Health Effects of Air Pollution

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Environmental Air Pollution - Two Major Categories

- Atmospheric Pollutants
  - Sulfur Dioxide
  - Particulate Matter
- Atmospheric Irritants
  - Nitrogen Dioxide
  - Ozone

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  - Particulate Matter
- Atmospheric Irritants
  - Nitrogen Dioxide
  - ***Ozone***

Atmospheric Irritants

- Nitrogen dioxide and ozone are the major components of photochemical smog
- Most studies have been performed on healthy adults and only a few have been performed on patients with chronic obstructive pulmonary disease and asthma

Atmospheric Irritants - Ozone

- Ambient levels
- Epidemiologic Evidence
- Experimental exposure studies
- Mechanisms of action

Ozone - Ambient Levels

- Environmental sources - Very few
- Indoor sources - primarily due to high voltage electrostatic devices
- Lower atmosphere sources
  - Hydrocarbons and NO2 reacting in the presence of ultraviolet radiation from the sun
  - Down-transport from the upper atmosphere (this makes only a partial contribution to lower atmospheric concentrations)

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Ozone - Lower Atmosphere Concentrations

- Daily variations of ozone
  - Starts low in the morning and peaks in the afternoon
  - The peak is dependent on atmospheric conditions and the concentration of exhaust emissions from vehicles powered by fossil fuel
  - Rapidly destroyed by NO at night
  - Daily variation of ozone is greater in urban areas than rural areas

Ozone - Lower Atmosphere Concentrations

- Seasonal Variation of ozone
  - highest during the summer months

Ozone - Background Concentrations

- Levels have been steadily increasing over the last century
- Average background is between 20 and 40 parts per billion (ppb) in most industrialized countries
- However, because of the large variations in the concentration, there are considerably higher exposure levels in a part of the population or over limited periods of time

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Ozone - Epidemiologic Evidence (1)

- Most studies have focused on acute effects of ozone
- Often studies were done at summer camps or on days of high ozone and compared with days of lower ozone
- Studies have consistently demonstrated an increase in pulmonary symptoms and decline in lung function proportional to the level of ozone

Ozone -
Epidemiologic Evidence (2)

- The studies give different estimates of the effects of ozone because the effects are dependent on duration and intensity of exposure, exercise level, and the patient population studied (children, COPD, asthma, etc)

Ozone -
Epidemiologic Evidence (3)

- The forced vital capacity (FVC) and forced expiratory volume exhaled in one second (FEV_1) are two numbers frequently used to measure lung function

Ozone -
Epidemiologic Evidence (4)

- In acute ozone exposure in normal individuals, both FVC and FEV_1 decrease between 0.1 and 1.3 ml per 1 ppb ozone
- These effects are felt to be transient but they may persist for weeks

Ozone -
Epidemiologic Evidence (5)

- The effects of acute ozone exposure in patients with chronic pulmonary disease are less clear
- Some studies have demonstrated an association between ozone levels and hospitalizations for asthma and some have not

Ozone - Epidemiologic Evidence (6)

- Some studies have looked at long-term ozone exposure and lung function by comparing individuals living in areas with different ambient levels of ozone
- Increased ambient levels of ozone has been associated with symptoms of chronic respiratory disease, decline in lung function, and increase in the annual rate of decline of FEV_1

Ozone - Epidemiologic Evidence (7)

- Bottom line:
  - Ozone acutely decreases lung function
  - There are probably adverse effects on asthma exacerbations and long-term exposure, but these studies are not as conclusive likely secondary to confounding variables

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Ozone - Experimental Exposure Studies

- Symptom scores and lung function
- Nonspecific airway responses
- Allergen responsiveness and immune response

Symptom scores and lung function

- Exposures at 2-3 times ambient concentrations have been studied
- The most characteristic symptoms include:
  - Cough
  - Shortness of breath
  - Sore throat
  - Chest pain
  - Pain on deep inspiration

Symptom scores and lung function (2)

- Studies have consistently demonstrated a decline in lung function with ozone exposure as a function of the total inhaled dose of ozone
- Total inhaled dose of ozone = concentration x ventilation x exposure time
- There is a large interindividual variability in response to ozone

