>
<td>OR (95% CI)</td>
<td>2-1 (2-1 to 5)</td>
<td>2.6 (5-2 to 9)</td>
<td>5.6 (2-1 to 9)</td>
</tr>
<tr>
<td>OR (95% CI)</td>
<td>1/0 (0-4 to 1)</td>
<td>2.9 (2-1 to 9)</td>
<td>6.5 (2-1 to 9)</td>
</tr>
<tr>
<td>Father with asthma</td>
<td>10/38 (26)</td>
<td>6/35 (17)</td>
<td>16/73 (23)</td>
</tr>
<tr>
<td>OR (95% CI)</td>
<td>4.2 (0-2 to 8)</td>
<td>3.6 (1-5 to 9)</td>
<td>4.4 (2-5 to 7)</td>
</tr>
<tr>
<td>One parent with allergic rhinitis</td>
<td>28/129 (9)</td>
<td>14/326 (8)</td>
<td>42/454 (7)</td>
</tr>
<tr>
<td>OR (95% CI)</td>
<td>1-1 (0-8 to 1)</td>
<td>0-8 (0-5 to 1)</td>
<td>0-7 (0-6 to 1)</td>
</tr>
<tr>
<td>One parent with atopic dermatitis</td>
<td>10/100 (6)</td>
<td>9/146 (6)</td>
<td>19/302 (6)</td>
</tr>
<tr>
<td>OR (95% CI)</td>
<td>0-8 (0-4 to 1)</td>
<td>0-8 (0-4 to 1)</td>
<td>0-8 (0-4 to 1)</td>
</tr>
</tbody>
</table>

### Table 4: Child's allergic rhinitis in relation to one allergic disease of one of the parents and exclusion of additional atopic diseases of first degree relatives. Results are number (%).

<table>
<thead>
<tr>
<th>Family history</th>
<th>Boys</th>
<th>Girls</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>No allergic family history</td>
<td>156/190 (8)</td>
<td>84/2074 (4)</td>
<td>240/974 (6)</td>
</tr>
<tr>
<td>OR (95% CI)</td>
<td>3-4 (2-5 to 4-5)</td>
<td>4-2 (2-9 to 7)</td>
<td>5-2 (2-9 to 7)</td>
</tr>
<tr>
<td>OR (95% CI)</td>
<td>3-7 (2-6 to 5-3)</td>
<td>4-2 (6-5 to 7)</td>
<td>5-1 (3-1 to 4)</td>
</tr>
<tr>
<td>Father with allergic rhinitis</td>
<td>16/37 (20)</td>
<td>18/135 (13)</td>
<td>34/272 (16)</td>
</tr>
<tr>
<td>OR (95% CI)</td>
<td>2-9 (3-9 to 5-4)</td>
<td>3-6 (2-9 to 4)</td>
<td>4-9 (2-6 to 4)</td>
</tr>
<tr>
<td>One parent with asthma</td>
<td>15/8 (17)</td>
<td>9/82 (11)</td>
<td>24/170 (14)</td>
</tr>
<tr>
<td>OR (95% CI)</td>
<td>2-3 (3-9 to 1)</td>
<td>2-8 (3-0 to 4)</td>
<td>3-3 (3-0 to 4)</td>
</tr>
<tr>
<td>One parent with atopic dermatitis</td>
<td>18/15 (11)</td>
<td>11/146 (8)</td>
<td>30/305 (10)</td>
</tr>
<tr>
<td>OR (95% CI)</td>
<td>1-4 (0-6 to 2-4)</td>
<td>1-8 (0-9 to 2)</td>
<td>1-1 (1-1 to 2)</td>
</tr>
</tbody>
</table>

### Table 5: Child's atopic dermatitis in relation to one allergic disease of one of the parents and exclusion of additional atopic diseases of first degree relatives. Results are number (%).

