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Acute respiratory effects of low level summer smog in primary school children

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Acute respiratory effects of low level summer smog in primary school children. C.E.J. Cuijpers, G.M.H. Swaen, G. Wesseling, G. Hoek, F. Sturmans, E.F.M. Wouters. ©ERS Journals Ltd 1995.

ABSTRACT: We aimed to study the possible effects of exposure to a summer smog episode on the respiratory health of 212 school children. Furthermore, the suitability of the forced oscillation technique (FOT) to demonstrate such effects was evaluated.

Acute respiratory symptoms were evaluated by questionnaire and lung function was assessed by spirometry and respiratory impedance measurements. For each child, comparisons were made between measurements performed at baseline (low levels of air pollutant: 55 µg·m^{-3} for SO_2 and 58 µg·m^{-3} for NO_2 (maximum 24 h means); O_3 levels ranged from 2–56 µg·m^{-3} (8 h mean)); and after a summer smog episode (characterized by 8 h O_3 levels >120 µg·m^{-3} (163 µg·m^{-3}) and 1 h levels >160 µg·m^{-3} (215 µg·m^{-3}).

No significant effects were observed on the prevalence of acute respiratory symptoms. When individual changes in lung function indices (ΔLF) were regressed on changes in previous day ozone (8 h mean) and changes in mean daily temperature (ΔMTemp), using multiple linear regression analysis, a significant negative association was observed with peak expiratory flow (PEF), but not with other spirometry indices. Although significant associations were observed with reactance at 8 Hz (*X*rs8), resonant frequency (*f*0) and frequency dependence of resistance (FD), the signs of the βs were opposite to the direction expected when O_3 adversely affected the impedance outcomes.

In conclusion, in this study short-term exposure to moderately high levels of ozone did not result in clear adverse effects on the respiratory health of the children. Further research into the applicability of the FOT in this type of field studies still seems to be advisable.

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In recent years, there has been increasing concern about the possible health consequences of air pollution episodes (smog). Such episodes happen during stagnant weather conditions in summer as well as in winter, though the pollutants of primary concern during these episodes usually differ. For summer smog, ozone is considered to be the component forming the major indicator of the much more complex mixture of pollutants. In contrast to the pollutants from winter type smog (sulphur dioxide, particulate matter), only little progress has been made in controlling ozone in ambient air [1]. In recent years, in The Netherlands, health effects due to photochemical episodes have constituted an important public health issue [2].

Prolonged exposure of moderately to heavily exercising subjects to ozone concentrations near ambient levels, can result in (transient) lung function decrements, respiratory and other symptoms, increased nonspecific bronchial responsiveness and inflammatory reactions [1, 3]. The lung function response to ozone increased with physical exercise and exposure time [4, 5]. Levels at which these effects have been observed are in the range 160–240 µg·m^{-3} ozone [4, 6, 7]. Children experimentally exposed to ozone levels in this range, showed lung function decrements comparable in magnitude to those found in adults. In contrast, no symptom responses were observed in these children [8, 9].

Epidemiological and field studies have demonstrated that exposure to ambient ozone levels near or below US standards was associated with transient decreases in pulmonary function of children [10–15], and in two studies the lung function was negatively associated with previous-day ambient ozone [14, 15]. Furthermore, hospital admissions for respiratory illnesses (asthma) were found to be significantly associated with ozone levels lower than those given as guidelines [16, 17].

The present study was undertaken to examine the relationship between acute exposure to ambient pollutants, including ozone (O_3), particulate matter with an aerodynamic diameter less than 10 µm (PM10), acid aerosol, sulphur dioxide (SO_2), nitrogen dioxide (NO_2) and black smoke (BS), and respiratory function in children, during a summer smog episode. Children were studied because cigarette smoking and exposure to occupational lung irritants are not likely to be confounding factors. Furthermore, children can easily be studied at school during their normal daily activities.

In addition to current spirometry, respiratory impedance measurements, using the forced oscillation technique (FOT), were performed in these children. Earlier studies have demonstrated that the FOT is a suitable tool to evaluate the mechanical characteristics of the respiratory system in (young) children [18–20]. The measurements are noninvasive and effort-independent, and 3–5 valid impedance measurements per child can be obtained in a relatively short time (5–10 min). In the present study, the complementary value of the FOT in the early detection of small changes in lung function due to exposure to air pollution episodes, suggested by PESLIN *et al.* [21] and WOUTERS [22], was investigated.

