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Short-term health effects of particulate and photochemical air pollution in asthmatic children

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Short-term health effects of particulate and photochemical air pollution in asthmatic children. J. Just, C. Ségala, F. Sahraoui, G. Priol, A. Grimfeld, F. Neukirch. ©ERS Journals Ltd 2002.

ABSTRACT: In a previous panel study in Paris, France, detrimental effects of moderately high levels of winter air pollution on the symptoms and lung function of asthmatic children were demonstrated. A new study was conducted, with the aim of assessing the short-term effects of photo-oxidant and particulate air pollution on childhood asthma during spring and early summer in Paris.

Eighty-two medically diagnosed asthmatic children were followed up for 3 months. Outcomes included the incidence and prevalence of asthma attacks, nocturnal cough, supplementary use of β_2-agonists, symptoms of airway irritation, and peak expiratory flow (PEF) value and its variability. The statistical methods controlled for the lack of independence between daily health outcomes, temporal trends and pollen and weather conditions.

Black smoke and nitrogen dioxide (NO_2) were associated with increases in the occurrence of nocturnal cough and respiratory infections. Ozone (O_3) was associated with an increase in the occurrence of asthma attacks and respiratory infections and with changes in lung function, as shown by an increase in PEF variability and a decrease in PEF. Statistically significant interactions were demonstrated between O_3 and temperature and between O_3 and pollen count for asthma attacks. O_3 levels had a greater effect on additional bronchodilator use and on irritations of the eyes, nose and throat on days on which no steroids were used. Particulate matter was associated with eye irritation only.

This study showed that, although within international air quality standards, the prevailing levels of photo-oxidant and particulate pollution in spring and early summer had measurable short-term effects on children with mild-to-moderate asthma.
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The short-term effects of air pollution in humans are predominantly assessed by means of time series studies. These recently reviewed [1] studies have shown broadly consistent associations between air pollutants and a number of related outcomes, such as total mortality, cardiorespiratory mortality and hospital admissions. To ensure that relationships observed are causal, it is necessary to check that studies with different designs show similar associations [2] and that there is coherence between a broad range of related health outcomes [3]. As recently reviewed [4, 5], panel studies provide these advantages. The health effects are measured on an individual basis, whereas the exposure data are mostly based on aggregated data. These studies are often conducted on the most susceptible subgroups of the population, such as children and asthmatics. Previously, a panel study was conducted in Paris, France [6], in which the detrimental effect of moderately high levels of winter air pollution on the symptoms and lung function of asthmatic children was demonstrated. As attention is increasingly focused on photo-oxidant air pollution episodes, a new study was conducted with the aim of assessing the short-term effects of photo-oxidant and particulate pollution on the health of medically diagnosed asthmatic children during spring and early summer.

Methods

Study subjects

The study population was recruited from outpatients at Armand Trousseau Children's Hospital, Paris, France. All asthmatic children attending the paediatric pneumology clinic from January–March 1996 were asked to participate. The children (volunteers) were included if they: were 7–15 yrs old; had at least one asthma attack in the past 12 months; were taking daily anti-asthma treatment; could spend $\geqslant 12\ h \cdot day^{-1}$ in Greater Paris; and had parents able to complete a diary. Fourteen of the children enrolled did not participate from the start of the study. During the 3 months of follow-up, children for whom the diary was not kept for 4 consecutive weeks, despite

Table 1. – Description of the children studied

Subjects n	82
Age yrs (SD)	10.9 (2.45)
Males %	65.9
Atopy %	90.2
Asthma attacks in the last 12 months %	79.3
Emergency care %	61.0
Hospitalisation %	28.4
Intensive care %	3.7
Medication %	
Inhaled β_2-agonists	
Regularly scheduled	48
Supplementary (as needed)	39
Inhaled cromones	6.1
Inhaled corticosteroids	
Regularly	74
Occasionally	17
Antihistamines	74.4
Methylxanthines	18.5

telephone reminders (n=2), or who gave inaccurate responses (n=2) were excluded. Table 1 summarises the characteristics and medication of the 82 participating children.

The protocol was approved by the relevant ethics committees: the Bichat Hospital Committee for the Protection of Persons Participating in Medical Research (Paris, France) and the National Committee of Data Processing and Freedom (Paris, France).

