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Effect of Moderate NO_2 Air Pollution on the Lung Function of Children with Asthmatic Symptoms

MICHAEL MOSELER, ANNELIESE HENDEL-KRAMER, WILFRIED KARMAUS,[1]
JOHANNES FORSTER, KATHARINA WEISS, RADVAN URBANEK,[2]
AND JOACHIM KUEHR[3]

University Children's Hospital, D-79106 Freiburg, Germany

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In the course of a 2½-year longitudinal study, the influence of outdoor NO_2 and of the heating device at home on lung function was investigated in 467 children of school age in the urban area of Freiburg. Data were gathered in three surveys using standardized interviews, lung function measurements, skin prick tests with inhalant allergens, and NO_2 measurements from October to April near the child's home. Regarding the lung function of a subpopulation with asthmatic symptoms (n = 106) in the three consecutive surveys, multivariate regression analyses adjusted for confounders indicate negative associations between five dependent variables, FEV_1%FVC (P = 0.004), FEV_1% (P = 0.02), MEF_{75}% (P = 0.038), MEF_{50}% (P = 0.052), and MEF_{25}% (P = 0.002), on the one hand, and outdoor NO_2 for average NO_2 concentrations exceeding 40 $\mu g/m^3$ on the other. The use of individual room heaters is associated with decreased lung function and is significant only for FEV_1%FVC (P = 0.033). Neither NO_2 nor individual room heating is significantly associated with one of the lung function parameters in the subpopulation without asthmatic symptoms (n = 361). In conclusion, children with asthmatic symptoms are identified as being susceptible to having reduced lung function under outdoor air pollution where average NO_2 concentrations exceed 40 $\mu g/m^3$.

INTRODUCTION

Since the London Fog period of 1952, which resulted in an increased incidence of respiratory tract illness, the detrimental effect of high levels of air pollution on human airways seems to be indisputable (Logan, 1953). Whether considerably lower levels of air pollution have any influence on respiratory morbidity is at present a controversial matter. A necessary corollary to the question of the extent to which air pollutants cause certain respiratory tract illnesses is how already existant illnesses and symptoms are affected by air pollutant concentrations. This latter question led to the development of analytic studies on susceptible groups.

Children are considered extremely sensitive to pollutants, more so than adults, due to increased metabolic activity as a result of lung growth and high lung volumes during breathing. Asthmatic children were reported to be particularly sensitive (Dockery *et al.*, 1989).

In addition to industrial sources, NO_2 is emitted by cars especially and thus shows little variability throughout the year. It can occur in combination with other pollutants and therefore may also be an indicator for the extent of a more complex

[1] NORDIG Institute for Health Research, Germany.
[2] University Children's Hospital, Vienna, Austria.
[3] To whom correspondence should be addressed at University Children's Hospital Freiburg, Mathildenstr. 1, D-79106 Freiburg, Germany.

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pollution of outdoor air. Furthermore, NO_2 can be present in significant concentrations indoors as well. For instance, combustion processes within the home can contribute to increased loads in indoor air.

The current study was designed to determine a period effect of outdoor NO_2 air pollution at low and moderate concentrations in the winter on the lung function of children. In addition to NO_2, the type of the heating system as a possible source of indoor air pollution was considered as a risk factor.

POPULATION AND METHODS

In September, 1987, a cover letter requesting participation in the study was sent to 81% (n = 5078) of families with school children (birth between 9/1/1971 and 8/31/1980) in the Freiburg area. The region is characterized as having a homogeneous climate with very low intraseasonal changes (Rhine valley). Of these families, 7.5% agreed to participate, making an initial study population of 569 children. One account of the low response proportion, a telephone survey of a randomly selected group of nonresponders was carried out. The results of this survey do not suggest a selection bias with respect to doctor's diagnosed asthma (Table 1) or with respect to the educational level of the parents (Table 1, Kühr *et al.*, 1991).

The children were first examined in October, 1987, and then twice more at intervals of 11 months until May, 1990, thus providing three measurements for each child. At the end of the study completed data for 467 children (82.1% of the initial population) were available. The following instruments were used for data collection in each of the three surveys: standardized interview with the mother, skin prick test, lung function test, measurement of the outdoor NO_2 concentration.

TABLE 1
COMPARISON OF PERCENTAGES OF NONPARTICIPATING FAMILIES, THE TOTAL STUDY POPULATION IN THE LONGITUDINAL STUDY, AND THE STUDY POPULATION WITH THREE CONSECUTIVE LUNG FUNCTIONS

Questions	Sample of nonresponders (n = 291) (participation: 71.8%)	Total study population (n = 569) (participation of all families with children: 7.5%)	Study population with three consecutive lung functions (n = 467)
Doctor's diagnosis of asthma (lifetime prevalence)	4.2	4.6	6.2
Social status			
Tertiary education	40.0	36.9	40.0
Technical college	18.7	18.3	18.4
Apprenticeship	32.8	36.7	34.9
Unskilled	8.7	8.1	6.6

Group with asthmatic symptoms. Using standardized interviews, the following asthmatic symptoms occurring during the 12-month period prior to each interview were ascertained: any dyspnoea including dyspnoea with wheezing, exercise-induced dyspnoea, nocturnal dyspnoea, morning cough on most days, cough in spring and summer on most days. Of the total sample (n = 467) 106 children with at least one of these symptoms in one of the three surveys were categorized as the group with asthmatic symptoms (22.7%).

