

Increased prevalence of sensitization against aeroallergens in adults in West compared with East Germany

T. NICOLAI*, B. BELLACH, E. V. MUTIUS*, W. THEFELD and H. HOFFMEISTER

Robert Koch Institut, Berlin and *Universitätskinderklinik München, Dr v. Haunersches Kinderspital, München, Germany

Summary

Background An increased prevalence of allergic diseases and atopic sensitization as assessed by skin-prick testing in children in West compared with East Germany has been reported.

Objectives This study was designed to evaluate whether such a difference is also present in adults, and if this can be shown when using a serological test for allergic sensitization.

Methods Two large samples representative for all adults between 25 and 69 years of age were drawn in West (1991, $n = 5313$) and East Germany (1992, $n = 2617$). A serological test screening for IgE-antibodies to common aeroallergens (SX1) was performed. A questionnaire was used to assess the presence of clinical respiratory allergy, known possible risk factors for allergies and confounding variables.

Results Allergic sensitization decreased with age. Significantly more subjects <45 years of age had a positive allergy test in West as compared to East Germany. The prevalence of clinical allergy was also higher in West Germany. This difference was significant in younger adults and was independent of other risk factors identified. These additional risk factors encompassed younger age, higher educational level, male sex, and living in a community with more than 100 000 inhabitants.

Conclusion Sensitization to common aeroallergens as determined by a multiple allergen RAST test in adults below 45 years of age living in West Germany is increased compared to East Germany. This increase cannot be explained by genetic differences and is similar to the West to East decreasing gradient in allergies reported from studies in children employing skin-prick tests.

Keywords: allergy, adults, Phadiatop-SX1, prevalence, community size

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Introduction

Allergic diseases cluster in families [1], but studies in twins [2] have shown that, although concordance for atopy is significantly higher among monozygotic pairs than among dizygotic pairs, concordance among the former is relatively low when compared with that of other genetically determined illnesses. Thus, environmental factors must have a strong influence in determining which genetically predisposed subjects will develop allergic sensitization. As the German reunification process provided a unique opportunity to assess the effect of radically different lifestyles and air

pollution exposure, etc., the study reported here was conceived and performed by the Robert Koch Institute (as federal health monitoring agency) almost immediately after the political reunification made it possible.

Differences in the prevalence of allergic diseases and atopic sensitization (as assessed by skin-prick testing) between children in East and West Germany have been reported [3–5]. The life-time prevalence of doctor diagnosed asthma and hay fever was higher in Munich than in Leipzig. In Munich, rhinitis symptoms showed a strong peak during the summer months (when pollen counts are high), whereas in Leipzig this was not the case. Atopic sensitization to mites, pollen and cats as assessed by skin-prick tests were all significantly more frequent in children in West Germany. In a multivariate logistic regression analysis

Correspondence: T. Nicolai, Universitätskinderklinik München, Dr v. Haunersches Kinderspital, Lindwurmstrasse 4, D-80337 München, Germany.

of these data, sensitization to mites, pollen, cats or dogs fully accounted for the higher prevalence of asthma in the West German study area [4]. Other paediatric studies conducted after the fall of the iron curtain showed a decreasing slope of positive skin-prick test results from Sweden to the Baltic states, and as far East as Uzbekistan [6]. This could be interpreted as confirmation of the notion that Western living conditions induce the development of allergic sensitization, at least in children. However, it is unclear whether the results reported for children reflect a difference in sensitization rates in the population as a whole.

Also, some methodological questions remain for the interpretation of these paediatric data: first, the studies cited here used skin-prick testing as indicators of allergic sensitization. This method is subject to observer bias and the results can depend on cut-off points of weal size [7]. In one study, sensitivity of the skin-prick test as compared with specific IgE was lower in Poland and Estonia than in Sweden, possibly exaggerating the differences in sensitization between East and Western European study areas [8]. The weal size of positive controls was decreased in the East German study children as compared with West German children [4]. This may represent an observer bias or increased non-specific reactivity of the skin in the West. Secondly, questionnaire-derived prevalence rates of allergic diseases may reflect differences in public awareness and diagnostic labelling by doctors in the areas compared rather than real differences in disease frequencies. Thirdly, in studies involving different regions in eastern Europe, genetic differences as causes of different sensitization rates cannot be excluded. The first problem can be circumvented by using serological tests for allergen-specific IgE-antibodies, and the latter one does not arise when populations from East and West Germany are compared.

