

The excess of atopic eczema in East Germany is related to the intrinsic type

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Summary

Background Prevalence data for atopic eczema based on a dermatological examination have not so far been available for East and West Germany. Possible differences in the proportions of extrinsic and intrinsic types of eczema, and how far these could explain differences in the prevalence of eczema, need to be clarified.

Objectives To compare the prevalence of atopic eczema in pre-school children between different locations in East and West Germany, and over a period of 7 years, at three time points. Additionally, to determine the proportions of intrinsic and extrinsic types of eczema by taking skin prick test reactivity into account.

Methods Repeated cross-sectional studies in 1991, 1994 and 1997 in 5–6-year-old pre-school children at five different locations in West Germany ($n = 2075$) and six in East Germany ($n = 1926$) were carried out. Individuals with eczema were identified by an examination performed by physicians of the Department of Dermatology. In addition, a skin prick test and a standardized questionnaire were used.

Results The overall prevalence of atopic eczema in these children was 10.4%. At all three times of investigation (1991, 17.5% vs. 11.2%; 1994, 12.6% vs. 8.7%; 1997, 11.2% vs. 4.5%) and in the total group (12.9% vs. 8.2%), the prevalence was significantly higher in East than in West Germany. After controlling for influences of sex, parental history of atopic diseases, observer and socio-economic status in multiple logistic regression analyses, these differences remained significant for 1991, 1994 and for the overall group (odds ratio, OR 1.78, 95% confidence interval, CI 1.43–2.21). Girls (OR 1.56, 95% CI 1.27–1.92) and children whose parents had a higher level of school education (OR 1.17, 95% CI 1.00–1.37) were affected more frequently. Of all children, 26.6%, and of those with eczema, 41.9% exhibited at least one reaction in the prick test (OR 2.21, 95% CI 1.75–2.80; sensitization in eczema vs. no eczema). Whereas 50.4% of the children with eczema in West Germany were sensitized, only 36.5% of the diseased children in East Germany reacted positively in the prick test (OR 1.77, 95% CI 1.12–2.79).

Conclusions These results are in accordance with findings regarding allergic sensitization and hay fever and might indicate that factors other than allergy are responsible for the higher prevalence of atopic eczema in East Germany.

Key words: atopic eczema, epidemiology, geographical variation, prick testing

The world-wide increase of atopic diseases (allergic bronchial asthma, allergic rhinoconjunctivitis, atopic eczema/dermatitis) in Western countries is so far unexplained.¹ Hypothetical considerations include

genetic, environmental and individual parameters among which 'life-style factors' have been summarized as most likely candidates contributing to this trend.^{2–5} In this context the reunification of Germany in 1990 offered a unique opportunity to study a kind of political experiment ('experimentum dicturae'), in which populations of an ethnically similar background and under

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similar climatic conditions were exposed, beside other unequal living conditions, to different degrees and patterns of air pollution. So far these studies have revealed some unexpected results. Allergic sensitization and hay fever, for example, were found to be more frequent in West Germany.^{6–10} In most of these studies the number of locations was restricted to a comparison of one single town each in East and West. Little attention has been paid to atopic skin diseases, including eczema, but according to questionnaire-based investigations no significant differences between East and West German cities have been reported. We have conducted a dermatological examination of about 4000 pre-school children at three different time points between 1991 and 1997 in multiple locations both in East and West Germany. Thereby we were able to compare the prevalences of atopic eczema in representative study sites and with a longitudinal perspective. Furthermore, we determined the proportions of an 'extrinsic' and an 'intrinsic' type of atopic eczema according to concomitant allergic sensitization as measured by skin prick test.

