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Susceptibility to air pollution in elderly males and females

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ABSTRACT: It is important to know which individuals in the general population have increased susceptibility to air pollution. The aim of this study was to identify susceptible subgroups by studying airways hyperresponsiveness (AHR), high total immunoglobulin (Ig)E and sex.

Diary data on lower and upper respiratory symptoms (LRS and URS, respectively), cough, and morning and evening peak expiratory flow (PEF) were collected in 327 elderly patients (50–70 yrs) for a period of 3 months. Acute effects of particulate matter with a diameter <10 μm, black smoke, sulphur dioxide and nitrogen dioxide on symptoms and PEF were estimated using logistic regression.

In total, 48 (14.7%) subjects had AHR+/IgE+, 112 (34.3%) had AHR-/IgE+, 42 (12.8%) had AHR+/IgE- and 125 (38.2%) had AHR-/IgE-. In the AHR+/IgE+ group, each 10 $\mu g \cdot m^{-3}$ increase in air pollution was associated with a significant increase in prevalence of URS (odds ratio ranging 1.03–1.19), cough (1.03–1.08) and fall in morning PEF (1.04–1.26). In the AHR+/IgE+ group, males responded predominantly with symptoms and females with a fall in morning PEF.

In conclusion, elderly individuals with both airway hyperresponsiveness and high total immunoglobulin E are especially susceptible to air pollution. Identifying susceptible subgroups might enlarge insight into the actual mechanisms by which air pollution evokes specific modes of response.

KEYWORDS: Air pollution, airway hyperresponsiveness, elderly, immunoglobulin E, sex, susceptibility

Epidemiological studies have previously described small but consistent acute adverse health effects of ambient air pollution on respiratory health in individuals with self-reported respiratory symptoms and/or doctor-diagnosed asthma [1–3]. Results of air pollution studies in individuals without such respiratory symptoms are less consistent and, thus, less clear. This might result from only a minor negative acute effect of air pollution in subjects with good respiratory health. Thus, effects may be missed in relatively small-panel studies that focus on individual risks in specific groups. However, in large time series studies performed in the general population, acute negative effects of higher levels of various air pollutants on respiratory hospital admissions, respiratory mortality and overall mortality have been found [1]. Therefore, it is important to identify which individuals in the general population have increased susceptibility to air pollution.

There are indications that an allergic constitution determines whether an individual has an acute response to increasing levels of air pollution. Children with increased levels of serum total immunoglobulin (Ig)E are more susceptible to air pollution, especially if they have airway hyperresponsiveness (AHR) [4, 5].

Adult airway hyperresponders might have increased susceptibility to air pollution [6], due to the fact that they have increased deposition of particles compared with nonresponders [7]. Whether adults with both allergic features and AHR are also more susceptible to the effects of air pollution has not been the subject of any specific study so far. The aim of the current study was to establish whether elderly adult individuals with both AHR and allergic features are more prone to the negative health effects from air pollution. Moreover, to further explore individual risk factors for susceptibility to air pollution males and females were investigated separately. Females are known to have a higher degree of AHR than males, which has been related to increased susceptibility to the effect of environmental exposures, such as tobacco smoke, irritants and allergens [8–11]. Therefore,

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females with increased IgE and AHR may constitute a group at high risk for effects of air pollution on the respiratory system.

METHODS

Population sample and setting

Study design and methods have been described extensively by VANDER ZEE *et al.* [12]. Briefly, data were collected as a part of a panel study on acute effects of air pollution on respiratory health among elderly adults. A panel study was performed in both rural (Meppel, Nunspeet) and urban (Amsterdam) areas in The Netherlands, over two consecutive winters, using the protocol of the Pollution Effects on Asthmatic Children in Europe (PEACE) study [13]. A random sample of names and addresses from subjects with Dutch nationality, aged 50–70 yrs was obtained from the municipal authorities of Amsterdam, Meppel, and Nunspeet. Subjects were approached by mail with a screening questionnaire and invited to participate in the current panel study. Screening questionnaires were used to obtain information on respiratory symptoms and consisted of selected questions from the European Community Respiratory Health Survey (ECRHS) [14]. Complete data on forced expiratory volume in one second (FEV_1), AHR, serum total IgE, and daily data on lower respiratory symptoms (LRS), upper respiratory symptoms (URS), cough and morning and evening peak expiratory flow (PEF) were collected from 327 elderly subjects (aged 50–70 yrs). The study was approved by the medical ethical committee of the University Hospital of Groningen (Groningen, The Netherlands).