The objective of this study was to assess the prevalence of allergic sensitization among adults living in East and West Germany by a serological test for IgE antibodies against common aeroallergens, taking known risk factors and confounders into account. The studies were part of an ongoing health survey conducted by the former Bundesgesundheitsamt (Federal Health Office) and had been approved by the appropriate ethics commission.

Methods

Subjects

A large representative sample of randomly drawn adults was available for this study as part of a nationwide screening programme of the federal health authorities. A sample representative (with regard to age, sex and community size) of all (34.7 million) German adults between 25 and 69 years of age in West Germany was identified in 1991. A

sample representative of all (12.1 million) people in the same age group in East Germany was drawn using the same method in 1992. Details regarding the method of sample generation (using a standard programme of a large German polling company [Infratest, Munich, Germany]) have been published elsewhere [9]. In short, the sample population was modelled to reflect the results of the federal 'microcensus' performed by the 'Statistisches Bundesamt' in the West and the centralized population registry in the East with respect to regional population distribution, community size, gender and age. In a first step, communities in different regions (Bundesländer) were selected (according to local population registry data) to represent the distribution of communities in the census. Age and gender were then used to generate local strata. The final selection of individual probands from the local registries was performed using a weighed randomizing programme, where the weighing function which defined the likelihood to be selected reflected the size of the respective strata in the general population census.

Allergy test

In order to avoid some of the above mentioned problems with the interpretation of skin-prick tests, a serological method screening for the presence of IgE-antibodies to common aeroallergens (SX1, Pharmacia, Uppsala, Sweden) was used. It is less expensive and cumbersome than multiple tests for individual allergen-specific IgE antibodies (RAST-tests), seems to have advantages over the use of total IgE and avoids the problems associated with skin prick testing. This test is based on the RAST technique and has recently been evaluated and particularly recommended for epidemiological studies [10–15].

The allergens included in the test are house dust mite, cat and dog epithelium, *cladosporium herbarum*, pollen of timothy grass, rye, birch and mugwort. It is assumed that these allergens include 90% of all relevant inhalation allergens in Central Europe [16]. The result of the test is a numerical value ('allergy test value'). According to the recommendations of the test manufacturer (Pharmacia, Uppsala, Sweden), the final test result is recorded as positive or negative using a predefined cut-off (<2) of the allergy test value. For the purpose of this paper, a positive Phadia-top-SX1 test is reported as 'atopy', because it indicates the presence of specific IgE antibodies to at least one of the allergens included [16]. Blood sampling was done throughout the respective study year.

Questionnaire

Participants came to the study centres and a self-administered questionnaire was completed. A second questionnaire was administered by a physician who was part of the study

team. The self-administered questionnaire was used to assess known possible risk factors for allergies and confounding variables. Questions included passive (people who had never smoked currently living or working in rooms where others smoke regularly) and active smoking (pack-years), educational level (school grade finished), community size (number of inhabitants), heating system and presence of pets at home. Clinical allergy was assumed when the participant reported (in the physician-administered questionnaire) hay fever or allergies to pollen, house dust mite, house dust, wood dust, horses, cats or dogs.

Statistical methods

The yes/no result of the allergy test was used to identify subjects as sensitized or non-sensitized to aeroallergens ('atopy'). Persons were defined as having clinical allergic disease according to the answers given in the questionnaire (see above).

A logistic regression analysis was performed, stratified for age, with 'atopy' as dependent variable. Region, sex, smoking, community size, educational level and other possible risk factors and confounders (as available from the questionnaire, see above) were introduced as independent variables into the model. Only stable significant factors were retained in the final model. Estimated odds ratios were calculated as an approximation of relative risks [17]. In a second step, the above analysis was repeated stratified by region and age, in order to clarify if the effects of risk factors differed between East and West Germany.

Statistical significance was accepted at $P < 0.05$. All calculations were performed with the software package SPSS/PC⁺ (Version 4.01).

Results

Participation rates

The participation rates, age and sex distribution for the Western and Eastern part of the study are given in Table 1. No differences were found between West and East Germany in response rates, age and sex distribution.

