An Overview of Ongoing Oxidant Research at Brookhaven National Laboratory *

MASTER

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My role at this meeting is two-fold: first, to provide you with an overview of the biological programs at Brookhaven National Laboratory that are dealing with health effects of oxidant air pollutants, and secondly, to discuss recent research that we have done in my group concerning the interaction of oxidants and hypertension.

Brookhaven National Laboratory is located approximately 70 miles east of New York City in the geographic center of Long Island. While the major focus at Brookhaven has been in high energy physics, there are a number of departments which are conducting life sciences research. The Safety and Environmental Protection Division devotes a portion of its efforts towards studying health effects of radiation. The relatively new Department of Energy and Environment has several programs associated with health effects research. One group is assessing health effects of population exposure at the national level and is also assessing health effects of a variety of energy alternatives. A second group in DEE is developing the ability to assess mutagenic and carcinogenic effects of chemicals using short term in vitro systems. Within the Biology Department the major effort, of course, is in biological research of all kinds. With regard to oxidants, the effort that may be of interest to this group is a program developed by the late Dr. Arnold Sparrow investigating the mutagenic effects of air pollutants on the higher plant *tradescantia*. This program is on-going at the present time with trailers set up in and adjacent to industrial complexes in the northeast.

Inhalation toxicology is a fairly new effort within the Medical Department. Prior to my joining Brookhaven in 1976 the only research involving oxidants was being conducted by Drs. Borg and Schaich, who are also

*Research carried out under the auspices of the United States Department of Energy under contract No. DE-AC02-76CH00016

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attending this symposium. Some of those studies will be described in a few minutes. The majority of my time since coming to Brookhaven has been spent in developing a laboratory for exposure of rodents to any compound, regardless of the hazard associated with that compound.

The lay-out of the new facility is shown in the first two figures. The inset in figure 1 describes the conceptual lay-out of the space. On the right hand side we have non-regulated space and on the left hand side, regulated space. The chambers and gloves boxes, indicated by the "C" in the inset, are maintained within the regulated space. The air handling system for the non-regulated space is a conventional system with common supply and local exhaust ventilation. The air handling system for the regulated space is completely separate and independent from that servicing the non-regulated space and has a common exhaust system providing several degrees of filtration for air exiting that space. A third separate supply and exhaust system is provided for the inhalation chambers and glove boxes. The air systems for both the regulated space and the chambers are totally redundant. In operation, the regulated air space is maintained at about minus .08 inches wg pressure less than the non-regulated space. Chambers are operated at minus one half to minus one inch (wg) with respect to the regulated air space.

The actual lay-out of the building is shown in figure 2. Within the non-regulated space we have the electron microscopy suite, two conventional laboratories, two offices, and a glass washing area. The regulated space consists of two large chamber rooms separated by a bank of small laboratories and arranged in such a fashion that a door between the two chamber rooms can be closed and can totally separate the two rooms. We intend to use chamber room A for highly hazardous materials and chamber room B for more conventional compounds. Two small animal rooms are adjacent to chamber room B. Access

to the regulated space is through three small vestibules, indicated in figure 1, which are ventilated at about 1 air change/minute with clean, fresh air. Two large viewing windows allow observation of operations behind the barrier (figure 3). Thus, visitors can view the exposure facilities without entering the regulated space. Cat-walks over the top of the inhalation chambers provide space for contaminant generation and for chamber monitoring (figure 4).

Figure 5 shows a close-up of our five foot inhalation chambers. As can be seen, they are installed in pits and arranged so that a rack of animals can be wheeled into the inhalation chamber. This rack houses 12 cage units, each capable of holding 8 rats in individual cages. Thus, we can expose up to 96 rats in one rack, or a total of 192 rats in one inhalation chamber. The cages are capable of housing either one rat, two hamsters, or three mice; thus this design is capable of exposing up to 576 mice in one system.

These facilities came on-line in December, 1979 and are now in operation. Chamber room A will be used to expose animals to highly hazardous compounds, such as polycyclic aromatic hydrocarbons and other known carcinogens. For these compounds we intend to use chambers with facilities for housing and exposing animals in a totally attached unit. The actual design of these chambers is presently underway.

My goal in developing this research effort was to build a team that was capable of measuring functional or physiological changes in small animals, anatomical changes, and biochemical changes. To that end I have recruited a small animal respiratory physiologist, Dr. Daniel Costa, who trained under Dr. Mary Amdur. He has purchased and assembled equipment necessary for measuring the physiological status of the pulmonary system of rats in terms of spirometry and mechanical function. We are using plethysmography and gas

dilution techniques and believe that our methods are representative of the current technology and state-of-the-art.

We will use a recently acquired scanning electron microscope to assess anatomical structure of lungs of animals exposed to a variety of airborne materials. Conventional pathologic evaluation will be used and we intend to develop morphometric techniques at the level of the light microscope. In addition to the histopathologic evaluation, we will also measure a number of biochemical indices in the lung which indicate a response to challenge by environmental agents.

Specific projects underway at this time include a study of the deposition and translocation of sized glass fibers, supported in part by the Thermal Insulation Manufacturers Association; a comparison of functional change versus anatomical change after exposure of rodents to a series of known pulmonary toxicants (the first compound of specific interest to this group that we have chosen as a model pulmonary toxicant is ozone); a study of the interaction between hypertension and air pollution, which I will describe in detail later on this morning; the use of bleomycin to produce a model of fibrosis in the rat; and exposure of animals to coal dust in order to develop a rodent model of coal workers pneumoconiosis.

Since it is clear from epidemiological evidence that people who are already sick are at a much greater risk during episodes of high air pollution, we intend to develop animal models of various aspects of chronic lung disease. Having developed these models we hope to then superimpose on these sick animals exposure to some of the common air pollutants such as nitrogen dioxide and ozone in an attempt to understand why these already stressed people are at a much greater risk during episodes of high air pollution.

This concludes the general description of the research on oxidants being carried out at Brookhaven National Laboratory. The remaining portion of the time devoted to BNL will be spent in describing three specific areas of research currently underway. First, Dr. Samuel C. Morris of the Biological and Environmental Assessment Division will describe the assessment activities underway within the Department of Energy and Environment. Next, I will describe in some detail experiments that we have carried out investigating the relationship between hypertension and both sulfur dioxide and ozone. Finally, Dr. Karen Schaich will present her results with regard to the effects of ozone exposure on red blood cells.

Figure Captions

Figure 1. Outline of Brookhaven Inhalation Toxicology Facility. Inset:
Separation of air handling systems. See text for description.

Figure 2. Floor plan of laboratory.

Figure 3. Chamber Room B looking through the viewing window.

Figure 4. Generation and monitoring equipment located above the chambers.

Figure 5. Caging units used inside the chambers.

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Fig 5.