Subjects and methods

The investigations of this repeated cross-sectional study took place in five locations in the West German Federal State of North Rhine-Westphalia and six regions in the East German Federal State of Saxony-Anhalt between the months February and May of the years 1991, 1994 and 1997. Locations and sample size are given in Table 1. The response regarding the dermatological examination ranged between 66.0% in 1991 and 76.2% in 1994 (1997: 70.4%). The gender ratio was balanced at all three time points (female: 47.5–49.2%). All parents whose 5–6-year old children were scheduled for the compulsory school entrance examination were contacted and asked for participation in this study using the same invitation letter over the study years. Written parental consent and permission of the Ethical Committee of the Ärztekammer Saxony-Anhalt were obtained. A standardized questionnaire was mailed to the parents and returned at the time of examination, which was performed at the local public health departments. By design, the observers rotated from location to location, and a minimum of two observers examined at each study site consecutively. The investigators followed a standardized examination protocol to assure comparable assessments and were supervised part-time by personnel who did the training.

Dermatological examination

All children underwent a standardized dermatological examination while wearing their underpants only. These examinations were done by experienced and specially trained physicians of the Departments of Dermatology of Hamburg and Munich University (1991 and 1997, $n = 19$; 1994, $n = 10$). All physicians received additional training in using the standardized record files and the instrument for severity assessment (SCORAD). Cases of atopic eczema were then diagnosed on a clinical basis. In addition, the extent was expressed as a percentage of the body surface; the degree of intensity (absent, mild, moderate, prominent) of six typical morphological skin features (erythema, oedema, oozing, lichenification, excoriation and dryness) was recorded. Extrinsic eczema was defined to be present in children who exhibited at least one positive reaction in the prick test.

Skin prick test

A standardized skin prick test was performed on the forearm of the children. In all years the four common aeroallergens birch pollen, grass pollen, house dust mite and cat dander, and two food allergens (hen egg, cow milk), were tested. Additionally, mugwort pollen and *Cladosporium* were tested in 1994 and 1997. In the first year we used a multipuncture device (Stallerkit, Stallergènes, Allmed-Pharma, Alpen, Germany), which was loaded with the allergens and with codeine phosphate and physiological saline as controls. Since 1994 a conventional lancette prick test (ALK-Scherax, Hamburg, Germany) with histamine as positive control was used. Results were read after 15 min and assessed as positive if the weal diameter was 2 mm or greater. Most children who underwent the dermatological examination also participated in the skin prick test; the proportion having prick tests was no different between East (91.4%) and West (92.9%) Germany. Results with positive reactions to saline or those which exhibited no positive reaction to any test (including the histamine/codeine phosphate controls) were excluded from further analyses. Furthermore, the readings of one observer each in 1994 ($n = 117$) and 1997 ($n = 88$) were excluded because of an unusual high frequency of positive readings (53.8 and 83%), which was not comparable with the results of other observers at the same location. Valid prick test readings from a total of 3061 children were included in the final analysis.

Table 1. Prevalence of atopic eczema (%) in 4001 pre-school children in East and West Germany during 1991–97 by single locations

Location	West Germany					East Germany					
	Duisburg N	Duisburg S	Essen	Cologne	Borken	Halle	Merseburg	Magdeburg	Gardelegen	Salzwedel	Osterburg
1991	5.7 (6/106)	7.3 (19/259)	15.3 (28/183)		14.6 (37/253)	17.5 (50/285)					
1994				7.3 (18/246)	10.1 (26/257)	14.6 (32/219)	13.4 (17/127)	11.5 (43/374)	9.1 (11/121)	14.4 (24/167)	
1997	4.1 (8/193)	6.3 (9/144)	3.0 (5/169)		4.9 (13/265)	11.2 (23/205)		13.8 (22/159)	8.6 (8/93)	11.7 (14/120)	7.1 (4/56)

Questionnaire

A standardized questionnaire was mailed before the actual examination. It covered the personal and parental history of atopic diseases (asthma, hay fever, atopic eczema), including a question regarding a history of physician-diagnosed eczema. The socio-economic status was approximated by the level of parental school education and transformed into three categories (< 10 years, = 10 years, > 10 years).

