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Short-term effect of winter air pollution on respiratory health of asthmatic children in Paris

C. Segala*, B. Fauroux+, J. Just+, L. Pascual+, A. Grimfeld+, F. Neukirch*

Short-term effect of winter air pollution on respiratory health of asthmatic children in Paris. C. Segala, B. Fauroux, J. Just, L. Pascual, A. Grimfeld, F. Neukirch. ©ERS Journals Ltd 1998.

ABSTRACT: There is controversy as to whether low levels of air pollution affect the symptoms and lung function in asthma. We addressed this by examining the short-term effects of winter air pollution on childhood asthma in Paris.

We performed a 6 month follow-up of 84 medically diagnosed asthmatic children classified into two groups of severity. The outcomes included incidence and prevalence of asthma attacks, symptoms and use of supplementary β_2-agonists, peak expiratory flow (PEF) value and its variability. The statistical analysis controlled the lack of independence between daily health outcomes, trends and meteorology.

Air pollution was associated with an increase in reports and duration of asthma attacks and asthma-like symptoms in mild asthmatic children. The strongest association was the risk of asthma attack for an increase of 50 $\mu g \cdot m^{-3}$ of sulphur dioxide (SO_2) on the same day (odds ratio (OR)=2.86). Maximum reduction in morning peak expiratory flow (PEF) (5%) and maximum increase in PEF variability (2%) were observed at a lag of 3 days for an increase of 50 $\mu g \cdot m^{-3}$ of SO_2 in the subgroup of mild asthmatics receiving no regular inhaled medication. In moderate asthmatic children, the duration of supplementary β_2-agonist use was strongly associated with air pollution.

The general pattern of our results provides evidence of the effect of the low levels of air pollution encountered in Western Europe on symptoms and lung function in childhood asthma.

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*Institut National de la Santé et de la Recherche Médicale, Unité 408, Epidémiologie, Faculté de Médecine, Bichat, Paris, France. +Centre de l'Asthme Hôpital Armand Trousseau, Paris, France.

Correspondence: C. Segala, INSERM U408, Epidémiologie, Faculté de Médecine Xavier Bichat, BP 416, 75870 Paris cedex 18, France
Fax: 33 1 42263330

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Numerous studies conducted since 1980 have led to a better understanding of the health consequences of outdoor air pollution [1]. The presence of chemical contaminants in the air at relatively low concentrations, as is now usual in Western countries, has harmful effects on subjects with pre-existing chronic respiratory disease [2], especially children [3]. This has been observed for asthmatic subjects in controlled human exposure studies [1, 4] and in various epidemiological studies using different methodologies. Several authors have studied the long-term effects of air pollution, comparing prevalence of asthma or bronchial hyperresponsiveness between areas with different air pollution levels [5–7]. Other studies have tested correlations between hospital visits for asthma and air pollutants [8–12]. Since hospital attendance for asthma reflects only severe asthma events, panel studies are used to evaluate the short-term health effect of air pollution on asthmatic adults [13–16], asthmatic children [17–21], or both [22–24]. These diary studies have given some controversial results, partly because they can be difficult to analyse [25], and also because asthmatics can manage their own symptoms and pulmonary function by medication [17]. Moreover, most studies were conducted in North America or Northern Europe, and their results cannot be generalized to areas with different pollution and meteorological conditions.

The purpose of the present study was to examine the short-term effects of winter air pollution on the respiratory health of medically diagnosed asthmatic children. We used a panel study, controlling for the lack of independence of daily health outcomes and considering both maintenance and supplementary medications taken by the subjects.

Methods

Study subjects

The population was recruited from out-patients of the Hôpital d'enfants Armand Trousseau. All asthmatic children attending the paediatric pneumology department from September to November 1992 were asked to participate. The first 100 voluntary subjects fulfilling the following selection criteria were included: age 7–15 yrs; having had at least one asthma attack in the past 12 months; spending at least 12 $h \cdot day^{-1}$ in Greater Paris; and having parents able to complete a diary. Four enroled children did not participate from the start of the study. During the 6 months follow-up, those children who did not keep the diary for four consecutive weeks despite telephone reminders (n=6) or gave inaccurate responses (n=6) were excluded.

The 84 children were classified into two groups according to the regularly scheduled inhaled medications that they received: one group of moderate asthmatics who received daily both inhaled steroids and inhaled β_2-agonists (n=41) and one group of mild asthmatics (n=43), among whom 21 received neither inhaled steroids nor regularly

scheduled inhaled β_2-agonists. Supplementary β_2-agonists were prescribed to all children as needed. Table 1 summarizes the characteristics of the two groups of children.