Air pollution, weather and pollen data measurements

Ambient air pollution was routinely measured at the stations of the monitoring network (AIRPARIF) in the Greater Paris area. Data was retained from the urban background monitoring sites, which were representative of ambient air pollution in the geographical area and are not directly exposed to local sources. Recorded air pollution data included values for black smoke (BS; suspended black particulates), suspended particles with an aerodynamic diameter <13 μm (PM), sulphur dioxide (SO_2), nitrogen dioxide (NO_2) and ozone (O_3) concentrations. PM (measured by β-radiometry at five stations), SO_2 (measured by ultraviolet (UV) fluorescence in 11 stations), and NO_2 (measured by chemiluminescence at 14 stations) levels were measured hourly and a mean value was calculated for each day. The 24-h mean levels of BS were determined by reflectometry (French standard method NF-X 43-005) at 22 stations. The 8-h mean of O_3 concentrations was measured (UV photometric analysers) at six stations. An overall mean of the mean daily readings at all stations was calculated because a previous study [7] demonstrated temporal and geographical homogeneity between data collected at the various stations. Mean daily temperature and relative humidity were determined at the Paris weather station (Météo France). Data on total pollen counts were collected by the French surveillance system for pollen counts (The Pasteur Institute, Paris, France, and the Aerobiological Monitoring Network, Paris, France).

Figure 1 shows the 24-h pattern of mean levels of PM, BS, NO_2 and O_3 during the study period. Pollution concentrations were moderate, with no pronounced peak. There was a very strong correlation between levels of NO_2 and BS, with weaker correlations observed between NO_2 and PM levels, and between O_3 levels and particulate matter levels. As expected, there was no correlation between NO_2 and O_3 levels. SO_2 was not considered in subsequent analysis because it was present only at low levels. High temperature was associated with high levels of O_3, whereas low humidity was associated with high concentrations of the four pollutants, especially O_3 (tables 2 and 3).

Symptom diaries and peak expiratory flow rate measurements

The children were examined by a paediatric pulmonologist, who obtained informed consent from the parents and completed a standardised 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 atopy testing. A positive result was defined as a wheal diameter of $\geqslant 3$ mm. Each participant was given a new peak flow meter (mini-Wright; Clement Clarke International Ltd, Edinburgh, UK) to measure peak expiratory flow (PEF). They were instructed how to measure PEF in a standing position. The subject's parents had to complete a diary.

Patients were followed for 3 months, from April 1, 1996 to June 30, 1996. 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 of >38°C) and the number of inhaled β_2-agonist puffs. They also recorded the severity of nocturnal cough, wheeze and symptoms of irritation, on a three-point scale as follows: 0=none, 1=moderate, 2=severe. Children recorded the best PEF of three attempts, three times per day (morning, afternoon and evening). Parents were asked to note if the child had spent the day outside the study area, and all such days were excluded from the analysis.

Diaries were collected weekly. Parents who did not return diaries or who returned incorrectly completed diaries were contacted by telephone. At the end of the study, two assessors that were not involved in the study checked the consistency of the responses. PEF measurements were considered invalid if values were identical for 1 week. Suitable data was available for a mean of 80% of the subjects per day.

Data transformation

For symptoms, days were classified as positive or negative with no account taken of the severity of symptoms for positive days. An incident episode for a given symptom was defined as the presence of the symptom on a given day when the previous day had