Symptom scores and lung function (3)

- Additionally, individuals with underlying lung disease have a greater response to ozone than other individuals
- Example: Kreit et al J Appl Physiol 1989;66:217-222

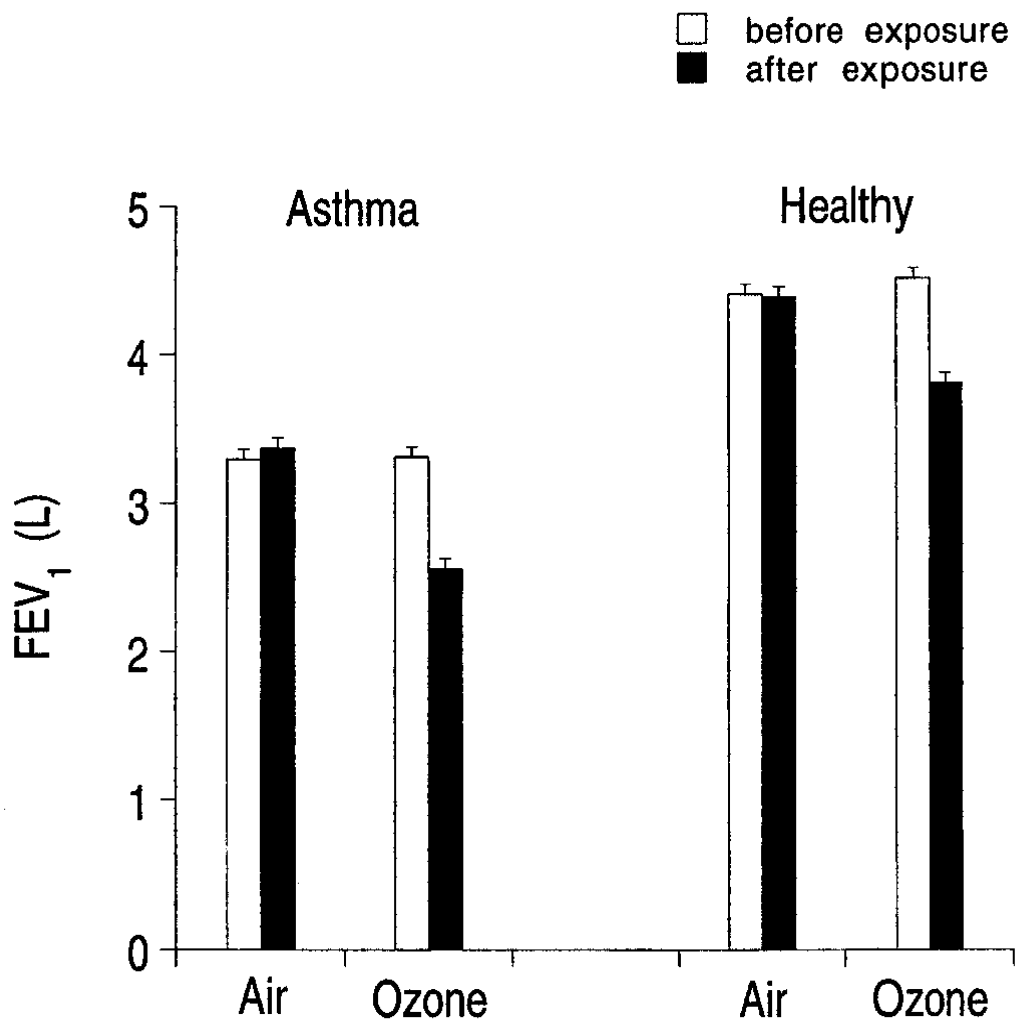


FIG. 6. Mean values (±SEM) of FEV_1 before (*open bars*) and after (*full bars*) exposure to 0.4 ppm ozone or purified air for 2 hr during intermittent exercise in asthmatic (n=9) and healthy (n=9) subjects. (From Kreit JN, Gross KB, Moore TB, Lorenzen TJ, D'Archy J, Eschenbacher WL. Ozone-induced changes in pulmonary function and bronchial responsiveness in asthmatics. *J Appl Physiol* 1989;66:217–222.)

