

# Environmental Risk Factors for Respiratory and Skin Atopy: Results from Epidemiological Studies in Former East and West Germany

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### Key Words

Allergy · Environment · Pollution · Germany · Eczema

### Abstract

The fall of the Berlin wall in 1989 offered the unique opportunity to compare populations of a similar genetic and geographic background which had been living under quite different environmental exposure conditions for over 40 years. Since 1990 comparative epidemiological studies were performed between various regions in former East and West Germany with yearly questionnaires and 3 years' physical, dermatological, allergological and exposure examination in a total of about 30,000 preschool children. There were striking differences between the various German regions with higher prevalence rates of respiratory atopy (hay fever, asthma) and atopic sensitization (prick test, RAST) in West Germany, while atopic eczema was significantly higher in East Germany (17.5 vs. 11.4% in West Germany). Total serum IgE levels were markedly higher in children in the east of Germany, similarly to the prevalence of parasitic infestation (questionnaire data as well as positive ascaris RAST). In multivariate logistic regression analysis the following factors were significantly associated with atopic eczema: animal contact (odds ratio, OR 2.9), animal furs in the bedroom (OR 2.2), use of gas without ventilation (OR 1.7) and living near road with heavy traf-

fic (OR 1.7). Furthermore, socioeconomic factors measured as parental educational status (university vs. elementary school) were significantly associated (OR 2.3) with atopy. Respiratory tract infections and irritant responses decreased together with decreasing SO<sub>2</sub> and suspended particulate air pollution in East Germany from 1991 to 1997. It is concluded that environmental factors from the physical, chemical, biological, and psychological environment (characteristic of a 'modern' or 'western' society) do influence the development of atopic sensitization and disease.

### Introduction

The prevalence of allergic diseases has increased worldwide during the last decades, but most strikingly in industrialized countries [4, 8, 19, 23, 36], now showing prevalence rates of the atopic diseases bronchial asthma, rhinoconjunctivitis or atopic eczema in the range between 10 and 20% in the general pediatric population [11, 13, 20, 26, 32]. The reasons for this increase in allergy prevalence are not known. However, there exists a variety of hypotheses, ranging from increased awareness, more intense allergen exposure, decreased stimulation of the immune system by improved hygiene ('jungle hypothesis'), influence of environmental pollution to psychosocial influences [5, 22, 23,

34]. Most of these hypotheses have been summarized as 'western life-style' [23, 34], promoting the development of allergies.

The fall of the Berlin wall in 1989 offered the unique opportunity to compare populations of a similar genetic and geographic background which had been living under quite different environmental exposure conditions for over more than 40 years (table 1). There were essentially four groups performing epidemiological studies comparing former East versus West German or European countries with regard to allergy prevalence [5, 6, 11, 15, 20, 29, 34, 35] (table 2). All of them had arrived at the striking and at first paradoxical results of a decreased allergy prevalence in the east compared to the west. Here, the results of our own East-West German comparison study are presented with a focus on selected aspects of environmental influence upon allergic sensitization and disease. More detailed information has been and will be published elsewhere [4, 5, 11, 12, 20, 26].

## Material and Methods

### Study Areas

The areas in former East Germany were chosen to represent a range of different airpollution levels. Halle and Leipzig are industrialized cities in Saxony-Anhalt, Magdeburg is the capital of Saxony-Anhalt with comparatively moderate pollution, and in the 'Altmark' three small towns with lower degrees of pollution were included. The areas in North Rhine-Westphalia in former West Germany were suggested by the clean-air plans ('Luftreinhaltepläne') of the state and included the cities of Duisburg, Essen, Gelsenkirchen, Dortmund (heavily industrialized towns in the Ruhr area) and the small town of Borken with low air pollution in Westphalia.

### Study Design, Subjects and Response

Since 1990 comparative epidemiological studies were performed in various regions in former East and West Germany with yearly questionnaires and 3 years' physical, dermatological, allergological and exposure examination in a total of 28,205 5- to 7-years old preschool children. All boys and girls entering the elementary school in the geographically defined areas were chosen. Blood and urine samples were collected. Lung function tests were done using body plethysmography. A dermatological and allergological workup included inspection of the whole skin by trained physicians from the Departments of Dermatology and Allergy in Hamburg (1991, 1994) and Munich (1997). Stigmata and signs of atopic eczema were registered; the severity of atopic eczema was measured using the scoring system of atopic dermatitis (SCORAD) index [25]. The serum-specific IgE was measured using the CAP-RAST system. More methodological details have been given previously [5, 11a, 25, 26].

### Statistical Analysis

Logistic regression was used for analysis. The parameter estimates of that model were transformed to adjusted odds ratios.