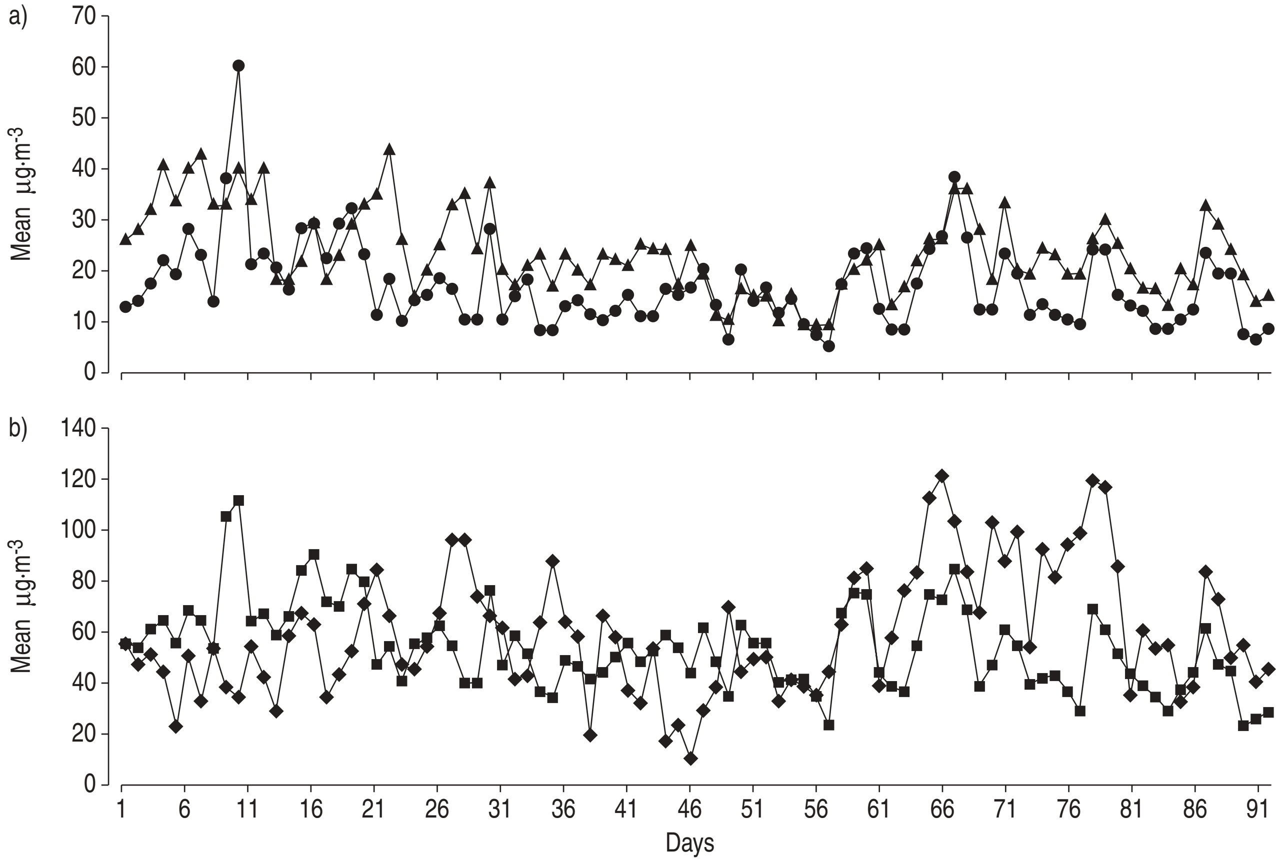

Fig. 1. – Mean daily concentrations of suspended black particles (BS), suspended particles with an aerodynamic diameter of <13 µm (PM), nitrogen dioxide (NO_2) and ozone (O_3) during the study period. Day 1 was April 1, 1996. ●: BS; ▲: O_3; ◆: PM; ■: NO_2.

Table 2. – Univariate statistics for pollution and weather for the study period

	Mean	SD	Minimum	Maximum
PM µg·m^{-3}	23.5	8.4	9.0	44.0
BS µg·m^{-3}	16.8	8.4	5.0	60.0
SO_2 µg·m^{-3}	11.6	5.7	3.0	30.0
NO_2 µg·m^{-3}	53.8	16.9	23.0	111.0
O_3 µg·m^{-3}	58.9	24.5	10.0	121.0
Temperature °C	14.4	4.8	3.7	27.6
Humidity %	63.7	11.8	34.8	87.8

PM: suspended particles with an aerodynamic diameter of <13 µm; BS: suspended black particulates; SO_2: sulphur dioxide; NO_2: nitrogen dioxide; O_3: ozone.

been symptom-free. A prevalent episode was defined as the presence of the symptom on a given day irrespective of whether or not that symptom was also present on the previous day. Additional bronchodilator use was coded as a yes/no variable: yes if the number of puffs used on a given day was greater than that for the previous day.