Lung function and AHR

Spirometry and methacholine (Mch) challenge tests were performed according to the standardised protocol of the ECRHS, which meets American Thoracic Society guidelines [2, 4, 14, 15]. Briefly, the FEV_1 was recorded from at least two and up to five technically satisfactory manoeuvres, which means a subject had to be able to perform a minimum of two technically acceptable curves (forced expiratory manoeuvres). The tests were stopped if subjects could not produce two technically acceptable curves out of a maximum of five attempts [15]. The highest FEV_1 was used in the analysis [14, 15]. Measurements were performed with a dry-seal Morgan Spiroflow Ds12 (P.K. Morgan Ltd, Kent, UK). Mch was administered in increasing concentrations by a Mefar MB3 dosimeter (Mefar, Brescia, Italy), and the maximum dose was 2.0 mg. The provocation was stopped if there was a $\geqslant$10% fall in FEV_1 following inhalation of diluent (relative to the baseline FEV_1) or a $\geqslant$20% fall in FEV_1 (relative to the post-diluent FEV_1) following inhalation of any cumulative dose of Mch (Mch_{cum}). Subjects with $\geqslant$20% fall in FEV_1 after inhalation of up to 2.0 mg Mch_{cum} were considered to have AHR+. Subjects without such a fall in FEV_1 were considered to be nonresponders (AHR-).

Serum total IgE

Serum total IgE was determined [16], and the median values of males and females were used separately as cut-off points for elevated values. The median value was similar for males and females, namely 20 $kU \cdot L^{-1}$. Serum total IgE levels $\leqslant$20 $kU \cdot L^{-1}$ were defined as low total IgE (IgE-) and those >20 $kU \cdot L^{-1}$ were defined as high total IgE (IgE+).

Daily symptoms and PEF

Subjects received a diary in which to record daily the presence of LRS (*i.e.* wheeze, attacks of wheezing with shortness of breath and shortness of breath), URS (*i.e.* sore throat, runny or stuffed nose), cough and morning and evening PEF for 3 months [4]. To avoid large changes in the composition of the reporting groups of subjects on separate days, subjects had to complete diary data for $\geqslant$60% of the days. Subjects who did not meet this criterion or who reported exactly the same PEF value for >1 week (which is suggestive of cheating) were excluded from the analyses. The prevalence of LRS on a given day was defined as the number of subjects who reported such symptoms on that day divided by the number of subjects who provided diary data for that given day. The prevalence of URS and cough was assessed in the same way.

Subjects were instructed to make three measurements of PEF on a mini-Wright PEF meter (Clement Clarke International, London, UK) every morning on waking, and again in the evening at bedtime. The highest of each of the three morning measurements and the highest of the three evening measurements were used for analysis. For each subject, the distributions of morning and evening PEF were determined, and decreases >10% below the 95th percentile of an individual's morning or evening PEF distribution were judged to be clinically relevant. The effects of air pollution were expressed as changes in daily prevalence of LRS, URS, cough and >10% fall in morning or evening PEF [4, 17].

Air pollution concentrations

Air pollution concentrations were measured continuously at fixed sites in Meppel, Nunspeet and Amsterdam. The particle measurement sites were selected so that they were close to the living area of the participating subjects, but not strongly influenced by local sources, such as traffic and industry. Concentrations of particulate matter <10 μm (PM_{10}), black smoke (BS), sulphur dioxide (SO_2) and nitrogen dioxide (NO_2) were measured from 03:00 until 03:00 h the next day.

Concentrations were characterised by a 24-h average on the day the health effects were measured (lag 0); 1 and 2 days preceding that day (lag 1 and lag 2); and the 5-day mean concentration of lag 0 to lag 4 preceding that day [12]. Effect estimates of air pollution on morning PEF were determined for lag 1, lag 2 and 5-day mean, as the morning PEF measurement was performed prior to the air pollution exposure of that same day (lag 0).

