

Allergic Sensitization and Disease in Mother-Child Pairs from Germany: Role of Early Childhood Environment

C. Cramer^{a,b} U. Ranft^a J. Ring^c M. Möhrensclager^c H. Behrendt^d
H. Oppermann^e M. Wilhelm^f U. Krämer^a

^aInstitut für umweltmedizinische Forschung (IUF), Heinrich-Heine-Universität Düsseldorf, Düsseldorf,

^bKreisgesundheitsamt Aachen, Aachen, ^cDepartment of Dermatology and Allergy Biederstein and

^dZAUM – Center for Allergy and Environment GSF/TUM, Division of Environmental Dermatology and Allergy,

Technical University Munich, Munich, ^eLandesamt für Verbraucherschutz des Landes Sachsen-Anhalt, Halle, and

^fDepartment of Hygiene, Social and Environmental Medicine, Ruhr University Bochum, Bochum, Germany

Key Words

Allergic diseases · Allergic sensitizations · East-West German comparison · Mother-child correlation · Western lifestyle

Abstract

Background: Early childhood influences are important for the development of the allergic phenotype. In East Germany, tremendous lifestyle changes took place after 1990 and it can be hypothesized that the allergic phenotypes in mothers and their children are less similar than in West Germany. This was investigated in our study done in mothers and their 6-year-old children from East and West Germany in the year 2000. **Methods:** 1,393 mother-child pairs participated. A subgroup of 774 pairs gave blood for the determination of specific IgE. Regional differences in mother-child correlations and in prevalence of mother-child combinations with respect to allergic sensitization and disease were examined by logistic regression analysis. **Results:** The adjusted association in positive allergic sensitization between mothers and their children was not significant in East Germany (OR 1.23, 95% CI: 0.68–2.24) but highly significant in West Germany (OR 2.89, 95% CI: 1.73–4.80). The probability for the

combination of ‘negative’ mother and ‘positive’ child was significantly higher in East than in West Germany. **Conclusions:** Mother-child transmission of atopy predisposition can even be cancelled by environmental changes.

Copyright © 2007 S. Karger AG, Basel

Introduction

Early life (including prenatal) exposure to a combination of factors characterized as ‘Western lifestyle’ is considered most important for the development of allergic diseases [1, 2]. As long as no changes in lifestyle occur, early life exposure is similar in mothers and their children and the allergic phenotypes will be similar because of shared genetic and environmental factors. In East Germany however, the fast transition from a socialist economic system to a market economy within a few years after reunification caused a change in lifestyle, quickly adapting to Western lifestyle. As a result, children born in East Germany a few years after the fall of the Berlin wall may in part have been exposed to Western lifestyle factors already during their first years of life, whereas their parents had grown up under ‘Eastern’ living condi-