<table>
<thead>
<tr>
<th>Family history</th>
<th>Boys</th>
<th>Girls</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>No allergic family history</td>
<td>248/1766 (14)</td>
<td>305/1924 (16)</td>
<td>553/3600 (15)</td>
</tr>
<tr>
<td>OR (95% CI)</td>
<td>3-8 (2-7 to 5-5)</td>
<td>3-6 (2-7 to 5-5)</td>
<td>5-6 (2-7 to 5-5)</td>
</tr>
<tr>
<td>OR (95% CI)</td>
<td>4-4 (3-1 to 7-0)</td>
<td>2-4 (1-9 to 2)</td>
<td>5-8 (2-9 to 5-2)</td>
</tr>
<tr>
<td>Father with atopic dermatitis</td>
<td>12/44 (27)</td>
<td>15/45 (33)</td>
<td>27/89 (30)</td>
</tr>
<tr>
<td>OR (95% CI)</td>
<td>2-3 (1-2 to 5-3)</td>
<td>2-7 (1-2 to 5-3)</td>
<td>2-7 (1-2 to 5-3)</td>
</tr>
<tr>
<td>One parent with asthma</td>
<td>56/320 (18)</td>
<td>70/310 (23)</td>
<td>126/330 (20)</td>
</tr>
<tr>
<td>OR (95% CI)</td>
<td>1-3 (0-9 to 1-8)</td>
<td>1-5 (0-9 to 1)</td>
<td>1-4 (1-1 to 1-8)</td>
</tr>
<tr>
<td>One parent with atopic dermatitis</td>
<td>12/35 (31)</td>
<td>21/777 (27)</td>
<td>33/350 (21)</td>
</tr>
<tr>
<td>OR (95% CI)</td>
<td>1-0 (0-5 to 1-9)</td>
<td>2-0 (1-0 to 3-3)</td>
<td>1-5 (1-0 to 2-2)</td>
</tr>
</tbody>
</table>

### Table 6: Risk of asthma, allergic rhinitis, and atopic dermatitis in families with two first degree relatives with an allergic disease. Results are number (%).

<table>
<thead>
<tr>
<th>Family history</th>
<th>Asthma</th>
<th>Allergic rhinitis</th>
<th>Atopic dermatitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>No allergic family history</td>
<td>257/3995 (6)</td>
<td>240/3984 (6)</td>
<td>553/3600 (15)</td>
</tr>
<tr>
<td>OR (95% CI)</td>
<td>18/144 (13)</td>
<td>27/149 (14)</td>
<td>42/135 (31)</td>
</tr>
<tr>
<td>One parent with atopic dermatitis</td>
<td>2-1 (2-1 to 2)</td>
<td>3-6 (2-3 to 5)</td>
<td>5-0 (2-3 to 6)</td>
</tr>
<tr>
<td>OR (95% CI)</td>
<td>3-8 (2-7 to 5-5)</td>
<td>4-5 (2-7 to 5-5)</td>
<td>5-2 (2-7 to 5-5)</td>
</tr>
<tr>
<td>OR (95% CI)</td>
<td>3-4 (1-6 to 7)</td>
<td>3-8 (1-8 to 7)</td>
<td>3-9 (1-8 to 7)</td>
</tr>
<tr>
<td>Asthma</td>
<td>10/38 (26)</td>
<td>6/38 (16)</td>
<td>9-35 (26)</td>
</tr>
<tr>
<td>OR (95% CI)</td>
<td>5-2 (2-5 to 10)</td>
<td>2-9 (2-5 to 1-9)</td>
<td>4-9 (2-5 to 4)</td>
</tr>
<tr>
<td>Allergic rhinitis</td>
<td>28/235 (12)</td>
<td>6/323 (27)</td>
<td>62/229 (27)</td>
</tr>
<tr>
<td>OR (95% CI)</td>
<td>2-0 (1-5 to 3-0)</td>
<td>5-7 (4-3 to 7-8)</td>
<td>2-3 (1-7 to 9-1)</td>
</tr>
<tr>
<td>Atopic dermatitis</td>
<td>22/174 (13)</td>
<td>21/174 (12)</td>
<td>71/168 (42)</td>
</tr>
<tr>
<td>OR (95% CI)</td>
<td>2-1 (1-5 to 3-4)</td>
<td>2-1 (1-5 to 3-4)</td>
<td>4-1 (3-0 to 5-7)</td>
</tr>
</tbody>
</table>
Genetic risk for asthma, allergic rhinitis, and atopic dermatitis

school leaving final qualification, more family histories of atopic dermatitis or allergic rhinitis were reported (41%) than in families where the parents had an elementary school qualification (23%). This was also true in households without cigarette smokers (36%) as opposed to families with smokers (27%) and was more so in families living in Munich (33%) rather than in southern Bavaria (30%). The same results were noted more often in German families (36%) than in families of other nationalities. There was no significant difference for the rate of reported asthma cases in the family in the different groups.

To estimate the effect of the different confounding variables, the OR for allergies in the child having one family member with an allergic disease was determined in different subgroups. There was no statistically significant difference between boys or girls, whether living in Munich or southern Bavaria, with parents smoking at home, or not, whether the questionnaire was filled in by the father or the mother, and between the different standard of parents' education. In nearly all of these subgroups, an OR of about 2 was observed.

Discussion

This population study showed that 40% of the children had an allergic family history and if grandparents were included this figure rose to 47%. It is hence necessary to differentiate between hereditary risk factors. As 15% of the families reported combined allergies, it is important to avoid the overlapping effects by excluding additional allergies in each case. This restriction appreciably reduces the number of the children included in the different evaluations.

