

Inner city air pollution and respiratory health and atopy in children

T. Hirsch*, S.K. Weiland**, E. von Mutius⁺, A.F. Safeca*, H. Gräfe[‡], E. Csaplovics[§],
H. Duhme**, U. Keil**, W. Leupold*

Inner city air pollution and respiratory health and atopy in children. T. Hirsch, S.K. Weiland, E. von Mutius, A.F. Safeca, H. Gräfe, E. Csaplovics, H. Duhme, U. Keil, W. Leupold. © ERS Journals Ltd 1999.

ABSTRACT: The impact of inner city air pollution on the development of respiratory and atopic diseases in childhood is still unclear.

In a cross sectional study in Dresden, Germany, 5,421 children in two age groups (5–7 yrs and 9–11 yrs) were studied according to the International Study of Asthma and Allergies in Childhood (ISAAC) phase II protocol. The prevalences of wheezing and cough as well as doctor diagnosed asthma and bronchitis were assessed by parental questionnaires. Children also underwent skin-prick testing, venipuncture for the measurement of serum immunoglobulin (Ig)E, lung function testing and a bronchial challenge test (4.5% saline) to assess airway hyperresponsiveness. Exposure was assessed on an individual basis by relating mean annual air pollution levels (SO₂, NO₂, CO, benzene, and O₃) which had been measured on a 1 km² grid, to the home and school address of each study subject.

After adjusting for potential confounding factors an increase in the exposure to benzene of 1 µg·m⁻³ air was associated with an increased prevalence of morning cough (adjusted odds ratio (aOR): 1.15; 1.04–1.27) and bronchitis (aOR: 1.11; 1.03–1.19). Similar associations were observed for NO₂ and CO. In turn, the prevalences of atopic sensitization, symptoms of atopic diseases and bronchial hyperresponsiveness were not positively associated with exposure to any of these pollutants.

It is concluded that in this study a moderate increase in exposure to traffic-related air pollution was associated with an increased prevalence of cough and bronchitis, but not with atopic conditions in children.

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The potential health effects of long-term exposure to outdoor air pollution on the respiratory tract of children has been the focus of much research in recent years. Several authors reported a significant association between increased exposure to particulate matter [1–4], SO₂ [1, 3, 4], O₃ [5] and nitrogen oxides [3, 4, 6] and the occurrence of respiratory tract illnesses. Not all reports attempted to discriminate between the different phenotypes of these conditions. Reports that provide detailed information suggest an effect on the prevalence of cough and bronchitis, but not on asthma and atopy [2, 7, 8].

Other epidemiological studies found an association between automobile [9, 10] or truck traffic frequency [11–13] and wheeze. Higher exposure to truck traffic and black smoke was also associated with impaired forced expiratory volume in one second (FEV₁) [14]. Some studies also reported an association between truck traffic frequency [12, 13] or black smoke exposure [11] and symptoms of allergic rhinitis. A large Italian study on 39,275 children [15] found a significant association between truck traffic exposure and wheeze, but the associations with other respiratory symptoms (cough and phlegm) were more pronounced. No positive associations were seen between traffic exposure and doctor-diagnosed asthma [9, 11],

atopy [11] or bronchial hyperresponsiveness (BHR) [9]. In contrast to these findings data from *in vitro* studies and laboratory experiments suggest that particles from diesel exhaust, one of the major contributors to particulate matter pollution in urban areas, specifically promote allergic reactions and BHR [16].

Limitations of study design and exposure assessment have hampered the interpretation of published epidemiological findings. Exposure to air pollution was often assessed through only one or a few monitoring stations supposed to represent air pollution levels over a large area. However, concentrations of certain pollutants such as NO₂ have been shown to vary substantially over short distances [17]. Surveys comparing prevalences of disease between regions with different air pollution concentrations are prone to confounding by factors characteristic of the respective study area such as meteorological or socio-economic conditions. Finally, studies focusing on traffic frequency as a global estimate of vehicle exhaust exposure do not take into account other potential sources of inner city air pollution.

The aim of this study was to relate the prevalence of respiratory and allergic diseases in childhood to measurements of outdoor air pollutant concentrations in the city of

*University Children's Hospital Dresden, Germany, **Institute of Epidemiology and Social Medicine, University of Münster, Germany, ⁺University Children's Hospital, Klinikum Innenstadt, Munich, Germany, [‡]Saxony State Agency for Environment and Geology, Radebeul, Germany, [§]Institute of Photogrammetry and Remote Sensing, University of Technology, Dresden, Germany.

Correspondence: T. Hirsch, Kinderklinik im Universitätsklinikum Carl Gustav Carus der Technischen Universität Dresden, Fetscherstr. 74, D-01307 Dresden, Germany. Fax: 49 3514585358

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Dresden, Germany. To distinguish asthma from other respiratory conditions objective measures of parameters closely associated with asthma such as BHR and atopic sensitization were analysed. The individual exposure to outdoor air pollutants was estimated using detailed measurements of annual mean concentrations of SO₂, NO₂, CO, benzene, and O₃ for a 1 km² grid in the city of Dresden.