Prevalence rates

Prevalence rates for 'atopy' (serological allergy test, Fig. 1) and reported clinical allergic diseases (from questionnaire data, Fig. 2) are given separately for women and men, and for East and West as percentage of respective age groups. Allergic sensitization decreased with age ($P < 0.0001$, Mantel-Haenszel test for trend), and significantly more subjects in the age groups below 40 years were atopic in West as compared to East Germany ($P < 0.0001$). This was

Table 1. Population description and response rate.

	East		West	
	Women	Men	Women	Men
Initial sample	1762	1568	4093	3907
Final sample	1646	1461	3965	3735
Responded	1160	1051	2688	2623
(Questionnaire)	(70.5%)	(71.9%)	(67.8%)	(70.2%)
Age distribution				
25–35 years $n=$	312	252	741	711
	4.1*/2.5 [#]	3.4/2.6	9.9/11.1	9.5/12.0
35–55 years $n=$	290	269	576	577
	3.9*/2.2 [#]	3.6/2.4	7.7/9.1	7.7/9.5
45–69 years $n=$	558	530	1371	1335
	7.3*/4.9 [#]	6.9/4.4	18.2/20.1	17.8/19.2

*% of sample

[#]% of population

The initial sample was selected to represent all adult Germans with regard to age, sex and community size. The final selection is slightly smaller than the initial sample due to persons who had either died or whose addresses turned out to be non-existent. The non-responders either declined participation, were not available at the time of the study, or could not be reached. The response rate for the allergy test was virtually identical, as both questionnaire and test were administered at the same occasion. The numbers of subjects in the different age groups are then given as well as the group size as % of the total sample. For comparison, the corresponding population groups (official data for 1991/1992 from Bayerisches Landesamt für Statistik und Datenverarbeitung, München, Germany) are also given as % of the total German population between age 29 and 69 years.

true for both women ($P < 0.0001$) and men ($P < 0.005$). The prevalence of clinical allergy as assessed from the questionnaire answers also showed a significant excess for women and men below 40 years living in West Germany ($P < 0.0001$). These effects disappeared in the older age groups. Atopy was more common in males living in West Germany when they were tested in summer as compared to the rest of the year ($P = 0.03$), but the differences between East and West Germany remained even when subjects tested in summer were excluded from analysis.

'Atopy': multiple logistic regression analysis

The relative risks for 'atopy' stratified into three age groups are shown in Table 2. A higher level of education increased the risk of sensitization. However, this effect reached statistical significance only in the age groups above 35 years. The risk of sensitization was significantly increased in persons living in communities with $> 100\,000$ inhabitants. In the age group between 25 and 35 years, female gender

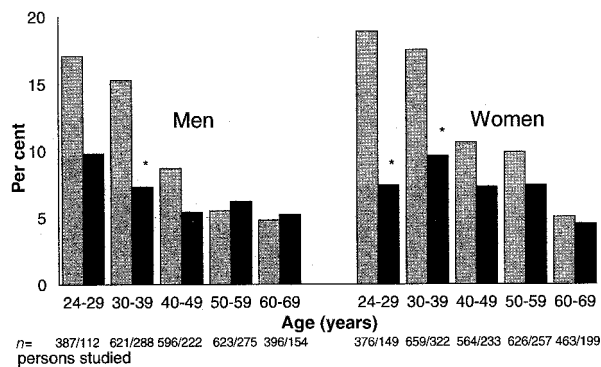


Fig. 1. Percentage of participants reporting clinical allergies in the different age groups in East and West Germany. * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$ for difference between East and West in the respective age group. The number of persons tested is given beneath each column. * $P < 0.05$ for East compared with West Germany.

implied a decreased risk to be sensitized. Living in West Germany resulted in an increased risk of allergic sensitization in the age groups below 45 years. The risk was increased by 83% in the age group 25–35 years, and by 55% in subjects 35–45 years of age. No such increased risk was seen in the oldest age group.