Variables of interest. The NO_2 measurement provided average concentrations near the child's home during three heating periods (October to April). The NO_2 concentrations were measured for periods of 1 week by the German Weather Service using fixed outdoor passive samplers at 31 locations (Palmes *et al.*, 1976). Palmes' tubes were placed in a wind and rain shielded instrument (device: Sigma-2) (Verein Deutscher Ingenieure, 1990). The fixed passive samplers were distributed all over the city, avoiding the direct vicinity of roads or other traffic. In the first winter half-year the NO_2 concentrations based on fixed passive sampling and continuous monitoring were highly correlated with each other (r = 0.79, n = 67 pairs). The heating system was chosen as an indicator of indoor air pollution with combustion products. The type of heating and heating fuel used were categorized by a dichotomous variable, differentiating wood and fossil fuel burning individual room heaters within the home from other heating systems.

Dependent variables. In each survey within the period of the outdoor measurements lung function tests were carried out on the day of the interview in a standardized manner with the same staff (Kühr *et al.*, 1989). The tests took place in the afternoon between 2 and 6 pm. No prior withdrawal of medication by asthmatic children was required. The lung function was tested in a sitting position using a nose clip and a mouth piece (Jaeger, Germany). On each occasion, following two to three complete flow volume envelopes for practice (and if reproducibility was assured), the definite measurement was ascertained. Five indicators of the lung function (FEV_1%FVC, FEV_1, MEF_{25}, MEF_{50}, MEF_{75}) were derived from the complete flow volume envelopes (Pneumoscop, Jaeger, Germany). Four parameters are expressed as a percentage of the predicted value (FEV_1%, MEF_{25}%, MEF_{50}%, MEF_{75}%) using reference values based on body surface (Zapletal, 1987).

Confounding variables. The extent of passive smoking was analyzed as a function of any current tobacco consumption in the living area. Furthermore, gender, age, asthmatic disposition (asthmatic history of parents and grandparents), frequent respiratory tract infections at preschool age, and social status (occupational training of the parents: tertiary education, technical college, apprenticeship, and unskilled) as reported in the interview were regarded as confounding variables. A skin prick test (SPT) with 10 common inhalant allergens (ALK, Denmark) was carried out in each survey (Kuehr *et al.*, 1992). The allergic reactivity was recorded as the largest ratio of the wheal diameter to one of the 10 allergens and the diameter to histamine obtained in the corresponding survey.

Statistical analysis. In order to estimate the weekly NO_2 concentration near the children's residences, a polynomial of fifth degree in x and y (x,y presents a measurement location in the city) was fitted based on the weekly NO_2 concentrations of 31 measurement locations (x,y) and taking the natural border of the town into account, which was defined due to meteorological and geographical points of view.

The median of these weekly NO_2 values during each of the three surveys (October to April 1987/88, 1988/89, and 1989/90) was used in the analysis.

To explain the five dependent variables in each of the three measurements by the variables of interest (NO_2, individual room heating) under mutual control of the confounding variables, multivariate linear regression was applied. Since all three measurements of lung function had been carried out within a time period of 21 months, on average chronological effects were considered individual differences over time (Kessler *et al.*, 1981). All chronological effects could be discounted with one exception: for $FEV_1\%$ a combined effect of gender and time had to be considered. With this exception it could be assumed that each child had three measurements taken almost concurrently. In a repeated-measurement model all three surveys were used to assess the strength of effects (Schluchter, 1988). The statistical procedure can be briefly described as follows (Jennrich *et al.*, 1986; Schluchter, 1988):

If Y_i is the dependent variable, X_{ij} the jth explanatory variable, and ϵ_i the measurement error to time i, then the relationships between the dependent and the explanatory variables can be expressed as:

$$Y_1 = \beta_0 + \beta_1 X_{11} + \ldots + \beta_k X_{1k} + \epsilon_1$$

$$Y_2 = \beta_0 + \beta_1 X_{21} + \ldots + \beta_k X_{2k} + \epsilon_2$$

$$Y_3 = \beta_0 + \beta_1 X_{31} + \ldots + \beta_k X_{3k} + \epsilon_3.$$

For the residual vector $\epsilon = (\epsilon_1, \epsilon_2, \epsilon_3)$, a normal distribution and a compound symmetry structure of its covariance matrix are required:

$$\text{cov}(\epsilon_i,\epsilon_j) = \begin{cases} V(i = j) \\ C(i \neq j) \end{cases}$$

The statistical program applied calculates the maximum likelihood estimates for values from β_0 to β_k, V and C (Jennrich *et al.*, 1986; Schluchter, 1988).

Since the requirement of linearity for the effect of NO_2 on the lung function variables was invalidated (Fig. 1) the approach of a linear regression had to be reconsidered. Of two alternatives, the use of dummy variables and the application of a threshold model, we favored the latter. The reasons are (a) a previous finding of a threshold relation (Schwartz, 1989), (b) loss of information in applying indicator (dummy) variables, and (c) biological plausibility for a threshold effect of NO_2 in the range of low doses. Thus the NO_2 concentrations were transformed assuming no effect below 40 $\mu g/m^3$ and a linear effect above 40 $\mu g/m^3$ (range: 12 to 51 μg/m3). The latter values were diminished by 40 $\mu g/m^3$.