Methods

Study population and health outcome measurements

Dresden, a city with 480,000 inhabitants and an area of 226 km², is located in the south-east of Germany. Between September 1995 and June 1996 all children participating in the school entry examinations (n=3,866) and a random sample of school children attending fourth grade classes (n=3,668) were studied using the Phase II modules of the International Study of Asthma and Allergies in Childhood (ISAAC) [18]. Because all school beginners were 5–7 yrs of age at the time of investigation, and most fourth grade pupils were 9–11 yrs old (98.8%) the authors will refer in the following text to 5–7 and 9–11 yr old children, respectively.

Parental questionnaires were distributed through the community health department which conducts the school entry examinations for 5–7 yr olds and through the schools for 9–11 yr olds. A completed questionnaire was returned by parents of 3,312 (83%) children of ages 5–7 yrs and of 3,045 (85.7%) children of ages 9–11 yrs. The questions on respiratory and allergic disorders included those developed for the ISAAC-project [19]. The focus of this analysis is on responses to the ISAAC questions on "wheeze in the last 12 months", "number of wheezing attacks in the last 12 months", and on "sleep-disturbing" and "speech-limiting" wheezing in the last 12 months. Symptoms of allergic rhinoconjunctivitis ("sneezing or runny, or blocked nose without a cold" and "itchy-watery eyes") and atopic eczema ("itchy-rash") during the last year were also assessed *via* ISAAC core questions.

In addition, a question on morning cough as a symptom of nonspecific airway irritation was asked ("Did your child frequently cough in the morning right after waking up in the last 12 months?"). This question had been developed for questionnaires of the British Medical Research Council [20]. Parents were furthermore asked: "Did a doctor ever diagnose any of the following diseases in your child? a) asthma; b) asthmatic, spastic or obstructive bronchitis; c) bronchitis. Children were defined as having asthma, if a doctor had diagnosed "asthma" at least once or "asthmatic, spastic or obstructive bronchitis" more than once. Children were classified as having bronchitis, if a doctor had diagnosed "bronchitis" more than once, and if these children did not meet the definition criteria for asthma. The questions on doctor's diagnoses of asthma and bronchitis included in this study were validated against BHR to cold air in Bavarian schoolchildren [21]. Finally, questions on living conditions, family background and traffic density on the street of residence were evaluated.

All 9–11 yr olds and a random subsample of 5–7 yr olds (n=2,328) were invited to take part in skin-prick tests (SPT) and blood sampling (ISAAC Phase II modules). The SPTs were performed on the left forearm using ALK lancets and standardized allergen extracts of mixed grass

pollen, mixed tree pollen, *Alternaria tenuis*, *Dermatophagoides pteronyssinus* and *D. farinae*, and cat (ALK laboratories, Hörsholm, Denmark). The wheal size was calculated as the mean of the long axis and its perpendicular. Atopic sensitization was defined as a wheal of ≥ 3 mm to at least one allergen after subtraction of the reaction to the negative control. SPT results of children reacting negative to histamine (wheal <2 mm, n=72) were excluded from the analysis. Specific serum immunoglobulin (Ig)E against a panel of aeroallergens was determined by Fluorescence Enzyme Immuno Assay (SXI CAP; Pharmacia, Lund, Sweden). SPTs were performed in 1,360 (58.4%) children aged 5–7 yrs and 2,260 (61.6%) children aged 9–11 yrs. Blood samples were drawn from 954 (41.0%) children in the younger and 2,083 (56.8%) children in the older age group.

Measurements of lung function were offered only to a random subsample of the 9–11 yr old children (n=1,999). Spirometric measurements (Master Scope 4.1, Jäger, Würzburg, Germany) were performed according to the quality control criteria of the American Thoracic Society [22, 23]. The FEV₁ and the forced expiratory flow over the middle half of the vital capacity (FEF_{25–75%}) were expressed as a percentage of the predicted values based on sex and height [24]. Bronchial responsiveness was assessed only in children with an FEV₁ >75% predicted. These children inhaled nebulized hypertonic (4.5%) saline for periods of increasing duration (0.5, 1, 2, 4, 8 min). After each inhalation period the FEV₁ was measured. Children were classified as BHR if the FEV₁ had fallen by $\geq 15\%$ from baseline [25]. One thousand two hundred and fifty-six children (62.8%) took part in spirometry. Among these, 140 subjects could not be challenged because of technical or organisational problems, 61 children did not complete the bronchial challenge because of health complaints (*e.g.* cough, nausea) or limited motivation, and 7 children were not challenged at all because of a baseline FEV₁: $\leq 75\%$ pred. The bronchial challenge was successfully completed by 1,048 (52.4%) children.

Written informed consent was obtained from the parents for each study instrument separately. The study was part of a multicentre project (ISAAC Germany Phase II) and was approved by the ethics committee of the University of Münster.

Air pollution monitoring

Between April 1994 and April 1995, outdoor air pollution in the populated area of Dresden was monitored in a 1 × 1 km grid in the Gauss-Krüger (GK)-coordinate system [26]. For 182 grid-points 0.5 h mean concentrations of SO₂ (ultraviolet fluorescence), NO₂ (chemiluminescence), CO (infrared absorption), and O₃ (ultraviolet photometry) were determined 26 × 4 m above ground by monitoring stations placed on caravans meeting the standards set by the Federal Ministers of the Interior [27] and Environment [28]. The monitoring stations were placed as close to each GK-gridpoint as possible but never more than 200 m away from it. The majority of the monitoring sites was situated at small and very small streets in residential districts or field-paths in the surroundings of Dresden representing "city background sites". Twenty-nine (15.9%) of the 182 monitoring stations were situated in streets with dense traffic (>5000 cars·24 h⁻¹).