For PEF values, data for the first 7 days were excluded from the analysis, as this period was considered to be a learning period. To eliminate the effect of the large differences between subjects' absolute PEF, each PEF value was converted into a Z score by subtracting the mean PEF for that child and dividing the result by the SD of all PEF values for that child [8]. Daily PEF variability was calculated as the

Table 3. – Pearson correlation coefficients for pollution and weather for the study period

	PM	BS	SO_2	NO_2	O_3	Temperature	Humidity
PM	1.0						
BS	0.59***	1.0					
SO_2	0.70***	0.65***	1.0				
NO_2	0.54***	0.92***	0.69***	1.0			
O_3	0.21#	0.21*	-0.02	0.09	1.0		
Temperature	0.04	0.12	-0.34***	-0.01	0.65***	1.0	
Humidity	-0.41**	-0.26*	-0.27**	-0.32**	-0.70***	-0.35***	1.0

PM: suspended particles with an aerodynamic diameter of <13 µm; BS: suspended black particulates; SO_2: sulphur dioxide; NO_2: nitrogen dioxide; O_3: ozone. *: p<0.05; **: p<0.01; ***: p<0.001; #: p<0.10.

amplitude % mean [9]:

$$\frac{(\text{highest} - \text{lowest PEF value}) \times 100}{\text{mean}} \quad (1)$$

Total pollen counts were log-normally distributed, and were log-transformed before analysis.

Statistical methods

Incident and prevalent episodes of asthma attacks, nocturnal cough, wheeze, symptoms of irritation, respiratory infections and supplementary use of 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 evaluated by regression analysis based on the generalised estimating equations (GEE) proposed by LIANG and ZEGER [10, 11]. These models correct for the repeated measurements in response data. The standard error of the regression estimate is therefore adjusted for the fact that responses from any one subject are likely to be correlated. This method generates robust estimators regardless of the specifications of the covariance matrix, and as autocorrelation is included in the covariance, coefficients can be interpreted as usual. The models are marginal logistic models for binary outcomes and marginal linear models for PEF variables.

The analysis was conducted in stages. According to the fit of the model, the procedure first determined the following covariates of the regression models: time trends (included as linear and if necessary, quadratic and cubic terms of the number of days since the start of the study), day of the week, pollen count (same day) and meteorological variables (with the inclusion, in some cases, of a quadratic term for temperature). Various temperature and humidity lags were investigated ($\leqslant$6 days), and, in the final model, the meteorological variables with the lag showing the strongest association with health outcomes were included (mostly lag 0, 1 or 2).

Pollutant measures (day 0) and cumulative pollutant measures (0–2 mean and 0–4 mean) were then entered in turn into the model. The effect of each pollutant on health was estimated by entering it separately into the models. Possible interactions between temperature and humidity, temperature and O_3, and pollen and O_3 were also assessed. If a significant interaction was found ($p<0.05$), an interaction term was introduced into the models. Finally, multipollutant models were conducted in which particles and O_3 levels or NO_2 and O_3 levels were correlated with the same health outcome in one-pollutant models. An analysis restricted to person-days on which no steroid was used (979 person-days) was also carried out.

For binary response data, results are expressed as odds ratios (OR) with 95% confidence intervals (CI) for an increase of 10 $\mu g \cdot m^{-3}$ in pollutant concentration.

Table 4. – Frequency of asthma attacks, symptoms, respiratory infections and use of supplementary β_2-agonists and mean values of morning peak expiratory flow and daily variability

	Incident episodes	Prevalent episodes
Asthma attacks	1.0	1.9
Nocturnal cough	3.1	7.9
Wheeze	3.7	9.2
Respiratory infections	0.4	0.8
Eye irritation	3.6	9.0
Throat irritation	3.7	10.0
Nose irritation	5.2	17.1
Morning values $L \cdot min^{-1}$	332.3 (87.5)	
Daily variability %	8.7 (9.2)	

Data are presented as % or mean±SD. Total incidence rate: (total number of incident cases×100)/total number of person-days at risk; total prevalence rate: (total number of prevalent cases×100)/total number of person-days.

Results

Total incidence and prevalence rates of binary health outcomes over the study period and mean values of PEF variables are shown in table 4. As expected in this well-treated asthmatic population, the incidence of asthma attacks was lower than the incidence of nocturnal cough, wheeze and symptoms of irritation. The mean duration of episodes was 2–3 days. At this time of year, respiratory infections were rare.