In order to evaluate whether the effects of smoking, educational level, gender and community size differed between East and West Germany, risk factor analysis was repeated stratified for age and region. The general direction and size of the risk factors were similar in East and West Germany. Active smoking had no significant influence on the results of the allergy test. Passive smoking increased the risk of allergic sensitization in older adults living in West

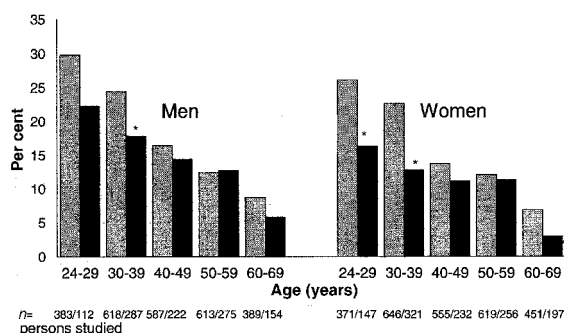


Fig. 2. Percentage of participants with a positive serological test for respiratory allergy (SX1, Pharmacia, Sweden; 'atopy', for definition see text, methods) in the different age groups in East and West Germany. * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$ for difference between East and West in the respective age group. The number of persons tested is given beneath each column.

Germany. The educational level became significant as a risk factor only in the older age groups in West Germany. The increased risk in males reached statistical significance only in younger people living in East Germany, while the effect of the community size $> 100\,000$ was seen in all groups but did not reach statistical significance in younger people in the East.

Discussion

The data presented show that self-reported clinical allergy as well as a positive screening test for IgE antibodies to common aeroallergens was more prevalent in younger adults living in West Germany as compared with those living in former East Germany. The increased risk in West Germany for 'atopy' remained significant when other risk factors and confounders were taken into account.

These results extend and are in accordance with data reported for school children from other studies, where the prevalence of hay fever, asthma, and skin-test reactivity to common aeroallergens was considerably higher in 10-year-old children in West as compared to East Germany [3,4,18]. In accordance with our data, a lower prevalence of asthma and nasal allergies in adults living in Erfurt, East Germany, as compared to Hamburg, West Germany, has been reported [19], and data from similar studies have been reviewed in this journal [20]. Our results are in agreement with data indicating a West to East decreasing slope of allergic sensitization in children (comparing Sweden and Eastern European states) [6,8,21]. Considerable regional differences in asthma prevalence have also been reported recently from the EC respiratory health survey [22].

One advantage of the data reported here is that genetic differences cannot explain the increased allergies in West compared to the former East Germany. This implies that environmental exposure or living conditions (lifestyle) are factors causing the differences in sensitization rates in East and West Germany.

Most studies involving children used skin-prick tests to evaluate atopic sensitization to aeroallergens. These tests are subject to interobserver differences and methodological difficulties regarding allergen stability, size of positive controls, etc. Only small studies have used RAST tests when comparing East and West Germany: 6-year-old children in East Germany (Halle) [23,24] had fewer positive RAST results for house dust mite or pollen compared with the same age group in the West (Cologne and Düsseldorf). A survey in two vocational schools using allergen specific IgE showed higher sensitization rates among adolescents in West compared to East Germany [25].

In the study reported here, a serological test based on a multiple allergen RAST technique was employed. Although it has not been widely used for epidemiological purposes as

Table 2. Relative risk for sensitization stratified for age and region [() = 95% confidence interval]

Risk factors	25–35 years	35–45 years	45–69 years
Smoking habits			
Non-smoker	1	1	1
Passive smoker	0.82 (0.58–1.16)	1.05 (0.73–1.51)	1.28 (0.91–1.80)
Smoker (in pack years)	0.98 (0.97–1.00)	0.98 (0.97–0.99)	1.00 (0.99–1.00)
Educational level			
8th grade	1	1	1
10th grade	1.07 (0.80–1.42)	1.64 (1.12–2.40)	1.32 (0.85–2.06)
Final examination (12th or 13th year)	1.13 (0.83–1.53)	1.66 (1.20–2.28)	1.61 (1.18–2.21)
Community size			
Population <20 000	1	1	1
Population 20 000–100 000	1.05 (0.74–1.49)	1.36 (0.92–2.00)	1.55 (1.06–2.29)
Population >100 000	1.48 (1.15–1.92)	1.50 (1.12–2.01)	1.77 (1.32–2.38)
Sex			
Male	1	1	1
Female	0.72 (0.58–0.90)	0.94 (0.73–1.21)	0.82 (0.64–1.06)
Region			
east	1	1	1
west	1.83 (1.34–2.49)	1.55 (1.10–2.19)	1.04 (0.77–1.40)

yet, it has been evaluated and recommended as an epidemiological tool for population based studies of allergy prevalence [10]. As a screening method for atopy, it offers advantages over skin tests (less observer bias), total IgE (higher sensitivity and specificity) and multiple RAST testing (less expensive) [10].