The measurements were carried out approximately every fortnight at varying times between 06:00h and 23:00h (10% of the measurements on holidays). An equal distribution of times and weekdays was ensured for all sets of 104 measurements at the corners of a 1 × 1 km square but was also aspired for the 26 measurements at the single points. Measurement quality was controlled by daily calibration with internal standards (accepted range $\pm 10\%$ about the reference), and unannounced control measurements with external standards [26]. In addition, at each measurement 50 L of air were vacuumed separately over activated carbon, and analysed by gas chromatography for benzene (Siemens GC 1/4; Siemens AG, München-Berlin, Germany) according to guideline 3482/4 of the "Verein Deutscher Ingenieure". Annual mean immission at a given grid-point was calculated as the arithmetic mean of the 26 values determined at this point.

Estimation of individual exposure

Home addresses of all children and school addresses of the 9–11 yr olds were assigned to GK-coordinates by means of a geographical information system (SICAD; Siemens/Nixdorf AG, München-Paderborn, Germany; theoretical exactness 0.1 m). One hundred and three home addresses not included in this database were located on topographic maps with an accuracy of about ± 50 m and then assigned to GK coordinates. The children's exposure at the home address or the school address was estimated using the annual mean immission values from the nearest monitoring station in each of the four geographical directions (in most cases at the corners of the 1 × 1 km square in which the address was located). These four values, weighted by the inverse of the square of their distance to the respective address, were averaged (Stuttgarter Contour Programme (SCOP)) to create, maintain and apply digital terrain models. Institute of Photogrammetry and Remote Sensing, University of Technology, Vienna, Austria, 1994). The 95th percentile of the 104 values measured at these four stations during the year was used as a proxy of the peak exposure of each child. In 168 children living in

the periphery of the monitored area, one or two of the four monitoring stations were located >1 km from the others. Values from these stations were not used for the assessment of peak exposure. For 9–11 yr old children, a combined estimate was also calculated as the mean of the estimates of exposure at home and at school.

The exposure estimates could be validated against a continuous monitoring station in the city 100 m from a street with dense traffic (>5000 cars·24 h⁻¹). The yearly mean concentrations of SO₂, NO₂ and O₃ measured continuously at this station were compared with estimates based on the noncontinuous measurements at the four nearest gridpoints: SO₂ 42.3 $\mu\text{g}\cdot\text{m}^3$ (continuous) versus 46.1 $\mu\text{g}\cdot\text{m}^3$ (noncontinuous); NO₂ 25.5 $\mu\text{g}\cdot\text{m}^3$ versus 32.1 $\mu\text{g}\cdot\text{m}^3$; O₃ 44.1 versus 48.9 $\mu\text{g}\cdot\text{m}^3$. The values estimated by discontinuous measurements might be slightly higher because no gridpoint measurements were performed between 23:00h and 06:00h at night.

Data analysis

The analyses were restricted to children with complete addresses who had lived in Dresden for at least 12 months and, because of concerns regarding the validity of questionnaire responses, who had German nationality. This reduced the number of children to 2,796 and 2,625 with completed questionnaires, 1,138 and 2,050 with SPT, as well as 870 and 1,887 with serum IgE measurements in the younger and older age groups, respectively. Measurements of lung function were analysed for 1,137 children aged 9–11 years. When comparing the questionnaire responders selected for the analyses ($n = 5,421$) with those excluded ($n = 936$), no significant differences were found with respect to all health outcomes as listed in table 1. In the selected group, exposure to maternal smoking (26.6 versus 21.4%) and lower parental education (72.8 versus 67.1%) were more prevalent as compared to the nonselected group. Furthermore, slightly more children of the higher age group were selected (48.5 versus 44.9%). No significant differences were found for the other potential confounders included in the multivariate models (see below).

Table 1. – Respiratory health and atopy in the study population

	5–7 yr olds	9–11 yr olds
Symptoms in the past 12 months		
Wheeze	188/2730 (6.9)	210/2595 (8.1)
Morning cough	279/2737 (10.2)	310/2592 (12.0)*
Symptoms of allergic rhinoconjunctivitis	153/2727 (5.6)	325/2567 (12.7)*
Symptoms of atopic eczema	317/2737 (11.6)	409/2588 (15.8)*
Doctor's diagnosis		
Asthma	158/2700 (5.9)	203/2582 (7.9)*
Bronchitis	826/2512 (32.9)	920/2478 (37.1)*
Pulmonary function		
Bronchial hyperresponsiveness	ND	156/956 (16.3)
FEV ₁ <85% pred.	ND	72/1137 (6.3)
FEF _{25–75%} <70% pred.	ND	150/1123 (13.4)
Atopy		
Specific IgE to aeroallergens >0.7 kU·L ⁻¹	190/870 (21.8)	605/1887 (32.1)*
SPT reaction ≥ 3 mm to at least one allergen***	146/1138 (12.8)	534/2050 (26.0)*