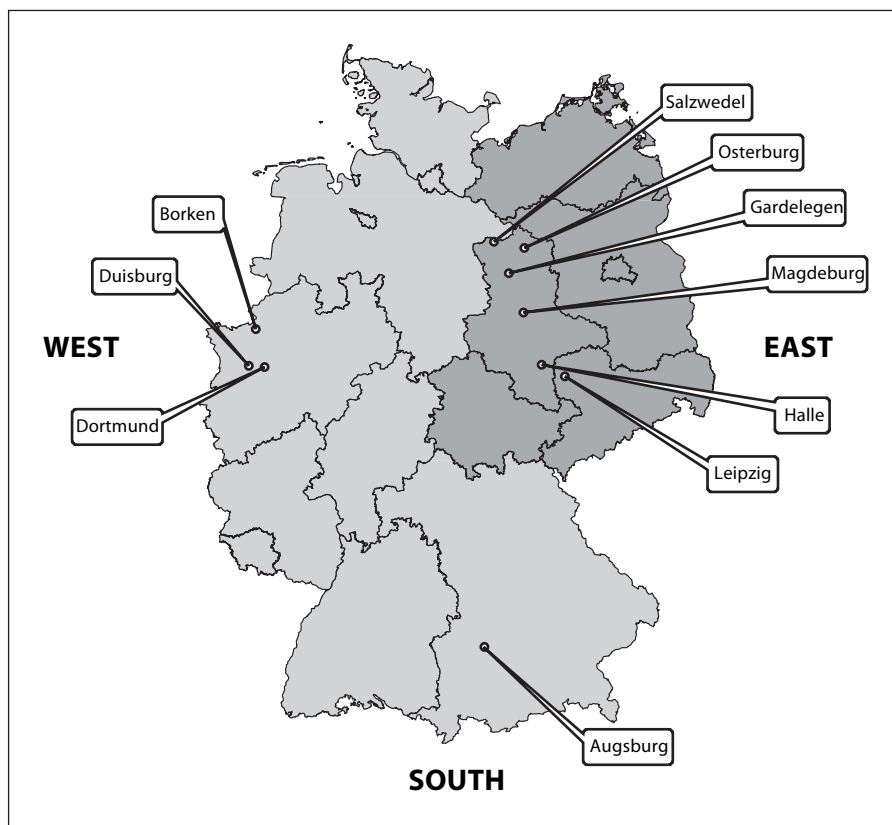


Fig. 1. Study areas in West, South and East Germany. Before 1990 the regions shaded in dark belonged to the former German Democratic Republic.

tions. This might be reflected in less strong mother-child correlations for allergic diseases in East Germany compared to other regions of Germany (West and South Germany), where no such changes took place. Therefore, the aim of this study was to compare the prevalence patterns of allergic diseases and specific sensitizations in mother-child pairs from East, West and South Germany investigated in 2000 and to show how far these findings go along with the hypothesis of a special importance of early life environmental exposure.

In 1990, allergic disease had been significantly less prevalent in East than in West Germany [3, 4]. Recent data indicate an upward trend of the prevalence rates of hay fever and allergic sensitizations in East German children reaching West German rates in the year 2000 [5–7]. In the parental generation, different environmental and lifestyle factors during childhood should have led to lower prevalence rates for the mothers of the 6-year-old children in East Germany compared with those in West Germany. As a result, East German children with allergies should more frequently have mothers without allergies than allergic children from West Germany. In other words, the proportion of the pair combination ‘mother without al-

lergy’ and ‘child with allergy’ ($M^- \wedge C^+$) is expected to be significantly higher 10 years after reunification in East than in West Germany, whereas the proportion of the combination ‘mother with allergy’ and ‘child with allergy’ ($M^+ \wedge C^+$) should be lower in the East. This can be formulated in mathematical terms of probability as:

$$(I) P[M^- \wedge C^+ | East] > P[M^- \wedge C^+ | West] \text{ and} \\ P[M^+ \wedge C^+ | East] < P[M^+ \wedge C^+ | West]$$

As the shift in the prevalence patterns is only expected for the group of children with allergy, the proportions of the other 2 possible combinations, i.e. ‘mother with allergy’ and ‘child without allergy’ ($M^+ \wedge C^-$) and ‘mother without allergy’ and ‘child without allergy’ ($M^- \wedge C^-$), are expected to be similar in East and West Germany:

$$(II) P[M^+ \wedge C^- | East] \approx P[M^+ \wedge C^- | West] \text{ and} \\ P[M^- \wedge C^- | East] \approx P[M^- \wedge C^- | West]$$

If early childhood exposure largely drives mother-child correlations in allergy phenotypes, then these correlations should be similar in children from West and South Germany which – as depicted in figure 1 – had not been part of the former German Democratic Republic. This

should be true, despite the known higher prevalence of allergic sensitizations in southern compared to western regions of Germany [8]. The composite hypothesis of the South-West comparison reads as follows:

$$(III) P[M^+ \wedge C^+ | \text{South}] > P[M^+ \wedge C^+ | \text{West}] \text{ and} \\ P[M^- \wedge C^- | \text{South}] < P[M^- \wedge C^- | \text{West}]$$

The proportions of the discordant mother-child pairs $M^+ \wedge C^-$ and $M^- \wedge C^+$ should be similar in both regions:

$$(IV) P[M^+ \wedge C^- | \text{South}] \approx P[M^+ \wedge C^- | \text{West}] \text{ and} \\ P[M^- \wedge C^+ | \text{South}] \approx P[M^- \wedge C^+ | \text{West}]$$

