Acute Exposure to Realistic Acid Fog: Effects on Respiratory Function and Airway Responsiveness in Asthmatics

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INTRODUCTION

Water collected from naturally occurring fogs often is found to be contaminated by acidic air pollutants (Waldman et al., 1982; Jacob et al., 1985; Johnson et al., 1987). The pH of polluted fogwater may be as low as 3 (Jacob et al., 1985; Johnson et al., 1987). Acid fogs are formed via heterogeneous phase reaction of sulfur dioxide (SO₂) or nitrogen oxides (NOₓ) with atmospheric water droplets. Sulfuric acid (H₂SO₄) and nitric acid (HNO₃) are the most common acid air pollutants.

Sulfuric acid aerosols have been noted to cause significant decrement of pulmonary function in asthmatics by Utell and co-workers (1983) and Koenig and co-workers (1983) after exposure to H₂SO₄ in concentrations of 450 and 100 μg/m³, respectively. Exposure to sulfuric acid aerosols has also been associated with increased bronchial responsiveness (Utell et al., 1984).

On the basis of the limited measurements of ionic strengths in liquid fogwater reported to date (Waldman et al., 1982; Jacob et al., 1985; Johnson et al., 1987), we can calculate that fogs usually have an osmolarity lower than 30 mOsm. Inhalation of hypoosmolar aerosols is also a well-established stimulus to bronchoconstriction (Schoefl et al., 1987; Anderson et al., 1983; Sheppard et al., 1983). Therefore, the effects of hypoosmolarity of fog could theoretically enhance the effects of acidity on the respiratory tract. However, studies addressing the effects of acid aerosols considered aerosols of dry submicrometer particles and may be less relevant in relation to fog exposures: typical fog droplets are at least an order of magnitude larger in diameter and do not have the same pattern of deposition in the respiratory tract, which might change their health risk.
The aim of this study was to assess the acute effects of a realistic acid fog on respiratory function and bronchial responsiveness. The first step of this multidisciplinary work was the characterization of acid fog in an urban area. In a second step we exposed volunteer asthmatics to a fog as similar as possible to natural acid fog.

METHODS

Brussels Fog Assessment

Site

Samples were collected at eight different sites in the city of Brussels, Belgium, depending on the presence of fog (Fig. 1). The city is located within a dense traffic system; most of the industries and the international airport are located North and Northeast of the downtown area. Brussels is also subject to external anthropogenic sources of pollution due to the proximity (a few hundred miles) of several other large industrial concentrations such as the German Ruhr area, Rotterdam, and Belgian cities (Antwerp, Ghent, Liège, Charleroi). Brussels is a densely populated (one million inhabitants) and moderately industrialized city.

Sampling

Fogwater was sampled using a screen collector (Jacob et al., 1985a). Droplets are collected by inertial impaction on an angled screen made of six layers of 500-µm-diameter polyamide strands. Droplets coalesce rapidly on these strands and flow downward due to gravity and aerodynamically drain into a funnel, which drains the fogwater into a preweighted polyethylene collection bottle. The size cut for 50% collection efficiency, predicted from inertial impaction theory (Friedlander, 1977; Johnson et al., 1987), corresponds to a droplet diameter of 6 µm. The screen collector samples 9.8 m³ air/min with an efficiency of 90%. A collection rate of approximately 55 ml/h is yielded in a fog with a typical LWC¹ of 0.1 g⁻³. Prior to sample collection, the collector is rinsed thoroughly with ultrapure water (MQ water). Forty-five fogwater samples corresponding to 18 fog events were taken between 22 October 1991 and 16 February 1993.

Analytical Procedures

As soon as possible after collection, samples were filtered through 0.45-µm-pore membrane filters (Sartorius, cellulose nitrate) to prevent as much as possible any changes in the concentrations of the chemical species primarily caused by the solubilization processes of the particulate matter. The conductivity and the pH were measured immediately after sample filtration. The samples were then stored in a refrigerator at 4°C until analyses. NH₄⁺ and NO₃⁻ were analyzed by visible colorimetry on an autoanalyzer. Depending on the concentration range of the sample, Cl⁻ and SO₄²⁻ were measured by high pressure liquid chromatography or by visible colorimetry. Major cations (Ca²⁺, Mg²⁺, Na⁺, K⁺) were determined by atomic absorption spectrophotometry.