Air pollution and weather data measurements

Ambient air pollution was routinely measured in stations of the existing monitoring network (AIRPARIF), all located in the Greater Paris area. Only data from background sites were retained, excluding street sites. Air pollution data recorded included values for sulphur dioxide (SO_2), suspended black particulates (black smoke) with an aerodynamic diameter smaller than 5 μm (BS), suspended particulates with an aerodynamic diameter close to 10 μm (PM_{13}) and nitrogen dioxide (NO_2). SO_2 (measured by ultraviolet (UV) fluorescence in 11 stations), PM_{13} (measured by β-radiometry in four stations) and NO_2 (measured by chemiluminescence in eight stations) were measured hourly and a mean value was calculated for each day. The 24 h mean levels of BS were measured by reflectometry (French standard method NF-X 43-005) in 15 stations. Ozone had an 8 h mean (SD) of 14.9 (12.5) $\mu g \cdot m^{-3}$ during the study period (winter and beginning of spring); it was, therefore, not considered. The average of the mean daily readings at all stations was calculated, since a previous study [26] verified the temporal and geographical homogeneity between data collected in the various stations. Thus, the subjects were considered as all having a similar exposure. Daily average temperature and relative humidity were measured at the Paris weather station (Meteo France).

Figure 1 depicts the temporal pattern of 24 h average levels of PM_{13}, BS, SO_2 and NO_2, during the study period. Pollution concentrations were moderate, with no pronounced peak. There were very high correlations between the measures of SO_2, BS and PM_{13} and weaker correlations between these three pollutants and NO_2. Low temperature was associated with higher levels of SO_2 and particulates, and low humidity with higher concentrations of NO_2 (table 2).

Table 1. – Description of the children studied

	Mild asthmatics	Moderate asthmatics
Subjects n	43	41
Age yrs (SD)	9.6 (2.3)	10.6 (2.5)
Males %	58	68
Atopy %	89	89
FEV_1		
>80% pred %	98	89
70–80% pred %	2	11
Medications %		
Inhaled β_2-agonists		
Regularly scheduled	12	100
Supplementary (as needed)	37	27
Inhaled cromones	42	7
Inhaled corticosteroids	40	100
Antihistamines	79	88
Methylxanthines	26	56

FEV_1: forced expiratory volume in one second.