Methods

The data presented in this paper were collected in 2000 within the framework of 2 larger studies on school beginners in Germany. In East and West Germany, the study was part of a series of repeated cross-sectional studies on the health impact of air pollution (SAWO) after Germany's reunification from 1991 to 2000; in South Germany (in Augsburg), it was part of 2 repeated cross-sectional studies in 1996 and 2000 on air pollution and allergy and eczema morbidity (MIRIAM). A detailed description of subjects and methods has been presented elsewhere [4, 5, 9]. In the year 2000, the investigations of the about 6-year-old school beginners were supplemented with investigations of their mothers. Figure 1 depicts the study areas. These include cities as well as smaller rural towns (Salzwedel, Gardelegen, Osterburg and Borken).

Every school beginner and his or her mother from these pre-selected geographical areas was invited to participate in a questionnaire investigation and to donate a blood sample for testing allergic sensitization. The ethical committees of the Medical Associations of Saxony-Anhalt and Bavaria approved the studies. Written informed consent was obtained from the parents and mothers.

For all study areas, the applied methods to determine the prevalence of allergic diseases and sensitizations were identical. A standardized questionnaire which included the parental ISAAC core questionnaire [10] on asthma, rhinitis and eczema for 5- to 8-year-old children asked the parents about any diseases ever diagnosed by a physician as well as symptoms and, furthermore, about socioeconomic and environmental factors as potential confounders. Mothers additionally were asked about their own diagnoses and symptoms. Allergic sensitization was tested by determining specific immunoglobulin E (IgE) antibodies against common allergens in the blood serum by an enzyme immunoassay [Radio Allergo Sorbent Test (RAST), CAP-FEIA; Pharmacia & Upjohn, Uppsala, Sweden].

Only complete mother-child pairs with German nationality of the mother were analyzed in this report. This was done to not confound ethnic differences with East/West differences (very few non-German participants lived in East Germany).

Statistical Analysis

For assessing allergic diseases and sensitizations we defined 2 binary outcome variables. First, based on the information of the

questionnaire, participants were classified as having 'allergic diseases and symptoms' (or shortly 'allergies') either if they had ever had physician-diagnosed asthma, eczema or hay fever, or if they had experienced wheezing, attacks of sneezing with reddened eyes or a longer-lasting itchy skin rash in the last 12 months. Second, based on the results of the RAST, participants were classified as having 'allergic sensitization' if they had at least 1 specific sensitization (specific IgE ≥ 0.35 kU/l) against birch pollen, grass pollen, mugwort pollen, or cat or house dust mites.

Logistic regression was used to describe the association of 'allergic sensitization' and 'allergic diseases and symptoms' between children and their mothers. The results of this analysis are presented as raw and adjusted odds ratios (OR).

Furthermore, the prevalence patterns for 'allergic sensitization' and 'allergic diseases and symptoms' for the 4 different mother-child combinations $M^+ \wedge C^+$, $M^- \wedge C^+$, $M^+ \wedge C^-$ and $M^- \wedge C^-$ in East, West and South Germany were given and compared with logistic regression analysis. Additional variables (from a list of 15) were included into all regression models, if their prevalence was different between West and East or West and South Germany and if they were significantly ($p \leq 0.1$) associated with 1 of the 4 possible mother-child combinations. The dichotomous variable for urbanization (urban or rural study area) was always included into the regression models if applicable.

To test the composite hypotheses of the East-West and the South-West comparison given in the introduction [(I) and (III)], Holm's procedure for multiple testing was applied.

Statistical analyses were performed using the statistical analysis package SAS for Windows, version 8.2 (SAS Institute, Cary, N.C., USA).

Results

Participation and Response Rates

In the predefined areas 1,393 mother-child pairs with German nationality participated in the study. Referring to the children invited for school entrance examination, the response rate in the children's group was 70% in East Germany, 65% in West Germany and 71% in South Germany. A nonresponder analysis was performed in Leipzig ($n = 66$), Duisburg ($n = 289$) and Borken ($n = 104$), where nonresponders filled in a short questionnaire. The responding and nonresponding children did not differ with respect to any of the questions asked in the short questionnaire (gender, number of siblings, number of colds, and physician diagnoses of allergies, asthma and hay fever).