Association between pollutants and asthma

The results are reported in table 5 (incident episodes) and table 6 (prevalent episodes). Wheeze, whether incident or prevalent, was not correlated with the levels of any type of pollutant (not shown). Incident episodes of nocturnal cough were correlated with 0–2 mean BS ($p=0.05$) and with NO_2 concentration at lag 0 ($p=0.007$). Prevalent episodes of nocturnal cough were correlated with 0–2 mean BS ($p=0.02$). Incident asthma attacks were significantly correlated at lag 0 with O_3 level ($p=0.02$), only if the model included significant interactions between O_3 and pollen ($p=0.002$) and O_3 and temperature ($p=0.01$).

O_3 levels were also significantly associated with the supplementary use of β_2-agonists on days on which no steroids were used by children: OR=1.41, 95% CI 1.05–1.89 at lag 0; OR=1.66, 95%CI 1.12–2.46 at 0–2 mean; and OR=1.43, 95%CI 1.03–2.0 at 0–4 mean.

Association between pollutants and respiratory infections

Incident episodes of respiratory infections (table 5) were correlated at lag 0 and 0–2 mean with BS ($p=0.0003$ and $p=0.04$, respectively) and NO_2 levels ($p=0.0002$ and $p=0.04$, respectively). Prevalent episodes of respiratory infections (table 6) were correlated at lag 0 and 0–2 mean with BS ($p=0.0005$ and $p=0.01$, respectively) and at lag 0 with NO_2 levels ($p=0.0003$). If a term was included for the significant

Table 5. – The effects of an increase of 10 μg·m^{-3} in suspended black particles (BS), suspended particles with an aerodynamic diameter of <13 μm (PM), nitrogen dioxide (NO_2) and ozone (O_3) levels on incident episodes

	Lag days	BS	PM	NO_2	O_3#
Asthma	0	1.24 (0.89–1.73)	1.06 (0.61–1.83)	1.16 (0.95–1.41)	0.99 (0.88–1.12)
	0–2	1.15 (0.72–1.84)	1.09 (0.48–2.49)	1.17 (0.88–1.41)	1.18 (0.81–1.40)
	0–4	1.31 (0.75–2.26)	1.07 (0.44–2.65)	1.17 (0.87–1.56)	1.09 (0.88–1.34)
Nocturnal cough	0	1.22 (0.99–1.51)¶	1.10 (0.88–1.37)	1.22 (1.05–1.42)*	1.04 (0.92–1.18)
	0–2	1.36 (1.00–1.86)*	1.03 (0.77–1.37)	1.17 (0.97–1.43)¶	0.94 (0.83–1.06)
	0–4	1.23 (0.85–1.78)	1.11 (0.86–1.42)	1.13 (0.92–1.40)	0.95 (0.84–1.07)
Respiratory infections	0	1.96 (1.35–2.84)*	0.64 (0.35–1.15)	1.69 (1.28–2.22)*	0.97 (0.73–1.37)
	0–2	2.08 (1.03–4.21)*	0.74 (0.38–1.43)	1.71 (1.01–2.90)*	0.97 (0.72–1.30)
	0–4	2.15 (0.78–5.96)	0.99 (0.58–1.68)	1.57 (0.76–3.24)	0.90 (0.68–1.18)

Data are presented as odds ratios (95% confidence intervals). Each odds ratio was obtained with a generalised estimating equations logistic model, adjusted for the effects of time trend, day of the week, weather and pollen levels. #: models without interaction terms, results of those including interaction terms are given in the text; ¶: 0.05<p<0.10; *: p<0.05. n=82.

Table 6. – Effects of a increase in 10 μg·m^{-1} of suspended black particles (BS), suspended particles with an aerodynamic diameter of <13 μm (PM), nitrogen dioxide (NO_2) and ozone (O_3) levels on prevalent episodes