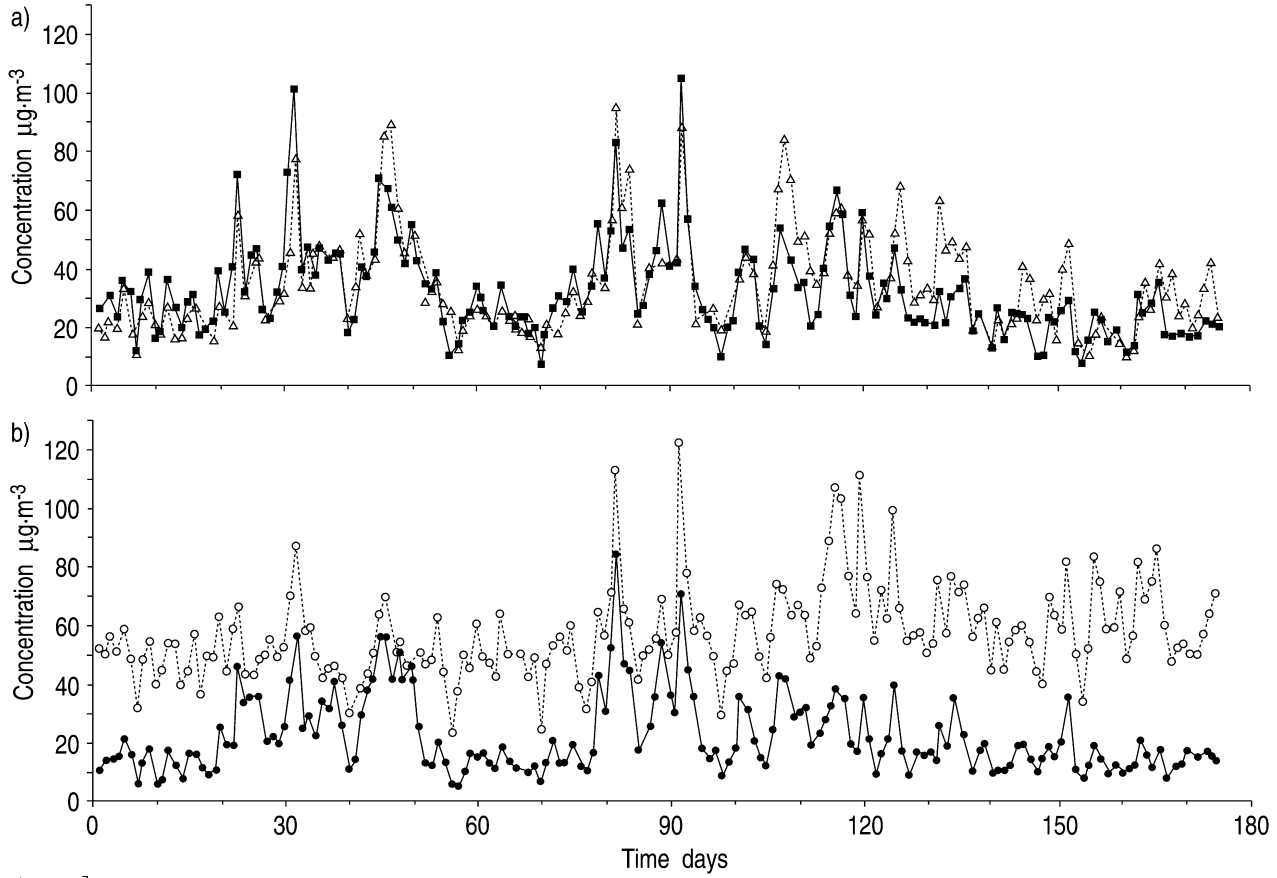

Fig. 1. – Mean daily values of: a) black smoke (▪) and particles with an aerodynamic diameter close to 10 mm (Δ); b) sulphur dioxide (•) and nitrogen dioxide (○). Measurements were made throughout the study period, starting on November 15 1992 (day 0).

Symptom diaries and peak expiratory flow rate measurements

The children were examined by their paediatric pulmonologist, who obtained informed consent from the parents and filled out a standardized form including demographic data, medical history, allergic status based on skin-prick tests, maintenance therapy and spirometry measurements. Twenty one common allergen extracts were used for testing atopy. Positivity was defined as any wheel diameter Š3 mm. Each participant was given a newly purchased peak flow meter (mini-Wright) to measure peak expiratory flow (PEF). They were instructed how to perform PEF measurements in a standing position. The subject's parents were given a diary and instructed how to complete it. Participants were told that this was an investigation of factors related to severity of asthma but not that the principal factor of interest was air pollution.

Patients were followed for 25 weeks, from November 15 1992 to May 9 1993. At the end of each day the parents recorded the presence or absence of asthma attacks, upper or lower respiratory infections with fever (defined as body temperature above 38°C) and the use of supplementary inhaled β_2-agonists. They also recorded the severity of three symptoms (wheeze, nocturnal cough and shortness of breath) graduated as follows: 0=none, 1=moderate and 2=severe. Children recorded their best PEF out of three attempts, three times a day (morning, afternoon and evening). Patients were asked to note the days spent outside the study area, and these days were excluded from the analysis.

Diaries were collected weekly. Subjects failing to return diaries or returning incorrectly completed diaries were contacted by telephone. At the end of the study, two persons not involved in the study checked the consistency of responses. PEF measurements were considered invalid if values were the same in the morning, afternoon and evening for 1 week. On average, suitable data was available for 79% of the subjects per day.

Data transformation

For asthma-like symptoms, days were classified as positive or negative irrespective of the severity. The factors that increase the risk of acquiring a symptom (incident episode) are not necessarily the same as those that increase its duration (approximated by prevalence data). An incident episode for a given symptom was defined as the presence of the symptom on a given day when the previous day has been symptom-free. A prevalent episode was defined as the presence of the symptom on a given day irrespective of the presence of the symptom on the previous day.

For the PEF records, the first 7 days were dismissed, as they were considered to be a learning period. To eliminate the effect of the large differences between subjects in absolute PEF, each PEF value was converted into a Z score by subtracting the mean PEF of that child and dividing the result by the standard deviation of all PEF values for that child [19].

The daily PEF variability was calculated as the amplitude percentage mean [16]: (highest-lowest PEF value)× 100/mean.

Statistical methods

Incident and prevalent episodes of asthma attacks, related symptoms, respiratory infection and use of supplementary β_2-agonist, Z-transformed morning PEF and daily PEF variability were used as health outcomes.

The association between air pollutants and health outcomes was examined by regression analysis based on the generalized estimating equations (GEE) proposed by Liang and Zeger [27] and Zeger and Liang [28]. These models correct for the repeated measurements in the response data. Thus, the standard error of the regression estimate is adjusted for the fact that responses from any one subject are likely to be correlated. Also, this method generates robust estimators regardless of the specification of the covariance matrix, and autocorrelation being in the covariance, coefficients have the usual interpretation. The models are marginal logistic models for binary outcomes and marginal linear models for PEF variables.

The analysis was conducted in stages. The procedure first determined the covariates that belong to the regression models: day of the week (weekday *versus* weekend) and time trend (included as linear and quadratic terms of the number of days since the start of the study) and meteorological variables. Different temperature and humidity lags were investigated (up to six days) and in the final model, the meteorological variables with the lag showing the strongest association with health outcomes were included (mostly at lag 0, 1 or 2 days). Then, the concurrent and lagged pollutant measures for up to 6 days were entered in turn into the model. The effect of each pollutant on health was estimated by entering it separately into the models. We considered the possibility of nonlinear relationships between pollution and health outcomes by examining logarithmic transformations of each pollutant. The linear forms of pollution are reported, sine they were always more significant than the logarithmic transforms. We also tested interaction terms between temperature and humidity, and between weather variables and pollutants; none were found.