Data are presented as absolute numbers, with percentages in parentheses. *: $p < 0.05$ for Chi-squared test for comparison of age groups; **: Fluorescence Enzyme Immuno Assay (SX1 panel; Pharmacia, Lund, Sweden): timothy grass, rye, birch, hazel, *Cladosporium herbarum*, *Dermatophagoides pteronyssinus*, cat dog; ***: Skin-prick test solution (ALK, Hørsholm, Denmark): Grass mixture, tree mixture, *D. pteronyssinus*, *D. farinae*, cat, *Alternaria tenuis*. Bronchial hyperresponsiveness was assessed with 4.5% NaCl. FEV₁: forced expiratory volume in one second; FEF_{25–75%}: forced mid-expiratory flow; IgE: immunoglobulin E; ND: not done.

Only 31 children (0.5%) were excluded because of foreign nationality.

At first the crude association between pollutant exposure and the health outcomes shown in table 1 was assessed. The crude association between categories of benzene concentrations, a close indicator of traffic emissions, and the health outcome variables was analysed using the Mantel-Haenszel Chi-squared tests for linear trends. Multivariate logistic regression analyses were performed to assess the effects of the following putative confounding variables: sex, age group, birth weight, parental education, maternal smoking, season of testing, central heating, furry pets, damp housing, carpets, and floor level of the dwelling. Variables were included as potential confounders into the multiple logistic regression model if they were associated with at least one health outcome in the crude analysis (Chi-squared test, $p < 0.25$) and changed at least one pollutant's effect estimate by $>20\%$ when included in the multivariate model. Five variables (sex, age group, birth weight, furry pets, carpets) were included although they failed to change the effect estimates significantly because they were strongly associated with at least one outcome ($p < 0.05$) and were regarded as potential confounders in comparable studies [8, 14]. Each covariate in the multivariate model was tested for interaction with the pollutant effects (likelihood ratio test $p < 0.05$). The estimated individual air pollutant exposure was treated as continuous linear variable in all logistic regression models. Odds ratios were calculated for concentration differences (approximately interquartile ranges) as they are common in inner cities. The analyses were performed using SPSS for Microsoft Windows 6.01 (SPSS Inc., Chicago, IL, USA).

Results

The mean \pm SD age of the studied children was 5.3 ± 0.8 yrs in the younger age group, and 9.7 ± 0.6 yrs in the older age group. Fifty-two per cent were male. The prevalence of atopy and all respiratory symptoms and diagnoses except wheeze was significantly higher in 9–11 yr old children (table 1). The estimated individual exposures to different air pollutants at the home address are given in table 2. The exposure to SO_2 , NO_2 , CO and benzene at school was on average 2.8–3.4% higher than at home.

A significant increase in the prevalence of morning cough in the past 12 months ($p = 0.0007$) and the lifetime prevalence of doctor diagnosed bronchitis ($p = 0.01$) across categories of rising benzene exposure ($<3 \mu\text{g}\cdot\text{m}^3 \rightarrow 4.5 \mu\text{g}\cdot\text{m}^3$) was seen (table 3). Similar, but less pronounced trends were found for the prevalence of wheeze in the past

12 months ($p = 0.05$), the proportion of children with reduced FEF_{25–75%} values ($p = 0.06$) and a doctor's diagnosis of asthma ($p = 0.15$). In contrast, no trend was seen for the occurrence of airway hyperresponsiveness or reduced FEV₁ values over increasing exposure categories. Furthermore, atopic sensitization as assessed by SPT and specific IgE tended to be inversely associated with rising benzene concentrations.

After adjusting for potential confounding factors morning cough in the past 12 months showed the most consistent positive association with the annual mean exposure to several air pollutants: SO_2 , NO_2 , CO and benzene (table 4). For example, the prevalence of morning cough was estimated to increase by $\sim 20\%$ per increase of $1 \text{ mg}\cdot\text{m}^3$ benzene. Likewise, the lifetime prevalence of bronchitis was significantly and positively associated with levels of NO_2 , CO and benzene (but not SO_2). In contrast, yearly mean ozone exposure tended to be negatively associated with morning cough and bronchitis.

In an attempt to disentangle the specific effect of ozone from that of the other traffic related pollutants O_3 was introduced into the multivariate model in combination with other traffic related pollutants. This procedure generally reduced the point estimates of the odds ratios and widened the confidence intervals probably due to colinearity of these strong inversely correlated gases (O_3 – NO_2 : $r = 0.66$, O_3 –CO: $r = -0.55$, and O_3 –benzene: $r = -0.59$). However the general pattern of the observed associations remained unchanged (data not shown).

No clear pattern emerged for the associations between air pollutant exposure and asthmatic conditions. There was a trend towards a positive association between exposure to several pollutants and the lifetime prevalence of doctor diagnosed asthma, but this association reached statistical significance only for the combined estimate of exposure to benzene at home and at school address. No significant association was found between the mean level of air pollution and wheeze in the past 12 months (table 4). Moreover, neither the frequency of wheezing episodes nor the prevalence of speech limiting or sleep disturbing asthma attacks in the past 12 months was significantly associated with exposure to any of the pollutants (data not shown).