Exposure to Acid Fog

Subjects

All the subjects were volunteers and were informed of the risks of the experimental protocol, which was approved by the institutional review board for human studies. Exposed subjects were asthmatics. Asthma was defined by a history of recurrent episodes of wheezing, chest tightness, and reversible airway obstruction (reversibility > 10% of predicted value of FEV₁) and/or airway hyperresponsiveness (PD₂₀ < 7.8 µM metacholine).

Theophylline preparations, inhaled β adrenergic agents, or ipratropium were stopped 18 hr before the bronchial responsiveness testing. No subject took oral corticosteroids within the 2 weeks before the test and inhaled corticosteroids were withheld 1 week before the test. All subjects denied a history of upper or lower respiratory infection within 4 weeks before study. Smokers had to stop smoking 18 hr before the test. Compliance of smoking subjects with the 18-hr cessation interval was difficult to judge objectively. Only two subjects were ruled out because they admitted having smoked during this period. For the rest of the group, compliance was considered relatively good. Perhaps this is due to a relatively moderate level of tobacco consumption in our smoking subjects (mean + SEM: 10.5 ± 2.5 cigarettes per day).

Fog Generation and Exposure

Fog was generated by an air-compressed nebulizer (Hudson Updraft 2, Hendley Medical Supplies, Ltd). The air we used (Oxyhydrique Internationale SA) did not contain significant concentrations of atmospheric pollutants (H₂O < 15 ppm, CO < 5 ppm, SO₂ < 0.1 ppm, NO–NO₂ < 1 ppm, NH₃ < 1 ppm, Cl₂

¹ Abbreviations used: MMAD, mass median aerodynamic diameter; LWC, liquid water content; FEV₁, forced expiratory volume in 1 s; Fₐw, airflow resistance; SRₐw, specific airflow resistance; FRC, functional residual capacity; RV, residual volume; ERV, expiratory reserve volume; PD₂₀, cumulative dose of metacholine responsible for a 20% fall of FEV₁; SEM, standard error of the mean; Mch, metacholine; SGₐw, airflow conductance; VMD, volume median diameter
< 0.1 ppm). Subjects were exposed to acid fog through a face mask (covering mouth and nose). Granulometry was controlled by an optical aerodynamic particle counter (Polytec-Waldbrown, RFA) under conditions of temperature (~18°C) and relative humidity (~75%) identical to exposure conditions. The physical and chemical characteristics of the fog are summarized in Table 1. In the first step, H₂SO₄ was suspended in NaCl solution to produce an isoosmolar acid fog with H₂SO₄ concentration 500 µg/m³. In this step we investigated only the effects of acidity in fog. In the second step, the hypooosmolar and acid reconstituting conditions of the fog were very similar to those of naturally occurring fog. Both exposure conditions corresponded to that of very dense fog (LWC ≥ 0.5 g/m³).

Measurement of Pulmonary Function

Subjects performed pulmonary function studies in an integrated-flow, pressure-corrected body plethysmograph (Leith and Mead, 1974). Airway resistance (Rₑₑ) was measured during panting as described by Leith and Mead (1974) and Dubois and co-workers (1956). Airway resistance was corrected for volume and expressed as specific airway resistance (SRₑₑ).

Before measurements of SRₑₑ, a 30-s period of normal breathing was monitored on oscilloscope to avoid reflex changes in bronchial tone induced by rapid changes in lung volume. Then, beginning at the end of a normal tidal breath, the subject panted against a closed shutter for measurement of functional residual capacity (FRC). To calculate the residual volume (RV), the subject expired maximally and expiratory reserve volume (ERV) was subtracted from FRC. After this, the subject inspired maximally and TLC was calculated by adding RV and inspiratory forced vital capacity. Finally, the subject expired forcefully to RV and the forced expiratory volume in 1 sec (FEV₁) was measured. A minimum of three maneuvers were performed and we used acceptability and reproducibility criteria recommended by the American Thoracic Society (1987) to select the measurement we recorded.