Table 2. – Distribution of 24 h averages of pollution and weather data during the study period

	Mean±SD (range)	Pearson correlation coefficients					
		SO_2	NO_2	PM13	BS	Temp.	Humidity
SO_2 µg·m^{-3}	21.7±13.5 (4.4–83.8)	1.0					
NO_2 µg·m^{-3}	56.9±15.5 (23.8–121.9)	0.54***	1.0				
PM13 µg·m^{-3}	34.2±17.2 (8.8–95.0)	0.83***	0.55***	1.0			
BS µg·m^{-3}	31.7±16.3 (6.6–104.6)	0.89***	0.61***	0.82***	1.0		
Temp. °C	8.0±4.6 (-4.4–20.1)	-0.58***	0.10	-0.48***	-0.46***	1.0	
Humidity %	85.9±11.4 (46.8–100.0)	0.003	-0.30***	-0.07	0.14†	-0.17*	1.0

†: p<0.10; *: p<0.05; ***: p<0.001. SO_2: sulphur dioxide; NO_2: nitrogen dioxide; PM13: particles with an aerodynamic diameter close to 10 µm; BS: black smoke; Temp.: temperature.

The two groups of children were analysed separately. All analyses were performed using the Statistical Analysis System (SAS; SAS Institute Inc., Cary, NC, USA) macro procedure GEE [29].

Results

Total incidence and prevalence rates of binary health outcomes over the study period and mean values of PEF variables are shown in table 3 for the two groups of children. Both frequency and duration of asthma attacks and asthma-like symptoms were greater in moderate asthmatics than in mild asthmatics. The frequency and duration of respiratory infections were low in all the children, whereas supplementary β_2-agonists were used twice as often and for three times longer by mild than moderate asthmatics.

Table 3. – Frequency of asthma attacks, symptoms, respiratory infections and of use of supplementary β_2-agonists. Mean values of morning peak expiratory flow (PEF) and daily variability

	Mild asthmatics	Moderate asthmatics
Asthma attacks*	0.7/2.0	1.7/3.6
Wheeze*	1.7/7.5	4.7/12.4
Nocturnal cough*	3.7/16.1	5.3/18.4
Shortness of breath*	2.3/9.1	5.6/18.3
Respiratory infections*	0.9/3.0	0.8/3.2
Supplementary β_2-agonists*	0.8/2.9	0.4/0.8
PEF_{am} L·min^{-1}+	301.2±80.6	302.2±87.0
PEF_{var} L·min^{-1}+	11.6±11.7	14.1±13.9

*: values are presented as incidence rate/prevalence rate, per 100 person days·days at risk^{-1}. +: mean±SD. Total incidence rate: (total number of incident episodes × 100)/(total number of person/days at risk); total prevalence rate: (total number of prevalent episodes × 100)/(total number of person/days at risk). PEF_{am}: morning PEF rate; PEF_{var}: daily PEF variability.

Association between meteorological variables and health outcomes

Temperature was negatively correlated with both incident and prevalent episodes of asthma and with prevalent episodes of nocturnal cough and shortness of breath. Temperature decrease was associated with PEF decrease. Humidity was positively correlated with both incident and prevalent episodes of wheezing and with incident episodes of shortness of breath and respiratory infections.

Association between pollutants and symptoms. Results in mild asthmatics are reported in table 4 (incident episodes) and table 5 (prevalent episodes). SO_2 was associated with: both incident and prevalent episodes of asthma; use of supplementary β_2-agonists; incident episodes of nocturnal cough; prevalent episodes of shortness of breath; and respiratory infection. Associations between health outcomes and the three other pollutants followed similar patterns, but the effects were weaker. Symptoms were more strongly associated with lagged (mostly lag 3 and 4 days) than concurrent-day pollutant levels, except for asthma attack for which the risk for an increase of 50 $\mu g \cdot m^{-3}$ of SO_2 was the highest on the same day: odds ratio (OR)=2.86, 95% confidence interval (95% CI): 1.31–6.27.

No significant association was found at lag 5 or 6 days for incident episodes or at lag 6 days for prevalent episodes (not shown). In contrast, among moderate asthmatics (table 6), associations between symptoms and pollutants were

Table 4. – Odds ratios (ORs) of the effects of an increase of 50 $\mu g \cdot m^{-3}$ of pollutants on incident episodes in mild asthmatics (n=43)