BHR was negatively associated with NO_2 and CO, and positively associated with O_3 . No increased risk of atopic sensitization was seen for any pollutant. Likewise, neither a doctor's diagnosis of hay fever and eczema nor symptoms of allergic rhinoconjunctivitis and atopic eczema in the past 12 months were associated with outdoor air pollution exposure (data not shown).

When stratifying children with doctor diagnosed asthma into atopic (SX1 CAP; Pharmacia; $>0.7 \text{ kU}\cdot\text{L}^{-1}$) and nonatopic asthmatics no significant association was found between pollutant exposure and atopic asthma. Nonatopic asthma, however, was significantly associated with pollutant exposure (except for O_3). Similar differences were found when comparing the adjusted prevalence odds ratios (aPOR) for morning cough and bronchitis in atopic and nonatopic children. For wheeze the difference was less pronounced (table 5).

The subgroups of children with doctor diagnosed asthma, BHR, or a parental history of atopic diseases were not at a higher risk for adverse health effects of air pollution than the total population (data not shown). Information on

Table 2. – Estimated mean annual exposure to air pollutants at home address

		mean	minimum	25–75 percentile	maximum
SO_2	$\mu\text{g}\cdot\text{m}^3$	48.3	29.0	42.7–54.3	69.3
NO_2	$\mu\text{g}\cdot\text{m}^3$	33.8	17.1	29.3–37.8	56.0
CO	$\text{mg}\cdot\text{m}^3$	0.69	0.32	0.55–0.76	1.54
Benzene	$\mu\text{g}\cdot\text{m}^3$	4.0	1.9	3.3–4.4	8.7
O_3	$\mu\text{g}\cdot\text{m}^3$	46.0	30.3	43.1–49.1	64.0

asthma medication was available for 180 of the 361 asthmatic children. Among these children increasing levels of pollutant exposure were not associated with an increased use of inhaled steroids (data not shown). There was no effect modification by age group.

The associations between 95th percentile pollutant exposures and morning cough or bronchitis were somewhat weaker but still significantly positive for NO₂ and benzene when considering the home address (data not shown). In turn, the significant inverse association with annual mean O₃ exposure was not seen for high exposure to O₃ (aPOR for morning cough 0.92 (0.81–1.05) and bronchitis 1.04 (0.65–1.67)). Current wheeze was marginally positively associated with peak exposure to NO₂ (aPOR: 1.16 (1.01–1.33)) and SO₂ (aPOR: 1.06 (1.00–1.12)) at home address but these associations were not found for doctor diagnosed asthma, baseline pulmonary function, or BHR. No significant associations were found between peak pollutant exposure and atopic sensitization.

Discussion

The results of this survey suggest that moderate increases in inner city air pollution well below the national ambient air quality standards [29, 30] are associated with an increased prevalence of morning cough and doctor diagnosed bronchitis, but not of airway hyperresponsiveness, atopic sensitization, or symptoms of atopic diseases in children.

Inner city air pollution has many sources of which car traffic is one important contributor. In Dresden the pollutant measurements presented here have also been related to actual traffic counts. In these estimates 87% of the total benzene emission was attributable to road traffic [31]. For other pollutants the association with traffic was lower: 46% of the NO₂ emission, 48% of the CO emission, and only 1.7% of the SO₂ emission could be ascribed to motor

vehicle exhausts [32]. Anthropogenic O₃ is produced by photochemical reactions involving NO₂. It is reduced in the presence of high NO concentrations which occur in areas with dense traffic. Therefore, the measured O₃ levels were inversely correlated with concentrations of NO₂, CO, and benzene.

The adverse health effects were related to exposure to several pollutants. The prevalence of morning cough and bronchitis was positively associated with exposure to benzene, NO₂ and CO, and inversely related to O₃. Benzene concentrations are almost exclusively attributable to motor vehicle emissions. Concentrations of NO₂ and CO are also determined to a substantial degree by traffic but also by other sources (e.g. indoor heating and industrial combustion). Thus, traffic is an important but not the only source of agents which may account for the observed associations.

SO₂ was positively associated with current morning cough but not with bronchitis. This pollutant predominantly represents other sources than traffic therefore its longterm effects may differ from those of the other pollutants. The inverse associations of annual mean O₃ exposure with morning cough and bronchitis were not seen for peak exposures to O₃. Exposure to high concentrations of O₃ are known to induce airway irritation [33] and impairment of pulmonary function [34]. This may counteract the inverse effects of low traffic exposure in some districts of the Dresden area.

There was no positive association between exposure to benzene, NO₂ and CO and the prevalence of symptoms or diagnoses of hay fever and eczema, atopic sensitization, and BHR. The associations between pollutant exposure and respiratory symptoms and diagnoses were clearly stronger in nonatopic than in atopic children. These findings are in line with the hypothesis that these air pollutants induce nonspecific irritative rather than allergic inflammatory changes in the airway mucosa. Irritative effects would affect the clinical course in nonatopic children more

Table 3. – Prevalence of respiratory symptoms and diseases, reduced pulmonary function, and atopy in all children* by categories of exposure to benzene