Assessment of Bronchial Responsiveness

Bronchial responsiveness was assessed pharmacologically using a classic Mch challenge (Sterk et al., 1993). Metacholine was delivered by a MEFAR MB dosimeter (calibrated output: 14 µl per puff; droplets size, polydisperse aerosol from 0.5 to 5 µm).
For each metacholine dose, subjects inhaled five times to their TLC. FEV₁ was measured 30 and 90 sec following each five inhalations and the best value was chosen. The metacholine concentrations were progressively increased (0.125–0.250–0.5–1–2–5–10–20–25 mg/ml). The FEV₁ measured after inhalation of diluent (NaCl 0.9%) was taken as the pretest value and the test was stopped when FEV₁ had decreased at least 20%. For each subject a dose–response curve was established where the percentage fall in FEV₁ was plotted against the cumulative dose of metacholine on a log scale (maximal cumulative dose of metacholine, 22.5 μM). PD₂₀ values were measured on these curves.

Variability of pulmonary function measurements is not a specific characteristic of smokers but is found in all the asthmatic subjects. It is related to level of bronchial hyperresponsiveness. Bronchial responsiveness assessed by PD₂₀ at baseline was not significantly higher in smokers than in nonsmokers in our study (PD₂₀ at baseline: mean in smokers = 1.84 μM Mch and in nonsmokers = 1.6 μM Mch). To reduce effects of variability of pulmonary function in time we used minimal delay between assessment of baseline situation and exposure situation in the experimental protocol. Also, to minimize effects of variability of pulmonary function between subjects, we compared paired differences and used nonparametric statistical methods to analyze results.

Experimental Protocol

On the first day, respiratory function and bronchial responsiveness were assessed for each subject. The next day, respiratory function was reassessed and these measure was considered as baseline respiratory function.

Prior to exposure, subjects gargled grapefruit juice to reduce levels of oral ammonia that might neutralize inhaled acid. Subjects were then exposed to acid fog for 1 hr at rest. Exposure time included three periods of 5 min of voluntary hyperventilation alternating with tidal breathing periods. One-half hour after exposure, respiratory function and bronchial responsiveness tests were performed at the same hour in the day.

**Statistical Analysis**

The paired differences of FEV₁, SRₐw, and PD₂₀ were each noted not to be normally distributed, and therefore nonparametric statistical methods were used throughout the analysis. The FEV₁, SRₐw, and PD₂₀ were expressed as means ± SEM (standard error of the mean). Paired differences for values of FEV₁, SRₐw, and PD₂₀ before and after fog exposure were compared using the Wilcoxon matched-pairs signed-rank test. A P < 0.05 was considered significant.

**RESULTS**

**Brussels Fog Assessment**

The fogwater composition, shown in Table 1 and Fig. 2, is dominated by NH₄⁺ and SO₄²⁻ and to a lesser extent by NO₃⁻ and Cl⁻. Earlier fog studies in urban environments (Waldman et al., 1982; Jacob et al., 1985; Johnson et al., 1987) have reported similar patterns. The frequency distributions show maxima for the following classes of concentrations: 1.5 to 2 mEq/liter for NH₄⁺, 0.5 to 1 mEq/liter for SO₄²⁻ and Cl⁻, and 0.0 to 0.5 mEq/liter for NO₃⁻. The mean cations/anions balance is equal to 1.22, which means that all major species have been accounted for. However, the maximum value (1.63) suggests that anions are missing in some samples. This anion deficiency (“Deficit” in Fig. 2), probably corresponds to highly soluble organic species such as formaldehyde, acetic acid, and formic acid, as reported elsewhere (Jacob et al., 1983; Munger et al., 1983, 1990). The composition of fogwaters collected at different times and places is found to be highly variable because it depends on a great number of chemical, physical, and meteorological factors such as temperature in-