Lag days	SO_2	BS	PM_{13}	NO_2
Asthma				
0	2.86 (1.31–6.27)*	1.57 (0.79–3.12)	1.92 (0.88–4.21)+	2.33 (1.18–4.64)*
1	2.45 (1.01–5.92)*	1.35 (0.62–2.96)	1.30 (0.59–2.85)	1.51 (0.62–3.64)
2	1.40 (0.43–4.54)	-	-	-
3	1.52 (0.57–4.04)	-	1.39 (0.70–2.76)	-
4	2.33 (0.96–5.62)+	1.61 (0.81–3.20)	1.90 (0.79–4.59)	2.18 (1.10–4.32)*
Wheeze				
0	1.47 (0.90–2.41)	-	-	-
1	1.27 (0.48–3.38)	-	-	-
4	1.37 (0.57–3.32)	-	-	-
Nocturnal cough				
3	1.93 (1.18–3.15)*	1.65 (1.11–2.44)*	1.73 (1.17–2.57)*	1.62 (0.99–2.64)+
4	2.12 (1.43–3.13)*	1.86 (1.26–2.75)*	1.27 (0.95–1.71)	2.09 (1.28–3.42)*
Shortness of breath				
2	-	-	1.56 (0.86–2.80)	-
3	1.57 (0.79–3.11)	1.31 (0.73–2.36)	1.27 (0.64–2.51)	-
4	1.73 (0.79–3.78)	1.46 (0.74–2.91)	1.46 (0.74–2.91)	1.32 (0.60–2.89)
Respiratory infections				
1	1.52 (0.38–5.98)	-	1.46 (0.50–4.28)	-
2	1.66 (0.62–4.43)	-	1.36 (0.62–2.98)	-
3	2.39 (0.90–6.37)+	2.09 (0.96–4.58)+	2.50 (1.06–5.48)*	2.29 (1.05–5.02)*
4	1.80 (0.75–4.35)	2.06 (1.04–4.09)*	1.52 (0.63–3.66)	1.81 (0.83–3.96)
β_2-agonist				
3	1.58 (0.65–3.81)	1.41 (0.64–3.08)	-	1.38 (0.77–2.48)
4	1.63 (1.00–2.66)*	1.41 (0.78–2.54)	-	-

Each OR was obtained using a generalized estimating equations logistic model, adjusted for the effects of age, sex, weather data and time trend terms. ORs less than 1.2 are omitted for brevity. The 95% confidence intervals are shown in parentheses. +: p=0.05–0.10; *: p<0.05. For further definitions see legend to table 2.

Table 5. – Odds ratios (ORs) of the effects of an increase of 50 μg·m^{-3} of pollutants on prevalent episodes in mild asthmatics (n=43)

	Lag days	SO_2	BS	PM13	NO_2
Asthma	0	1.71 (1.15–2.53)*	1.32 (0.89–1.96)	1.32 (0.89–1.96)	1.31 (0.73–2.35)
	1	1.55 (0.86–2.78)	1.21 (0.74–1.97)	-	-
	4	1.23 (0.68–2.21)	-	-	1.20 (0.73–1.95)
Wheeze	2	1.26 (0.77–2.06)	-	-	-
	3	1.32 (0.81–2.15)	-	-	-
	4	1.48 (0.90–2.41)+	1.23 (0.83–1.83)	-	-
Nocturnal cough	4	1.32 (0.89–1.96)	1.27 (0.95–1.71)	-	1.28 (0.96–1.72)
Shortness of breath	1	1.36 (0.92–2.01)	-	-	-
	2	1.45 (0.98–2.14)+	1.20 (0.89–1.20)	1.22 (0.83–1.81)	-
	3	1.52 (1.03–2.25)*	1.22 (0.91–1.64)	1.22 (0.82–1.80)	-
	4	1.51 (1.02–2.24)*	1.25 (0.93–1.68)	1.25 (0.93–1.68)	-
	5	1.23 (0.83–1.82)	-	-	-
Respiratory infections	0	1.58 (0.72–3.46)	-	-	-
	1	1.91 (0.79–4.62)	1.40 (0.70–2.77)	1.37 (0.69–2.72)	1.22 (0.61–2.41)
	2	2.13 (0.97–4.67)+	1.54 (0.70–3.36)	1.66 (0.84–3.30)	1.23 (0.62–2.43)
	3	2.09 (1.05–4.15)*	1.55 (0.86–3.07)	1.67 (0.93–3.00)+	1.52 (0.93–2.48)
	4	2.05 (1.14–3.68)*	1.66 (1.02–2.71)*	1.47 (0.90–2.39)+	1.55 (1.04–2.29)*
	5	1.40 (0.71–2.79)	1.35 (0.83–2.20)	1.23 (0.75–2.00)	1.23 (0.76–2.01)
β_2-agonist	3	1.41 (0.78–2.53)	-	-	-
	4	2.02 (1.02–4.01)*	1.21 (0.61–2.40)	-	-
	5	1.96 (0.99–3.88)+	-	-	-

Each OR was obtained using a generalized estimating equations logistic model, adjusted for the effects of age, sex, weather data and time trend terms. ORs less than 1.2 are omitted for brevity. The 95% confidence intervals are shown in parentheses. +: p=0.05–0.10; *: p<0.05. For definitions see legend to table 2.