Statistical analysis

Logistic regression was performed on the data, with additional modelling of first-order autocorrelation in the residuals, and adjustment for daily minimum temperature, linear, quadratic and cubic time trend, weekend/holidays, and influenza incidence for the rural and urban areas and the two winters separately [18], which gave four effect estimates. These four effect estimates were weighted with the inverse of the square of their standard error, which resulted in a weighted mean estimate. Odds ratios (OR) for symptoms and fall in morning and evening PEF were expressed for each 10 $\mu g \cdot m^{-3}$ increase in PM_{10}, BS, SO_2 and NO_2. OR were considered to be significantly increased with increasing levels of air pollution if the 95%

confidence intervals (CI) did not include the value 1. Groups were considered to have increased susceptibility to air pollution when the effect estimates of PM10, BS, SO_2 and NO_2 for the groups with AHR+/IgE+, AHR-/IgE+ or AHR+/IgE- were outside the 95% CI of the effect estimates for the group with AHR-/IgE-, which served as the control group [19].

RESULTS

Air pollution concentrations and population characteristics

The 24-h mean air pollution concentrations during the two winters are shown in table 1. The median values of PM10, BS, SO_2 and NO_2 were somewhat higher in the urban compared with the rural area, but there were no significant differences. In total, 48 out of the 327 subjects (14.7%) had AHR+/IgE+, 112 subjects (34.3%) had AHR-/IgE+, 42 (12.8%) had AHR+/IgE-, and 125 (38.2%) had AHR-/IgE- (table 2). Within the AHR+ subgroups the number of current smokers was significantly higher than within the AHR- subgroups. Females had AHR more often than males (30.6 and 24.3% respectively), but this difference was not statistically significant.

Response to air pollution in the four groups

The associations between the daily prevalence of URS, cough and >10% fall in morning PEF with increase of the different air pollutants for the four groups are shown in tables 3–5. No consistent positive or negative associations were found between the prevalence of LRS or >10% fall in evening PEF and increases in level of air pollution in any of the four groups (data not shown).

Response to air pollution in the group with AHR+/IgE+

Within the AHR+/IgE+ group, the large majority of the OR were >1, indicating a consistent positive relationship between increased prevalence of URS, cough, and >10% fall in morning PEF and higher levels of air pollution. The prevalence of URS was significantly increased with increases in PM10 (lag 1 and 5-day mean), BS (lag 1, lag 2 and 5-day mean), SO_2 (lag 1) and NO_2 (lag 2 and 5-day mean). The prevalence of cough was significantly increased with increased levels of PM10 and BS on the same day (lag 0) and NO_2 the previous days (5-day mean). The prevalence of >10% fall in morning PEF was increased significantly with increased levels of PM10 (lag 1), and BS and SO_2 (both lag 1, lag 2 and 5-day mean). All but two of these estimates were outside the 95% CI of the effect estimates in the control group AHR-/IgE- (tables 3–5).

TABLE 2 Population characteristics of subjects with and without airway hyperresponsiveness (AHR) and relatively high serum total immunoglobulin (Ig)E

	IgE+		IgE-	
	AHR+	AHR-	AHR+	AHR-
Subjects n (%)	48 (14.7)	112 (34.3)	42 (12.8)	125 (38.2)
Males/females	25/23	66/46	11/31	58/67
Age yrs	60.5±6.7	58.8±6.0	59.5±6.4	59.2±6.1
FEV_1 % pred	92.5±17.8	113.8±14.0	97.7±19.4	115.6±14.6
VC % pred	106.4±16.3	115.6±14.3	108.3±16.8	117.7±14.7
Never-/ex-/ current smokers	53/20/27	60/23/17	49/19/32	71/16/13
Atopy	54	37	17	17
Median daily prevalence of				
LRS	21.8	6.3	15.0	6.1
URS	28.0	18.6	23.7	16.9
Cough	29.2	18.6	25.0	16.4
>10% fall in morning PEF	35.0	17.2	30.0	15.6

Data are presented as mean±SD or as %, unless otherwise stated. AHR+: ⩾20% forced expiratory volume in one second (FEV_1) decline at ⩽2.0 mg cumulative methacholine; AHR-: <20% FEV_1 decline at 2.0 mg cumulative methacholine; IgE+: high serum total IgE, >20 $kU \cdot L^{-1}$; IgE-: low serum total IgE, ⩽20 $kU \cdot L^{-1}$; % pred: % predicted; VC: vital capacity; LRS: lower respiratory symptoms; URS: upper respiratory symptoms; PEF: peak expiratory flow.

