

## *Synopsis of Research Report Number 90*

# **A Pilot Study of Potential Biomarkers of Ozone Exposure**

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### **Background**

Ozone, a major constituent of smog and a lung airway irritant, induces transient declines in lung function and respiratory tract inflammation in some people. Studies with laboratory animals have demonstrated that pathologic and physiologic effects of ozone on the respiratory system depend on the dose and duration of exposure. Although sensitive and accurate methods are available to measure the levels of ozone in ambient air, no methods have been developed to determine the dose of ozone that reaches tissues in the respiratory tract. Such methods would aid researchers conducting clinical studies and those seeking to extrapolate the results of animal studies to humans. Some inhaled pollutants react with tissue constituents to form products that can be measured in blood, urine, or other fluids and reflect the dose received by a tissue. These products are referred to as *biomarkers of dose*. No biomarkers for ozone exposure have been identified. Ozone is a highly reactive gas and is unlikely to penetrate far beyond the fluid that lines the lung's epithelial cell layer. Ozone's harmful effects are thought to be mediated by products of its reaction with components of the lining fluid and the epithelial cell membrane. These products include aldehydes which, although rapidly metabolized, can be toxic to cells. Thus, the levels of aldehydes in lung fluids may serve as biomarkers of the dose of ozone received by the lung.

HEI supported Dr. William A. Pryor of Louisiana State University to develop methods for measuring ozone reaction products in *in vitro* models of lung lining fluids exposed to ozone and in lung fluids from rats exposed to ozone. During the study, Dr. Mark Frampton of the University of Rochester provided Pryor with lung fluids from humans exposed to air or ozone under controlled conditions. In the current pilot study, Pryor and colleagues analyzed these fluids for two aldehydes that are known to be ozone reaction products. This report describes the results of the collaborative study between Drs. Pryor and Frampton.

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### **Approach**

In an earlier study, Frampton and colleagues exposed exercising smokers and nonsmokers to filtered air or to 0.22 parts per million (ppm) ozone for four hours. They obtained lung fluid samples from the subjects either immediately after or 18 hours after exposure ended. Pryor and collaborators analyzed the samples for two aldehydes, nonanal and hexanal. These aldehydes are formed by ozone reacting with unsaturated fatty acids found in the lung lining fluid and cell membranes.

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### **Results and Implications**

The investigators reported that nonanal levels were significantly higher in lung fluid samples obtained immediately after ozone exposure ceased and returned to control levels (established from exposures to filtered air) 18 hours after exposure ceased. (Changes in hexanal were not statistically significant at either time point.) Smokers and nonsmokers showed similar increases.

The increased level of nonanal suggests that aldehydes may be useful markers of ozone exposure. (Nonanal is also a toxic compound that may play a role in the adverse effects caused by ozone exposure.) However, aldehyde identification was not rigorously quantified in this study; therefore, the results must be considered as qualitative rather than quantitative. In addition, because the subjects in this study were exposed to only one concentration of ozone, studies using a range of ozone levels are required to confirm this preliminary observation and substantiate the relation between nonanal formation and ozone exposure level.



# Aldehydes (Nonanal and Hexanal) in Rat and Human Bronchoalveolar Lavage Fluid After Ozone Exposure

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