**TABLE 1**

<table>
<thead>
<tr>
<th>Physical and Chemical Characteristics of Reconstituted Fogs</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MMAD</strong>&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>------------------------</td>
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<tr>
<td>Naturally occurring fog</td>
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<tr>
<td>Means ± SEM</td>
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<tr>
<td>Limit values</td>
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<tr>
<td>First artificial fog</td>
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<tr>
<td>Second artificial fog</td>
</tr>
</tbody>
</table>

<sup>a</sup> MMAD, mass median aerodynamic diameter (means ± SEM and limit values observed for naturally occurring fogs; means ± SEM for artificial fogs); LWC, liquid water content; Osm, osmolality.
version, adjacent sources of a specific pollutant, and liquid water content.

The equivalent proportion between NH$_4^+$ and SO$_4^{2-}$ is found to be remarkably constant for most fog events. NH$_4^+$ concentration plotted versus SO$_4^{2-}$ concentration shows a very good correlation, with the exception of the highest concentrations of NH$_4^+$. The slope of the linear regression (without the data corresponding to [NH$_4^+$] > 5 mEq/liter) is 1.9. Such a feature was also described by Sigg et al. (1985) and Behra et al. (1989).

Thus, SO$_4^{2-}$ is partially neutralized by NH$_4^+$ in most samples. The NH$_4^+$ cation, acting as the main acid-neutralizing component, originates from gaseous NH$_3$. Intensive cattle breeding and agricultural activities provide important sources of NH$_3$. We can summarize by saying that Brussels fogwater can be largely assigned to a solution of ammonium salts such as (NH$_4$)$_2$SO$_4$ and NH$_4$HSO$_4$. These salts are primarily present in the aerosol phase and act as condensation nuclei for the growth of fog droplets, where they are subsequently partially dissolved.

Exposure to Acid Fog

Effects of Sulfuric Acid Fog

Subjects characteristics, lung function testing, and bronchial responsiveness challenge tests are summarized in Table 2 and Fig. 3. The means ± SEM were as follows: FEV$_1$ (% of predicted value) before exposure: 79 ± 4.9% and after exposure: 76 ± 5.6% (NS; $P = 0.14$); SR$_{aw}$ (L x cm H$_2$O/L/s) before exposure: 8.19 ± 1.7 and after exposure: 8.83 ± 2.5 (NS; $P = 0.87$); PD$_{20}$ (µM Mch) before exposure: 1.267 ± 0.5 and after exposure: 1.041 ± 2.4 (NS; $P = 0.36$).

Differences observed in FEV$_1$ and SR$_{aw}$ before and after fog exposure were not significant. Only 8 of the 14 subjects demonstrated an increase of SR$_{aw}$ after fog exposure. Moreover, changes were very small: increased SR$_{aw}$ exceeded 10 L x cm H$_2$O/L/s (considered as normal range) in only two cases and the mean change of SR$_{aw}$ was 4%. Significant change of bronchial responsiveness after H$_2$SO$_4$ fog exposure was not observed ($P = 0.36$). When an increase of bronchial responsiveness was observed, this change remained very tenuous. The mean change of bronchial reactivity was -18% of PD$_{20}$ in the sense of an increase of bronchial responsiveness.

Effects of Ammonium Sulfate Fog

Subjects characteristics, lung function testing, and bronchial responsiveness assessment are sum-
TABLE 2
Individual Characteristics and Responses to H₂SO₄ Fog Exposure

<table>
<thead>
<tr>
<th>Subject</th>
<th>Sex</th>
<th>FEV₁ (-before)</th>
<th>FEV₁ (after)</th>
<th>FVC (before)</th>
<th>FVC (after)</th>
<th>SRₜₜwat (L x cm H₂O/L/s)</th>
<th>PD₂₀ (µM Mch)</th>
<th>Reversibility¹ (-% of predicted value)</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>M</td>
<td>61</td>
<td>69</td>
<td>86</td>
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<td>6.8</td>
<td>0.25 1.88</td>
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<td>M</td>
<td>76</td>
<td>64</td>
<td>112</td>
<td>100</td>
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<td>5.9</td>
<td>0.608 0.51</td>
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<td>M</td>
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<td>55</td>
<td>77</td>
<td>68</td>
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<td>96</td>
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<td>113</td>
<td>115</td>
<td>3.5</td>
<td>5</td>
<td>1.17 1.69</td>
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</table>