	Lag days	BS	PM	NO_2	O_3#
Asthma	0	1.10 (0.77–1.57)	1.07 (0.72–1.59)	1.05 (0.84–1.33)	1.03 (0.93–1.13)
	0–2	1.02 (0.50–2.06)	1.18 (0.64–2.17)	1.01 (0.67–1.52)	1.07 (0.84–1.35)
	0–4	1.04 (0.44–2.46)	1.16 (0.63–2.13)	1.02 (0.61–1.67)	1.06 (0.85–1.30)
Nocturnal cough	0	1.08 (0.95–1.25)	1.05 (0.83–1.34)	1.00 (0.91–1.10)	1.04 (0.97–1.10)
	0–2	1.33 (1.03–2.10)*	1.10 (0.81–1.50)	1.07 (0.95–1.21)	1.04 (0.92–1.18)
	0–4	1.15 (0.83–1.61)	1.09 (0.79–1.52)	1.04 (0.88–1.23)	0.95 (0.84–1.07)
Respiratory infections	0	1.57 (1.10–2.23)*	1.17 (0.68–2.03)	1.39 (1.04–1.86)*	1.08 (0.93–1.24)
	0–2	4.68 (1.45–15.1)*	1.31 (0.51–3.36)	1.88 (0.97–3.64)¶	1.12 (0.85–1.47)
	0–4	2.65 (0.70–10.0)	1.71 (0.71–4.12)	1.36 (0.59–3.09)	1.08 (0.79–1.48)

Data are presented as odds ratios (95% confidence intervals). Each odds ratio was obtained with a generalised estimating equations logistic model, adjusted for the effects of time trend, day of the week, weather and pollen levels. #: models without interaction terms, results of those including interaction terms are given in the text; ¶: 0.05<p<0.10; *: p<0.05. n=82.

interaction between O_3 and temperature, incident episodes of respiratory infections were correlated with 0–2 and 0–4 means for O_3 concentration (p= 0.009 and p=0.02, respectively). Similar results were obtained for prevalent episodes of respiratory infections. As incident episodes of respiratory infections were correlated with levels of O_3 together with BS or NO_2, multipollutant models were generated. BS level was not significant (p=0.15) in the multipollutant model that included BS, O_3 and an interaction term between O_3 and temperature. O_3 level was not significant (p=0.08) in the multipollutant model that included NO_2, O_3 and an interaction term between O_3 and temperature. As respiratory infections may confound the relationship between pollutants and health outcomes in asthmatic patients, all the models were re-run with respiratory infection as an additional explanatory variable. This slightly decreased the ORs obtained, but did not affect the significance of the effects observed (not shown).

Association between pollutants and symptoms of irritation

In the total population, incident episodes of nose or throat irritation were not correlated with the levels of any of the pollutants. Only incident episodes of eye irritation were correlated with O_3 concentration at lag 0 (p=0.02), if a significant term of interaction between O_3 and temperature was introduced. Prevalent episodes of eye irritation were significantly correlated with PM levels: OR=1.18, 95% CI 1.01–1.39 at lag 0; OR=1.28, 95% CI 1.03–1.59 at 0–2 mean; and OR=1.42, 95% CI 1.12–1.80 at 0–4 mean. Borderline associations were found between prevalent episodes of eye and throat irritations and BS and NO_2 levels (not shown).

If the analysis was restricted to days on which no steroids were used by the children (table 7), symptoms were more strongly related to O_3 and PM levels. O_3 concentration was associated with incident episodes of nose (0–2 mean and 0–4 mean, p=0.05) and throat irritations (0–2 mean, p=0.001) and with prevalent episodes of eye (mean 0–4, p=0.03) and nose irritations (lag 0, p=0.008; mean 0–2, p=0.009; mean 0–4, p=0.02). PM was associated with prevalent episodes of eye irritation (mean 0–4, p=0.04). The interactions between O_3 and temperature or pollen were not significant. In a multipollutant model assessing the independent effects of O_3 and PM on prevalent episodes of eye irritation (mean 0–4), the O_3 parameter remained stable but not significant (p=0.10), whereas the PM parameter decreased and was not significant (p=0.19).

Table 7. – The effects of an increase in 10 $\mu g \cdot m^{-3}$ in pollutant concentration on symptoms of irritation on days on which no steroid was used