TABLE 1 Mean and median air pollution concentrations (24-h mean) in $\mu g \cdot m^{-3}$ during winter

	Urban				Rural			
	Days n	Mean	Median	Min.–max.	Days n	Mean	Median	Min.–max.
Winter 1993/1994								
PM10	89	41.5	34.6	12.1–112.7	87	44.1	30.4	7.9–242.2
BS	90	14.2	11.3	0–47.8	92	13.5	9.5	1.5–58.1
SO_2	91	11.8	10.2	2.7–33.5	92	8.2	4.4	0.8–41.5
NO_2	92	46.0	47.0	22.2–75.9	92	26.6	24.0	6.5–54.3
Winter 1994/1995								
PM10	82	31.1	28.9	8.8–89.9	81	26.6	23.7	7.1–96.9
BS	74	8.8	6.7	2.0–28.0	81	8.7	5.6	0.0–43.0
SO_2	82	8.3	7.4	0.6–24.4	80	4.3	3.7	0.5–17.0
NO_2	82	46.7	48.3	26.0–82.3	80	23.7	21.4	1.6–57.1

Min.: minimun; max.: maximum; PM10: particulate matter with a diameter <10 μm; BS: black smoke; SO_2: sulphur dioxoide; NO_2: nitrogen dioxide. There were no significant differences between the urban and rural air pollution concentrations.

TABLE 3 Estimated odds ratios (OR) and 95% confidence intervals (CI) for the prevalence of upper respiratory symptoms associated with a 10-μg·m^{-3} increase in air pollutants

	AHR-/IgE-	AHR-/IgE+	AHR+/IgE-	AHR+/IgE+
PM_{10}				
Lag 0	0.99 (0.97–1.01)	1.01 (0.99–1.03)	0.99 (0.95–1.03)	1.01 (0.98–1.04)
Lag 1	1.01 (0.99–1.03)	1.02 (1.00–1.04)#	1.01 (0.97–1.05)	1.03 (1.00–1.05)#
Lag 2	1.00 (0.98–1.02)	1.01 (0.99–1.03)	0.99 (0.96–1.03)	1.02 (0.99–1.05)
5-day mean	1.00 (0.96–1.04)	1.08 (1.04–1.11)#,¶	0.98 (0.91–1.06)	1.06 (1.00–1.11)#,¶
BS				
Lag 0	1.00 (0.96–1.05)	1.01 (0.96–1.06)	1.03 (0.94–1.13)	1.06 (0.99–1.13)
Lag 1	1.02 (0.98–1.07)	1.03 (0.99–1.07)	1.06 (0.98–1.14)	1.12 (1.06–1.19)#,¶
Lag 2	0.99 (0.95–1.04)	1.02 (0.98–1.06)	0.94 (0.86–1.01)	1.06 (1.00–1.12)#,¶
5-day mean	1.04 (0.96–1.13)	1.10 (1.02–1.20)#	1.03 (0.89–1.20)	1.19 (1.06–1.33)#,¶
SO_2				
Lag 0	0.99 (0.93–1.05)	0.98 (0.92–1.03)	1.05 (0.94–1.17)	1.06 (0.97–1.15)
Lag 1	1.02 (0.97–1.08)	1.07 (1.01–1.12)#	1.07 (0.96–1.19)	1.13 (1.05–1.23)#,¶
Lag 2	0.99 (0.94–1.05)	1.02 (0.96–1.07)	0.96 (0.86–1.07)	0.99 (0.92–1.08)
5-day mean	0.99 (0.88–1.12)	1.15 (1.02–1.29)#,¶	1.04 (0.83–1.30)	1.18 (0.99–1.40)
NO_2				
Lag 0	1.01 (0.98–1.04)	1.01 (0.98–1.04)	1.03 (0.97–1.09)	1.02 (0.98–1.07)
Lag 1	1.01 (0.98–1.04)	0.98 (0.96–1.01)	1.03 (0.98–1.08)	1.04 (1.00–1.08)#,¶
Lag 2	0.99 (0.96–1.02)	0.99 (0.96–1.01)	0.98 (0.94–1.03)	1.03 (0.99–1.07)
5-day mean	1.01 (0.94–1.08)	0.96 (0.90–1.03)	1.03 (0.91–1.16)	1.16 (1.06–1.27)#,¶

AHR+: ⩾20% forced expiratory volume in one second (FEV_1) decline at ⩽2.0 mg cumulative methacholine; AHR-: <20% FEV_1 decline at 2.0 mg cumulative methacholine; IgE+: high serum total immunoglobulin (Ig)E, >20 kU·L^{-1}; IgE-: low serum total IgE, ⩽20 kU·L^{-1}; PM_{10}: particulate matter with a diameter <10 μm; BS: black smoke; SO_2: sulphur dioxide; NO_2: nitrogen dioxide. #: significant associations; ¶: OR outside the 95% CI of the control group (AHR-/IgE-).