Methods

Design

In November and December 1990, baseline health measurements were carried out in 534 children (mean age 9±2 yrs). The parents of 614 children were approached by a letter given to children from two, randomly selected, primary schools in Maastricht, The Netherlands. Written informed consent was obtained for 534 (87%) children, 251 boys (47%) and 283 girls (53%). After a summer air pollution episode, defined as a time period with 8 h average levels of O_3 higher than 120 $\mu g \cdot m^{-3}$ on at least two consecutive days [23], occurring in July 1991, 212 randomly selected children (102 boys and 110 girls) were re-examined (mean age 9±2 yrs). The lung function measurements were carried out from 8–16 July; on each day, on average, 30 children were measured. The study was approved by the Medical Ethics Committee of the University of Limburg.

Air quality measurements

Part of the information about ambient levels of air pollutants was obtained from the nearest site of the National Air Pollution Monitoring Network, Wijnandsrade. The gaseous component SO_2 was registered by continuous monitors based on fluorescence and NO_2 and O_3 were registered by continuous monitors based on chemiluminescence. Twenty four hour average concentrations of black smoke were measured using the method of the Organization for European Co-operation and Development (OECD) [24]. Data on the ambient minimum temperature were also collected. Additional measurements were carried out for particulate matter and acid aerosol. Twenty four hour average concentrations of PM_{10} were made with an instrument described by LIU and PUI [25], with an inlet design similar to the Sierra Andersen 241 dichotomous sampler. No separation into fine (<2.5 μm) and coarse particles (>2.5 μm) is accomplished with this sampler. Acid aerosol was sampled by an Annular Denuder system, described by VAN DER MEULEN *et al.* [26], and analysed for H^+, sulphates, nitrates and ammonium. The system consisted of two sodium carbonate coated denuders, one citric acid coated denuder, and a filter pack with a Teflon and nylon backup filter. The measurements of PM_{10} and acid aerosols took place every eighth day during the baseline period. During the summer smog episode, these measurements were taken on a daily basis, between 7.00 a.m. and 7.00 p.m. (12 h average).

Effect parameters

Main health outcome measures in this study are changes in lung function determined by FOT and spirometry, and the prevalence of acute respiratory symptoms measured by a written questionnaire. The lung function measurements took place at school during school hours. Directly after the smog episode, the summer holiday started. Consequently, the parents and their children were difficult to reach and no further measurements were made.

The questionnaire. During the baseline period, the prevalence of acute and chronic respiratory symptoms was evaluated by means of a written questionnaire, completed by the parents of the children. The questionnaire is a Dutch version of the children's questionnaire of the World Health Organization published by FLOREY and LEEDER [27]. Except for "chronic cough", the reproducibility of the answers of the Dutch questionnaire for chronic respiratory symptoms has been found to be good [28]. During the summer smog episode, a condensed form of the original questionnaire was used, especially aimed at respiratory symptoms in the previous week (see table 1) and relevant changes in the indoor environment, such as exposure to parental smoking, home dampness, gas appliances and pets. The parents completed these questionnaires between 8–16 July.

Forced oscillation technique. The FOT used in this study was similar to the method described by LÀNDSÉR *et al.* [29]. The measurements are performed during spontaneous quiet breathing and enable the assessment of mechanical characteristics of the respiratory system. The technique, which has been extensively described elsewhere [30], yields values for the total resistance and reactance of the respiratory system. The total resistance (R_{rs}) comprises the resistance of the airways, the lungs and the chest wall. The reactance (X_{rs}) is determined by the inertial and capacitive properties of the respiratory system. In normal adults, resistance values increase slightly with increasing frequency. Reactance is usually slightly negative at lower frequencies and becomes positive at frequencies between 5–10 Hz (resonant frequency, f_0). In the presence of airway obstruction, there is an increase in resistance values especially at lower frequencies, which decrease with increasing frequency (negative frequency dependence of resistance, FD).

Table 1. – Questions on acute respiratory symptoms as included in the questionnaire

Did your child have one of the following symptoms in the previous week (=the week before receiving the questionnaire)?		
*	dry throat/hoarseness	yes/no
*	expectorate/cough up phlegm	yes/no
*	wheeze	yes/no
*	stuffed nose/runny nose	yes/no
*	sore throat	yes/no
*	shortness of breath	yes/no
*	tightness of the chest	yes/no
*	irritated eyes/red eyes	yes/no
*	a lot of sneezing	yes/no
*	earache	yes/no
*	feeling of sickness/stomach	yes/no
*	headache	yes/no
*	fever	yes/no
Has/did your child in the previous week		
*	been using medication	yes/no
*	stay ill at home	yes/no
*	see a doctor	yes/no

Reactance values are more negative and resonant frequency is increased in patients with airflow obstruction [31]. In healthy children, negative frequency dependence of resistance, between 8–28 Hz, is a common finding, which progressively decreases during growth, advancing to the values found in healthy adults [18, 19].