Statistical analysis

To compare effects in East and West Germany the single locations were transformed into a dichotomous variable. Beside descriptive statistics, χ^2 -tests for trend were performed when appropriate. Multiple analysis of variance (MANOVA) techniques was used to investigate observer influences within West Germany in 1991 where data on observer were not available for the East German location of Halle. We report odds ratios (ORs) and the corresponding 95% confidence intervals (CIs) as measures of association and stability. Multiple logistic regression analyses were performed for each single year and the entire population. Actual diagnosed atopic eczema was included as a dependent variable, and sex, parental history of allergic diseases, location (East/West), observer and parental school education were taken as independent variables. As data on observer status were not available for all locations in 1991, the model for this year and the calculation for the entire group was not controlled for observer.

Results

Prevalence of atopic eczema in East and West Germany

In total, 4001 children were examined during the years 1991–97. Of these, 10.4% exhibited actual lesions of atopic eczema. The prevalence data and sample size for each location are given in Table 1. The prevalence was

found to be significantly higher in East (12.9%) as compared with West (8.2%) Germany. Significant differences between East and West Germany occurred in all 3 years of investigation. The corresponding prevalence data (percentages) for the total sample, for East and for West Germany in the single years were: 1991 (12.9, 17.5, 11.2), 1994 (11.3, 12.6, 8.7) and 1997 (7.5, 11.2, 4.5). When adjusting for important confounders such as sex, parental history of allergic diseases, parental school education and observer in logistic regression models, these differences remained significant for the years 1991, 1997 and the total group (Table 2). When testing for differences between locations and observers within West Germany in 1991 there was no indication for heterogeneity between observers ($P = 0.47$), whereas significant differences within locations were observed ($P = 0.005$). Significant influences of the investigators were also not observed in the regression models for 1994 and 1997.

History of atopic eczema

Of all children, 15.3% had a history of physician-diagnosed eczema. There was a significant higher overall cumulative incidence of reported eczema in East (18.0%) as compared with West (12.8%) Germany (OR 1.50, 95% CI 1.27–1.77). The corresponding data (%) of cumulative incidence for the overall group, for

Table 2. Differences in prevalence of atopic eczema in pre-school children in East and West Germany during 1991–97

East vs. West Germany	Crude OR	Adjusted OR ^a
1991	1.68 (1.13–2.49)	1.82 (1.22–2.71)
1994	1.50 (1.03–2.19)	1.44 (0.99–2.12)
1997	2.66 (1.71–4.13)	1.88 (1.01–3.50)
1991–97	1.66 (1.35–2.06)	1.78 (1.43–2.21)

OR, odds ratio; 95% confidence interval in parentheses. ^aAdjusted for sex, parental history of atopic diseases, socio-economic status (parental school education), observer (in 1994 and 1997) and year of investigation (in 1991–97).

Table 3. Prevalence of allergic sensitization (%) in pre-school children with and without atopic eczema from East and West Germany in different years of investigation

Year	West Germany			East Germany			Total			
	Eczema	No eczema	OR (95% CI)	Eczema	No eczema	OR (95% CI)	Overall	Eczema	No eczema	OR (95% CI)
1991	54.8	35.3	2.22 (1.37–3.62)	42.9	26.1	2.12 (1.07–4.22)	35.2	50.4	32.8	2.08 (1.42–3.07)
1994	51.6	22.9	3.59 (1.58–8.18)	38.3	25.8	1.78 (1.10–2.87)	27.0	41.6	24.9	2.15 (1.43–3.22)
1997	34.6	17.5	2.50 (0.99–6.19)	29.4	17.4	1.98 (1.08–3.62)	18.5*	30.9	17.4	2.12 (1.29–3.46)
1991–97	50.4	26.3	2.84 (1.97–4.10)	36.5	22.6	1.97 (1.43–2.71)	26.6	41.9	24.6	2.21 (1.75–2.80)

OR, odds ratio; CI, confidence interval; *trend test $P < 0.0001$.