Complete information on all 6 items, each combined to the allergy indicator 'allergic diseases and symptoms', was available from 1,165 mother/child pairs. Not all mothers and children in this voluntary investigation gave blood. Therefore, the result of the RAST ('allergic sensitization') was known for 774 mother-child pairs (56% of 1,393). Furthermore, in the subgroup with a

Table 1. Prevalence of specific allergic sensitizations and diagnoses, symptoms of allergic diseases and frequencies of potential risk factors among German mothers and their children by region in Germany

	East		West		South	
	%	n	%	n	%	n
Mothers						
Allergic sensitization ¹	28.3	315	31.7	382	50.6**	77
Allergic diseases and symptoms	33.8**	473	43.2	579	45.1	113
Children						
Allergic sensitizations ¹	23.5	315	22.8	382	36.4*	77
Allergic diseases and symptoms	30.2	473	31.8	579	35.4	113
Living in an urban area ²	87.7***	610	70.0	639	100***	144
Male sex of child	51.6	610	47.7	639	54.9	144
Parental education ≤10 years school	55.2***	601	69.3	625	62.7*	137
Premature birth ³	6.6*, ⁴	602	9.2	621	3.5*, ⁴	143
Breastfeeding (at least 1 week)	90.0***	577	74.2	613	83.1*, ⁵	130
Age of the mother at birth of the child						
≤19 years ⁶	7.9***	610	3.1	639	2.1	142
≥33 years ⁷	9.5***	610	22.5	639	22.9	142
No siblings	35.0***	600	21.6	633	11.9*	137
Indoor dampness	8.0**	602	4.4	636	7.2	139
Current environmental tobacco smoke	39.4	597	36.2	630	22.4+, ⁸	143
Smoking of the mother during pregnancy	14.2**, ⁸	593	21.2	628	15.6	141
Environmental tobacco smoke exposure						
during the first 3 years of the child's life	29.7*, ⁸	600	35.6	633	18.3***	142
Child's father with allergy	16.0	563	18.2	614	27.7*	130
Bedroom sharing at time of study	37.0*, ⁴	593	41.1	633	52.4+, ⁸	126
Contact with pets at time of study	58.4	605	55.7	639	56.3	140

Significance in χ^2 test/Fisher's exact test when comparing with West Germany: + $p \leq 0.1$; * $p \leq 0.05$; ** $p \leq 0.01$; *** $p \leq 0.001$.

¹ To at least 1 tested allergen.

² At least 100,000 inhabitants.

³ As given in questionnaire.

⁴ Only significant for the subgroup with data of allergic sensitizations.

⁵ Not significant for the subgroup with data of allergic diseases and symptoms.

⁶ 5 percentile of distribution in East Germany 1991.

⁷ 95 percentile of distribution in East Germany 1991.

⁸ Not significant for the subgroup with data of allergic sensitizations.

RAST result, information on 'allergic diseases and symptoms' was missing in 109 mother-child pairs. One hundred and nineteen mother-child pairs had missing information on 'allergic diseases and symptoms' and 'allergic sensitization'. However, the subgroup with complete information did not differ from the whole group in respect to gender of child, education of parents and any allergy diagnoses and symptoms. Incomplete questionnaire information was significantly more prevalent in younger mothers; however, this was not related to the allergic outcomes.

Description of the Study Population and Potential Confounding Variables

The distributions of prevalence rates of 'allergic sensitization' and 'allergic diseases and symptoms' in mothers and children as well as the distributions of sociodemographic and environmental factors are listed in table 1. Generally the prevalence of the 2 outcome measures was higher in mothers than in children. Twenty-eight to 51% of the mothers had at least 1 allergic sensitization, whereas the proportion in children was between 23 and 37%. Up to 45% of the mothers and 35% of the children had 'allergic diseases and symptoms'. Mothers in South Ger-

Table 2. Allergic sensitizations and diagnoses and symptoms of allergic diseases in children dependent on allergic sensitization and symptoms of allergic diseases in mothers