In the present study, impedance measurements with a coherence function less than 0.95 at 8 or 28 Hz or at more than three frequencies were rejected. LÀNDSÉR *et al.* [32] demonstrated that for measurements with a coherence function exceeding 0.95 the error of the measurement due to the presence of noise or nonlinearities is less than 10%. All measurements were performed with the child seated, wearing a noseclip and with the cheeks and the floor of the mouth being supported with the hands of either the investigator or the child. Each child performed at least three valid impedance measurements. Data recorded were the mean values for the resistance at 8 and 28 Hz (*R*rs8, *R*rs28), the reactance at 8 Hz (*X*rs8), the frequency dependence of resistance (FD) defined as the difference between the *R*rs28 and *R*rs8 divided by 20, and the resonant frequency (*f*0) *i.e.* frequency at which *X*rs=0.

When exposure to elevated levels of air pollution results in airway obstruction, one would expect an increase in resistance and in resonant frequency, more negative reactance values and negative frequency dependence of resistance [22].

Spirometry. Spirometry was performed according to the European Coal and Steel Community (ECSC) protocol [33], with the exception that five instead of three acceptable manoeuvres had to be collected out of a maximum of eight attempts. Measurements were performed with the child in standing position using a dry spirometer (Vitalograph Ltd, Buckingham, UK). Body temperature and pressure saturated with water vapour (BTPS) corrected readings were obtained directly from the spirometer. From the valid manoeuvres the highest values for the forced vital capacity (FVC), the forced expiratory volume in one second (FEV1) and peak expiratory flow (PEF) were selected. The forced expiratory flow between 25 and 75% of the vital capacity (FEF25–75%) was selected from the measurement with the highest sum value for the FVC and the FEV1 [33].

Analyses

Using the data of the total group (n=534) the cross-sectional association between pulmonary function and age (in days) was calculated, by simple linear regression analysis. This was done for impedance and spirometry, and for boys (n=251) and girls (n=283) separately. The time lag between baseline and summer episode measurement was about 7 months. The associations from the linear regression models were used to adjust for the difference between the first and the second pulmonary function test result, for the changes in pulmonary function due to the increased age of the children. The growth rates resulting from this model are presented in table 2.

Firstly, differences in the prevalence of acute respiratory symptoms between baseline and smog episode were determined. Next, for each child, the absolute change in lung function parameters was calculated for FVC, FEV1, PEF, FEF25–75%, *R*rs8, *X*rs8, *f*0 and FD. Therefore, the growth corrected baseline values were subtracted from the episode values. In addition, differences in previous day ozone concentrations were calculated (8 h and 1 h means) by smog episode value minus baseline value and, likewise, the changes in mean daily temperature were calculated. Changes in the individual lung function parameters were regressed on changes in previous day ozone (1 and 8 h means) and changes in mean daily temperature, using multiple linear regression analysis. If the growth rates were mismodelled the intercept would be expected to deviate from zero, however the pollution slope would not be affected. In order to

Table 2. – Growth rates for spirometry and impedance parameters; based on the coefficients of the linear regression analysis of lung function on age (n=534)

	Girls (n=283)		Boys (n=251)	
Spirometry				
FVC	231*	(14)	210	(15)
FEV1	204	(11)	165	(13)
PEF	493	(29)	438	(31)
FEF25–75%	237	(20)	153	(21)
Impedance				
*R*rs8	-0.479◆	(0.050)	-0.362	(0.058)
*X*rs8	0.181	(0.028)	0.470	(0.025)
*f*0	-1.47†	(0.21)	-1.06	(0.24)
FD	0.008	(0.002)	0.005	(0.002)

Data are presented as mean, ±SEM in parenthesis. FVC: forced vital capacity; FEV1: forced expiratory volume in one second; PEF: peak expiratory flow; FEF25–75%: forced mid-expiratory flow; *R*rs8: resistance of the respiratory system at 8 Hz; *X*rs8: reactance of the respiratory system at 8 Hz; *f*0: resonant frequency; FD: frequency dependence of resistance. *: $\mathrm{mL \cdot yr^{-1}}$ or $\mathrm{mL \cdot s^{-1} \cdot yr^{-1}}$; ◆: $\mathrm{cmH_2O \cdot L^{-1} \cdot s \cdot yr^{-1}}$; †: $\mathrm{Hz \cdot yr^{-1}}$.

investigate differences in sensitivity to ozone exposure, the analyses were performed separately for a group of 43 children who reported one or more chronic respiratory symptoms at baseline. The SPSS-X statistical package was used to perform the analysis [34].