TABLE 4 Estimated odds ratios (OR) and 95% confidence intervals (CI) for the prevalence of cough associated with a 10-μg·m^{-3} increase in air pollutants

	AHR-/IgE-	AHR-/IgE+	AHR+/IgE-	AHR+/IgE+
PM_{10}				
Lag 0	1.00 (0.99–1.02)	1.01 (0.99–1.03)	1.00 (0.97–1.02)	1.03 (1.01–1.06)#,¶
Lag 1	0.99 (0.98–1.01)	0.99 (0.98–1.01)	1.01 (0.98–1.03)	1.00 (0.98–1.02)
Lag 2	1.00 (0.98–1.01)	1.00 (0.98–1.02)	0.99 (0.96–1.02)	0.99 (0.97–1.01)
5-day mean	0.98 (0.95–1.01)	1.01 (0.97–1.05)	1.02 (0.96–1.08)	0.99 (0.95–1.04)
BS				
Lag 0	1.02 (0.99–1.07)	1.01 (0.96–1.05)	1.03 (0.97–1.10)	1.08 (1.02–1.14)#,¶
Lag 1	1.00 (0.97–1.03)	1.00 (0.96–1.04)	0.99 (0.94–1.05)	1.01 (0.96–1.06)
Lag 2	0.97 (0.93–1.00)#	0.99 (0.95–1.03)	0.99 (0.94–1.04)	1.01 (0.96–1.06)
5-day mean	0.98 (0.92–1.04)	0.99 (0.91–1.08)	1.00 (0.89–1.11)	1.06 (0.96–1.16)
SO_2				
Lag 0	1.03 (0.98–1.08)	1.01 (0.95–1.07)	1.03 (0.95–1.12)	1.02 (0.94–1.11)
Lag 1	0.97 (0.93–1.02)	1.02 (0.96–1.08)	1.01 (0.93–1.09)	1.02 (0.94–1.10)
Lag 2	0.97 (0.93–1.02)	1.02 (0.96–1.08)	1.01 (0.93–1.08)	0.99 (0.92–1.07)
5-day mean	0.92 (0.84–1.01)	1.10 (0.97–1.25)	0.99 (0.83–1.18)	0.99 (0.84–1.15)
NO_2				
Lag 0	1.01 (0.98–1.03)	1.00 (0.97–1.03)	1.00 (0.96–1.04)	1.03 (0.99–1.07)
Lag 1	0.99 (0.97–1.02)	1.00 (0.97–1.02)	1.00 (0.97–1.04)	0.99 (0.97–1.03)
Lag 2	0.99 (0.97–1.01)	1.00 (0.97–1.02)	0.98 (0.94–1.01)	1.02 (0.98–1.05)
5-day mean	0.98 (0.92–1.04)	0.99 (0.94–1.05)	1.00 (0.93–1.09)	1.09 (1.02–1.17)#,¶

AHR+: ⩾20% forced expiratory volume in one second (FEV_1) decline at ⩽2.0 mg cumulative methacholine; AHR-: <20% FEV_1 decline at 2.0 mg cumulative methacholine; IgE+: high serum total immunoglobulin (Ig)E, >20 kU·L^{-1}; IgE-: low serum total IgE, ⩽20 kU·L^{-1}; PM_{10}: particulate matter with a diameter <10 μm; BS: black smoke; SO_2: sulphur dioxide; NO_2: nitrogen dioxide. #: significant associations; ¶: OR outside the 95% CI of the control group (AHR-/IgE-).

TABLE 5 Estimated odds ratios (OR) and 95% confidence intervals (CI) for the prevalence of a >10% fall in morning peak expiratory flow associated with a 10-$\mu g \cdot m^{-3}$ increase in air pollutants