Symptom scores and lung function (4)

- There seems to be some degree of tolerance to the effects of ozone on the decline in pulmonary functions
- Figure 7.A.

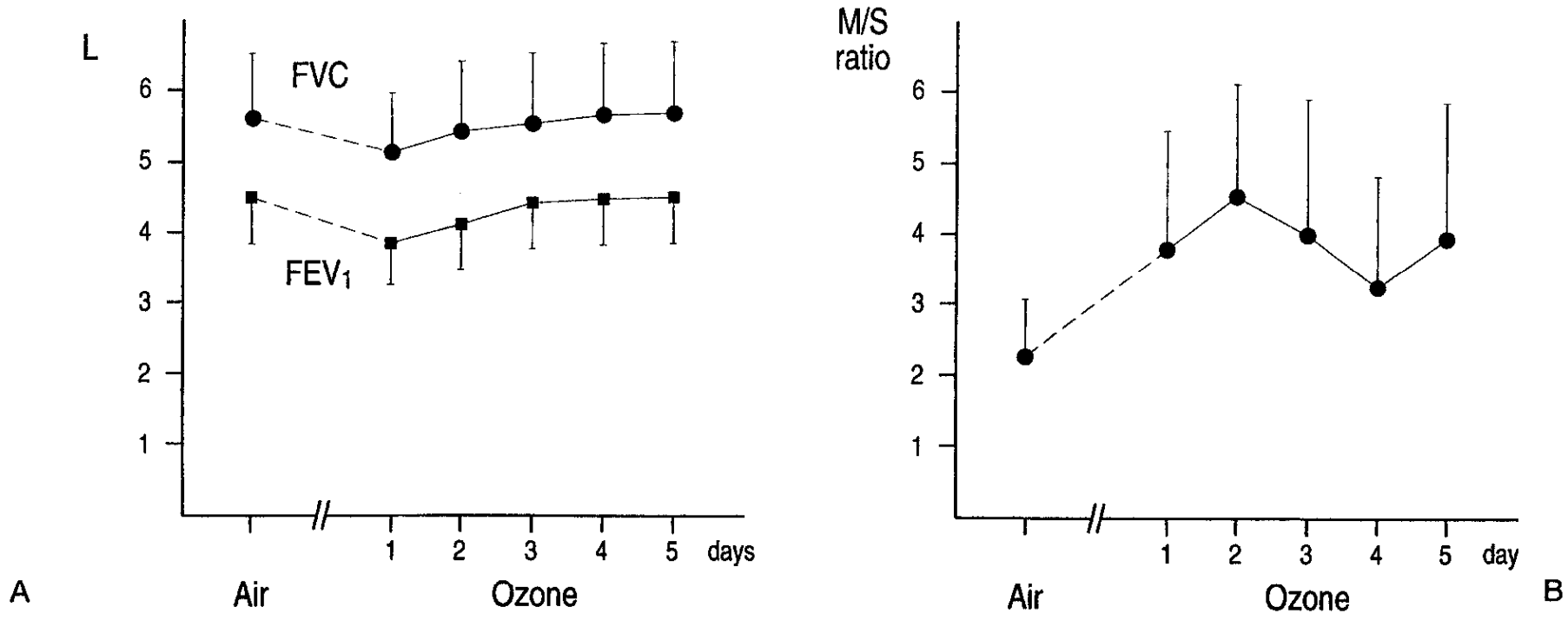
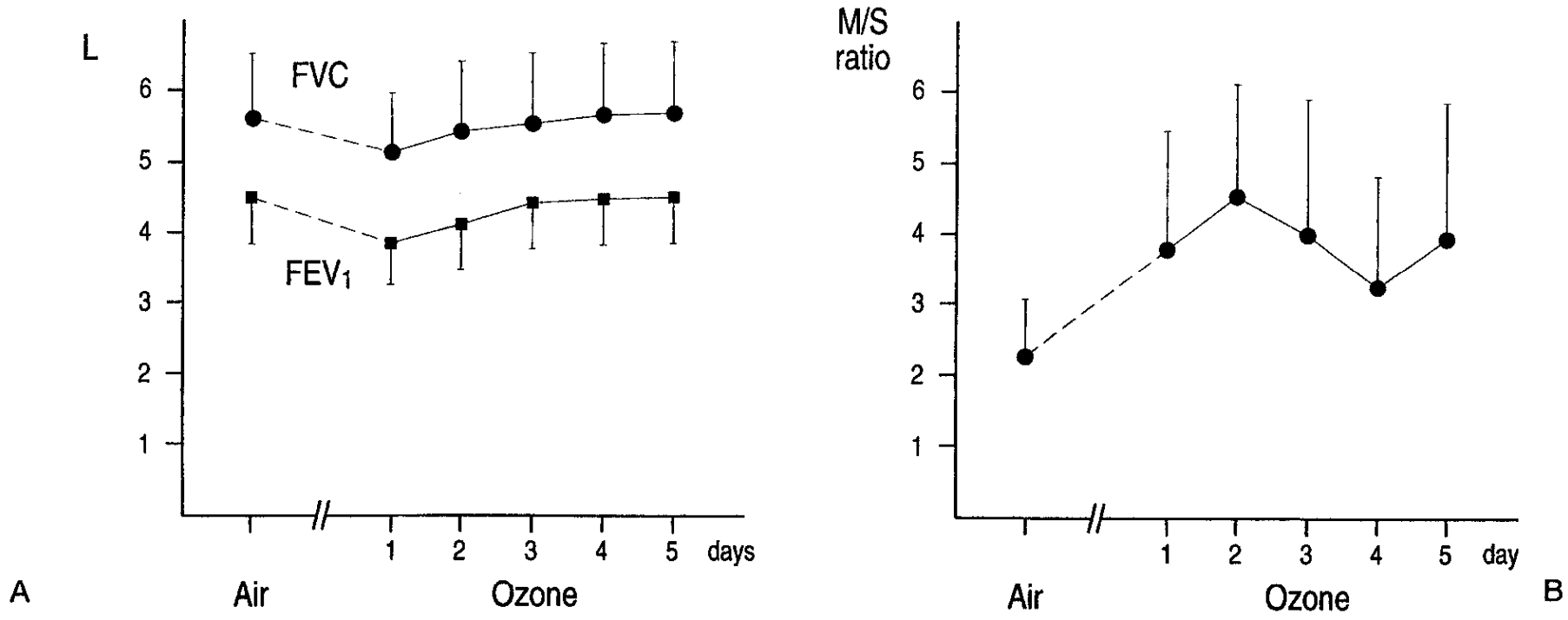