Table 6. – Odds ratios (ORs) of the effects of an increase of 50 μg·m^{-3} of pollutants in moderate asthmatics (n=41)

	Lag days	SO_2	BS	PM13	NO_2
On incident episodes					
Asthma	2	-	-	1.29 (0.79–2.10)	-
	3	-	-	-	1.43 (0.80–2.58)
	4	1.20 (0.55–2.62)	-	-	-
Wheeze	0	-	-	-	1.35 (0.91–2.00)
	3	1.23 (0.68–2.21)	1.26 (0.77–2.06)	1.26 (0.77–2.06)	1.37 (0.84–2.24)
	4	-	-	1.23 (0.92–1.65)	-
Nocturnal cough	2	1.34 (0.90–1.98)	1.22 (0.83–1.81)	-	1.54 (1.04–2.27)*
Shortness of breath	4	-	-	-	1.24 (0.92–1.66)
Respiratory infections	3	1.32 (0.37–4.71)	1.32 (0.60–2.90)	1.84 (0.76–4.45)	1.50 (0.62–3.63)
β_2-agonist	0	-	1.65 (0.46–5.89)	1.97 (0.45–8.58)	1.80 (0.41–7.82)
	4	-	-	-	1.28 (0.27–6.12)
On prevalent episodes					
Asthma	2	1.37 (0.76–2.47)	1.37 (0.92–2.03)	1.37 (0.93–2.03)	1.31 (0.80–2.13)
	3	1.41 (0.86–2.30)	1.44 (0.97–2.13)+	1.23 (0.76–2.02)	1.64 (1.11–2.43)*
	4	1.26 (0.77–2.06)	-	-	1.37 (0.84–2.23)
Wheeze	3	-	-	-	1.26 (0.85–1.86)
	4	1.31 (0.89–2.15)	-	-	1.26 (0.77–2.06)
	5	1.21 (0.82–1.79)	-	-	-
Nocturnal cough	4	1.23 (0.83–1.82)	1.22 (0.91–1.64)	-	-
	5	1.20 (0.90–1.62)	-	-	-
β_2-agonist	0	3.67 (1.25–10.8)*	3.29 (1.36–7.95)*	4.73 (1.96–11.4)*	2.36 (1.08–5.17)*
	1	4.60 (2.10–10.1)*	2.86 (1.59–5.15)*	5.29 (2.42–11.6)*	2.76 (1.69–4.51)*
	2	7.01 (3.53–13.9)*	2.95 (1.99–4.36)*	4.44 (2.47–8.00)*	2.53 (1.27–5.02)*
	3	4.74 (1.96–11.5)*	2.84 (1.58–5.12)*	2.85 (1.30–6.25)*	2.21 (0.83–5.90)+

Each OR was obtained using a generalized estimating equations logistic model, adjusted for the effects of age, sex, weather data and time trend terms. ORs less than 1.2 are omitted for brevity. The 95% confidence intervals are shown in parentheses. +: p=0.05–0.10; *: p<0.05. For definitions, see legend to table 2.

Table 7. – Regression coefficients* of the effects of an increase of 1 $\mu g \cdot m^{-3}$ of pollutants on peak expiratory flow (PEF) variables in the mild asthmatic group taking no corticosteroids and no regularly scheduled β_2-agonist (n= 21)

	Z-transformed morning PEF values+			PEF daily variability $\%\cdot\mu g^{-1}\cdot m^{-3}$†	
Pollutant	Lag days	β (±SE)	p-value	β (±SE)	p-value
SO_2	1	-		0.029±0.015	0.06
	2	-		0.026±0.022	NS
	3	-0.300±0.163	0.06	0.038±0.020	0.05
	4	-0.222±0.163	NS	0.020±0.018	NS
	5	-		0.035±0.020	0.08
	6	-		0.035±0.019	0.06
BS	3	-0.247±0.145	0.09	0.022±0.013	0.09
	4	-0.183±0.117	NS	-	
PM13	3	-0.181±0.134	NS	-	
	4	-0.209±0.108	0.05	-	
NO_2	3	-0.275±0.150	0.06	-	
	4	-0.200±0.157	NS	-	

*: each parameter was obtained using a generalized estimating equations linear model, adjusted for the effects of age, sex, weather data and time trend terms; +: coefficients that correspond to a decrease of less than 3% in morning PEF for an increase of 50 $\mu g \cdot m^{-3}$ of pollutants are omitted for brevity; †: coefficients that correspond to an increase of less than 1% in PEF variability for an increase of 50 $\mu g \cdot m^{-3}$ of pollutants are omitted for brevity. For definitions, see legend to table 2.

weaker, but prevalent use of supplementary β_2-agonists was strongly associated with each of the four pollutants on the same day and at lag l, 2 and 3 days. The strongest risk was for an increase of 50 $\mu g \cdot m^{-3}$ of SO_2 at lag 2 days: OR=7.01, 95% CI 3.53–13.9.

Respiratory infections might confound the relationships between pollutants and health outcomes in asthmatic patients. We therefore re-ran all the models with respiratory infection as an additional explanatory variable. This slightly decreased the ORs, but the effects remained significant independently of infection (data not shown).