	AHR-/IgE-	AHR-/IgE+	AHR+/IgE-	AHR+/IgE+
PM_{10}				
Lag 1	1.01 (0.98–1.04)	0.99 (0.97–1.02)	0.99 (0.95–1.03)	1.04 (1.00–1.07)#
Lag 2	0.97 (0.94–1.00)	0.99 (0.97–1.02)	0.99 (0.95–1.03)	1.03 (0.99–1.06)
5-day mean	0.97 (0.92–1.02)	0.97 (0.93–1.01)	0.99 (0.93–1.06)	1.05 (0.99–1.11)
BS				
Lag 1	0.99 (0.94–1.05)	0.97 (0.91–1.03)	0.93 (0.85–1.02)	1.08 (1.01–1.16)#,¶
Lag 2	0.99 (0.94–1.05)	0.99 (0.93–1.04)	0.96 (0.88–1.04)	1.08 (1.02–1.16)#,¶
5-day mean	0.92 (0.84–1.02)	0.91 (0.84–1.00)#	0.84 (0.73–0.96)#	1.16 (1.04–1.29)#,¶
SO_2				
Lag 1	1.00 (0.92–1.08)	1.00 (0.92–1.08)	0.99 (0.87–1.12)	1.15 (1.04–1.27)#,¶
Lag 2	1.00 (0.92–1.09)	1.01 (0.93–1.08)	0.92 (0.81–1.05)	1.18 (1.07–1.30)#,¶
5-day mean	0.92 (0.79–1.08)	0.90 (0.79–1.02)	0.78 (0.61–0.98)#,¶	1.26 (1.07–1.49)#,¶
NO_2				
Lag 1	0.99 (0.95–1.03)	0.98 (0.94–1.01)	0.99 (0.94–1.05)	1.03 (0.98–1.07)
Lag 2	0.99 (0.96–1.03)	1.02 (0.98–1.05)	0.99 (0.94–1.04)	1.01 (0.96–1.05)
5-day mean	0.88 (0.81–0.96)#	0.95 (0.88–1.02)	0.90 (0.82–0.99)#	0.99 (0.91–1.08)

AHR+: ⩾20% forced expiratory volume in one second (FEV_1) decline at ⩽2.0 mg cumulative methacholine; AHR-: <20% FEV_1 decline at 2.0 mg cumulative methacholine; IgE+: high serum total immunoglobulin (Ig)E, >20 $kU \cdot L^{-1}$; IgE-: low serum total IgE, ⩽20 $kU \cdot L^{-1}$; PM_{10}: particulate matter with a diameter <10 μm; BS: black smoke; SO_2: sulphur dioxide; NO_2: nitrogen dioxide. #: significant associations; ¶: OR outside the 95% CI of the control group (AHR-/IgE-).

Response to air pollution in groups with AHR-/IgE+, AHR+/IgE- and AHR-/IgE-

In subjects with AHR-/IgE+ the prevalence of URS increased significantly with increases in PM_{10} and SO_2 the previous day (lag 1), and increases in PM_{10}, BS and SO_2 the days before (5-day mean) (table 3). The 5-day mean estimates for PM_{10} and SO_2 were outside the 95% CI of the effect estimates in the control group AHR-/IgE- (table 3).

The present study found no significant positive associations between the prevalence of cough or >10% fall in morning PEF and increasing levels of air pollution in the AHR-/IgE+ group (tables 4 and 5). One negative significant association was found between the prevalence of >10% fall in morning PEF and BS (5-day mean); however, this estimate was not outside the 95% CI of the estimate in the control group (table 5). No consistent positive associations were found between prevalences of URS, cough or >10% fall in morning PEF and increasing levels of the different air pollutants (lag 0 through 5-day mean) in subjects with AHR+/IgE- or AHR-/IgE- (tables 3–5).

Response to air pollution according to sex within the AHR+/IgE+ group

The response to increasing levels of air pollution in the most susceptible group with AHR+/IgE+ was, in some aspects, different between males and females (table 6). Males had consistent, and most often significant, increased prevalences of URS with increasing levels of air pollution, whereas this was not the case in females. All but one of the estimates in males were outside the 95% CI of the effect estimates in females.

The prevalence of cough also increased significantly in males with increasing levels of BS and NO_2, whereas in females it did not. Males also had a significantly increased prevalence of cough with increasing levels of SO_2 2 days before (lag 2), whereas females had not.

In the susceptible group, females had consistently increased prevalences of >10% fall in morning PEF with increasing levels of air pollution, whereas males had not. In females, the prevalence of >10% fall in morning PEF was significantly increased with higher levels of SO_2 (lag 1, lag 2 and 5-day mean) and BS the day before (lag 1).