In order to obtain a multivariate normal distribution, which is required for linear regressions, the natural logarithm (ln) of the $FEV_1\%$, $MEF_{25}\%$, $MEF_{50}\%$, and $MEF_{75}\%$ was taken. Variables (confounders) influencing the relationship between the variables of interest and the outcome variable by less than 10% were eliminated from the regression model (Greenberg *et al.*, 1985).

RESULTS

The total population comprises children with and without asthmatic symptoms. Table 2 shows the frequency of characteristic features in the group with symptoms and the remaining nonsymptomatic population. Of the former group, 23.6% had been earlier diagnosed as having asthma by a practitioner (lifetime prevalence). Furthermore, in 65.1% of the symptomatic children a positive skin prick test occurred. Of the 106 children with asthmatic symptoms, complaints were reported for 62% in one, for 22% in two, and for 16% in all three interviews (Table 3). In the group with asthmatic symptoms the median values of all lung functions are lower than in the subpopulation without asthmatic symptoms and are significant for each of the parameters and in each of the three surveys (Table 4).

Figure 1 illustrates the relationship between the outdoor NO_2 concentration and the five lung function variables. On average, the lung function values decrease with NO_2, all five parameters starting from the concentration of 40 $\mu g/m^3$. In order to fulfill linearity required for linear regression, the NO_2 concentrations were transformed as follows: NO_2 below 40 $\mu g/m^3$ (threshold value) was put at zero, and all other NO_2 concentrations were diminished by 40 $\mu g/m^3$.

Table 5 shows the parameter estimates and significances of the final models for the group of children with (n = 106) and without (n = 361) asthmatic symptoms, each based on three individual lung function measurements. In the group with asthmatic symptoms NO_2 shows a significantly ($P \leq 0.05$) negative association with four of the five lung function parameters (Table 5). For $MEF_{50}\%$ the association is negative but without statistical significance ($P = 0.052$). Individual room heating is associated with diminished lung function in the susceptible group, being significant only for $FEV_1\%FVC$.

The parameter estimates indicate changes of the dependent variable, e.g., $FEV_1\%FVC$, for an increase per unit of the explanatory variables under statistical control of all other variables in the model (Table 5). For instance, an increase in NO_2 of 1 $\mu g/m^3$ exceeding the threshold level of 40 $\mu g/m^3$ is associated with a decline of $FEV_1\%FVC$ of 0.437%. The use of individual room heating is associated with a $FEV_1\%FVC$ reduction of 3.536%.

In order to test whether the effects of NO_2 also exist in each cross section, regression analyses were repeated for each observation period. Table 6 indicates a consistent effect of NO_2 in the three winter periods with the exception of $MEF_{75}\%$. Regarding the group without asthmatic symptoms, neither NO_2 nor individual room heating has any obvious significant effect. Of the confounding variables, increased allergic reactivity in SPT has a negative association with lung function in both subpopulations, and is significant ($FEV_1\%FVC$, $MEF_{75}\%$, $MEF_{25}\%$) in the susceptible group. Children with frequent respiratory tract infections at preschool age and boys show a decrease of lung function parameters in both groups. The relationship of age and lung function varies with the parameter and the group.