East and for West Germany were: 1991 (13.4, 16.0, 12.5; OR 1.33, 95% CI 0.89–1.97), 1994 (14.8, 15.9, 13.0; OR 1.27, 95% CI 0.98–1.64) and 1997 (17.6, 23.4, 12.8; OR 2.07, 95% CI 1.56–2.76).

Confounding factors

Girls suffered significantly more often from atopic eczema than boys. These differences were significant in each single year and in the total group after adjustment for several confounders (12.2% vs. 8.7%, OR 1.56, 95% CI 1.27–1.92).

We also observed a strong impact of parental school education on the prevalence of this skin disease. In bivariate analysis a significant linear trend to a higher prevalence of eczema with increasing length of school education (< 10 years, 10 years, > 10 years) was revealed (5.7%, 10.4%, 11.6%; trend test $P = 0.0004$). The association held true in regression analysis of the total group (OR 1.17, 95% CI 1.00–1.37).

The parental history of allergic diseases influenced the prevalence of eczema in the children significantly in the groups of 1991 (OR 1.61, 95% CI 1.09–2.36) and 1994 (OR 2.04, 95% CI 1.43–2.90). No significant effect was detected in 1997 (OR 1.06, 95% CI 0.68–1.66) or in the overall group (OR 1.22, 95% CI 0.98–1.52).

Intrinsic and extrinsic eczema

Allergic sensitization to common aeroallergens and food allergens as measured by skin prick test was

demonstrated in 26.6% of all children. Those with current atopic eczema had a significantly higher frequency of positive tests (41.9%) than those without current skin involvement (24.6%). This difference was significant throughout all years of investigation as well as in the entire sample (Table 3).

The percentage of extrinsic eczema, however, was found to be as low as 30.9% in 1997 and did not exceed 41.9% in the total population. We furthermore observed an overall decreasing trend in the prevalence of positive prick tests over the years. This trend was obvious in both parts of Germany. When analysing extrinsic and intrinsic eczema in East and West Germany it became clear that the percentage of extrinsic eczema was consistently and significantly higher in West Germany (50.4%) as compared with East Germany (36.5%). While the overall prevalence of extrinsic eczema was not different (West 4.8%, East 4.9%), the prevalence of intrinsic eczema was found to be almost twice as high in East (8.5%) as compared with West (4.7%) Germany (Table 4).

Discussion

In this study we have determined the prevalence of atopic eczema in pre-school children at various locations in East and West Germany between 1991 and 1997 by a dermatological examination and have further classified intrinsic and extrinsic eczema by taking prick test reactivity into account. The major results were of three kinds. The prevalence of atopic eczema was found to be consistently higher in East

Table 4. Prevalence of extrinsic and intrinsic atopic eczema (%) in pre-school children from East and West Germany in different years of investigation

Year	West Germany			East Germany			Intrinsic eczema East vs. West OR (95% CI)
	Extrinsic	Intrinsic	Overall	Extrinsic	Intrinsic	Overall	
1991	6.9	5.6	12.5	7.8	10.3	19.0	1.61 (0.75–3.50)
1994	5.2	4.9	10.1	5.1	8.3	13.4	1.72 (0.70–4.21)
1997	1.8	3.3	5.1	3.3	8.1	11.4	1.27 (0.44–3.67)
1991–97	4.8	4.7	9.5	4.9	8.5	13.4	1.77 (1.12–2.79)

OR, odds ratio; CI, confidence interval.

Germany. The percentage of extrinsic eczema was 41.9% overall and was significantly lower in East Germany. Over the study period the point prevalence of atopic eczema has decreased in both parts of Germany.

This is so far the only study on atopic eczema in East and West Germany that is based on an actual dermatological examination. Existing diagnostic criteria for atopic eczema have been validated against actual dermatological examination.^{11–14} In our study multiple trained physicians of University Departments of Dermatology performed skin examinations, and analyses of variance did not reveal any significant influence of interobserver variability.