**Table 1.** Similarities and distinctions between East and West Germany at the time of the reunification in 1990

Similarities	Distinction
Genetic background	'Experimentum dictaturae' (politics)
Language	Pollution
Geographic situation	Life-style
Climate	Public health

**Table 2.** Large epidemiological studies with actual medical examination comparing former East and West Germany or Europe with regard to allergy prevalence

Authors	Ref. No.	Countries
von Mutius et al.	29	Munich-Leipzig
Behrendt et al.	4	North Rhine-Westphalia, Saxony-Anhalt, Saxony
Wichmann, Magnussen	15, 35	Hamburg-Erfurt
Björkstén	6	Sweden-Poland Sweden-Estonia

**Table 3.** Prevalence (%) of atopic eczema (dermatological examination) in former East and West Germany

Year	West	East	Total
1991	11.2 (n = 986)	17.5 (n = 287)	12.9 (n = 1,273)
1994	8.7 (n = 503)	12.6 (n = 1,008)	11.3 (n = 1,511)

## Results

In 1991 there were striking differences between the various German regions with higher prevalence rates of respiratory atopic diseases (hay fever, allergic bronchial asthma) and atopic sensitization (skin prick test, specific IgE in the RAST) in West Germany compared to the east, while upper respiratory tract infections and symptoms of irritation (e.g. dry cough) were more frequent in East Germany. There was a clear correlation between outdoor pollutant exposure regarding SO<sub>2</sub> and suspended particles and the frequency of upper respiratory tract infection and symptoms of irritation within East German study regions [11a, 26]. Contrary to the respiratory atopic diseases, there was a significantly higher prevalence of atopic eczema in East Germany compared to West Germany [25] (table 3). Total serum IgE levels were

markedly higher in children in the east of Germany compared to the west [5]. Similarly the prevalence of parasitic infestation (questionnaire data as well as positive RAST to ascaris) was higher in the east. In a multivariate logistic regression analysis the following factors were significantly associated with atopic eczema: animal contact (OR 2.9), animal furs in the bedroom (OR 2.2), use of gas without hood (OR 1.7), living close to a road with heavy traffic (OR 1.7).

Furthermore socioeconomic factors as evaluated by parental educational status (academic career vs. elementary school) were significantly associated with parameters of atopy both in the clinical evaluation (questionnaire data, dermatological examination) as well as in the skin prick test and in the RAST [11].

In 1991 air pollution patterns between East and West Germany were also different, with highly elevated air concentrations of SO<sub>2</sub> and suspended particulate matter in the east, whereas air concentrations of nitrogen dioxide (NO<sub>2</sub>) were higher in the urban regions in the west. These two types of qualitatively different air pollution patterns were referred to as type I and type II air pollution [4]. In the years from 1991 to 1997 there was a marked decrease of prevalence of upper respiratory tract infections and irritative symptoms together with a decrease in the outdoor pollution of SO<sub>2</sub> and suspended particulate matter. These trends were highly significant. In Leipzig 24.5% (n = 503) of the children had more than five colds in 1991. In 1994 it was 18.9% (n = 280) and in 1997 10.1% (n = 188). Over the same time SO<sub>2</sub> pollution declined from 160 µg/m<sup>3</sup> annual mean in 1991 to 60 µg/m<sup>3</sup> in 1994 to 13 µg/m<sup>3</sup> in 1997. Suspended particles changed from 80 to 54 and to 51 µg/m<sup>3</sup>. In the years from 1991 to 1997 there was an increase in the prevalence of hay fever in East Germany which was more pronounced than in the west. In Leipzig it changed from 1.0% in 1991 to 3.6% in 1997, in Duisburg from 2.4 to 2.3%. No association with SO<sub>2</sub> or particle pollution was detected.

## Discussion

The results of this epidemiological study regarding the prevalence of atopic disease and sensitization in the east and west of Germany are partly in agreement with those of the other investigators (table 2), reflecting the higher prevalence of hay fever and bronchial asthma in the eastern German or European regions. In some aspects, however, we either have additional findings (e.g. the higher prevalence of atopic eczema, the increased serum total IgE concentrations in the east) or we disagree with the interpretation regarding the influence of environmental pollution or the definition of

'western life-style'. In the following some specific aspects regarding the factors of allergy development possibly having an influence are discussed briefly.

### *Genetic Background*

The genetically determined susceptibility to develop atopic diseases is not a satisfactory explanation for the increase in allergy prevalence. In a rather homogeneous population we found striking differences (see table 1). Furthermore, there were also striking differences within West or East German study areas being sometimes even more pronounced than the difference in prevalence between East and West Germany as a whole. These regional differences can so far not be explained by the parameters investigated, especially not be the parental atopy history.

### *Allergen Exposure*

Allergen exposure per se does not seem to be able to explain the differences in the hay fever prevalence. Pollen counts measured in former East Germany compared to West Germany were equally high [4, 5] with some qualitative differences, e.g. higher prevalence of mugwort in East Germany compared to the west. At the same time – with equal birch pollen concentrations in the air – there were significantly lower prevalences of positive skin prick tests to birch pollen in German children in the east compared to the west [4, 20, 25].