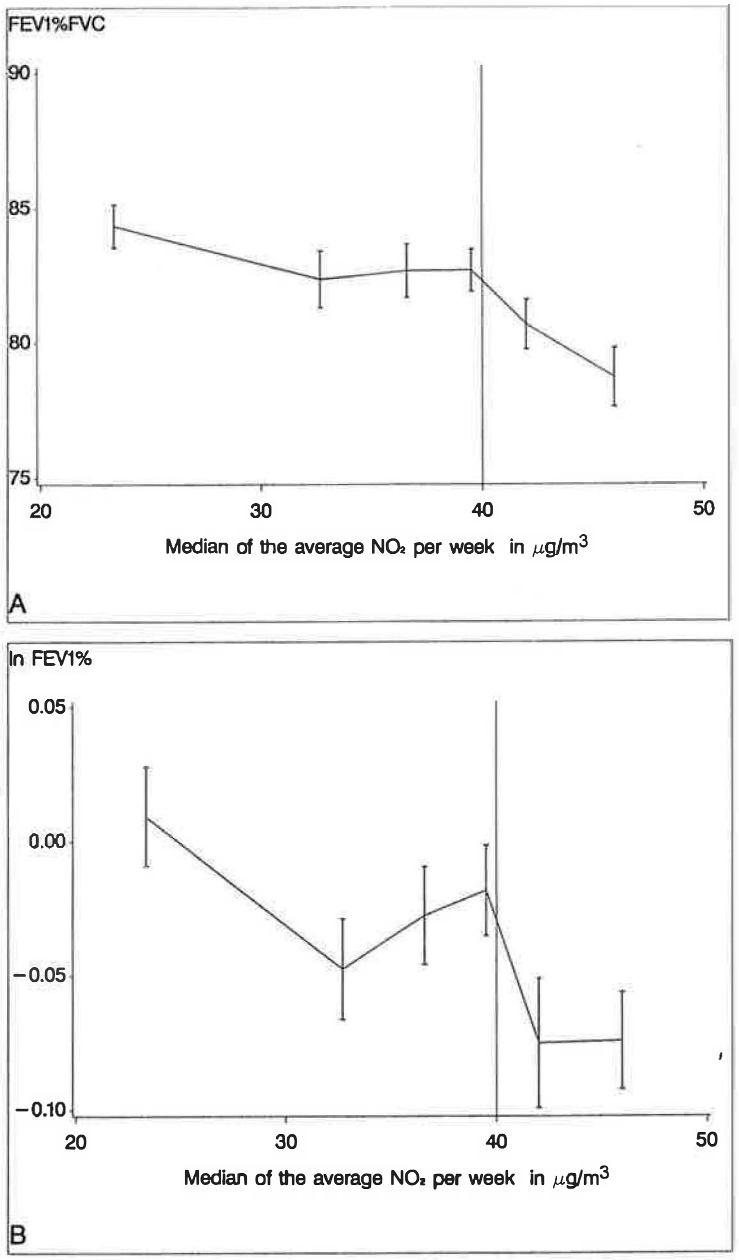

FIG. 1. Bivariate analysis of the relationships between outdoor NO_2 and $FEV_1\%FVC$ (A), $FEV_1\%$ (B), $MEF_{25}\%$ (C), $MEF_{50}\%$ (D*), $MEF_{75}\%$ (E) for the group with asthmatic symptoms (n = 106). For the purpose of illustration, the 318 NO_2 measurements (range 12–51 μg/m^3) were divided into six classes each comprising 53 measurements. Within each class the arithmetic means of the lung function values and the corresponding NO_2 values were calculated, respectively, and these averages form the shape of the curve. Additionally the standard error of mean of the lung function parameter is indicated by vertical bars for each NO_2 class. *For correspondence with multivariate models (see Table 5), only the relationships in the second and third survey are provided.

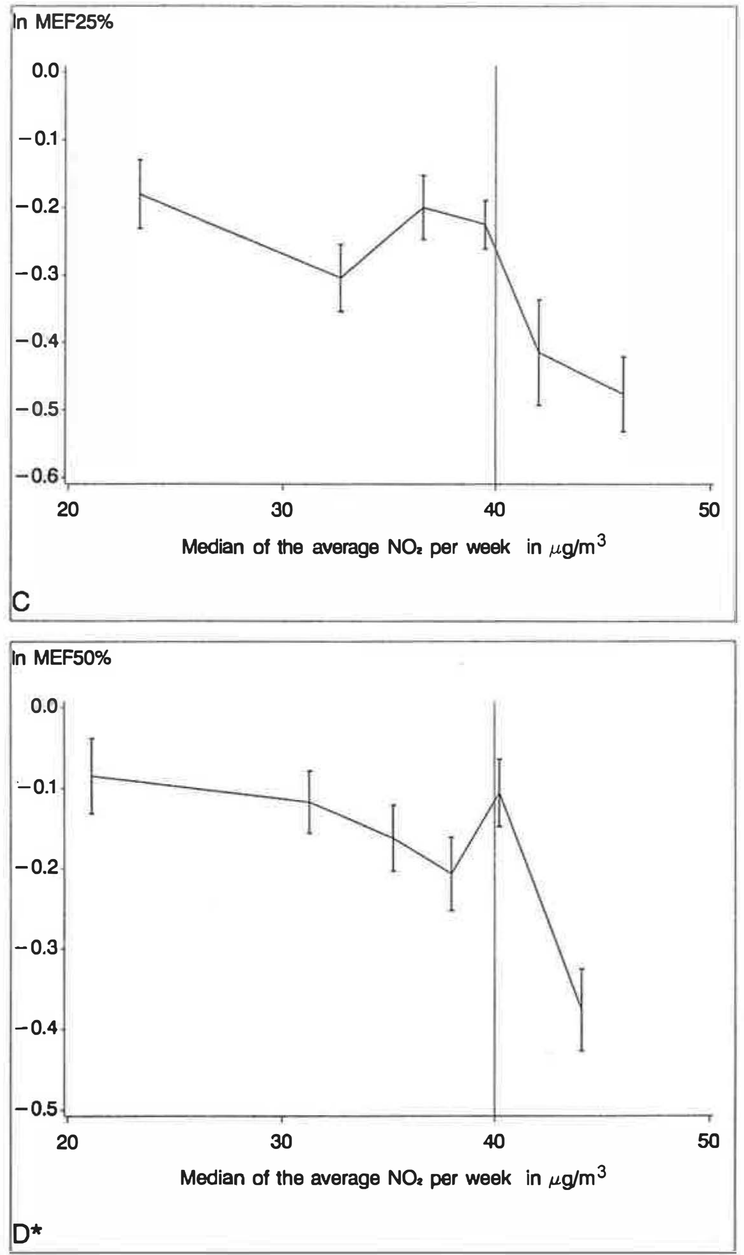

FIG. 1—*Continued*

DISCUSSION

Our study suggests that moderate air pollution, indicated by average NO_2 concentrations, affects lung function in a susceptible subgroup of school-aged children, being significant for four of five parameters. On the other hand, no significant effect of a variable of interest on one of these lung function parameters could