Results

Air quality measurements

At the time of the baseline measurements, ambient air pollution levels were low. The highest 24 h averages for SO$_2$, black smoke and NO$_2$ in that period were 55, 54 and 58 $\mu g \cdot m^{-3}$, respectively. Ozone levels were also low; the highest observed 8 h average was 56 $\mu g \cdot m^{-3}$ (minimum 2 $\mu g \cdot m^{-3}$) and the highest observed 1 h average was 66 $\mu g \cdot m^{-3}$ (minimum 1 $\mu g \cdot m^{-3}$). During the baseline period, PM10 and acid aerosol were measured on six different days. The mean PM10 concentration over these six days was 65 $\mu g \cdot m^{-3}$. Ambient levels of acid aerosol were low, the highest concentration of H$^+$, expressed as equivalent sulphuric acid was 0.4 $\mu g \cdot m^{-3}$. The 24 h mean ambient temperature in November was 5.9°C (range 1.1–11.2°C; maximum 1 h 13.1°C) and in December 3.2°C (range -0.8–7.1°C; maximum 1 h 9.4°C). In calculating these means, we included only those days on which baseline lung function measurements of the 212 children were performed.

During the summer smog episode from 2–14 July, O$_3$ levels were increased (table 3). On about 11 days, the ozone concentration exceeded the 160 $\mu g \cdot m^{-3}$ with a maximum of 215 $\mu g \cdot m^{-3}$. The highest observed 8 h average concentration was 163 $\mu g \cdot m^{-3}$. There was a relatively large variation in ozone concentrations between individual measurement days, the highest 8 h averages during the lung function measurement period occurred on July the 7th, 10th and 11th.

The PM10 levels remained low, the highest observed concentration was 54 $\mu g \cdot m^{-3}$ (24 h average). There was no increase in acid aerosols, the H$^+$ levels were near zero. The concentrations of SO$_2$, NO$_2$ and black smoke also remained low during the summer episode, maximum 24 h values were 23, 51 and 24 $\mu g \cdot m^{-3}$, respectively. The 24 h mean ambient temperature was between 20 and 25°C and the 1 h maximum was 32°C (on July 11th). Table 4 presents the mean previous-day ozone concentrations (1 and 8 h) and the mean daily temperature during baseline and episode, and the mean differences of these variables, between both measurement periods.

Table 3. – Levels of air pollutants during the summer smog episode (July 1991)

Day	O$_3$ (8 h) $\mu g \cdot m^{-3}$	PM10 (24 h) $\mu g \cdot m^{-3}$	SO$_4$ (12 h) $\mu g \cdot m^{-3}$	H$^+$ (12 h)
02/07	138			
03/07	163			
04/07	140			
05/07	133			
06/07	130			
07/07	154	42	10.4	0.00
Start HM				
08/07	90		5.4	0.00
09/07	80	24*	1.2	0.00
10/07	136	54*	8.2	0.00
11/07	143	35*	5.7	0.00
12/07	94	23*	Error	0.00
13/07 W	50			
14/07 W	85	23	0.0	0.00
15/07	50			
16/07	58			

*: 12-hour average (day-time); HM: start health measurements; W: weekend; Error: measurement error; PM10: particulate matter with an aerodynamic diameter less than 10 µm.

Table 4. – Mean previous-day ozone concentrations during baseline and during the summer smog episode, and means of the maximum 1 h temperature during both periods (of the baseline measurement period only those days on which one or more children of the present episode study were measured, were used)

Description		
Ozone concentration $\mu g \cdot m^{-3}$		
Previous day ozone, 1 h, baseline	35.7	(21.5)
Previous day ozone, 8 h, baseline	20.7	(15.5)
Previous day ozone, 1 h, episode*	119.2	(40.3)
Previous day ozone, 8 h, episode*	103.8	(36.4)
Δozone, 1 h, (episode - baseline)	83.5	(46.1)
Δozone, 8 h, (episode - baseline)	83.1	(41.1)
Temperature °C		
Mean daily temperature, baseline	5.2	(3.3)
Mean daily temperature, episode	19.5	(2.7)
Δmean temperature (episode - baseline)	14.2	(4.7)

Data are presented as mean, ±SD in parenthesis. *: July 7th to 15th.