A microscopic and electron-microscopic analysis revealed differences in pollen grains collected in the east compared to the west, particularly with regard to the pollen-pollutant interaction. It has been shown that air pollutants can interfere with the pollen surface and give rise to increased and altered allergen release from the pollen cytoplasm [2–4].

### *Decreased Stimulation of the Immune System*

In our multivariate logistic regression analysis we did not find an association between vaccination habits with BCG and prevalence of atopic eczema in East or West Germany. There was a higher prevalence of upper respiratory tract infections in the east [26].

Furthermore, we observed an increased prevalence of parasitic infestation in children in the east of Germany as determined by the questionnaire ('did your child ever have a worm infestation?' or '...a worm infestation in the last weeks?') as well as by measuring specific IgE against parasitic allergens (ascaris) [5]. In an earlier parasitological study in Halle it was found that more than 90% of the preschool children had *Enterobius vermicularis* infestation [Ockert, pers. commun.]. However, it was not possible to

measure IgE against this parasite. This increased parasite infestation might also possibly explain the markedly higher total serum IgE levels in German children in the east as compared to the west [5]. The natural defense mechanisms against parasites – namely IgE antibodies – might, due to the lack of appropriate challenge in the western areas, be more easily directed against ‘innocent’ environmental substances such as pollen (‘jungle hypothesis’) [5, 14, 22].

#### *Socioeconomic Aspects*

Both in former East and West Germany the educational status of parents seemed to be an important influencing factor, whereas this was not the case for variables describing irritative upper airway reactions. The odds ratio for higher parental education was highest for hay fever (OR 3.7, CI 1.2–11.7) but also significant for atopic eczema both in the history as well as on the day of examination, skin prick tests and serum IgE antibodies against environmental allergens. This cannot be explained by increased awareness of the ‘atopic mother’. When confounding variables such as ‘smoking habit’, ‘low birth weight’, ‘no breast feeding’ or ‘damp apartment’ were excluded there was no change in this association. However, not adjusting for parental education leads to a number of false-positive associations between other variables and allergy prevalence [11]. Therefore in our analysis, in the multivariate logistic regression, parental education was always used as confounding variable among others. Purely economic reasons are not able to explain this finding since the associations were similar in West and East Germany. Also the number of siblings did not explain this effect in our study.

#### *Environmental Pollution*

There is evidence from many studies that air pollution is associated with a higher prevalence of upper respiratory disease and maybe also allergic diseases [1, 4, 7, 9, 10, 17, 20, 24, 33, 35, 36]. The paradoxical finding in the East-West German comparisons, that in highly polluted formerly communist countries of Eastern Europe there were less respiratory atopic diseases, can be at least partly explained when the quality of air pollution is considered, namely the distinction between the type I and the more modern type II air pollution pattern [4]. While type I air pollution is not associated with allergy or even inversely correlated, there are some studies showing that exposure to type II of air pollution may be associated with a higher prevalence of allergic sensitization and disease [5, 7, 17, 20, 33] in western countries.

**Table 4.** The four ‘antinomies’ emerging from the results of East/West German allergy comparison studies (paradoxical findings in the east)

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- (1) Air pollution is high – atopy is low
  - (2) Airway atopy is low – skin atopy is high
  - (3) Total serum IgE is high – atopy is low
  - (4) Allergen-specific IgE is low – parasite infestation is frequent
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## **Conclusions**

The results from the East-West German comparison studies regarding the prevalence of atopic diseases are complex and difficult to understand. At first glance we and others were struck by seemingly paradoxical results not fitting the original hypothetical considerations [23]. We name here at least four ‘antinomies’ (a term used by Immanuel Kant, describing a pair of two obviously correct sentences not fitting together; table 4). These antinomies, however, can be resolved by more detailed analysis and differentiation.

(1) Air pollution is not ‘one parameter’ but has to be analyzed critically qualitatively and quantitatively and with respect to outdoor and indoor exposure. (2) Atopy is a complex phenomenon, maybe not based on only one mechanism as described in allergic rhinoconjunctivitis. Obviously skin atopy behaves differently from respiratory atopy. This has to be taken into consideration in future studies. (3) Although immunoglobulin E is the predominant antibody of atopic disease, the value of total serum IgE as parameter of atopy is highly questionable. In our study high total serum IgE levels are combined with low levels of atopy in East Germany. The nature and origin of total serum IgE content has to be taken into consideration. As predictors of atopy specific IgE against common environmental allergens seem to be more reliable. (4) The influence of parasitic infestation upon the development of atopy deserves further investigation. The TH1-favoring effect of some bacterial and viral infections has to be considered. The TH2-inducing effect of parasites might not necessarily be in favor of respiratory atopic disease; however, there might be a connection to atopic eczema.

There is more and more evidence that not only one but many factors from different categories and originating both from the physical, chemical, biological and psychosocial environment can influence the development of allergy. The scientific elucidation of factors or substances responsible for the development of specific parameters of atopy is crucial before rational consequences for primary prevention of allergy can be taken.

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