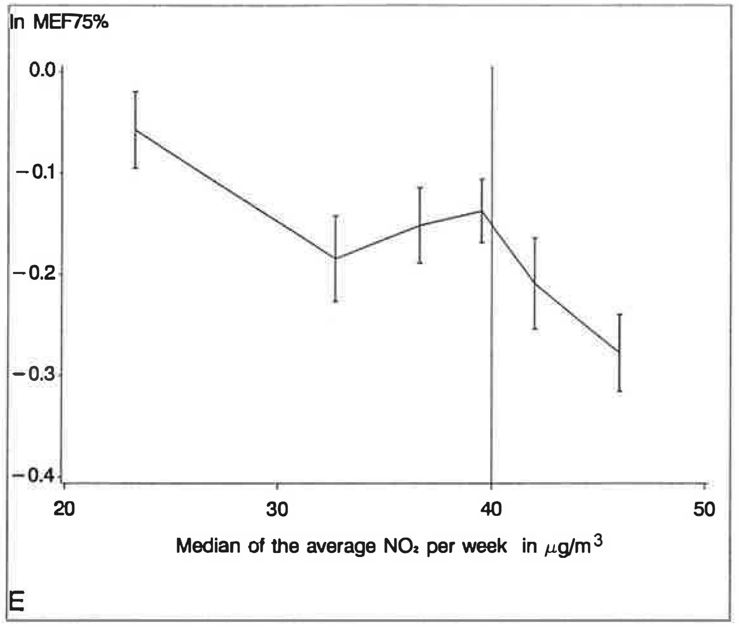

FIG. 1—*Continued*

be identified for the remaining population. In contrast to the others, asthmatic symptoms are reported at least once throughout the study in the case of susceptible children. The difference between the two subpopulations regarding respiratory health is furthermore suggested by the fact that the lung function in the susceptible group is significantly reduced on the basis of all five parameters in each of the three surveys compared to the symptom-free children (Table 4). Since the susceptible group shows homogeneity regarding asthmatic history as well as relatively reduced lung function, it seemed appropriate to us that an effect of NO_2 air pollution on lung function among these children should be presented separately.

The three measurements of the children's lung function took place within the periods of the corresponding NO_2 measurement. In order to estimate a medium- to long-term rather than a short-term effect, the median of the NO_2 concentration of the respective winter season was used. The median indicates that a child spent roughly half the heating period at an exposure at equal or higher level. In comparison to the mean value, the median is less affected by single outlying measurements. In addition to the median of the heating period, the NO_2 median of the 6 weeks preceding the lung function measurement was used showing similar but weaker associations (not shown). The latter suggests an effect expressed within months rather than within days.

The recent work of a Swiss group (Braun-Fahrländer *et al.,* 1992) compared the annual mean of NO_2 on the incidence and mean symptom duration with a 6-week average, showing a stronger effect for the 6-week period. Our study, however, concentrates on an effect of air pollution on lung function in the heating period, which is not described by the annual mean.

TABLE 2
CHARACTERISTIC VARIABLES IN THE SUBPOPULATION WITH AND WITHOUT ASTHMATIC SYMPTOMS

Variable	Asthmatic symptoms: Yes (n = 106)	Asthmatic symptoms: No (n = 361)
Doctor's diagnosis of asthma	23.6%	1.1%
Positive skin prick test	65.1%	35.7%
Frequent respiratory tract infections at preschool age	50.0%	24.1%
Family history of asthma	55.7%	38.2%
NO_2 concentration (median, 5%, and 95% values)		
1st survey	42 (26–47)	42 (29–49)
2nd survey	35.2 (18.7–44)	35.2 (20.9–45)
3rd survey	37.4 (19.8–44)	36.3 (23.1–47.3)
Individual room heating	10.4%	6.9%
Gender		
Male	55.7%	50.1%
Female	44.3%	49.9%
Age in 1987		
≤10 years	50.9%	46.5%
<10 years	49.1%	53.5%
Passive smoking		
1st survey	29.2%	27.1%
2nd survey	30.2%	26.0%
3rd survey	31.1%	24.6%
Social status		
Tertiary education	34.9%	41.6%
Technical college	17.9%	18.6%
Apprenticeship	37.7%	34.1%
Unskilled	9.4%	5.8%

Since the group of children with asthmatic symptoms encompasses 21.8% of the total study population, a relatively large proportion of children are shown to be at risk of being sensitive to NO_2 at moderate concentrations. However, the definition based on their history is not the only characteristic of this group. From Table 2 it can be seen that compared to the symptom-free population, a relatively higher

TABLE 3
TYPE AND FREQUENCY OF ASTHMATIC SYMPTOMS

Period prevalence in	Dyspnoea including wheezing	Exercise-induced dyspnoea	Nocturnal dyspnoea	Morning cough	Cough spring/summer	At least one symptom
3 surveys	7.5	6.6	0.9	3.8	—	16.0
2 surveys	12.3	9.4	8.5	0.9	2.8	22.0
1 survey	37.7	26.4	17.0	22.6	18.9	62.0
Never	42.5	57.66	73.6	72.6	78.3	—
Total	100.0% (n = 106)	100.0% (n = 106)	100.0% (n = 106)	100.0% (n = 106)	100.0% (n = 106)	100.0% (n = 106)

TABLE 4
MEDIAN AND 90% INTERVAL (90% I) OF FIVE LUNG FUNCTION PARAMETERS IN THE THREE SURVEYS STRATIFIED FOR THE HISTORY OF ASTHMATIC SYMPTOMS