Table 5. – Prevalence of acute respiratory symptoms (in the previous week) and medical prescription, during baseline and summer smog episode (n=112)

	Baseline		Summer smog episode	
Respiratory symptoms	n	%	n	%
Dry throat/hoarseness	18	16	15	13
Expectorate/cough up phlegm	19	17	12	11
Wheeze	7	6	8	7
Stuffed nose/runny nose	40	36	28	25
Sore throat	21	19	21	19
Shortness of breath	6	5	10	9
Tightness of the chest	5	5	5	5
Irritated eyes/red eyes	13	12	19	17
A lot of sneezing	21	19	18	16
Earache	12	11	9	8
Feeling of sickness/stomach	28	25	24	21
Headache	39	35	21	19
Fever	7	6	5	5
Medical prescription	24	21	21	19
Staying ill at home	14	12	8	7
Doctors consultation	13	12	13	12

Effect parameters

The questionnaire. During the summer smog episode, adequately completed questionnaires were obtained for 122 of the 212 children (58%). This low response is due to the fact that directly after the episode the summer holiday started so that the parents were difficult to contact. For 10 of the 122 children, we did not have a full completed baseline questionnaire. These children were excluded from the symptom analysis, leaving 112 children.

Comparisons were made between the prevalence of acute respiratory symptoms (in the previous week) at baseline and during the summer smog episode. The results are presented in table 5. No statistically significant changes were observed in the prevalence of acute symptoms. Except for shortness of breath and irritated eyes/red eyes the symptom prevalence was higher during baseline. No major changes in exposure to the measured indoor pollutants, such as parental smoking, home dampness, gas appliances and pets, occurred between baseline and smog episode (data not shown).

Spirometry and respiratory impedance. Valid impedance measurements (baseline and smog episode) were available from 212 (100%) children, and valid spirometry (baseline and smog episode) from 208 children (98%). Their mean (±SEM) values during baseline for spirometry were: FVC 2.34 (±0.52) L, FEV1 2.0 (±0.44) L, PEF 265.28 (±67.10) L·min^{-1}, FEF25–75% 2.23 (±0.62 L·s^{-1}; and for the respiratory impedance parameters were: *R*rs8 6.03 (±1.59) cmH$_2$O·L^{-1}·s, *X*rs8 -1.025 (±0.69) cmH$_2$O·L^{-1}·s, *f*0 15.14 (±5.84) Hz, and FD -0.007 (±0.047) cmH$_2$O·L^{-1}·s.

In the unadjusted linear regression analyses, changes in spirometry and impedance parameters were regressed on changes (Δ) in previous day (PD) ozone levels, for ΔO_3PD-1 (1 h mean) and ΔO_3PD-8 (8 h mean) separately. For spirometry, ΔPEF was significantly negatively related to changes in ozone levels. The associations with ΔFVC, ΔFEV1 and ΔFEF25–75% were not significant, with small, positive values for their βs (not plausible). For impedance, significant associations were observed with Δ*X*rs, Δ*f*0 and ΔFD, but again the direction of the slopes were not plausible. Next, changes in spirometry and impedance parameters were regressed on ΔO_3PD-8, adjusted by differences in daily mean temperature (ΔMTemp). Although the correlation between ΔMTemp and ΔO_3PD-8 was 0.65 ($p \leq 0.01$), both variables could be added in the model, simultaneously. The results of these regression models are presented in table 6. For spirometry, ΔPEF was still significantly negative related to ΔO_3PD-8, indicating a decrease in PEF with increasing ozone concentration. (To illustrate this relationship a plot of ΔO_3PD-8 by ΔPEF was made (fig. 1), demonstrating a large scatter of points). Although no significant associations were found with other spirometry indices, the signs of the observed βs were now

Table 6. – Results of the multiple linear regression analysis, ΔO_3PD-8 + ΔMTemp together in one model (lung function indices as dependent variables; spirometry (n=208), impedance (n=212)