Data collected from questionnaires always suffer from various problems. The information given about a child or family member's atopic disease relies on memory and retrospective interpretation by the person who answered the questionnaire. However it is not possible to diagnose asthma, allergic rhinitis, or atopic dermatitis by means of a single examination of the child, because these allergic diseases occur mostly episodically. Nevertheless questionnaires offer a unique opportunity to collect information from a large and representative group in the population. As this survey comprised only children aged 9 to 11 years, the different groups are very comparable. It should be noted that the estimated risk for an allergic disease is valid for this age group and could vary for older children.

Earlier studies on allergic inheritance which also determined the prevalence of a family history of allergic disease in individuals with and without allergies, reported a positive family history in 40 to 80% of individuals with an allergic disease compared with 20% or fewer of individuals without an allergic disease. Our observation that 35% of children without a reported allergic disease have a positive family history is in keeping with a surprisingly high number of children with an allergic family history.

Studies evaluating the genetic role in allergies often differentiate only between families with and without atopic diseases or take only the number of atopic family members into account. Furthermore, investigations which distinguished between the genetic risk of different atopic diseases did not consider the effect of combinations of multiple allergies. In families with single allergic disease of one parent only asthma, not allergic rhinitis, is a predisposing factor for asthma in the offspring. A longitudinal study in a cohort of children aged 5–9 years observed an increase of the relative risk only for parental asthma. On the other hand, asthma of the mother or the father raises the risk of allergic rhinitis. This one sided relationship supports the hypothesis that allergic rhinitis could be a minor form of bronchial asthma. This is in accordance with the results of a follow up study of college students demonstrating an increased risk of developing asthma for persons with allergic rhinitis.

The prevalence of asthma is higher in boys than in girls, but the risk factors of parental asthma are comparable for both sexes. The finding of a study of 4–6 year old children in New Zealand that parental asthma and atopic dermatitis are only associated with asthma in boys could not be confirmed by our data.

The differentiation between allergies of the mother and of the father shows that for asthma in the child only paternal asthma has a strong influence, while for allergic rhinitis and atopic dermatitis the influence of the mother is more decisive. The estimated differences between the influence of the mother and of the father must be interpreted with caution, as 80% of the questionnaires were filled out by mothers. Allergies of the mother are probably overrepresented and allergies of the fathers may include more of the acute and severe type.

A cross sectional study of atopic disease in 1325 school entrants found that children whose parents have an identical type (respiratory or skin) of atopic disease more frequently develop an atopic disease (72%) than children with nonidentical types of allergies in the parents (21%). We could not find a difference in the prevalence of allergies between the whole group of children with both parents allergic (56%) and children of parents with an identical type of allergic manifestation (55%). But children with two allergic family members with an identical type of allergy have the highest risk of developing that type of allergy. Combinations with different types of allergies do not show a clear relationship to one form of allergy. Additive effects also increased the risk for other types of allergic manifestations.

The proved relationship between atopy of a sibling and atopy of the examined child, which exists independently of parental disease, cannot be explained by a simple hereditary model. The increase in prevalence of allergies in children with one affected sibling and no reported parental disease and the additional increase with three or more family members compared with the group with both parents allergic could be explained by an incomplete genetic penetrance.

Various other types of studies have provided additional insight into the genetic basis of allergies. The results of case-control studies,
which are based on clinical diagnosis, support
the relationship between parental atopy and
allergic disease, but due to the small numbers of
cases they do not allow differentiation of family
allergies.

The differences between monozygotic and
dizygotic twins and a tendency for the same type
of manifestations as evaluated in a large twin
study provides evidence for the genetic nature of
atopy.5 Concordance rates for asthma and
allergic rhinitis of monozygotic twins reared
apart are quite similar to those of twins reared
together, suggesting a substantial genetic com-
ponent for the development of asthma and
allergic rhinitis.22 But twin studies are unable to
identify the pattern of transmission.

Investigations of bronchial hyperreactivity
using the methacholine test in healthy family
members of asthmatics and in twins support the
hypothesis of a separate transmission of hyper-
reactivity23–25 which corresponds with the find-
ing of a separate transmission of asthma. Family
studies of serum IgE concentrations show a
clear concordance,17 19 and a genetic determina-
tion in the form of an IgE regulating gene has
been suggested.8 Investigations in extended
families have suggested that the propensity to
produce IgE in response to common, usually
inhaled, allergens is inherited as an autosomal
dominant linked to chromosome 11.26 27 But
the clinical expression depends on interaction
with other factors which may be, to some
extent, also genetic. The concentration of IgE in
an infant’s cord blood has been found in many
studies to predict the allergic predisposition of
the child. Presumably the cord blood IgE
concentration is a reflection of the genetic risk
of developing atopic disease.15 Recent data
about the IgG immune responsiveness to grass
pollen allergen suggest that it is strongly asso-
ciated with a specific HLA sequence.16

In the clinical situation it is not so important
to decide whether genetic transmission is
dominant, recessive, or polygenic but to estimate
the increased risk in an allergic family constel-
lation. The distinction between defined allergic
family situations in this study allows a differen-
tiated statement about the risk in certain family
situations, as well as the prediction of the
probable type of allergy.