Mean: 79 76 99 96 8.19 8.8 1.26 1.041
±SEM: ±4.9 ±5.6 ±4.7 ±5.4 ±1.8 ±2.5 ±0.5 ±0.4

¹ Reversibility of airway obstruction was assessed only in subjects presenting with obstructive ventilatory impairment at baseline.
² Abbreviations used: A, ß adrenergic agonist (d = daily; o = occasionally); IC, inhaled corticosteroids; T, theophyllin; SC, systemic corticosteroids (during exacerbations); ND, not done.

marized in Table 3 and Fig. 4. The means ± SEM were as follows: FEV₁ (% of predicted value) before exposure: 76 ± 7% and after exposure: 73 ± 6% (NS; P = 0.15); SRₜₜwat (L x cm H₂O/L/s) before exposure: 6.93 ± 2.12 and after exposure: 7.33 ± 1.81 (NS; P = 0.2); PD₂₀ (µM Mch) before exposure: 1.68 ± 0.71 and after exposure: 1.71 ± 0.61 (NS; P = 0.8). We did not observe significant change in FEV₁ and SRₜₜwat before and after exposure to ammonium sulfate fog. In 7 of the 10 subjects, SRₜₜwat was increased but this increase was relatively small (mean increase = 36.4%) and in only 2 subjects, values of SRₜₜwat

![FIG. 3. Effects of H₂SO₄ fog exposure on airway resistance (SRₜₜwat) and bronchial responsiveness (PD₂₀).](image-url)
**TABLE 3**

<table>
<thead>
<tr>
<th>Subject</th>
<th>Sex</th>
<th>FEV(_{1}) (% of predicted value) Before</th>
<th>After</th>
<th>FVC (% of predicted value) Before</th>
<th>After</th>
<th>SR(_{aw}) (L × cmH(_2)O/L/s) Before</th>
<th>After</th>
<th>PD(_{20}) (µM Mch) Before</th>
<th>After</th>
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<th>Smoker</th>
<th>Reversibility(^a) (% of predicted value)</th>
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<td>2.01</td>
<td>Ao, IC</td>
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Mean: 76.5 ± 7 to 91.1 ± 8.3, 6.9 ± 7.3, 1.68 ± 1.71
±SEM: ±6.2 to ±6.04, ±2.1 to ±1.8, ±0.7 to ±0.6

\(^a\) Reversibility of airway obstruction was assessed only in subjects presenting with obstructive ventilatory impairment at baseline.

\(^b\) Abbreviations used: Ao, 

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reached 10 L × cmH\(_2\)O/L/s (considered as normal range).

Sulfate ammonium exposure did not significantly change bronchial responsiveness (\(P = 0.87\)). In all subjects, changes in bronchial responsiveness were small and the mean change of PD\(_{20}\) from preexposure baseline was +2% in the sense of a decrease of bronchial responsiveness.

The statistical power of Wilcoxon matched-pairs signed-rank test in these studies (assessing importance of \(\beta\), the type II error) (Freiman et al., 1978) was as follows:

- concerning exposure to H\(_2\)SO\(_4\) fog: 10.36% for FEV\(_{1}\), 7.44% for SR\(_{aw}\), and 9.06% for PD\(_{20}\);
- concerning exposure to ammonium sulfate fog: 9.52% for FEV\(_{1}\), 6.59% for SR\(_{aw}\), and 5.37% for PD\(_{20}\);

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**FIG. 4.** Effects of ammonium sulfate fog exposure on airway resistance (SR\(_{aw}\)) and bronchial responsiveness (PD\(_{20}\)).
DISCUSSION

In this study, exposure of asthmatics at rest to a realistic acid fog did not cause significant change in respiratory function or bronchial responsiveness. The challenge with H₂SO₄ fog was designed to isolate the causal role of acidity among the effects of acid fogs. To rule out a possible combined effect of hyposmolarity, fog solution was made isoosmolar. The pH of solution was extreme but realistic. LWC of this fog was chosen very high to increase sensitivity of the experiment. Lack of bronchoconstrictor effect and lack of bronchial reactivity change observed after exposure to H₂SO₄ fog in this first part suggest that, after short-term exposure, acidity of natural fogs does not influence respiratory function and bronchial responsiveness in asthmatics.