FIG. 7. A: mean values (±SD) of FEV_1 and FVC after a single exposure to filtered air and after repeated exposures to 120 ppb of ozone on 5 consecutive days. Exposures were performed for 6.6 hr with 50 min of exercise each hour in healthy subjects (*n*=17). **B:** mean (±SD) of the ratio of specific airway resistance measured after inhalation of methacholine to specific airway resistance measured after inhalation of saline (*M/S*) as assessed 75 min after each of the exposures. (Data from Folinsbee LJ, Hortsman DH, Kehrl HR, Harder S, Abdul-Salaam S, Ives PJ. Respiratory responses to repeated prolonged exposure to 0.12 ppm ozone. *Am J Respir Crit Care Med* 1994;149:98–105.)

Nonspecific Airway Responsiveness

- Exposure to ozone may increase bronchial hyperreactivity (airway twitchiness)
- This does not seem to increase with time, but it does not return to normal with repeated exposures in contrast to the effects on baseline lung function
- Figure 7.B.



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Allergen Responsiveness and Immune Response

- One recent study demonstrated an increase in allergic responsiveness when patients were exposed to ozone

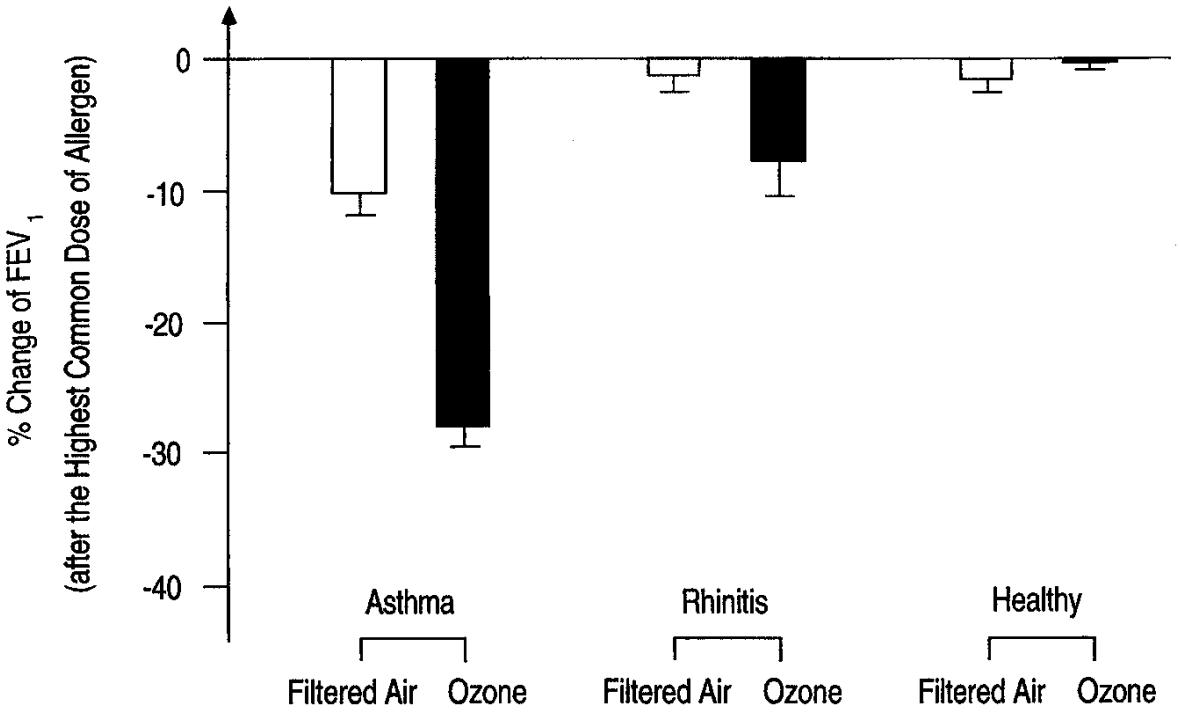

FIG. 8. Mean values (±SEM) of the maximum percent fall of FEV_1 after inhalation of the highest dose of allergen that was given during allergen provocation testing after exposure to ozone (*full bars*) or filtered air (*open bars*). The study included 24 persons with allergic asthma, 12 persons with allergic rhinitis, and 10 healthy persons. (Modified from Jörres R, Nowak D, Magnussen H. The effect of ozone exposure on allergen responsiveness in subjects with asthma or rhinitis. *Am J Respir Crit Care Med* 1996;153:56–64.)