Model	Coefficients	SE	p-value
* ΔFVC = β_1 ΔMTemp + β_2 ΔO_3PD-8+C	β_1 = 0.019994	0.004897	0.0001
	β_2 = -8.64479×10^{-4}	5.6239×10^{-4}	0.1258
	C = -0.223571	0.055845	0.0001
* ΔFEV1 = β_1 ΔMTemp + β_2 ΔO_3PD-8+C	β_1 = 0.014414	0.004241	0.0008
	β_2 = -4.45513×10^{-4}	4.8711×10^{-4}	0.3615
	C = -0.200044	0.048370	0.0001
* ΔPEF = β_1 ΔMTemp + β_2 ΔO_3PD-8+C	β_1 = 3.500892	0.957132	0.0003
	β_2 = -0.451271	0.109923	0.0001
	C = -4.033821	10.915364	0.7121
* ΔFEF25–75% = β_1 ΔMTemp + β_2 ΔO_3PD-8+C	β_1 = 0.022065	0.007920	0.0058
	β_2 = -0.001337	9.0963×10^{-4}	0.1413
	C = -0.288570	0.090326	0.0016
* Δ*R*rs8 = β_1 ΔMTemp + β_2 ΔO_3PD-8+C	β_1 = 5.53555×10^{-4}	0.022989	0.9808
	β_2 = -0.002705	0.002606	0.3006
	C = -0.245533	0.264980	0.3553
* Δ*X*rs8 = β_1 ΔMTemp + β_2 ΔO_3PD-8+C	β_1 = -0.005718	0.012622	0.6510
	β_2 = 0.003815	0.001431	0.0083
	C = -0.185823	0.145488	0.2030
* Δ*f*0 = β_1 ΔMTemp + β_2 ΔO_3PD-8+C	β_1 = 0.075448	0.103796	0.4682
	β_2 = -0.028079	0.011768	0.0180
	C = 1.491599	1.196399	0.2140
* ΔFD = β_1 ΔMTemp +β_2 ΔO_3PD-8+C	β_1 = -0.001378	8.7485×10^{-4}	0.1167
	β_2 = 2.51437×10^{-4}	9.9191×10^{-5}	0.0120
	C = -0.006329	0.010084	0.5310

Δ: difference between smog episode and baseline. FVC, FEV1 in L, PEF in L·min^{-1}, FEF25–75% in L·s^{-1}. *R*rs8, *X*rs8 and FD in cmH$_2$O·L^{-1}·s, *f*0 in Hz. O_3PD-8: previous day ozone level in µg·m^{-3}, 8 h mean; MTemp: mean daily temperature, in °C. For further abbreviations see legend to table 1.

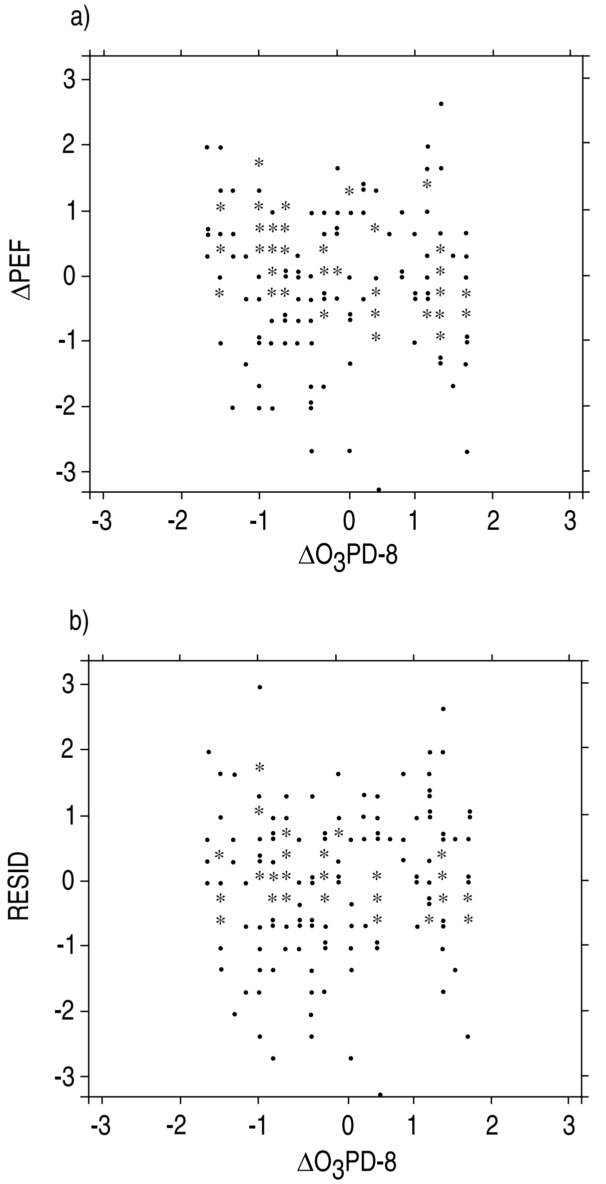

Fig. 1. – a) Standardized Scatter plot of ΔO$_3$PD-8 by ΔPEF. b) Standardized Scatter plot of ΔO$_3$PD-8 by the residuals (RESID) of ΔPEF. Maximum frequencies: a) •=1; ⁚ =2–7; *>7; b) •=1; ⁚ =2–6; * >6. Δ: difference between smog episode and baseline; O$_3$PD-8 previous day ozone level, 8 h mean; PEF: peak expiratory flow.