	Estimated outdoor exposure to benzene at home address**					p-value***
	-3 µg·m ³	-3.5 µg·m ³	-4 µg·m ³	-4.5 µg·m ³	>4.5 µg·m ³	
Symptoms in the past 12 months						
Wheeze	37/660 (5.6)	72/1035 (7.0)	80/1079 (7.4)	117/1334 (8.8)	92/1217 (7.6)	0.054
Morning cough	58/657 (8.8)	92/1036 (8.9)	120/1089 (11.0)	171/1334 (12.8)	148/1213 (12.2)	0.00073
Doctor's diagnosis						
Asthma	32/643 (5.0)	71/1022 (6.9)	74/1081 (6.8)	99/1316 (7.5)	85/1220 (7.0)	0.15
Bronchitis	205/612 (33.5)	316/975 (32.4)	348/1007 (34.6)	444/1251 (35.5)	433/1145 (37.8)	0.011
Pulmonary function						
Bronchial hyperresponsiveness	14/77 (18.2)	33/149 (22.1)	30/226 (13.3)	47/290 (16.2)	32/214 (15.0)	0.20
FEV ₁ <85% pred.	5/118 (4.2)	13/201 (6.5)	15/251 (6.0)	26/334 (7.8)	13/233 (5.6)	0.56
FEF _{25-75%} <70% pred.	9/117 (7.7)	25/198 (12.6)	31/248 (12.5)	52/327 (15.9)	33/233 (14.2)	0.064
Atopy						
Specific IgE to aeroallergens >0.7 kU·L ⁻¹	109/317 (34.4)	137/526 (26.0)	191/611 (31.3)	206/692 (29.8)	152/611 (24.9)	0.045
SPT reaction ≥3 mm to at least one allergen	87/372 (23.4)	123/609 (20.2)	169/681 (24.8)	172/816 (21.1)	129/710 (18.2)	0.069

*: The results are presented for 5–7 and 9–11 yr olds combined, with percentages in parentheses. **: categories of benzene exposure are characterized by their upper limits except for the highest category. The extreme categories represent larger ranges of exposure in order to achieve sufficiently large sample sizes; ***: Mantel-Haenszel Chi-Square test for linear trend. Bronchial hyperresponsiveness was assessed with 4.5% NAC. FEV₁: forced expiratory volume in one second; FEF_{25-75%}: forced mid-expiratory flow; IgE: immunoglobulin E.

Table 4. – Association of respiratory symptoms and diseases, pulmonary function, and atopy in children with exposure to inner city air pollutants at home (EHA) and at home and school address (EHSA)

	Subjects n*	SO ₂ +10 µg·m ³	NO ₂ +10 µg·m ³	CO +0.2 µg·m ³	Benzene +1 µg·m ³	O ₃ +10 µg·m ³
Symptoms in the past 12 months						
Wheeze						
EHA	4518	1.07 (0.92–1.24)	1.13 (0.93–1.37)	1.05 (0.93–1.18)	1.05 (0.93–1.18)	0.84 (0.66–1.07)
EHSA	2218	1.09 (0.86–1.38)	0.95 (0.72–1.26)	1.02 (0.85–1.22)	1.08 (0.90–1.29)	0.79 (0.56–1.13)
Morning cough						
EHA	4515	1.16 (1.02–1.31)	1.22 (1.04–1.44)	1.12 (1.01–1.23)	1.15 (1.04–1.27)	0.80 (0.65–0.98)
EHSA	2211	1.30 (1.06–1.59)	1.21 (0.96–1.52)	1.13 (0.98–1.30)	1.21 (1.04–1.40)	0.71 (0.53–0.96)
Doctor's diagnosis						
Asthma						
EHA	4477	1.06 (0.90–1.24)	1.16 (0.94–1.42)	1.07 (0.94–1.21)	1.11 (0.97–1.25)	0.79 (0.61–1.02)
EHSA	2203	1.05 (0.83–1.34)	1.14 (0.86–1.51)	1.16 (0.97–1.38)	1.21 (1.01–1.45)	0.62 (0.43–0.89)
Bronchitis						
EHA	4228	0.92 (0.85–1.00)	1.23 (1.11–1.38)	1.19 (1.11–1.27)	1.11 (1.03–1.19)	0.83 (0.73–0.96)
EHSA	2114	0.91 (0.80–1.04)	1.27 (1.09–1.49)	1.24 (1.12–1.38)	1.16 (1.04–1.29)	0.83 (0.67–1.02)
Pulmonary function						
BHR						
EHA	838	0.92 (0.68–1.23)	0.61 (0.45–0.84)	0.79 (0.63–0.99)	0.80 (0.62–1.03)	1.52 (1.00–2.31)
EHSA	838	0.94 (0.66–1.34)	0.58 (0.41–0.82)	0.77 (0.60–0.99)	0.81 (0.62–1.06)	1.60 (1.02–2.52)
FEV ₁ <85% pred.						
EHA	992	1.24 (0.83–1.83)	0.95 (0.62–1.44)	1.09 (0.81–1.47)	1.19 (0.86–1.64)	1.20 (0.70–2.07)
EHSA	992	1.44 (0.89–2.33)	0.85 (0.54–1.36)	1.01 (0.73–1.41)	1.17 (0.81–1.67)	1.34 (0.76–2.37)
FEF _{25–75%} <70% pred.						
EHA	981	1.18 (0.90–1.56)	1.14 (0.86–1.51)	1.15 (0.94–1.39)	1.27 (1.03–1.58)	0.75 (0.51–1.10)
EHSA	981	1.25 (0.90–1.73)	1.05 (0.78–1.43)	1.07 (0.86–1.34)	1.17 (0.92–1.50)	0.89 (0.59–1.32)
Atopy						
Specific IgE against aero-allergens >0.7kU·L ⁻¹						
EHA	2361	1.02 (0.90–1.16)	0.96 (0.82–1.12)	0.95 (0.86–1.06)	0.98 (0.88–1.09)	0.93 (0.76–1.13)
EHSA	1629	0.87 (0.74–1.03)	0.89 (0.73–1.08)	0.94 (0.83–1.06)	0.92 (0.81–1.05)	1.06 (0.82–1.35)
SPT reaction ≥3 mm to at least one allergen						
EHA	2729	1.03 (0.90–1.17)	1.01 (0.86–1.19)	0.99 (0.89–1.10)	1.02 (0.92–1.14)	0.94 (0.76–1.16)
EHSA	1760	0.92 (0.78–1.08)	1.02 (0.84–1.24)	1.01 (0.90–1.15)	1.01 (0.89–1.15)	0.98 (0.76–1.26)

