STATEMENT
Synopsis of Research Report 109

HEALTH EFFECTS INSTITUTE

Effects of Ozone on Airway Hyperresponsiveness in Guinea Pigs

INTRODUCTION

Asthma is one of the most common chronic and potentially disabling diseases among children and adults. It is characterized by three findings involving the airways: reversible airway obstruction, inflammation, and hyperresponsiveness. The last characteristic is defined as a heightened tendency of the bronchial airways to constrict. The airways of people with asthma also constrict when they inhale an allergen to which they are sensitive, and the airways constrict more when they inhale a nonspecific airway irritant such as acetylcholine. Some people without asthma develop nonspecific airway hyperresponsiveness after inhaling irritants. Controlled clinical studies have shown that exercising humans exposed to ozone (an irritant) develop airway hyperresponsiveness. Therefore, it is possible that people with asthma and others sensitive to allergens may be more susceptible to allergen-induced airway hyperresponsiveness during periods when levels of ozone are elevated.

Studies with laboratory animals have shown that short-term exposure to ozone induces airway hyperresponsiveness. However, we have little information on the effects of longer-term ozone exposures. The study by Dr Richard Schlesinger and colleagues of the New York University School of Medicine sought to determine whether long-term, intermittent exposure to ozone induces or exacerbates airway hyperresponsiveness.

APPROACH

Schlesinger and colleagues used a well-established animal model of airway hyperresponsiveness and allergic asthma to determine whether ozone can induce airway hyperresponsiveness or exacerbate existing airway hyperresponsiveness. They exposed three cohorts of male and female guinea pigs to 0.1 or 0.3 ppm ozone for 4 hours per day, 4 days per week, for 24 weeks. Control animals breathed clean air. The ozone concentrations were relevant to those encountered by humans during periods of ozone pollution. For example, levels ranging from 0.12 to 0.4 ppm have been recorded in the United States. The investigators exposed one cohort of nonsensitized animals to ozone alone. They induced hyperresponsiveness in a second cohort by sensitizing them to the allergen ovalbumin by inhalation before ozone exposure began. They induced hyperresponsiveness in a third cohort by sensitizing them to ovalbumin at the same time ozone exposure began.

Schlesinger and colleagues measured nonspecific airway hyperresponsiveness in each cohort by periodic challenge with acetylcholine. They measured specific airway hyperresponsiveness in the second and third cohorts by periodic challenge with ovalbumin. At the end of the challenge period, half of the animals in each cohort were killed for biochemical and cellular measurements of markers of inflammation in lung fluids and tissue. The remaining animals breathed clean air for 8 weeks, during which time the investigators performed similar measurements.

RESULTS AND INTERPRETATIONS

Animals exposed to ozone (but not ovalbumin) did not develop airway hyperresponsiveness. Ozone exposure exacerbated nonspecific and specific airway hyperresponsiveness in both cohorts of animals exposed to ovalbumin. The effects generally depended on the dose but were independent of gender. The levels of nonspecific and specific hyperresponsiveness were quantitatively similar and persisted for 4 weeks after exposure ceased. Ozone did not affect the levels of selected markers of inflammation; therefore, the results do not support an association of the inflammatory parameters assessed in this study with airway hyperresponsiveness.

The response of the ovalbumin-sensitized animals to ozone is consistent with studies of short-term ozone exposure on allergen-induced airway hyperresponsiveness in laboratory animals. The results of this study add to these findings by documenting the effects on hyperresponsive animals exposed to ozone for extended periods. They suggest that people with hyperresponsive airways may experience an increased response during periods of elevated ozone levels. This possibility should be evaluated in human studies.

This Statement, prepared by the Health Effects Institute, summarizes a research project conducted by Dr Richard Schlesinger at New York University School of Medicine, Tuxedo NY. The complete report, *Ozone-Induced Modulation of Airway Hyperresponsiveness in Guinea Pigs*, can be requested from HEI (see reverse side).
SCHLESINGER 109

Ozone-Induced Modulation of Airway Hyperresponsiveness in Guinea Pigs

INVESTIGATORS' REPORT

Richard B Schlesinger, Mitchell Cohen, Terry Gordon, Christine Nadziejko, Judith T Zelikoff, Maureen Sisco, Jean F Regal, and Margaret G Ménache

COMMENTARY Health Review Committee

RELATED HEI PUBLICATIONS

HEALTH EFFECTS INSTITUTE

Charlestown Navy Yard
120 Second Avenue
Boston MA 02129 USA

+1-617-886-9330
+1-617-886-9335 fax

pubs@healtheffects.org
www.healtheffects.org

Recycled Paper