Although various investigations have shown
the role of genetic factors in allergies, it should
be kept in mind that 23% of the children
without any familial disposition also develop
allergies. The study of this group of children
would be of special interest in exploring the role
of environmental factors.

This study was supported by the ‘Bayerischen Staatsministerium
für Landesentwicklung und Umweltfragen’. We would like to
dank Dr E Frhr von Loefelholz-Colberg, Professor Dr
W Lehmacher, and Dr T Nicolai for planning and supervising
this study; all 182 participating schools for their support of the
study, as well as the children and their parents, whose commit-
tment was essential for the survey.

1 Coca AF, Cooke RA. On the classification of the phenomena of
2 Bray GW. The hereditary factor of asthma and other allergies.
3 Marsh DG, Meyers DA, Bus BW. The epidemiology and
4 Kielland M. Prediction and prevention of atopic allergy.
Allergy 1982;37:463–73.
5 Edwards-Lubs ML. Allergy in 7000 twin pairs. Acta Allergol
1971;26:249–85.
6 Ferguson DM, Horwood LJ, Shannon FT. Parental asthma,
parental eczema and asthma in early childhood. Journal of
7 Blumenthal MN, Amos DB. Genetic and immunologic basis of
8 Levits R, Micnzer W, Klebeberger SR. A genetic approach to
the study of lung physiology: understanding biological
258:157–64.
9 McConnell KM, Roggmann KJ. Parental smoking, asthma,
eczema of older siblings, and family history of asthma
increase risk of bronchial asthma. Am J Dis Child 1986;
140:106–12.
10 Poets C. Atopy in children with and without a family history
of atopy. II. Skin reactivity. Acta Paediatr Scand 1989;
78:902–6.
11 Sibbald B, Horn MEC, Gregg IA. Family study of the genetic
basis of asthma and wheezy bronchitis. Arch Dis Child 1980;
12 Luoma R, Koivikko A, Viander M. Development of atopic
allergy and atopic dermatitis by the age of five years.
13 Kuester W, Petersen M, Christophers E, Goos M, Sterry W.
A family study of atopic dermatitis. Clinical and genetic
characteristics of 138 patients and 2151 family members.
14 von Mutius E, Dold S, Watt M, et al. Münchener Asthma-
und Allergiestudie. Prädvalenz der atopischen und
asthmatischen Erkrankungen im Kindesalter in Bayern.
15 Owensby DR. Environmental factors versus genetic deter-
minants of childhood inhalant allergies. J Allergy Clin
16 Kielland M. Atopic disease in seven-year-old children. Acta
17 Turner KJ, Rosman DL, O’Mahony J. Prevalence and
familial association of atopic disease and its relationship
to serum IgE levels in 1061 school children and their families.
International Archives of Allergy 1974;47:650–64.
18 Horwood LJ, Ferguson DM, Shannon FT. Social and
familial factors in the development of early childhood
19 Lebowitz MD, Barbee R, Burrows B. Family concordance
of atopy, asthma, and disease. J Allergy Clin Immunol
1984;73:259–64.
20 Sherman CR, Tossteden TD, Tager IB, Speizer FE, Weiss
ST. Early childhood predictors of asthma. Am J Epidemiol
21 Hagy GW, Sertipane GA. Risk factors for developing asthma
22 Hansson B, McGue M, Roitman-Johnson B, Segal NL,
Bouchard TJ, Blumenthal MN. Atopic disease and
immunglobulin E in twins reared apart and together. Am
23 Kung P, Godfrey S. Exercise-duffed bronchial ability in
monozygotic (identical) and dizygotic (non-identical) twins.
24 Hopp RJ, Bewsra AK, Watt GD, Nair NM, Townley RG.
Genetic analysis of allergic disease in twins. J Allergy Clin
25 Longo G, Strinati R, Poli F, Fumi F. Genetic factors in
141:531–4.
26 Cookson WO, Hopkin JM. Dominant inheritance of
atopic immunoglobulin E responsiveness. Lancet 1986;i:
86–8.
27 Cookson WO, Sharp PA, Faux JA, Hopkin JM. Linkage
between immunoglobulin E responses underlying asthma
28 Ansari AA, Shionoya N, Zullo P, Marsh DG. HLA-D
gene studies in relation to immune responsiveness to a grass