	Lag days	Incident episodes	Prevalent episodes
Eye irritation			
O_3	0	1.12 (0.98–1.29)#	1.06 (0.90–1.24)
	0–2	1.17 (0.64–2.16)	1.34 (0.96–1.87)#
	0–4	1.09 (0.71–1.69)	1.31 (1.08–1.60)*
PM	0	1.07 (0.66–1.71)	1.20 (0.88–1.65)
	0–2	0.83 (0.45–1.53)	1.71 (0.97–3.01)
	0–4	0.92 (0.46–1.83)	1.97 (1.03–3.76)*
Throat irritation			
O_3	0	1.11 (0.84–1.46)	1.05 (0.96–1.16)
	0–2	1.36 (1.08–1.73)*	1.11 (0.99–1.25)#
	0–4	1.22 (0.72–2.07)	1.07 (0.85–1.36)
PM	0	1.33 (0.66–2.69)	1.23 (0.83–1.82)
	0–2	1.28 (0.58–2.80)	1.08 (0.68–1.73)
	0–4	1.06 (0.38–2.95)	0.91 (0.47–1.73)
Nose irritation			
O_3	0	1.05 (0.83–1.32)	1.09 (1.00–1.20)*
	0–2	1.24 (1.0–1.54)*	1.27 (1.06–1.52)*
	0–4	1.16 (1.0–1.35)*	1.15 (1.02–1.29)*
PM	0	0.74 (0.48–1.13)	1.20 (0.91–1.58)
	0–2	0.76 (0.42–1.36)	1.09 (0.78–1.52)
	0–4	0.96 (0.53–1.73)	1.09 (0.73–1.61)

Data are presented as odds ratios (95% confidence intervals). Each odds ratio was obtained with a generalised estimating equations logistic model, adjusted for the effects of time trend, day of the week, weather and pollen levels. Models without interaction terms, results of those including interaction terms are given in the text. O_3: ozone; PM: particles with an aerodynamic diameter of <13 μm. #: 0.05<p<0.10; *: p<0.05.

Association between pollutants and peak expiratory flow variables

Daily PEF variability increased by 2.6% with an increase of 10 $\mu g \cdot m^{-3}$ of 0–2 mean O_3 concentration (p=0.05) and 3.3% with an increase of 10 $\mu g \cdot m^{-3}$ of 0–4 mean O_3 concentration (p=0.09). These percentages doubled, but were not significant, if the analysis was restricted to days on which no steroids were used. Morning PEF correlated with O_3 concentration (mean 0–2, p=0.006; mean 0–4, p=0.009) only if a significant interaction between O_3 and temperature was introduced in the models. No relationship was found between PEF variables and levels of the other three pollutants.

Discussion

In asthmatic children, photochemical air pollution and particulate air pollution had various effects on health. Moderately high levels of BS and NO_2 were associated with increases in both the incidence and prevalence of nocturnal cough and respiratory infections. Moderately high levels of O_3 were associated with an increase in the incidence of asthma attacks, respiratory infections and eye irritation. Statistically significant interactions were demonstrated between O_3 concentration and temperature for these three health outcomes, and between O_3 concentration and pollen count for asthma attacks. O_3 concentration had a greater effect on additional bronchodilator use and irritations of the eyes, nose and throat on days on which no steroids were used. PM was only associated with prevalent episodes of eye irritation. O_3 was the only pollutant associated with changes in lung function, as shown by an increase in PEF variability and a decrease in PEF. Statistically significant interaction was demonstrated between O_3 concentration and temperature for this decrease.

In a previous study [6], it was shown that moderately high levels of winter air pollution were associated with increases in the incidence and prevalence of asthma attacks and asthma-like symptoms in children with mild asthma and with changes in lung function, as shown by the decrease in PEF and increase in PEF variability. In the study, only 49% of the asthmatic children (classified as moderately asthmatic) received both inhaled steroids and inhaled β_2-agonists daily, and in this group only supplementary β_2-agonist use was strongly associated with air pollution. By the time this study was performed, 74% of children received both inhaled steroids and inhaled β_2-agonists daily and it was not possible to distinguish between subgroups of asthmatics according to treatment. Nevertheless, the effect of air pollution on asthmatic children was still detectable during the spring and summer. In well-treated asthmatics, weaker associations between pollutant levels and asthma attacks or asthma-like symptoms would be expected, because asthmatics with an efficient maintenance treatment are able to manage their symptoms with supplementary medication. Indeed, the association between O_3 levels and supplementary use of β_2-agonists was found only on days on which no steroids were used. Pope *et al.* [12] also reported weaker associations, except for the use of supplementary asthma medication, in a sample of asthmatic patients than in a school-based sample.