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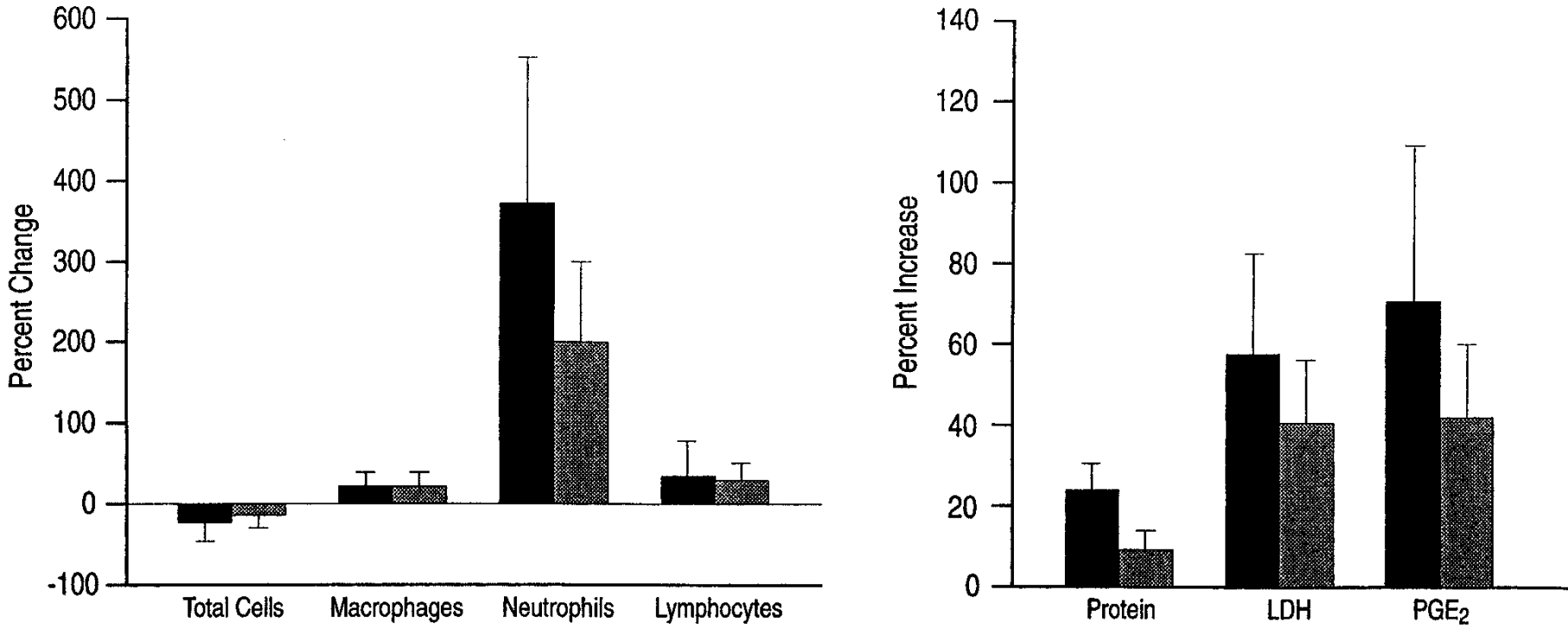
Ozone - Mechanisms of Action

- Ozone penetrates into the peripheral regions of the lung because of its relatively low water solubility
- Approx 40% of the inhaled dose is absorbed into the extrathoracic airways
- Approx 55% of the inhaled dose is absorbed into the intrathoracic airways
- Cell membranes are the main target of the effects of ozone

Ozone - Mechanisms of Action

- Once absorbed, there are increased chemicals of inflammation in the airways
- One way of measuring this is washing out areas of the lung (bronchoscopy and bronchoalveolar lavage) and measuring markers of lung inflammation



A

FIG. 9. A: Mean values (±SEM) of percent changes in total cell number and differential cell counts of macrophages, neutrophils, and lymphocytes in BAL fluid after a single exposure to 100 ppb of ozone (*full bars, n*=10) or 80 ppb of O_3 (*shaded bars, n*=18) relative to the values obtained after filtered air exposure. Exposures were performed for 6.6 hr by healthy volunteers, with 50 min of exercise for each hour, and bronchoscopies were performed 18 hr after exposure. **B:** corresponding mean (±SEM) changes of the levels of total protein, lactate dehydrogenase (*LDH*), and prostaglandin (PG) E_2 in BAL fluid. (Modified from Devlin RB, McDonnell WF, Mann R, et al. Exposure of humans to ambient levels of ozone for 6.6 hours causes cellular and biochemical changes in the lungs. *Am J Respir Cell Mol Biol* 1991;4:72–81.)