	East		West		West (urban) ¹		South	
	OR _{raw}	OR _{adj.}	OR _{raw}	OR _{adj.}	OR _{raw}	OR _{adj.}	OR _{raw}	OR _{adj.}
Allergic sensitization ² subjects	1.10 (0.62–1.95) 315	1.23 (0.68–2.24) 312	3.09*** (1.88–5.06) 382	2.89*** (1.73–4.80) 373	3.39*** (1.87–6.13) 264	3.17*** (1.72–5.86) 256	2.40 ⁺ (0.93–6.26) 77	2.39 (0.87–6.59) 72
Allergic diseases and symptoms ³ subjects	1.89** (1.26–2.84) 473	1.94** (1.27–2.97) 441	2.80*** (1.95–4.02) 579	2.45*** (1.68–3.58) 540	3.16*** (2.06–4.84) 404	2.89*** (1.84–4.56) 375	2.17 ⁺ (0.99–4.77) 113	2.74* (1.09–6.91) 95

Results of logistic regression with raw and adjusted OR presented. Figures in parentheses are 95% CI. ⁺ p ≤ 0.1; * p ≤ 0.05; ** p ≤ 0.01; *** p < 0.001.

¹ Urban level of the West German region only.

² OR and 95% CI are adjusted for urbanization level (only for East-West comparison), parental education and age of the mother at birth of index child.

³ OR and 95% CI are adjusted for urbanization level (only for East-West comparison), parental education, breastfeeding, siblings and indoor dampness.

many (Augsburg) more frequently had allergic sensitizations than mothers in West and East Germany. ‘Allergic diseases and symptoms’ were less frequent in the group of East German mothers than in mothers from West and South Germany. The proportion of children with at least 1 allergic sensitization was higher in Augsburg than in western parts of Germany and in East Germany.

Several sociodemographic and environmental factors differed significantly in the subgroups as indicated in table 1. By design, more children from urban areas were included in the study in East Germany than in West Germany. Children from the East German study areas further differed in some characteristics from West/South German children: they were more often breastfed, less often had siblings, their parents were better educated and their mothers were younger.

Allergies and Allergic Sensitizations in Mothers as Risk Factor for Allergies and Sensitization in Children

To study the relation of allergies and allergic sensitizations in children with those in their mothers, a logistic regression analysis was used. The results stratified by region are shown in table 2. In East Germany the OR of the effect of maternal atopy as risk factor for the development of allergic sensitizations in the child did not demonstrate a significant association. In contrast, a distinct association was shown for West Germany and even a stronger one for urban areas in West Germany, i.e. the odds for an allergic sensitization were 2–3 times higher for children

with an atopic mother than for those with a nonatopic mother. The OR in Augsburg was slightly lower but similar to that in West Germany. These associations were additionally evaluated for all single allergens (cat, house dust mites and grass, mugwort or birch pollen) separately. Whereas all of these OR were significantly greater than 1 in West Germany, this was not the case for any OR in East Germany. To analyze possible effect modification by variables with characteristic differences between East and West/South Germany, data were stratified by education of parents, breastfeeding, age of the mother (<30 and ≥30 when child was born) and number of siblings (no siblings, at least 1 sibling), and the analysis was repeated in each of these subgroups. The OR emerging in the subgroups were quite similar to those in the whole group, indicating no effect modification.

‘Allergic diagnoses and symptoms’ were also less strongly associated between mothers and their children in East than in West and South Germany, but in contrast to the results concerning sensitization, all OR were significantly greater than 1.

Regional Comparison of Mother and Child Combinations in Sensitizations and Allergies

Table 3 presents the crude prevalence of the 2 outcome measures in mother-child pairs by region. As Augsburg, the only study area in South Germany, is an urban area, the comparison with West Germany was restricted to Duisburg and Dortmund, the urban areas in West Germany.