Lung function parameter	Measurement in:	Asthmatic symptoms (n = 106) (median (90% I))	No asthmatic symptom (n = 361) (median (90% I))	Wilcoxon test (P)
FEV_1%FVC	Survey 1	82.3 (71–93)	84.1 (74–94)	0.016
	Survey 2	82.0 (69–92)	84.7 (73–93)	<0.001
	Survey 3	83.2 (70–93)	85.0 (75–94)	0.004
FEV_1%	Survey 1	96.5 (78–119)	100.8 (80–121)	0.004
	Survey 2	96.8 (72–118)	102.0 (81–123)	<0.001
	Survey 3	98.7 (79–122)	101.7 (82–125)	0.008
MEF_{75}%	Survey 1	86.6 (57–132)	94.5 (61–136)	<0.001
	Survey 2	85.5 (53–124)	94.1 (60–133)	0.002
	Survey 3	88.1 (57–128)	94.9 (64–135)	<0.001
MEF_{50}%	Survey 1	82.7 (59–138)	93.9 (62–133)	<0.001
	Survey 2	83.7 (52–119)	91.6 (61–131)	<0.001
	Survey 3	84.8 (58–124)	93.3 (63–131)	0.003
MEF_{25}%	Survey 1	71.9 (42–132)	85.7 (46–137)	<0.001
	Survey 2	77.8 (36–133)	86.4 (48–137)	0.001
	Survey 3	78.5 (38–132)	87.6 (52–145)	0.001

proportion of those children with symptoms has been diagnosed as having asthma and as having a positive family history of asthma. Furthermore, the high percentage of children in this group sensitized to inhalant allergens (65.1%) speaks in favor of the atopic origin of the history reported. Our data show that epidemiological studies on effects of air pollution on the airways of children depend on the preceding respiratory health of the study population. In accordance with this, the concept of "susceptibility" has been discussed extensively elsewhere (Brain *et al.*, 1988).

A detrimental effect of air pollutants on the airways of asthmatic children in particular has been recently pointed out (Dockery *et al.*, 1989). Mostardi *et al.* explored the influence of SO_2 and NO_2 on the lung function of 299 10- to 11-year-old children (Mostardi *et al.*, 1981). Within a 9-month period it was established that in a range of NO_2 concentrations between 36.9 and 54.5 $\mu g/m^3$ children with symptoms of acute respiratory illness at schools with higher pollutant exposure had lower FEV_1 values than those subjects attending schools with lower pollutant levels.

Studies on healthy children have shown NO_2 loads in quantities comparable to those of our study (range: 12–51 $\mu g/m^3$) affecting the incidence of respiratory tract infections. In a Swiss study of infants, a significantly higher number of respiratory symptoms was reported for children living in areas with an outdoor NO_2 concentrations between 30 and 39 $\mu g/m^3$ compared with children in areas with concentrations below 30 $\mu g/m^3$. Symptoms were reported most frequently in areas with NO_2 concentrations exceeding 50 $\mu g/m^3$ (Rutishauser *et al.*, 1990). In Helsinki, hospital admissions were associated with pollutants such as SO_2, NO_2, and total suspended particles (TSP) even though mean levels were low (e.g., NO_2: 38.6

TABLE 5
RESULTS OF LINEAR REGRESSION ANALYSES INCLUDING THREE REPEATED MEASUREMENTS FOR FIVE LUNG FUNCTION PARAMETERS AS DEPENDENT VARIABLES STRATIFIED FOR THE HISTORY OF ASTHMATIC SYMPTOMS: PARAMETER ESTIMATES (PE) AND PROBABILITIES (P) BASED ON t TEST

Subpopulation	Variables	FEV_1%FVC		ln FEV_1%		ln MEF_{75}%		ln MEF_{50}%[a]		ln MEF_{25}%	
		PE	P	PE	P	PE	P	PE	P	PE	P
With asthmatic symptoms (n = 106)	Intercept	90.339	0.000	−0.096	0.18[b]	−0.059	0.59	−0.373	0.04	−0.274	0.075
	NO_2 concentration ($\mu g/m^3$)	−0.437	0.004	−0.01	0.02	−0.011	0.038	−0.022	0.052	−0.029	0.002
	Indiv. room heating (yes/no)	−3.536	0.033	−0.054	0.16	−0.111	0.14	−0.114	0.14	−0.075	0.43
	Allergic reactivity in SPT	−1.41	0.006	−0.006	0.54	−0.054	0.008	−0.041	0.078	−0.09	0.003
	Frequent respiratory tract infections at preschool age	−2.832	0.006	−0.028	0.25	−0.091	0.05	−0.075	0.11	−0.101	0.083
	Male gender	−1.667	0.11	−0.059	0.016	−0.064	0.17	−0.06	0.21	−0.08	0.17
	Age (years)	−0.468	0.023	0.006	0.33	−0.001	0.87	0.022	0.031	0.01	0.42
Without asthmatic symptoms (n = 361)	Intercept	81.576	0.000	−0.105	0.000	−0.236	0.000	−0.219	0.000	−0.555	0.000
	NO_2 concentration ($\mu g/m^3$)	−0.049	0.5	−0.0001	0.97	0.003	0.25	0.004	0.16	0.003	0.54
	Indv. room heating (yes/no)	0.09	0.93	0.002	0.95	−0.035	0.41	−0.071	0.11	−0.034	0.54
	Allergic reactivity in SPT	−0.435	0.21	−0.006	0.39	−0.003	0.81	−0.005	0.68	−0.012	0.54
	Frequent respiratory tract infections at preschool age	−1.072	0.074	−0.016	0.25	−0.047	0.068	−0.041	0.11	−0.036	0.29
	Male gender	−2.543	0.000	−0.032	0.007	−0.048	0.03	−0.052	0.019	−0.067	0.019
	Age (years)	0.16	0.095	0.008	0.000	0.012	0.001	0.01	0.009	0.03	0.000