Association between pollutants and PEF variables

There was no relationship between pollutants and PEF variables in either asthmatic group studied. Nevertheless, pollutants correlated slightly with these outcomes in the subgroup of 21 mild asthmatics with no inhaled steroids and no regularly scheduled β_2-agonists (table 7). An increase of 50 $\mu g \cdot m^{-3}$ of one of the four pollutants resulted in a maximum decrease of 3–5% in morning PEF (based on the group average of 300.6 $L \cdot min^{-1}$). Lagged pollutants (mostly lag 3 and 4 days) were more strongly associated with PEF decrease than were concurrent day pollutant levels. Daily PEF variability increased by 1.9% for an increase of 50 $\mu g \cdot m^{-3}$ of SO_2 (maximum increase at lag 3 days). No relationship was found between PEF variability and the three other pollutants.

Discussion

We have shown that moderately elevated air pollutants levels were associated in mild asthmatic children with increases in the incidence and duration of asthma attacks and asthma-like symptoms and with alterations of lung function as measured by reduction in PEF and increase in PEF variability. In moderately asthmatic children receiving daily treatment, both with inhaled steroids and inhaled β_2-agonists, only supplementary β_2-agonists use was strongly associated with air pollution. All these associations were observed at levels below the current acceptable standard air quality in a homogeneous group of 84 currently asthmatic children diagnosed by their hospital pulmonary paediatricians. Most previous panel studies of winter air pollution used a screening questionnaire to recruit children with chronic respiratory symptoms [17–20] without a medical diagnosis of asthma.

In the mild asthmatic group, air pollution was related both to daily symptom incidence and symptom duration and we observed that incidence tended to be associated with pollutants at shorter lags than prevalence. Most panel studies of asthmatic children have only described associations between symptom prevalence and air pollution [17, 18, 20, 21]. The four pollutants were also associated with both incident and prevalent episodes of respiratory infections. Evidence of adverse effects of air pollution on respiratory illnesses has been related in several papers [30–35]. Since respiratory infections are related to asthma attacks [36, 37], they might have confounded the observed associations [20]. However, taking respiratory infections into account in the analysis did not substantially alter the association between pollutants and health outcomes. The reduction in PEF value and the increase of PEF variability were only reported in the subgroup of mild asthmatic children with no inhaled steroids and no regularly scheduled β_2-agonists, suggesting that anti-inflammatory treatment decreases the bronchial response to air pollution.

In the moderate asthmatic group, weaker associations between pollutants and asthma attacks or asthma-like symptoms were observed. This group is unlikely to be less susceptible to pollutants. It is possible that moderate asthmatics have a more efficient maintenance treatment and are better at managing their symptoms with supplementary medication. Indeed the association between air pollution and supplementary β_2-agonist use was strongest in the moderate asthmatic group. POPE *et al.* [17] similarly reported relatively weaker associations in a sample of asthmatic patients than in a school-based sample, except for the use of supplementary asthma medication.

Data were collected using daily diaries, thereby avoiding recall biases. This approach also detects relatively rare episodes [38]. Moreover, the classification of symptoms (none, moderate, severe) allowed for weak symptomatology to be recorded. Misclassifications in the reports of symptoms and PEF values in children by the parents were possible. This could have introduced a bias if reporting varied with perceived air pollution [39]. However, because air pollution was low in this study and because parents were not aware that air pollution was investigated by the study, it is unlikely that they modified their reporting according to exposure.

Daily measurements of PEF have been used in several panels of asthmatic children. Morning [22] or evening measurements [17, 18, 21, 24] or both [20] have been used to assess obstruction of proximal airways. We obtained the same pattern of results in our study by using evening PEF or mean value instead of morning PEF, but

the effects were weaker (not shown). In this study there was a significant training effect during the first days of the study and these days were, therefore, excluded from the analysis. Heterogeneity among individuals, which can introduce dependencies in the data [25] was taken into account by using daily mean Z-transformed peak flow values. We are not aware of any other panel study reporting relationships between air pollution and PEF variability in asthmatic children. Most of the children in our panel recorded three measurements every day. In a previous study, we showed that three daily measurements (and possibly two) are sufficient to assess bronchial lability in healthy adults [40].

Panel studies are a powerful method for assessing short-term effects of air pollution on human health. In such longitudinal studies, the subjects serve as their own controls. Therefore, it was assumed that personal characteristics and exposure to other factors were constant over the study period. Individual environmental exposures would have biased the results only if they had increased concomitantly with pollution levels, which is unlikely. GEE was used to measure the effects of day-to-day variations in ambient air pollution on health outcomes and this allowed the correlation between the repeated responses to be modelled. Prevalence data and PEF variables are obviously highly correlated, but correlation may exist even for incident cases [25]. Weather changes have been reported to be triggers of respiratory symptoms in asthmatic children [36, 41] and were, indeed, associated with health outcomes in our study. Therefore, all associations were adjusted for temperature and humidity. During a 6 month period, health outcomes, weather and pollutant data show short-term and seasonal variations. Consequently, time-trend variables which are factors that may confound the associations between outcomes and environmental data, were taken into account in the analysis.