Table 3. Prevalence of specific allergic sensitizations and diagnoses and symptoms of allergic diseases in German mother-child pairs by region

	East		West		West (urban)		South	
	mother-	mother+	mother-	mother+	mother-	mother+	mother-	mother+
Allergic sensitizations								
Child-	174 (55.2%)	67 (21.3%)	219 (57.3%)	76 (19.9%)	148 (56.1%)	55 (20.8%)	28 (36.4%)	21 (27.3%)
Child+	52 (16.5%)	22 (7.0%)	42 (11.0%)	45 (11.8%)	27 (10.2%)	34 (12.9%)	10 (13.0%)	18 (23.4%)
Total	315 (100%)		382 (100%)		264 (100%)		77 (100%)	
Allergic diseases and symptoms								
Child-	233 (49.3%)	97 (20.5%)	256 (44.2%)	139 (24.0%)	174 (43.1%)	93 (23.0%)	45 (39.8%)	28 (24.8%)
Child+	80 (16.9%)	63 (13.3%)	73 (12.6%)	111 (19.2%)	51 (12.6%)	86 (21.3%)	17 (15.0%)	23 (20.4%)
Total	473 (100%)		579 (100%)		404 (100%)		113 (100%)	

- = No 'allergic sensitization'/'allergic diseases and symptoms'; + = 'allergic sensitization'/'allergic diseases and symptoms' present.

Table 4. Regional differences in discordant and concordant mother-child pairs with respect to specific allergic sensitizations and diagnoses and symptoms of allergic diseases

	East-West OR (95% CI)	South-West (urban) ¹ OR (95% CI)
Atopic sensitizations²		
(n = 685)	(n = 328)	
Mother- and child+	1.68 (1.05–2.68)*	1.47 (0.66–3.25)
Mother+ and child-	0.87 (0.59–1.29)	1.44 (0.77–2.68)
Mother+ and child+	0.50 (0.29–0.89)*	1.94 (1.00–3.77)*
Mother- and child-	1.08 (0.78–1.48)	0.43 (0.25–0.75)**
Allergic diseases and symptoms³		
(n = 981)	(n = 470)	
Mother- and child+	1.39 (0.94–2.09)**	1.00 (0.50–2.01)
Mother+ and child-	0.77 (0.55–1.07)	0.99 (0.58–1.71)
Mother+ and child+	0.53 (0.36–0.76)***	0.96 (0.55–1.68)
Mother- and child-	1.48 (1.12–1.95)**	1.03 (0.64–1.67)

Results of logistic regression with OR referring to the combined hypotheses formulated in the introduction given in bold. - = No 'atopic sensitization'/'allergic diseases and symptoms'. + = 'atopic sensitization'/'allergic diseases and symptoms' present. Holm-adjusted p values: + p ≤ 0.1; * p ≤ 0.05; ** p ≤ 0.01; *** p < 0001.

¹ Urban level of the West German region only.

² OR and 95% CI are adjusted for urbanization level (only for East-West comparison), parental education and age of the mother at birth of index child.

³ OR and 95% CI are adjusted for urbanization level (only for East-West comparison), parental education, breast feeding, siblings and indoor dampness.

The results of the logistic regression analysis are given in table 4. The odds for the combination M⁻ ∧ C⁺ were higher in East than in West Germany, whereas the opposite was found for the combination M⁺ ∧ C⁺. The result is also significant after applying Holm's procedure for multiple testing. Contrary to our expectation, the odds for mother-child pairs with both free of 'allergic diseases

and symptoms' (M⁻ ∧ C⁻) were higher in East than in West Germany. Comparing sensitization between West and South Germany, the odds for the combination M⁺ ∧ C⁺ were higher in South than in West Germany and the odds for the combination M⁻ ∧ C⁻ were lower in South than in West Germany. This confirms the generally higher prevalence of sensitization in both genera-

tions in South Germany and thereby confirms hypothesis (III) formulated in the introduction. The result is also significant after applying Holm's procedure for multiple testing. Contrary to our expectation, no South/West differences could be detected for the outcome measure 'allergic diseases and symptoms'.

Discussion

In this study we compared the mother-child concordance with regard to allergic diseases, symptoms and sensitizations in different regions of Germany in the year 2000. The concordance was low and even not significant in East Germany where environmental changes were introduced in 1990. Concordance in West and South Germany, where no changes took place, was high.

East-West Comparison

It is well known that genetic factors influence the susceptibility to allergic sensitizations and diseases, but environmental factors seem to play a substantial role for the manifestation of atopy and atopic diseases [11, 12]. Especially influences characteristic of a 'Western society' are discussed to promote the development of allergy [2]. We found, that the adoption of Western lifestyle in East Germany after reunification led to noncorrelating allergic sensitization in mothers and their children and this was true irrespective of the type of sensitization.