Note. Negative parameter estimates indicate a negative association.
[a] Only for second and third survey since a statistical requirement (comparable effect in the surveys) for the first survey was not fulfilled.
[b] A combined effect of gender and time was accounted for since chronological effects could not statistically be neglected.

TABLE 6

EFFECT OF THE NO_2 CONCENTRATION WITH A THRESHOLD OF 40 $\mu g/m^3$ IN CROSSSECTIONAL ANALYSES ON DIFFERENT LUNG FUNCTION PARAMETERS IN THE GROUP WITH ASTHMATIC SYMPTOMS (n = 106)

Crosssectional observation:	$FEV_1\%FVC$		ln $FEV_1\%$		ln $MEF_{75}\%$		ln $MEF_{50}\%$		ln $MEF_{25}\%$	
	Parameter estimates	Probability	Parameter estimates	Probability	Parameter estimates	Probability	Parameter estimates	Probability	Parameter estimates	Probability
Winter period 1987/88 (survey 1)	−0.59	0.004	−0.04	0.004	−0.01	0.15	−0.02	0.049	−0.57	0.011
Winter period 1988/89 (survey 2)	−1.62	0.001	−0.09	0.004	−0.06	0.002	−0.06	0.009	−0.95	0.049
Winter period 1989/90 (survey 3)	−1.00	0.004	−0.04	0.016	−0.03	0.023	−0.03	0.026	−0.69	0.026

$\mu g/m^3$; Pönkä, 1991). An Austrian study with 510 children revealed a detrimental effect of NO_2 concentrations with mean values around 40 $\mu g/m^3$ preceding the lung function measurements (Frischer *et al.*, 1993). A recent analysis of the Swiss study including data from a large industrial area reported NO_2 and TSP to be correlated, with the consequence that part of the effect on symptoms must be attributed to TSP. In our study region only a few industrial sources contribute to outdoor air pollution. Thus the NO_2 load can be attributed mainly to vehicular traffic. NO_2 could be a risk factor in its own right with regard to reduced lung function. However, when studying natural exposure we cannot exclude that NO_2 is also an indicator for more complex air pollution, including other gaseous compounds as well as suspended particles.

In the present study the relationship of NO_2 and lung function was not linear. Lung function was reduced when NO_2 was higher than a threshold of 40 $\mu g/m^3$. A nonlinear relationship for NO_2 was also identified in a previous work by Schwartz (Schwartz, 1989). A steep decline of FVC occurred for NO_2 concentrations higher than 77 $\mu g/m^3$, however, in an unselected sample of children and youths aged 6–24 years. Therefore a threshold of 40 $\mu g/m^3$ for a susceptible group seems to be plausible. However, a limitation of the present study is that the threshold was not assumed a priori but introduced as an approach to deal with nonlinear relations in linear regressions. The relationship of NO_2 and lung function changes in this report is thus based on an increase of NO_2 in the range of 40 to 51 $\mu g/m^3$. In this range, however, we find 38.2% of the nonhyperreactive and 38.7% of the predisposed children. Assuming the threshold relationship to be valid, risk comparisons of TSP, NO_2 and other pollutants in the past could also be confounded by the nonlinearity of NO_2 effect, which has not been taken into account in a previous comparison.

In addition to outdoor air levels, several studies investigated effects of indoor NO_2. In homes with gas cooking extremely high short-term rises for NO_2 of up to 1100 $\mu g/m^3$ were found (Speizer *et al.*, 1980). Moreover, significantly lower lung function parameters were found for children living in houses with gas stoves compared to those who had electric stoves (Speizer *et al.*, 1980). In a Dutch study of 6- to 10-year-old children, however, the prevalence of respiratory symptoms was unaffected by indoor NO_2, whereas an effect on expiratory flow rates was evident in comparing the groups with lowest (up to 20 $\mu g/m^3$) and with highest (>60 $\mu g/m^3$) exposure (Dijkstra *et al.*, 1990).

An individual room heating unit burning wood or fossil fuels poses a significant risk factor for a reduction of $FEV_1\%FVC$, but only a tendency is seen for $FEV_1\%$ and two flow parameters. If the type of heating system used is taken as an indicator of the pollutant load indoors, the question of which specific components are responsible for the association is raised. Thirteen percent of all individual room heaters in our study (n = 46) burned oil, 33% wood or coal, and 54% natural gas. It can be assumed that all these heaters are vented according to statutory regulations. In a subsample of households (n = 33 with individual room heating, n = 348 without individual room heating) it was possible to carry out indoor measurements, indicating that in residences with individual room heating the relative humidity was significantly higher (11.1 hPa vs 9.6 hPa, Wilcoxon test: P = 0.02).