The use of stationary air pollution monitoring data to represent personal exposure is a weak point of this study, shared by most panel studies. Most of the child's time is spent indoors in winter. Nevertheless, studies comparing indoor and outdoor particulate concentrations have reported an average indoor/outdoor ratio of at least 0.5 [42, 43], and some authors found that indoor NO_2 correlated highly with outdoor NO_2 [31], suggesting that outdoor pollution measurement is a reasonable proxy for personal exposure. Moreover, several authors have suggested that misclassification of exposure, if random, would result in a downward bias of the association between air pollution and health outcomes [16, 19, 22].

The major local sources contributing to ambient air pollution in the Paris area are heating and automobile exhaust [44]. Although sulphur and particulate levels have decreased substantially over the last 30 yrs, the recent rise in vehicle traffic and the growing percentage of diesel engines [45] have, since 1985, contributed to an increase in emissions of nitrogen oxides, particulate matter and volatile organic compounds. During the winter of 1992–1993, levels of pollutants, other than NO_2, were well below European Community (EC) and World Health Organization (WHO) standards. It is not clear from our data what component(s) was responsible for the observed health effects. Similar findings were observed for each of the four pollutants, in single pollutant models. However, the pollutants studied may only be indicators for more complex air pollution, some of pollutants not being measured in our study and because of the likely interactions between pollutants [1, 4].

The finding of associations between winter air pollutants and respiratory effects in asthmatic children is consistent with a previous study correlating hospital admissions for asthma and air pollution in Paris [46] and with published panel studies. A recent study of 83 African-American asthmatic children in Los Angeles [20] has associated shortness of breath, but not cough and wheeze with suspended particulates with an aerodynamic diameter of 10 μm (PM10). In Utah valley, Pope *et al.* [17] showed that PM10 was associated with an increase in reported upper and lower respiratory symptoms and asthma medication, and decreased PEF values in 34 symptomatic schoolchildren. In a second study [18], children with chronic respiratory symptoms were estimated to report cough about twice as frequently for each 100 $\mu g \cdot m^{-3}$ increase in PM10. In these three US studies, no association were found with SO_2, but it may be not appropriate to extrapolate to other areas, as SO_2 levels were low. Likewise, in a panel of American children with persistent wheeze, Vedal *et al.* [22] failed to show any relationship between SO_2 and either respiratory illness or PEF levels. Recent panel studies in eastern Europe [21, 24] reported a decrease in PEF and an increase in symptom score associated with relative-ly high levels of air pollution. In the Netherlands, Roemer *et al*. [19] followed 73 children with chronic respiratory symptoms during three winter months. He did not observe any significant association between pollution levels and incident episodes of either asthmatic symptoms or medications. In contrast, PM10, black smoke and SO_2 were ass-ociated with increased prevalent episodes of wheeze and bronchodilator use, and decreased morning and evening PEF. Forsberg *et al.* [23] studied a panel of 31 asthmatic patients, aged 9–71 yrs, living in northern Sweden: shortness of breath was the only symptom that increased with increasing black smoke levels.

During our study period, NO_2 was the only pollutant to come close to the upper limit of the international guidelines (upper 24 h value: 122 $\mu g \cdot m^{-3}$ *versus* WHO 24 h guideline value: 150 $\mu g \cdot m^{-3}$). NO_2 has been reported to be a risk factor for reduced lung function. In a repeated cross-sectional survey, weekly NO_2 concentrations were found to affect the lung function of children with asthmatic symptoms [47]. Evidence for the health effects of outdoor NO_2 on asthmatic symptoms is scarce [48]. NO_2 was not related to any of the health outcomes in the study of Roemer *et al.* [19] and in the study of Higgins *et al.* [16] the effect of NO_2 disappeared when SO_2 was in-cluded in regression models.

Any effect of pollution exposure on asthmatic symptoms and/or pulmonary function is not necessarily contemporaneous, and in our study most of the significant associations between pollutants and health outcomes displayed a lag time. Previous panel studies have reported similar findings. Peters and co-workers [21, 24] reported weak same-day effects and stronger cumulative effects of air pollution on asthmatic children for both PEF and symptoms. In the study of Roemer *et al.* [19], weekly average pollution appeared to be more closely related than present day or previous day pollution to symptoms and PEF. Pope and Dockery [18] found that symptoms and PEF were more closely associated with 5 day moving average

PM10 levels than concurrent day pollution and suggested that the deficit in pulmonary function is immediate but continues to accumulate for several days [17]. This is consistent with previous studies of pollution episodes. DASSEN *et al.* [49] reported that the maximal deficit in lung function of children was observed two weeks after an episode of maximal total suspended particle (TSP) con-centration of 200 to 250 $\mu g \cdot m^{-3}$. BRUNEKREEF *et al.* [50] re-analysed data from a study published in 1982 [51] and showed a stronger statistical association with the 5 day mean than the previous day mean TSP.

In conclusion, we have shown that prevailing levels of winter air pollution, which are below international air quality standards, had consistent and measurable effects on children with mild to moderate asthma. These effects lasted several days after exposure, suggesting a persistent inflammatory process. We also showed that moderate asthmatic patients could manage their bronchial responses to air pollution by treatment.

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