Data are presented as absolute numbers (subjects) or prevalence odds ratio (POR) with 95% confidence intervals (95% CI) in parentheses (SO₂, NO₂, CO, benzene and O₃). POR and 95% CI were calculated by logistic regression analysis adjusting for the following putative confounding variables: sex, age group, birth weight, parental education, maternal smoking, season of testing, central heating, furry pets, damp housing, carpets, and floor level. Exposure at home address (EHA) was estimated for 5–7 and 9–11 yr olds combined. Exposure at home and school address (EHSA) was estimated for 9–11 yr olds only as the mean of exposures determined for home and school address. BHR: bronchial hyperresponsiveness; FEV₁: forced expiratory volume in one second; FEF_{25–75%}: forced mid-expiratory flow; IgE: immunoglobulin E; SPT: skin-prick test.

strongly than in atopics whose symptoms are also determined by allergen exposure.

The observation that the level of exposure was associated with nonatopic asthma and not with atopic asthma corroborates this notion. In this nonatopic subgroup, asthma may mainly be triggered or induced by viral infections. Some evidence suggests that the development of childhood respiratory tract infections is in fact related to increasing exposure to SO₂, NO₂ and particles [3, 4, 15]. Alternatively, irritative symptoms due to higher pollution exposure may result in more frequent visits to a physician who may then be more likely to misclassify a bronchitic child as asthmatic. In this case the association of pollutant exposure with asthma would have been overestimated and the association with bronchitis would have been underestimated in this study.

The selection of children with German nationality who had lived for ≥12 months in Dresden resulted in a population with slightly higher exposure to maternal smok-

ing and lower parental education. In such children outdoor pollution may contribute to a smaller amount to the overall effects of environmental hazards. Therefore the associations between outdoor pollution and respiratory health or atopy might have been underestimated in this study. The reduction of the study population by selection of children with German nationality was quantitatively negligible. In addition, ethnicity has been shown to be a significant determinant for the prevalence of atopic diseases in Germany [35].

When interpreting these findings it is important to bear in mind that in Dresden, as in many other areas of the former East Germany, exposure to air pollution has changed tremendously in the first years after German reunification in 1989. Levels of SO₂ have decreased substantially between 1989–1992 [36] and car traffic exposure has increased between 1990–1994 [37]. The adverse health effects seen in this study are therefore likely to reflect exposure in the past few years. The exposure

Table 5. – Association of respiratory symptoms and diseases with exposure to inner city air pollutants at home address* in atopic and nonatopic children

	Subjects n	SO ₂ +10 µg·m ³	NO ₂ +10 µg·m ³	CO +0.2 µg·m ³	Benzene +1 µg·m ³	O ₃ +10 µg·m ³
Symptoms in the past 12 months**						
Wheeze						
Atopic children ⁺	4391	1.03 (0.79–1.35)	1.05 (0.76–1.45)	1.00 (0.81–1.24)	1.02 (0.83–1.27)	0.81 (0.53–1.23)
Nonatopic children [#]	4379	1.36 (1.01–1.84)	1.16 (0.79–1.70)	1.05 (0.83–1.31)	1.09 (0.87–1.36)	1.08 (0.68–1.73)
Morning cough						
Atopic children ⁺	4316	1.22 (0.92–1.61)	1.09 (0.77–1.54)	1.03 (0.82–1.29)	1.08 (0.86–1.35)	0.67 (0.43–1.04)
Nonatopic children [#]	4306	1.32 (1.07–1.63)	1.42 (1.10–1.84)	1.22 (1.05–1.41)	1.26 (1.08–1.46)	0.84 (0.60–1.16)
Doctor's diagnosis						
Asthma						
Atopic children ⁺	4378	1.07 (0.79–1.45)	1.01 (0.70–1.46)	1.05 (0.83–1.32)	1.11 (0.88–1.40)	0.88 (0.54–1.41)
Nonatopic children [#]	4350	1.35 (1.00–1.82)	1.49 (1.04–2.16)	1.29 (1.05–1.59)	1.32 (1.07–1.62)	0.64 (0.40–1.03)
Bronchitis						
Atopic children ⁺	3634	1.04 (0.87–1.25)	1.00 (0.79–1.26)	1.00 (0.86–1.16)	0.95 (0.80–1.11)	1.07 (0.80–1.44)
Nonatopic children [#]	3585	0.99 (0.88–1.12)	1.37 (1.17–1.62)	1.21 (1.10–1.33)	1.13 (1.03–1.25)	0.83 (0.68–1.01)