The skin examinations may have missed potential cases without current overt skin changes. However, the clinical examination data and the reported lifetime cumulative incidence both showed the same East/West difference, suggesting that they are valid. This may also indicate that a differential influence of chronicity in both parts of Germany is unlikely. Overall, this outcome assessment may be considered as a strength of the study.

The prick test readings of two investigators were excluded because of unreliably high results. According to these changes the effect estimates of the association between eczema and sensitization as given in Table 3 have changed slightly for East Germany in 1994 (uncorrected OR 2.19, 95% CI 1.52–3.15) and for West Germany in 1997 (OR 1.65, 95% CI 0.74–3.63). The overall result and conclusion, however, was not affected by this correction.

Multiple urban as well as rural regions of two federal states within a similar degree of latitude were compared, which allowed for a more representative estimate of location-related differences. We approached a large population and achieved a reasonable response (which did not differ between East and West Germany), so the sample size also contributes to the power of the study. Furthermore, the observation period of 7 years enabled analyses of time-related changes. A decreasing trend of eczema prevalence over the study period was observed in both parts of Germany. This is in contrast to most other studies published between 1964 and 1994.^{15–20} It is not clear whether this trend is real or is a consequence of measurement error or of other confounding factors such as improved therapy. There is no obvious reason to suppose differential misclassification by the observers, but the trend is not reflected by the questionnaire data.

Girls in this study were at a significantly higher risk for atopic eczema than boys, as reported in earlier investigations.^{21–26} Also, the positive association with

parental socio-economic status as seen in this study has been described in previous reports on allergies.^{27–34} Differential reporting or access to medical care facilities can be excluded as a potential explanation in our, and in most of the other, studies.

A consistently higher prevalence of atopic eczema in East Germany between 1991 and 1997 confirms our initial result from 1991.³⁵ Questionnaire-based studies did not reveal significant differences.^{6,36} In contrast to the distribution of atopic eczema, we and others found a higher prevalence of hay fever and atopic sensitization in West Germany at least during the early period of these studies.⁸ This indicates that atopic eczema follows a risk pattern that is different from respiratory allergies and sensitization. Although there is indication that air pollutants^{35,37–40} contribute to the manifestation of eczema, it is not possible to show a direct link between the air pollution pattern of East Germany and the elevated prevalence of atopic eczema, mainly due to the lack of individual exposure data. The difference in frequency between East and West Germany holds true after adjusting for important confounders such as sex, parental history of allergic diseases and socio-economic status, although all of these proved to have a significant influence on the disease. Therefore, other factors such as allergens and irritants as well as nutritional factors and infections must be considered. In this context we reported earlier that levels of total IgE and parasitic infections were significantly higher in East Germany.⁴¹

Little is known of the proportion of extrinsic and intrinsic eczema from population-based studies. Hospital-based estimates for the percentages of extrinsic eczema from Hungary and France range from 84.5%⁴² to 54.2%.⁴³ According to a French report on 250 children, allergic sensitization to food allergens and aeroallergens was absent in mild cases, and detectable in 33% of moderate and all cases of severe eczema.⁴⁴ We know from previous population-based investigations that the severity of atopic eczema in children is mostly mild to moderate.⁴⁵ It therefore seems to be a valid estimate in this study that the overall proportion of extrinsic eczema is 41.9%. This also indicates that not all cases of atopic eczema are 'allergic' and that factors other than allergic sensitization contribute to the manifestation of the disease. In addition, we found the proportion of extrinsic eczema to be significantly lower in East as compared with West Germany. This is in accordance with the findings of overall allergic sensitization in both parts of the country^{6,9,35} and may indicate that environmental

factors play an important part and contribute to the excess of cases in East Germany.

These findings indicate that on a population basis the impact of allergic sensitization on atopic eczema is lower than expected. Future studies need to determine this association in different population-based samples and to identify other environmental risk factors, which then may lead to the development of additional preventive measures.

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