plausible (negative). ΔMTemp was significantly related to changes in all spirometry indices (positive values for β), except the ΔPEF. The impedance indices ΔX_{rs8}, Δf_0 and ΔFD were still significantly related to ΔO$_3$PD-8. However, the direction of the βs is just opposite to what one would expect if ozone adversely affects the impedance outcomes. The present βs indicate an increase in reactance, a decrease in resonant frequency and less negative frequency dependence of resistance with increasing ozone levels. No significant association was observed with resistance parameters. None of the respiratory impedance parameters was significantly associated with ΔMTemp.

When the 1 h mean for the previous day ozone level was used in the analysis, the results were almost identical to those presented for the 8 h mean. Furthermore, when, for the temperature correction, the mean daily temperature at baseline (with the hypothesis that low baseline temperature influences PEF rather than high "episode" temperature) was used instead of ΔMTemp, the results for spirometry were somewhat different. Again, only ΔPEF was significantly related to ΔO$_3$PD-8, but the signs of the βs for ΔO$_3$PD-8 with ΔFVC and ΔFEV$_1$ were now nonsignificantly positive comparable to the first analysis without temperature correction, which is less plausible. The associations with the impedance parameters were comparable to those observed with ΔMTemp.

Forty three children (20%) reported one or more chronic respiratory symptom(s) at baseline. When the regression analyses were performed for these 43 children separately, similar results were found to those just presented for the total group, although all associations were now nonsignificant (small group).

Discussion

The acute health effects of exposure to a short summer smog episode, with 8 h average ozone levels exceeding 120 μg·m^{-3}, were investigated in 212 primary school children. No significant increases in (acute) respiratory symptoms were reported in this study period. Regression of the changes in the individual lung function parameters showed a significantly negative slope for PEF and nonsignificant negative slopes for FVC, FEV$_1$ and FEF$_{25–75\%}$. Although the impedance indices, ΔX_{rs8}, Δf_0 and ΔFD were significantly associated with ΔO$_3$, the signs of the βs were opposite to the expected direction of an adverse effect. No significant relationship with previous day ΔO$_3$ was found for ΔR_{rs8}.

A problem in interpreting the data is that the results of a single baseline measurement are compared with episode measurements, performed about 7 months later. In particular, the comparison in symptom prevalence (between autumn and summer) therefore need to be interpreted with caution. The response rate of the second questionnaire was low (58%), and selection bias may have occurred. The occurrence of bias implies that the response of parents is related to the ozone exposure. This, however, seems unlikely. In fact, directly after the smog episode smog summer holiday started and many parents were difficult to contact. "Selection" (if it occurred) is, therefore, probably related more to whether the parents and their children had already gone on holiday or not. Moreover, if bias occurred, in particular parents of children who respond to the ozone exposure would have returned the questionnaire, which means that we would have observed an effect (=increase in symptom prevalence) but did not. Other factors which are known to affect the symptom prevalence, for instance indoor exposures or socioeconomic factors, can be regarded as constant over the 7 month period; in part, because each child is his/her own control and partly because we measured them and no major changes occurred.

Regression analyses of Δlung function (ΔLF) on Δozone

(ΔO_3) (previous day) were performed because of the relatively large variation in ozone levels on the different smog episode days as well as at baseline. Thus, in these analyses, individual changes in lung function parameters were related to individual changes in ozone levels. We observed a significant negative association with ΔPEF only; regression slopes for ΔFVC, ΔFEV_1, $FEF_{25-75\%}$ were negative, but not significant. In line with these observations are the results of two epidemiological studies, which also reported negative associations with ozone for PEF only [35, 36]. Very recently, HOEK *et al.* [15] reported responses on changes in ozone exposure to be largest for PEF, somewhat lower for maximum midexpiratory flow (MMEF) and lowest for FVC and FEV_1. Similar results have been reported from clinical studies [4, 7]. In contrast, significant negative associations with FVC and FEV_1 but not with PEF were found in a California summer camp study [11]. The impedance results of the present study do not support the spirometric findings, since no adverse effects on respiratory impedance parameters were observed. If the delta-analyses were repeated without adjusting the lung function data for growth, the pollution slopes stayed almost the same, suggesting that mismodelling of growth does not affect the association between ΔLF and ΔO_3.