The second part of the work was designed to assess global respiratory effects of fog with physical (granulometry) and chemical characteristics (pH and titratable acidity, major ions components, osmolality) similar to those of fogs measured in an urban area such as Brussels, Belgium. The negative results of the second part, again, suggest that naturally occurring fogs do not exert acute respiratory effects in asthmatics.

In our population sample, it was not possible to detect discriminating factors among subjects who worsened their bronchoconstriction or bronchial hyperresponsiveness and those who improved it or remained unchanged after exposure. Comparing severity of asthma (assessed by usual medication requirements), smoking habits, level of obstructive ventilatory impairment at baseline, and level of bronchial responsiveness at baseline in these subgroups of subjects, we did not find significant differences (p > 0.05 using nonparametric Wilcoxon test). This suggests that individual changes of SRaw or PD₂₀ likely are rather caused by random variations around the baseline than by the existence of reactive subgroups in the asthmatic population.

Our subjects, being ages 26 to 70 years old and having relatively moderate medication requirements, might not have been representative of the asthmatic population, but are likely comparable to asthmatics in previous studies. Because we studied subjects for a short period in this study, we cannot rule out the possibility that we missed delayed effects or effects of acid mist possibly occurring after a more prolonged exposure. Our experimental protocol did not include exercise during exposure (only three periods of hyperventilation). Exposure at rest could be a less sensitive method of assessing acid fog effects, but likely corresponds to more realistic exposure conditions for most of the asthmatic population. Although the two protocols reported here have limited statistical power, it is noteworthy that individual changes in SRaw and PD₂₀ are small, contrasting with situations observed with well-known bronchoconstrictors (histamine, SO₂, distilled water aerosols) or “bronchial responsiveness increaser” agents (SO₂, viral infections), where SRaw and PD₂₀ characteristically are modified by several hundred percentages in asthmatics.

Previous controlled exposure studies of the effects of H₂SO₄ involving subjects with asthma have generated conflicting data. Utell and co-workers demonstrated significant decreases in airway conductance (SGaw) after exposing asthmatic subjects to aerosols (MMAD 0.7 μm) containing 450 μg/m³ of H₂SO₄ for 16 min through a mouthpiece (1983). Koenig and co-workers exposed 10 adolescent asthmatics to 100 μg/m³ of H₂SO₄ and NaCl aerosol (MMAD 0.6 μm) through a mouthpiece and found a significant FEV₁ decrease immediately after a 10-min exercise period (1983). Utell also demonstrated that exposure to aerosol containing 450 μg/m³ H₂SO₄ increased bronchial reactivity to carbachol in asthmatics (1984).

Nevertheless, not all of the controlled exposure studies of the effects of H₂SO₄ aerosols in subjects with asthma demonstrated significant changes in pulmonary function and bronchial responsiveness. In the study of Sackner and co-workers there was no significant change in FEV₁ or total respiratory resistance in five adults with asthma exposed at rest to H₂SO₄ aerosols (MMAD 0.1 μm) at 10, 100, and 1000 μg/m³ for 10 min through a mouthpiece system (Sackner et al., 1978). Linn and co-workers exposed asthmatics to H₂SO₄ aerosols (MMAD 0.6 μm) at 122, 242, and 410 μg/m³ and did not find significant change in respiratory function, symptoms score, or bronchial reactivity to breathing cold dry air (1986).