Our results support the concept of a 'sensitization window' early in life. Accordingly, the tremendous changes in living and social conditions in East Germany after reunification have promoted the development of allergic diseases and sensitizations especially in children which were born after the fall of the Berlin wall, whereas their mothers seem to be less affected as the lifestyle changes had not occurred during their early childhood. Children of nonsensitized mothers were more often sensitized while children of sensitized mothers were less often sensitized than in West Germany, demonstrating that environmental influences early in life may override genetic influences. However none of the lifestyle factors identified as characteristic for children living in East Germany modulated mother-child correlations and may explain the different correlations. With regard to 'allergic diseases and symptoms', the higher probability for the combination $M^- \wedge C^-$ in East Germany might be due to the fact that changes in living conditions in East Germany occur only gradually, so one might expect that former disease patterns partly still continue in the year 2000.

Another explanation could be a higher underreporting rate of nonallergic mothers with respect to their children's allergies in East Germany compared to West Germany.

South-West Comparison

With regard to allergic sensitizations, differences between South and West Germany were only found for concordant mother-child pairs, thus confirming generally higher prevalence of sensitization in South than in West Germany. Furthermore, the OR for the mother-child association was about the same in West and South Germany, demonstrating similar transmission of the allergic predisposition in these parts of Germany. In contrast to the situation in East Germany, we did not assume substantial differences in early life influences between West and South Germany. The results for 'allergic diseases and symptoms' were different. This may indicate that a possibly existing German South-West gradient is restricted to allergic sensitizations, whereas prevalence patterns for manifest symptoms and diseases are equal in Augsburg and other urban regions in West Germany. However, our results for the South-West comparison have to be interpreted with caution, as South Germany is only represented by 1 study area (Augsburg). Furthermore, the sample size in Augsburg is comparably small and the possibility of chance errors has to be considered.

Strengths and Possible Limitations of the Study

A major strength of this investigation is the fact that our results are not only based on self- and parental-reported information about allergies, but also on so-called objective measures like RAST results. However, our outcome measure 'allergic diseases and symptoms' is questionnaire based. Therefore, a number of potential systematic errors have to be taken into consideration. The results may have been biased by the frequency of consultations, by an increased public awareness or by changes in diagnostic behavior [13, 14]. These influences might be causal for some of the above mentioned inconsistencies we have seen for the results of the outcome measure 'allergic diseases and symptoms' in comparison with the results for the outcome measure allergic sensitization'.

Another problem has to be considered regarding our questionnaire data. Allergic diseases or symptoms in a child may increase recall among mothers with an affected child and, therefore, give rise to a recall bias [15]. Furthermore, response bias is likely to occur as a result of a systematic drop out of nonatopic mothers, for example, who might be less interested in the study.

Although the original data we used from SAWO and MIRIAM were more detailed, we created pooled outcome measures to increase the case number and accordingly the power of our study. Generally, pooled outcome measures go along with a loss of information and do not allow detailed analyses. On the other hand, there is a characteristic age-dependent sequence of manifestation and remission of clinical symptoms as well as of certain IgE responses to environmental allergens ('atopic/allergic march') which has to be taken into consideration; e.g. an eczema in childhood may be reflected as hay fever or asthma in adulthood [16]. Therefore, with regard to mother-child concordance it seems advantageous to use pooled data, as they are more comprehensive and insensitive to age-dependent changes in special allergic diseases.

Conclusion

Our findings demonstrate that influences in early childhood are most important for allergy development. The manifestation of atopy in individuals with genetic

predisposition is largely determined and modified by environmental factors early in life. Mother-child transmission of atopy predisposition can even be cancelled by environmental changes.

Acknowledgements

The authors thank the local health departments in Augsburg, Borken, Cologne, Duisburg, Essen, Halle, Leipzig, Magdeburg, Osterburg and Salzwedel for their assistance in planning and organizing the study and their allowance to couple our investigations to the official school entrance examinations; they also thank Georg Eberwein for his help in organizing the study in West Germany. Thanks to Johanna Grosch (Munich) for the determination of specific IgE.