The concentration of NO_2, however, did not differ in homes with or without individual room heating (15.8 vs 14.7 $\mu g/m^3$). Several studies have shown humidity indoors to be a risk factor for the development of childhood respiratory illnesses (Brunekreef *et al.,* 1989; Waegemaekers *et al.,* 1989). Thus alterations of indoor climate in residences with individual room heating should be regarded as the basis of the association observed in our study.

The explanatory models of the multivariate analysis provided a number of potentially confounding variables. Of these, frequent respiratory tract infections at preschool age is of importance in two of the models for the susceptible group associated with reduced lung function. This could be interpreted as airway obstruction due to persistent chronic airway inflammation as a consequence of frequent infections (Strope *et al.,* 1991). This finding is in accordance with previous reports (Gold *et al.,* 1989). A negative association of the cutaneous allergic reactivity is obvious in the susceptible group of children. Such an association between atopy and decreased lung function parameters has been reported from previous studies (Clifford *et al.,* 1989). Regarding confounding caused by age ($FEV_1\%FVC$, $MEF_{50}\%$) and gender ($FEV_1\%$) in the susceptible group, a consistent tendency and statistical importance are lacking, respectively. However, while (absolute) age had to be adjusted for in each of the models presented, an influence of growing older in the course of the study (chronological effect) could be discounted with one exception ($FEV_1\%$).

In a subsample of 106 children with asthmatic symptoms, outdoor NO_2 (or NO_2 associated pollutants) on the one hand and individual room heating on the other are associated with a reduction of lung function parameters. In this subsample a family history of asthma, a doctor's previous diagnosis of asthma, and sensitization to inhalant allergens is more frequent than in the symptom-free population. Average outdoor NO_2 concentrations above 40 $\mu g/m^3$ are associated with a significant decrease of $FEV_1\%FVC$, $FEV_1\%$, $MEF_{75}\%$, and $MEF_{25}\%$ linear to the NO_2 level in the subpopulation with asthmatic signs, but not in those children without such symptoms. Our data suggest that, with respect to potentially susceptible groups of children, measures have to be taken to lower air pollution as far as possible.

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The Impact of Soil Lead Abatement on Urban Children's Blood Lead Levels: Phase II Results from the Boston Lead-In-Soil Demonstration Project

ANN ASCHENGRAU,* ALEXA BEISER,* DAVID BELLINGER,†
DONNA COPENHAFER,* AND MICHAEL WEITZMAN‡,§

**Department of Epidemiology and Biostatistics, Boston University School of Public Health, 80 East Concord Street, Boston, Massachusetts 02118; †Neuroepidemiology Unit, The Children's Hospital, 300 Longwood Avenue, Boston, Massachusetts 02115; and ‡The University of Rochester School of Medicine, and §Department of Pediatrics, Rochester General Hospital, 1425 Portland Avenue, Rochester, New York 14621*

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The Boston Lead-In-Soil Demonstration Project was a randomized environmental intervention study of the impact of urban soil lead abatement on children's blood lead levels. Lead-contaminated soil abatement was associated with a modest reduction in children's blood lead levels in both phases of the project; however, the reduction in Phase II was somewhat greater than that in Phase I. The combined results from both phases suggest that a soil lead reduction of 2060 ppm is associated with a 2.25 to 2.70 μg/dl decline in blood lead levels. Low levels of soil recontamination 1 to 2 years following abatement indicate that the intervention is persistent, at least over the short-term. Furthermore, the intervention appears to benefit most children since no measurable differences in efficacy were observed for starting blood and soil lead level, race, neighborhood, gender, and many other characteristics. However, soil abatement did appear to be more beneficial to children in the higher socioeconomic classes, with low baseline ferritin levels, and who spent time away from home on a regular basis and lived in nonowner occupied housing, and with adults who had lead-related hobbies and almost always washed their hands before meals. Children who lived in apartments with consistently elevated floor dust lead loading levels derived almost no benefit from the soil abatement. It was not possible to separate the effects of the variables that had a beneficial impact on efficacy because they were closely correlated and the number of subjects was small. We recommend that further research be conducted to identify subgroups of children to whom soil lead abatement might be targeted.

INTRODUCTION

Children are exposed to lead through different pathways including air, water, dust, and soil (ATSDR, 1988). Primary and secondary prevention efforts have focused mainly on reducing the lead levels in air, water, and dust, but recently lead-contaminated soil has gained attention (ATSDR, 1988; Mielke *et al.*, 1983; Duggan and Inskip, 1985). Most available data on soil lead exposure come from cross-sectional studies often conducted in communities with smelters (ATSDR, 1988; Mielke *et al.*, 1983; Duggan and Inskip, 1985; Sayre *et al.*, 1974; Charney *et al.*, 1980; Clark *et al.*, 1985; Landrigan *et al.*, 1975; Rabinowitz *et al.*, 1985; Roels *et al.*, 1980). Recently, three prospective intervention studies were conducted in Boston, Baltimore, and Cincinnati to determine the impact of reducing soil lead levels among urban children (Weitzman *et al.*, 1993; U.S. EPA, 1993a,b).

Phase I of the Boston Lead-In-Soil Demonstration Project found that lead-contaminated soil abatement resulted in a modest but statistically significant re-

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