The coefficients in table 6 translate into changes of FVC, FEV_1, PEF and $FEF_{25-75\%}$ of -4, -3, -20 and -7% associated with a change in 120 $\mu g \cdot m^{-3}$ of the 8 h average ozone concentration. These negative (although mostly nonsignificant) slopes are consistent with other epidemiological studies [1]. The magnitude of the PEF-slope in particular is large [1]. Based on the SEMS of the pollution slopes we calculated that decreases of 6% in FVC and in FEV_1 and of 10% in PEF and in $FEF_{25-75\%}$ would have been statistically significant. In contrast, respiratory impedance measurements did not show associations in the hypothesized direction. A nonsignificant change of -5% in resistance (R_{rs8}) and a significant decrement of -22% in resonant frequency was found. This might mean that impedance measurements do not demonstrate the type of effects caused by ambient ozone. Further (controlled exposure) research into the applicability of this technique seems necessary. Also, research to determine the dependence of impedance measurements on meteorological and other potential confounding factors seems necessary, given the observed associations opposite to the expected direction.

In healthy adults exercising outdoors, exposure to ambient ozone resulted in an increase of reported respiratory symptoms [37]. In contrast, field studies at summer camps for children failed to find increases in symptoms despite decrements in lung function, which were proportional to ambient O_3 concentrations [13]. The results of the present study appeared to be similar. However, the fact that baseline measurements took place in the autumn and smog episode measurements in the summer, could have resulted in a "downward bias" of the symptom prevalence. Although not significant, we did observe a slight increase in reported eye irritation. Photochemical air pollution is a causative factor in eye irritation, ascribed to non-ozone components of the photochemical mixture and occurring at ozone levels about 200 $\mu g \cdot m^{-3}$ (0.1 ppm) [38], which is somewhat higher than those in this study. Furthermore, the presence of airborne pollen during the summer season may, in part, be responsible for the observed increase in the prevalence of eye irritation.

It is not clear whether people who already suffer from respiratory diseases are more sensitive to the effects of exposure to ozone. Indeed, bronchial responsiveness to stimuli such as methacholine has experimentally been shown to be enhanced by exposure to ozone [4]. On this basis, it has been suggested that hyperresponsive subjects are at greater risk of airway narrowing due to irritative or allergic stimuli after exposure to ozone [39]. Therefore, we also investigated separately, children who reported one or more chronic respiratory symptom(s) at baseline. No differences were found in this group of symptomatic children compared with the healthy group. These data are in agreement with earlier observations, since similar negative associations with previous day ozone were found in children with and without chronic respiratory symptoms [15].

During this summer episode, ozone was the only reported pollutant which was increased. There is some evidence that ambient co-factors, such as H^+ in aerosols, potentiate the responses to ozone. However, in this study all other pollutants were low and H^+ levels were near zero. The latter probably results from neutralization by the high ammonia concentrations observed in The Netherlands. This has also been reported by others [14, 15].

The application of the forced oscillation technique in an epidemiological setting with children appeared to be good. Measurements were easy to perform for the child as well as the investigator. In contrast to spirometry, they are independent of the effort made by the child and are, therefore, less influenced by learning effects. Reported coefficients of variation (CV) of respiratory resistance parameters are about 10%, for healthy as well as asthmatic children [40–43]. Calculation of CV values using the data of the present study (SEM of the mean difference between baseline and smog episode divided by the mean value at baseline, maximum estimate) resulted in (1.17/6.03×100=) 19% for R_{rs8}, which is somewhat higher than for FVC and FEV_1, both 12%, but comparable to the CVs found for PEF and $FEF_{25-75\%}$, both 19%. Due to the fact that FD and X_{rs} fluctuate around zero as either a negative or a positive value and, consequently, their means approximate zero, much larger CV values were found for these parameters, as has been reported previously [43].

In summary, moderately elevated levels of ozone did not result in an increase of acute respiratory symptoms in primary schoolchildren. A statistically significant negative association with ozone was found for ΔPEF only, not supported by adverse effects on respiratory impedance indices. The data of the present study suggest that exposure to a mild summer smog episode, with 8 h average ozone levels exceeding 120 $\mu g \cdot m^{-3}$, did not result in clear, adverse effects on the respiratory health of primary school children.

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