DISCUSSION

The current study shows that individuals with both AHR and high levels of serum total IgE (AHR+/IgE+) are especially susceptible to air pollution. This susceptibility to increasing levels of air pollution occurs with respect to the prevalence of URS, cough and >10% fall in morning PEF, and is present as an acute (lag 0) and subacute effect (lag 1 through 5-day mean). Apart from some positive associations with URS in AHR-/IgE+ group, no consistent positive or negative associations were found between air pollutants and the prevalence of respiratory symptoms or fall in morning PEF in the other groups (AHR-/IgE+, AHR+/IgE- and AHR-/IgE-). When the susceptible group with AHR and high serum total IgE was studied in more detail, it was observed that males were likely to cough and have URS, whereas females were likely to have PEF decrements in the morning in response to air pollution exposure.

The current study clearly identifies the subgroup with AHR+/IgE+ as being the most responsive to air pollution. These results are in keeping with those of an earlier study, which showed that the prevalence of daily symptoms and PEF decrements increased with increasing levels of air pollution in

TABLE 6 Estimated odds ratios (OR) and 95% confidence intervals (CI) for the prevalence of upper respiratory symptoms (URS), cough and >10% fall in morning peak expiratory flow (PEF) associated with a 10-$\mu g \cdot m^{-3}$ increase in air pollutants for males and females with AHR+/IgE+

	URS		Cough		>10% fall in morning PEF	
	Males	Females	Males	Females	Males	Females
PM_{10}						
Lag 0	1.02 (0.97–1.07)	1.01 (0.97–1.04)	1.01 (0.98–1.04)	1.04 (1.00–1.08)$^{\#}$		
Lag 1	1.04 (0.99–1.08)	1.02 (0.98–1.06)	1.01 (0.98–1.03)	1.00 (0.96–1.03)	0.98 (0.93–1.04)	1.04 (0.99–1.09)
Lag 2	1.06 (1.02–1.10)$^{\#,\P}$	0.99 (0.95–1.02)	1.01 (0.98–1.03)	0.99 (0.96–1.03)	1.00 (0.95–1.05)	1.02 (0.98–1.07)
5-day mean	1.09 (0.99–1.18)	0.99 (0.93–1.06)	1.02 (0.97–1.08)	0.99 (0.92–1.05)	0.99 (0.91–1.07)	1.05 (0.97–1.14)
BS						
Lag 0	1.13 (1.02–1.25)$^{\#,\P}$	1.03 (0.93–1.12)	1.08 (1.01–1.16)$^{\#}$	1.07 (0.98–1.16)		
Lag 1	1.20 (1.10–1.30)$^{\#,\P}$	1.09 (1.01–1.18)	1.07 (1.01–1.14)$^{\#,\P}$	0.98 (0.91–1.05)	0.98 (0.87–1.10)	1.12 (1.01–1.24)$^{\#,+}$
Lag 2	1.09 (0.99–1.20)	1.02 (0.94–1.10)	1.03 (0.97–1.09)	1.00 (0.94–1.07)	0.97 (0.87–1.08)	1.09 (0.99–1.20)
5-day mean	1.43 (1.20–1.69)$^{\#,\P}$	1.05 (0.90–1.22)	1.16 (1.05–1.29)$^{\#}$	1.02 (0.89–1.18)	1.05 (0.87–1.26)	1.17 (0.99–1.37)
SO_2						
Lag 0	1.09 (0.95–1.25)	1.10 (0.97–1.24)	1.04 (0.95–1.13)	1.03 (0.91–1.18)		
Lag 1	1.12 (0.98–1.28)	1.12 (0.99–1.25)	1.00 (0.92–1.09)	1.00 (0.89–1.13)	1.04 (0.87–1.25)	1.18 (1.03–1.36)$^{\#}$
Lag 2	1.13 (0.99–1.28)	0.93 (0.83–1.05)	1.09 (1.00–1.18)$^{\#}$	0.97 (0.86–1.09)	0.92 (0.77–1.10)	1.24 (1.08–1.42)$^{\#,+}$
5-day mean	1.62 (1.25–2.11)$^{\#,\P}$	1.02 (0.82–1.28)	1.11 (0.95–1.30)	0.93 (0.73–1.18)	0.88 (0.64–1.21)	1.31 (1.03–1.66)$^{\#,+}$
NO_2						
Lag 0	1.08 (1.00–1.16)$^{\#,\P}$	0.99 (0.93–1.04)	1.02 (0.97–1.06)	1.03 (0.98–1.09)		
Lag 1	1.07 (1.01–1.14)$^{\#}$	1.04 (0.99–1.09)	1.02 (0.98–1.06)	0.97 (0.92–1.01)	0.97 (0.91–1.04)	1.03 (0.96–1.10)
Lag 2	1.03 (0.97–1.10)	1.04 (0.99–1.10)	1.02 (0.98–1.06)	1.01 (0.96–1.05)	0.98 (0.92–1.04)	1.00 (0.93–1.06)
5-day mean	1.22 (1.02–1.45)$^{\#,\P}$	1.07 (0.95–1.20)	1.17 (1.06–1.30)$^{\#,\P}$	1.00 (0.91–1.10)	1.02 (0.91–1.14)	0.89 (0.78–1.02)