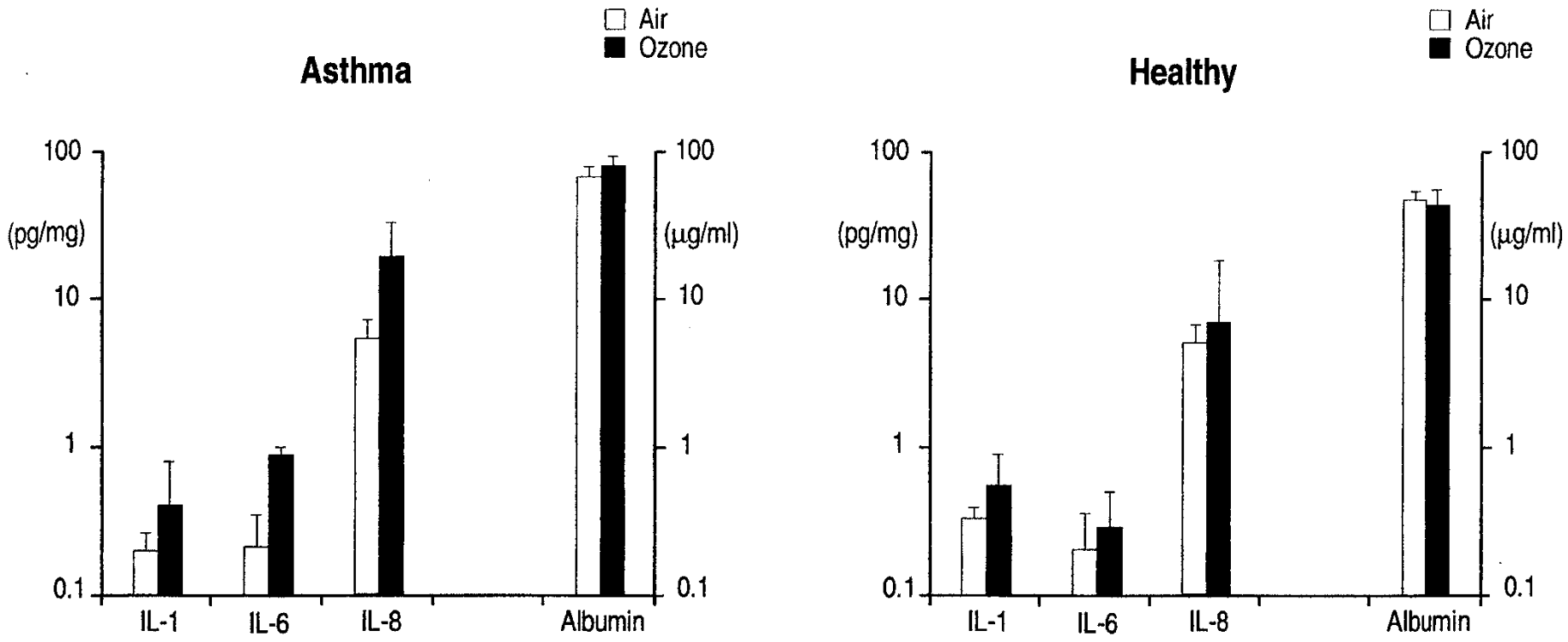


FIG. 10. Mean values (±SEM) of interleukin (*IL*) 1, IL-6, and IL-8, and albumin in the BAL fluid 18 hr after exposure to 200 ppb of ozone (*full bars*) or filtered air (*open bars*). Exposures were performed for 6 hr with intermittent exercise. Data were obtained in mild asthmatic (n=5) and healthy (n=5) subjects and are taken from Basha MA, Gross KB, Gwizdala CJ, Haidar AH, Popovich J Jr. Bronchoalveolar lavage neutrophilia in asthmatic and healthy volunteers after controlled exposure to ozone and filtered purified air. *Chest* 1994;106:1757–1765.

Effects of Ozone - Summary

- Ozone has been demonstrated to have significant effects on lung function especially in individuals with underlying lung disease
- The effects of ozone are dependent on concentration, activity of the individual, time of exposure, and specific response of that individual to ozone

Effects of Ozone - Summary

- The long-term effects of ozone exposure are still not well known