EXECUTIVE SUMMARY

ARB Contract A0-106-32

NEW APPROACH FOR DETECTING HEALTH HAZARDS OF NO_2 INHALATION

Period: April 29, 1981 - October 31, 1982

Principal Investigator: Arnis Richters, Ph.D.
Associate Professor
Department of Pathology
U.S.C. School of Medicine
2025 Zonal Avenue
Los Angeles, California 90033

Date Submitted: June 6, 1983

EXECUTIVE SUMMARY

The presence of air pollutants in the environment, especially those with carcinogenic properties, has been of great concern to environmental health scientists. In view of this, many studies have been carried out to isolate and to identify cancer causing agents from the air we breathe. However, little attention has been paid to the possibility that inhalation of a noxious air pollutant could facilitate the spread and dissemination of already existing cancer cells.

It is known that inhalation of ambient levels of nitrogen dioxide (NO_2), a common air pollutant, can alter the structure and function of lung blood capillaries or very small blood vessels, as well as suppress the body's defense system. Moreover, several investigators have demonstrated that damage to blood capillaries or alterations of the defense system favors the development of secondary cancer masses or metastases in cancer patients. Thus, we have reasoned that the damage incurred in the lungs and/or in the defense system by inhalation of NO_2, or polluted ambient air, could facilitate metastases development in lungs, particularly in the presence of circulating cancer cells. In order to test this new concept and see if the development of metastases could serve as an indicator for harmful NO_2 effects, an animal model system, utilizing mouse cancer cells, was developed.

Experiments usually had three groups of animals; one group was exposed to ambient levels of NO_2, the second group to filtered NO_2-free air and the third group to ambient room air. The NO_2 levels were continuously monitored. Before or after designated periods of exposure all animals received cancer cells (mouse melanoma cells) which were prepared from in vitro cultures and were infused into the blood stream of the animals. Three weeks later the lungs were examined for the development of cancer metastases.

The results of our previous studies have indicated that inhalation of 0.3, 0.4, or 0.8 parts per million (ppm) of NO_2 for a period of 10 weeks or longer increases the incidence of cancer metastases development in the lungs from circulating cancer cells, indicating adverse NO_2 effects. These small cancer masses, if permitted, continue to grow and eventually kill the animal. Of further significance was the finding that animals inhaling polluted ambient air for the same length of time also developed more lung metastases than the animals inhaling filtered clean air.

Our more recent experiments reinforce our earlier findings and provide new information about the role the specific exposure condition or exposure timing may play. Thus if 0.4 ppm NO_2 exposure follows immediately after cancer cell infusion into the blood stream then there is no facilitation of metastasis. The same is also true if NO_2 exposure of six weeks preceeds the infusion of cancer cells. However, a six-week exposure to <u>polluted ambient air</u> facilitates metastasis development in the lungs. This may mean that shorter exposures to polluted air may be more detrimental than the same length of exposure to a similar concentration of a single pollutant. Another finding of interest is that one-week clean air episodes between ambient level NO_2 exposures diminish the NO_2 effects, at least in the less sensitive portion of the test population. The sensitivity variability is well recognized among humans.

A preliminary study was also carried out to determine how the progression of lung metastases would affect the life span of the animals. The results of these experiments have indicated that animals inhaling NO_2 or ambient air had higher incidence of death due to progression of metastases. This was particularly noticeable during the first part of the survival period when there was highly significant increase in death rate among NO_2 and ambient air exposed animals.

We interpret that these animals were particularly sensitive to pollutant insult and could be compared to human counterpart with high sensitivity to air pollutants.

In view of these findings we have to raise a question whether the events described above are taking place in the urban human population. We do not have the answers yet. Answers could come from epidemiological studies designed to detect the incidence of metastases development in cancer patients who have lived or are living in polluted areas compared to those living in a clean air environment. Considering the fact that a significant segment of the population in the United States is already affected by cancer together with the probability that one in four individuals will develop cancer during their lifetime, the role air pollutants play in the dissemination of cancer and development of metastases becomes an important health issue. Most importantly, the data presented in this report provide additional support for the need of improved air quality and reduction of ambient air pollutants. Further studies are needed to evaluate other air pollutant effects on cancer metastasis and the mechanisms involved.

The details of the research described here can be found in the following publications: 1. Arch. Environ. Health, 36:36, 1981. 2. J. Surg. Oncology 17:159, 1981. 3. Environ. Health Perspectives 1982, in press. 4. Arch. Environ. Health, 1982, in press.