*: Exposure at home address was estimated for 5–7 and 9–11 yr olds combined; **: prevalence odds ratio (POR) and 95% confidence intervals (in parentheses) were calculated comparing atopic and nonatopic children with specified symptoms or diagnoses with the remaining population not meeting the criteria. The numbers of cases with information on symptoms or diagnoses differed in atopic and nonatopic children. Therefore different numbers of cases were included in the models. POR were calculated by logistic regression analysis adjusting for the following putative confounding variables; sex, age group, birth weight, parental education, maternal smoking, season of testing, central heating, furry pets, damp housing, carpets, and floor level; ⁺: specific immunoglobulin (Ig)E to aeroallergens >0.7 kU·L⁻¹; [#]: specific IgE to aeroallergens ≤0.7 kU·L⁻¹.

assessment preceded the measurement of health outcomes by ~1 yr. There were, however, no major changes in the immission of traffic related air pollutants in Dresden between 1994/95–1995/96 [36] and the questionnaire referred to symptoms in the preceding 12 months.

At the 29 monitoring stations in streets the NO₂ concentrations were significantly higher (mean 37.4 µg·m⁻³) than at the next monitoring sites in eastern (30.3 µg·m⁻³), western (32.5 µg·m⁻³), northern (30.4 µg·m⁻³), or southern (34.3 µg·m⁻³) direction (Wilcoxon matched-pairs signed-rank Test, each p<0.05). The measurements of the street monitors may result in an overestimation of exposure for some children living at a short distance from these monitors but not directly in the street where the measurement was done. In contrast, 17.5% of the children (948/5,421) lived in streets with dense traffic (>5000 cars·24 h⁻¹). For these children exposure may have been underestimated if none of the four monitoring sites used to estimate their exposure were placed in the street of residence. These types of misclassification of exposure may have led to an attenuation of the effect estimates.

The exposure estimate does not take building structures around streets into account, but covariates like "floor level of the dwelling" or "window of the child's room opening to a street" did not change the effect estimates significantly. Stratification by parental-reported traffic exposure did not eliminate the associations between pollutant exposure and reported cough or bronchitis. Thus, it is unlikely that preferential reporting of symptoms or diagnoses has distorted the findings.

Other studies have suggested that exposure to truck traffic and black smoke may be associated with asthma symptoms and reduced pulmonary function in children [11–15]. This specific association was not investigated in the current study, because black smoke had not been measured in the 1 km² grid. In studies which measured both, gases and particles, a close correlation was found

between concentrations of NO₂ and particulate matter <10 µm in diameter (PM₁₀) (r=0.94, [8]), or NO₂ and black smoke (r>0.70, [14]). However, PM₁₀ does not specifically represent diesel exhausts, and the black smoke concentrations were monitored in schools close to motorways where large variations in traffic density can increase correlations between all traffic dependent pollutants regardless of the specific source. Therefore, the current NO₂ exposure estimates cannot be regarded as specific markers of truck traffic exposure.

When including parental reports of truck traffic in the street of residence instead of the estimates of air pollutant exposure into the multivariate model significant associations with morning cough (aPOR for "constant" compared to "no truck traffic": 1.60 (1.06–2.42)) and wheeze (aPOR: 2.09 (1.24–3.53)) were found. Only nonsignificant tendencies towards higher prevalences with increasing traffic exposure were found for both doctor diagnosed asthma and bronchitis, and no association was observed with pulmonary function, BHR, and atopy. This is fairly consistent with the data from two other studies. The first study [11] presented data for chronic cough and found a similar association of this rather unspecific symptom with truck traffic and black smoke exposure as with wheeze. The second study [15] found an association of truck traffic exposure with current wheeze, cough and persistent phlegm, but not with current asthma and not with wheezing episodes in the first two years of life. These authors concluded that air pollution from truck traffic increases the risk for a wide range of adverse respiratory effects but may have a more important role in respiratory infections than in the aetiology of asthma. None of the studies on truck traffic exposure measured bronchial hyperresponsiveness or objective markers of atopy.

The results are also consistent with the findings of DOCKERY *et al.* [2] and BRAUN-FAHRLÄNDER *et al.* [8] who showed a significant association between cough and

bronchitis, but not asthma or atopic conditions with concentrations of particulate matter [2, 8], NO₂ and SO₂. [8]. Likewise, in children living in Munich, West Germany, high rates of road traffic increased respiratory symptoms, but were not associated with the prevalence of hay fever, asthma, and BHR [9].

In summary, the findings suggest that in children exposure to the traffic related air pollutants NO₂, CO, and benzene is associated with an increased prevalence of cough and bronchitis but not with the prevalence of atopic sensitization, symptoms of atopic diseases, and bronchial hyperresponsiveness.

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