There were some methodological limitations in this study that need to be considered. The survey in East Germany was conducted 1 year later than the study in West Germany. Although data collection was carried out throughout the respective study year, the pollen load could have been different in the 2 years, thereby influencing the titres of specific IgE against pollen. As a mixed aeroallergen test containing pollen together with others allergens was used, we have no way of knowing which allergen specific IgE caused the test to be positive more often in West German study subjects. In West Germany, males showed more often a positive atopy when tested in summer as compared to other seasons. However, the fact that the difference between East and West remained significant when subjects tested in summer were excluded from the analysis makes it unlikely

that the pollen load alone could explain the differences in serological allergy test results.

When analysing possible risk factors, we found that adults in both parts of the country living in communities with more than 100 000 inhabitants had an increased risk of allergic sensitization to aeroallergens. Others studies found increased RAST test positivity in urban regions of West Germany [18] and Austria [26], compared to rural areas of the respective countries. The American NHANES study reported increased rates of allergic diseases to be associated with larger community size [27].

Smoking had no consistent effect on atopy in this study. A higher educational level implied an increased risk of allergic sensitization in our study. The effect became statistically significant for subjects older than 35 years and was more prominent in the West. This might reflect the fact that people with a higher educational level are more likely to be affluent (particularly in the West), thereby having a more modern, or 'Western', and less traditional lifestyle, again implicating the association of a more modern lifestyle with increased rates of allergies. In the East, the socialist system

may have blunted this association between educational level and affluent lifestyle. The association of positive allergy tests and socio-economic status has also been reported by other authors [28].

A very intriguing aspect of these results lies in the fact that the regional differences in sensitization rates are only seen in adults who were below 45 years in 1991/2. This age dependence could either be due to the general decline in allergy frequency with age, making the effect of region less visible in the older age group, or a factor influencing allergic sensitization which operates only in the younger age group. If one assumes the latter, it is interesting to note that the younger age group encompasses all persons who grew up in the different socioeconomic background and living conditions in East and West after the border between the two parts of the country had become impermeable.

The reasons for the lower prevalence of atopic sensitization in East Germany are unknown. Other studies have suggested that outdoor air pollution by SO₂, particulate matter and vehicle exhausts [3,4,29] is not a strong determinant for the development of atopy. However, private car ownership and exposure to outdoor air pollution did differ significantly between East and West Germany and cannot be dismissed entirely as possible causal factors for the differences in allergic sensitization rates found. No relation was found between childhood asthma and atopy and the number of cars passing through the local neighbourhood where children lived in Munich [29]. However, the exhaust fumes produced by East German two stroke engine cars were quite different from the polycyclic aromates and NO which are a characteristic of private cars in the West. Two German epidemiological studies found an association of positive skin-prick tests with heavy metal [30] and airway hyperreactivity with NO₂ exposure [31].

Domestic factors characteristic of East European living conditions could interfere with allergic sensitization. Housing conditions and thus exposure to mites and other indoor allergens may differ between East and West Germany. Measurements of house dust mite allergen (Der p 1 and Der f 1) in dust of East and West German homes, however, showed a higher mite exposure in Eastern homes [32]. From the paediatric studies, dampness was found to be more prevalent in East German homes [4,18].

A characteristic of East German living conditions has been the easy access to early day care, since the great majority of women were working in the former German Democratic Republic. Day care was attended by about 70% of East German children aged 1–3 years, but only 7–8% of all children in this age group had access to day care in West Germany [4]. Therefore, a substantially greater proportion of the younger age group in our study may have spent their first years in day care if they grew up in East Germany. Early contact with respiratory infections has been suggested

to modify (and possibly decrease) the subsequent development of allergic sensitization [33,34]. A study of children from the Baltic area found that indices of domestic crowding (persons per room at home) were associated with fewer positive skin-prick test results [8].

This study shows increased allergic sensitization to common aeroallergens as determined by a multiple allergen RAST test in a large representative sample of adults living in the former West as compared to the former East Germany. This difference was significant in younger adults and was independent of the other risk factors identified. These additional risk factors encompassed younger age, a higher educational level, male sex, and living in a community with more than 100 000 inhabitants. The differences between East and West Germany cannot be explained by genetic differences and are similar to the West to East decreasing gradient in allergies reported from studies in children and employing skin-prick tests.

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