Studies with controlled exposure to acid fogs are less numerous than those with smaller droplets size aerosols. Avol and co-workers exposed normal and asthmatic adult subjects to fogs (MMAD 10 μm; LWC 0.1 g/m³) containing 0, 500, 1000, and 2000 μg/m³ H₂SO₄ in an exposure chamber for 1 hr; there was a statistically significant increase in respiratory symptoms, but there was no significant change in pulmonary function or bronchial responsiveness (Avol et al., 1988). Although some authors concluded that acid fog inhalation exposure is associated with increased mucociliary clearance (Laube et al., 1993), Aris and co-workers exposed asthmatic subjects to H₂SO₄ fogs (volume median diameter VMD 6 μm and LWC 1.8 or 0.5 g/m³) without demonstrating
effects on pulmonary function or on respiratory symptoms (1991). In a recent study, Morrow et al. exposed asthmatic subjects to near ambient levels of sulfuric acid aerosols (100 µg/m³ H₂SO₄) and did not observe significant change of lung function (1994).

In our study, exposure conditions combined several bronchial stimuli including hypooximolarity (Schoeffel et al., 1981; Anderson et al., 1983; Shepard et al., 1983), acidity (Utell et al., 1983; Koenig et al., 1983), and even titratable acidity (Fine et al., 1987). Despite association of all these potential bronchial effectors, exposure to this fog did not produce significant change in pulmonary function or bronchial responsiveness.

One hypothesis is that the lack of effect is, at least partly, linked to the physical properties of natural acid fog. In order to integrate our data with previous studies, it is possible that at the same pH values and H₂SO₄ concentrations, acid fogs consisting of large droplets (>7 µm) may be less toxic for the respiratory tract than aerosols of smaller droplets (<1 µm). Such findings have already been reported in animal exposure studies (Amdur et al., 1978) and suggested in some human exposure studies (Aris et al., 1991; Balmes et al., 1988). The specific mechanisms underlying acid-induced pulmonary functional changes are not known but, acting as irritant agents, acid aerosols likely exert respiratory effects by causing epithelial damage leading to inflammation and mediators release (Barnes and Lundberg, 1991) and by stimulating sensory receptors: the rapidly adapting irritant receptors and the C-fiber receptors (Corder and Coleridge, 1986; Sant'Ambrogio, 1987).

Since these receptors are mainly concentrated in subglottic large airways (in particular for the rapidly adapting irritant receptors), we can speculate that the preferential target site for acid aerosols to induce functional changes is likely located in the tracheobronchial region. Because of hygroscopic characteristics, deposition of fog in the respiratory tract is difficult to assess. Growth of hygroscopic particles during transit in humid respiratory airways makes extrapolation of data concerning dry aerosols deposition difficult (Morrow, 1986). However, isotopical studies demonstrated that, using monodisperse aerosol with MMAD = 10 µm, deposition in the tracheobronchial region did not exceed 25% of the total amount inhaled, the major part depositing in oropharynx (Bowes et al., 1989). Perhaps discrepancies of deposition sites between coarse (>7 µm) and fine (<1 µm) aerosols could explain the different respiratory effects previously described. In this regard it is interesting to note that Hackney and co-workers, comparing difference of effects between fine (MMAD = 0.9 µm) and coarse (MMAD = 10 µm) acid aerosols in asthmatics, observed that fine aerosols were more likely to change pulmonary function, while coarse aerosols were more likely to increase respiratory symptoms (Hackney et al., 1989). They suggested that this pattern might be explained by assuming that symptoms are caused primarily by large acid droplets deposited in upper airways and that disturbances of pulmonary mechanics in asthmatics are caused primarily by smaller acid droplets deposited more distally in the bronchial tree.

Moreover, fine aerosols usually have a lower LWC than coarse aerosols: for the same concentration of H₂SO₄ in air, acid pollutants and H⁺ ions are thus more concentrated in droplets of fine aerosols than of coarse aerosols, where they are diluted. These very concentrated particles could be more effective on irritant receptors in stimulating bronchoconstriction.

In conclusion, short-term exposure to realistic acid fog does not cause significant change in respiratory function or bronchial responsiveness in asthmatics at rest. The understanding of the discrepancies of effects between acid fogs and finer acid aerosols requires further investigations, addressing hygroscopic aerosol deposition in the respiratory tract and mechanisms of respiratory toxicity of acid aerosols.

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