AHR+: ⩾20% forced expiratory volume in one second (FEV_1) decline at ⩽2.0 mg cumulative methacholine; IgE+: high serum total immunoglobulin (Ig)E, >20 $kU \cdot L^{-1}$; PM_{10}: particulate matter with a diameter <10 μm; BS: black smoke; SO_2: sulphur dioxide; NO_2: nitrogen dioxide. $^{\#}$: significant associations; ¶: OR outside the 95% CI of the control group (AHR-/IgE-); $^{+}$: OR of females outside the 95% CI of males.

children with the same AHR+/IgE+ characterisation [4]. While both the study in children and the current study in adults showed that *a priori* state of AHR and allergy predisposes to susceptibility to ambient air pollution, data on whether air pollution stimulates the development of AHR and allergy are contradictory. SOYSETH *et al.* [20] found that exposure to higher levels of air pollution during the first 3-yrs of life were associated with a higher prevalence of AHR in later childhood, whereas a study by VON MUTIUS *et al.* [21] showed that AHR was less prevalent in children who had been exposed to higher levels of air pollution. However, both were cross-sectional studies, which makes it difficult to draw conclusions about the sequence of air pollution exposure and development of AHR.

The current finding that females are likely to develop a fall in morning PEF after air pollution exposure suggests a relatively high susceptibility of the females airways to nonspecific stimuli compared with males. This finding is in accordance with data that show females have a relatively strong airway responsiveness during Mch provocation testing compared with males [8–11, 22]. It has been suggested that the greater female airway responsiveness is due to the fact that females have a smaller airway calibre than males [22]. BENNETT *et al.* [23] showed that females have a significantly greater aerosol deposition than males, partially associated with a greater airway resistance. Females may have enhanced particle deposition, as they have smaller conducting airways than males of comparable total lung size. Furthermore, because females have a smaller anatomical dead space than males, they may generally bring particles deep into the lung, where these deposit in the alveoli. Compared with females, males have a relatively large airway calibre [22], with lower resistance, resulting in particle deposition higher up, at the beginning of the respiratory tract. Particles that are deposited at that site have a direct irritating effect on the bronchial tract, and may stimulate irritant receptors, which results in coughing and coughing up of phlegm [24]. This might explain why, in the current study, the overall mode of response to increasing air pollution in males is URS and cough, whereas females more often have a drop in their lung function (PEF) after air pollution exposure.

This is the first epidemiological panel study in elderly patients that examined the response to air pollution for both sexes separately. So far, researchers have not addressed the issue as to whether females have a different response to air pollution exposure than males [9, 10]. The effect of environmental factors has often been assumed to be equal for both sexes. Here it was found that males had a significantly increased risk of developing symptoms such as URS and cough when exposed to increasing concentrations of air pollution, whereas in females no significant association was found. This does not exclude an effect on females. A simple explanation may be that males are exposed for longer times during the day due to

outdoor activities [9]. For instance, the differences in effect of NO_2 and BS may be explained by sex differences in daily exposure to traffic exhaust. Further exploration of possible sex differences in response to air pollution seems worthwhile.

The splitting up of the susceptible groups into males and females inevitably led to reduced power to detect health effects of air pollution. Despite this, significant associations were shown between increasing levels of air pollution and respiratory outcome measurements in these two relatively small groups. It is important to notice that without stratification for sex, the association between increasing levels of air pollution and increasing prevalence of cough in males would have remained unobserved. However, as this is the first study looking at susceptible groups in an elderly population, the results and conclusions should be interpreted with caution, and be confirmed in larger groups of elderly patients.

In conclusion, air pollution studies should focus on identifying individuals with susceptibility characteristics, such as airway hyperresponsiveness and high total immunoglobulin E. Careful medical characterisation, taking sex into account, may provide greater insight into the actual mechanisms by which air pollution evokes, sometimes individual-specific, modes of response.

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