Synopsis of Research Report Number 88

Alveolar Changes in Rat Lungs After Long-Term Exposure to Nitric Oxide

Background

Nitric oxide (NO) in the environment is produced by the combustion of fossil fuels and tobacco. At high concentrations, NO is considered an environmental pollutant and, when inhaled, may be converted to several potentially toxic nitrogen-containing compounds, which can have complex diverse effects in people. However, NO is also formed in the body and, at low concentrations, mediates some important physiologic functions. It also has been used therapeutically to treat several pulmonary conditions, including adult respiratory distress syndrome and pulmonary hypertension.

No National Ambient Air Quality Standard for NO has been established, although NO in the atmosphere is readily converted to nitrogen dioxide (NO_2), and the National Ambient Air Quality Standard for NO_2 may provide some control of NO levels. Ambient concentrations of NO generally range from 0.01 to 0.18 parts per million (ppm); little is known about health effects or the range of exposures that may be toxic. Dr. Mercer previously reported that rats exposed to 0.5 ppm NO developed holes in the alveolar septa, the walls that separate individual tiny air sacs (alveoli) in the lung. He also reported that the number of holes was significantly greater in animals exposed to NO than in animals exposed to NO_2. The Health Effects Institute supported the follow-on study described in this report to learn more about the toxicity of NO so as to compare it with two other important oxidants, ozone and NO_2.

Approach

Dr. Mercer exposed three groups of rats continuously for six weeks to 2 or 6 ppm NO or to filtered air. The NO was free of ozone and NO_2. At the end of the exposure period he used an electron microscope to measure the number of holes in the alveolar septa and to observe other structural changes, such as in the surface area and the number and type of other abnormalities in the alveolar septa. The investigator also collected samples of fluid from the large and small airways and analyzed them for markers that would indicate inflammation and cell damage. He compared these results with those obtained previously in experiments using ozone and NO_2.

Results and Interpretation

Dr. Mercer found no increase in the number of holes in the alveolar septa and no change in the thickness of individual alveolar wall compartments in animals exposed to 2 or 6 ppm NO compared with control animals exposed to air. These results differ from those of an earlier study, in which he and his colleagues used a lower concentration of NO (0.5 ppm). The discrepancy between findings of increased holes in the alveolar septa in Dr. Mercer's previous study and no increase in the present study is an unaddressed issue and possible explanations should be explored. Analyses of the lung fluid showed no increase in chemical or cellular indicators of inflammation in animals exposed to NO. This study is one of the first to explore the toxicity of NO on lung structure and establishes a basis for future studies of the health effects of this air pollutant and therapeutic agent.

This Statement, prepared by the Health Effects Institute and approved by its Board of Directors, is a summary of a research project sponsored by HEI from 1995 through 1997. The study was conducted by Robert R. Mercer at the Department of Medicine, Duke University, Durham, NC. The complete report, *Morphometric Analysis of Alveolar Responses of F344 Rats to Subchronic Inhalation of Nitric Oxide*, can be requested by mailing or faxing the enclosed order form to HEI. With questions, please contact the HEI offices by phone, fax, or e-mail (see reverse side).

Morphometric Analysis of Alveolar Responses of F344 Rats to Subchronic Inhalation of Nitric Oxide

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Commentary

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