Thanks also to Dorothea Sugiri and Elke Link for the excellent data management as well as Gabriele Seitner and Tamara Schikowski (all IUF) for their help with the manuscript and language corrections.

The study was financially supported by the NRW State Ministry of the Environment, by the Saxony-Anhalt State Ministry of Social Affairs and by a grant (No. 01 EE 9501/2) from the Federal Ministry of Technology.

References

- 1 Matricardi PM: Prevalence of atopy and asthma in eastern versus western Europe: why the difference? *Ann Allergy Asthma Immunol* 2001;87:24–27.
- 2 Ring J: Allergy and modern society: Does 'Western life style' promote the development of allergies? *Int Arch Allergy Immunol* 1997; 113:7–10.
- 3 von Mutius E, Martinez FD, Fritzsche C, Nicolai T, Roell G, Thiemann HH: Prevalence of asthma and atopy in two areas of West and East Germany. *Am J Respir Crit Care Med* 1994;49:358–364.
- 4 Krämer U, Behrendt H, Dolgner R, Ranft U, Ring J, Willer HJ, Schlipkötter HW: Airway diseases and allergies in East and West German children during the first five years after reunification: time trends and the impact of sulfur dioxide and total suspended particles. *Int J Epidemiol* 1999;28:865–873.
- 5 Krämer U, Link E, Oppermann H, Ranft U, Schäfer T, Thriene B, Behrendt H, Ring J: Die Schulanfängerstudie in West- und Ostdeutschland (SAWO): Trends von Allergien und Sensibilisierungen 1991–2000. *Das Gesundheitswesen* 2002;64:657–663.
- 6 Heinrich J, Hoelscher B, Frye C, Meyer I, Wjst M, Wichmann HE: Trends in prevalence of atopic diseases and allergic sensitization in children in Eastern Germany. *Eur Respir J* 2002;19:1–7.
- 7 Weiland SK, von Mutius E, Hirsch T, Fritzsche C, Werner B, Hüsing A, Stender M, Renz H, Leupold W, Keil U: Prevalence of respiratory and atopic disorders among children in East and West of Germany five years after unification. *Eur Respir J* 1999;14:862–870.
- 8 Ring J, Wenning J (eds): *Weissbuch: Allergie in Deutschland*. München, Urban & Vogel, 2000.
- 9 Krämer U, Lemmen CH, Behrendt H, Link E, Schäfer T, Scherer G, Gostomzyk J, Ring J: The effect of environmental tobacco smoke on eczema and allergic sensitization in children. *Br J Dermatol* 2004;150:111–118.
- 10 Asher MJ, Keil U, Anderson HR, Beasley R, Crane J, Martinez FD, Mitchell EA, Pearce N, Sibbald B, Stewart AW, Strachan D, Weiland SK, Williams HC: International Study of Asthma and Allergies in Childhood (ISAAC): rationale and methods. *Eur Respir J* 1995;8:483–491.
- 11 Strachan DP, Wong HJ, Spector TD: Concordance and interrelationship of atopic diseases and markers of allergic sensitization among adult female twins. *J Allergy Clin Immunol* 2001;108:901–907.
- 12 Nolte H, Backer V, Porsbjerg C: Environmental factors as a cause for the increase in allergic disease. *Ann Allergy Asthma Immunol* 2001;87:7–11.
- 13 Magnus P, Jaakkola JJ: Secular trend in the occurrence of asthma among children and young adults: critical appraisal of repeated cross sectional surveys. *BMJ* 1997;314:1795–1799.
- 14 Wieringa MH, Vermeire PA, Brunekreef B, Weyler JJ: Increased occurrence of asthma and allergy: critical appraisal of studies using allergic sensitization, bronchial hyperresponsiveness and lung function measurements. *Clin Exp Allergy* 2001;31:1553–1563.
- 15 Kulig M, Bergmann R, Edenharter G, Wahn U: Does allergy in parents depend on allergy in their children? Recall bias in parental questioning of atopic diseases. *Multicenter Allergy Study Group. J Allergy Clin Immunol* 2000;105:274–278.
- 16 Wahn U: Der allergische Marsch. *Allergologie* 2002;25:66–73.