Panel studies are a powerful method for assessing the short-term effects of air pollution on human health. They have some limitations, which were discussed in detail in a previous paper [6]. To date, most panel studies on asthmatic children have been conducted in winter [8, 13–18], with few focusing on the effects of spring and summer air pollution. Two studies were conducted in Los Angeles, CA, USA. In the first [19], in which 83 African-American asthmatic children were studied during a 4-month summer period, particles with a 50% cut-off aerodynamic diameter of 10 μm (PM_{10}) and O_3 were associated with shortness of breath, but not coughing and wheezing. In the second study [20], which included 138 children, the occurrence of shortness of breath, cough and wheeze was associated with PM_{10}, particles with a 50% cut-off aerodynamic diameter of 2.5 μm ($PM_{2.5}$), NO_2 and moulds, but not with O_3 and pollen, and the use of extra asthma medication was associated to PM_{10} and O_3. During summer asthma camps in Connecticut, USA, O_3 and fine particles (sulphate and hydrogen ions) were found to be significantly correlated with asthma exacerbation, chest symptoms, medication use and decreases in lung function [21]. In San Diego, CA, USA, asthma symptoms were found to be significantly associated with PM10 and O_3, and in agreement with the results of this study, stronger relationships were found in the subgroup of patients with mild asthma who were not taking anti-inflammatory medication [22]. In two other panel studies [23, 24] conducted in Mexico City, Mexico, where there are high levels of pollution, symptoms and decreases in PEF were associated with O_3 and PM10 levels. In a study conducted in the Netherlands [25], BS was associated with a decrease in PEF, acute respiratory symptoms and medication use. Weaker associations were found for PM10 and O_3 levels.

The present study shows that O_3 has detrimental effects on the following health outcomes in asthmatic children: occurrence of asthma attacks, additional bronchodilatator use, changes in lung function (as shown by the decrease in PEF and increase in PEF variability), and symptoms of irritation of the eyes, nose and throat. These results are consistent with the "Evaluation des Risques de la Pollution Urbaine sur la Santé" (ERPURS) study, which is part of the Air Pollution on Health, a European Approach (APHEA) project, conducted in Paris. Positive associations were observed for increases in levels of pollutants in children [26]: a 3–8% increase in hospital admissions for asthma was observed for a 50 $\mu g \cdot m^{-3}$ increase in particle concentrations and a 1–3% increase in hospital admissions was observed for a 50 $\mu g \cdot m^{-3}$ increase in O_3 or NO_2 levels. A 50 $\mu g \cdot m^{-1}$ increase in particle or NO_2 concentration was associated with a 30% increase in the number of doctors' house calls for asthma [27]. In a similar manner to the present results, the relationship between asthma and O_3 concentrations was restricted to days on which the temperature was high (>20°). O_3 and temperature have a synergistic effect on several outcomes: asthma attacks, morning PEF and eye irritation. Together with climate and pollutants, ambient aeroallergens also influence asthma [20, 28]. In the present study, only pollen count was available, and O_3 and pollen count had a synergistic effect on the risk of asthma attacks. Recent experimental studies have shown that O_3 may interact with air suspended allergens by amplifying the response to the allergen [29, 30].

The principal local source contributing to ambient air pollution in the Paris area at this time of the year is automobile exhaust fumes [31]. The increases in vehicle traffic and the percentage of diesel engines [32] have contributed to the increase, since 1985, in emissions of nitrogen oxides, fine particulate matter, volatile organic compounds and O_3 during spring and summer. Nevertheless, during the study period, levels of pollutants were well within European Community and World Health Organization standards. During the study period, NO_2 and BS levels were highly correlated and both can, at this time of year, be considered as indicators of air pollutants emitted by diesel engines. This study also suggests that in an urban environment in spring to early summer, BS is more important than PM as an air pollution indicator associated with two acute effects in asthmatic children, nocturnal cough and respiratory infections. Only eye irritation was related to PM. A number of recent studies have suggested that PM2.5 is more strongly associated with health outcomes than PM10 [33–35]. The stronger associations observed for BS than for PM are consistent with the results of other studies conducted in Paris and elsewhere in Europe [25]. Two multipollutant models were created to study the independent effect of O_3 and particles, and found that particles made no independent contribution to respiratory infections and eye irritation. This finding is consistent with some other studies [21, 24]. In contrast, OSTRO *et al.* [20] reported greater effects of exposure to PM10 than exposure to O_3 on asthmatics.

In conclusion, this study shows that, although within international air quality standards, the prevailing levels of photo-oxidant and particulate pollution in spring and early summer had measurable short-term effects on children with mild-to-moderate asthma.

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