AD NUMBER: AD0857130

LIMITATION CHANGES

TO:

Approved for public release; distribution is unlimited.

FROM:

Distribution authorized to U.S. Gov't. agencies only; Administrative/Operational Use; 27 Jun 1969. Other requests shall be referred to the Office of Naval Research, Code 441, Washington, DC 20360.

AUTHORITY

ONR LTR, 29 AUG 1973

WRIGHTSVILLE MARINE BIO-MEDICAL LABORATORY

7205 WRIGHTSVILLE AVENUE
WILMINGTON, NORTH CAROLINA 28401

Operated jointly by

SCHOOL OF MEDICINE
OF THE UNIVERSITY
OF NORTH CAROLINA
AT CHAPEL HILL

THE BOWMAN GRAY
SCHOOL OF MEDICINE
OF WAKE FOREST COLLEGE

SCHOOL OF MEDICINE
AT DUKE UNIVERSITY

BABIES HOSPITAL
RESEARCH CENTER, INC.

June 27, 1969

FINAL AND FIRST ANNUAL REPORT

December 1, 1968 through February 28, 1969

Contract Number N00014-68-C-0376

Contract Title - The effect of Altitude Acclimatization upon the Susceptibility of Mammals to Oxygen Poisoning.

A SUMMARY IS GIVEN OF PROGRESS IN THE FOLLOWING AREAS:

Progress During the Above Period: Investigations under this contract were directed at (a) quantitating the protective effect due to altitude acclimatization in rats exposed to 1 atm. O_2 partial pressure: (b) fully describing the time relation governing development and subsequent dissipation of this type of protection; and (c) developing a working hypothesis regarding the mechanisms responsible for these changes and significance of the effects thus elicited.

Description of basic phenomena and of the time course of declimatization have been incorporated into a scientific paper communicated to the Journal of Applied Physiology. These results may be summarized as follows:

a. Prior acclimatization to hypoxia (air at 510 mb) increases the survival times of Sprague Dawley rats in 53% O_2/ 47% N_2 at P_{O_2} = 1100 mb from a mean of 51 $\pm$ 3 hours to 18% $\pm$ 49 hours. Histopathological and clinical evidence of pulmonary damage under these conditions does not appear until the sixth day of exposure in altitude acclimatized animals, but toward the end of the second day in non-acclimatized ones. In contrast to lung damage, oxygen convulsions produced by exposure to 7 atm. O_2 occur sooner in acclimatized than in control rats. Intravenous injection of

4

level between the hypoxia acclimatization and the high O_2 exposure shortens survival time, but after 11, and even after 30 days of declimatization, the effect of a prior altitude acclimatization is roughly equivalent to 25% reduction in P_{O_2} during hyperoxic exposure. Hematocrit levels have returned to those of control rats after 11 days.

The data indicate that under conditions in which pulmonary injury was the dominant toxic effect of oxygen, prior acclimatization to hypoxia markedly augmented the survival times of rats. The histological observations as well as the absence of protection against the CNS effects of high oxyge pressures indicate that the potection was exerted largely at the level of the pulmonary parenchyma. Comparison of the time courses of mortality in the several differently pretreated groups of rats, with the time sequence of development of symtoms and with the histopathological observations suggests that the protective effects of altitude acclimatization have two separable aspects: (a) protection of the lung tissues against oxygen injury; and (b) increase of the survival potential of rats in which the pulmonary lesion has become well established.

It now appears that this latter effect is related largely to elevation of the hematocrit in altitude acclimatized rats and that its dissipation follows in general the time course of the return of the hematocrit to normal levels. With regard to protection of the pulmonary parenchyma against injury, the most important leads would appear to come from deacclimatization studies. Changes which may be expected to persist long enough at sea level to contribute to the specific tissue protection against hyperoxia in the partially deacclimatized rats possibly include biochemical adaptations at the tissue level and very probably microcirculatory changes.

Vascular changes are coming to be recognized increasingly as the earliest evidence of pulmonary damage at elevated oxygen tensions. These changes are associated with an increase in alveolar capillary surface area and with evidence of circulatory congestion in the pulmonary bed. This development appears to be related to an increased resistance in the pulmonary veins and venules the cause of →

p 3

which is not yet clear. Altitude acclimatization, too, has been reported to be uniformly associated with an increased number and surface area of alveolar and adventitial capillaries. Congestion and pulmonary edema are prominent parts of the acute high altitude syndrome, especially as observed in previously well acclimatized subjects. The lung of the altitude acclimatized subject thus appears to have been placed under the necessity of becoming adapted to functioning under the very circulatory conditions which form a prominent part of the pathology of hyperoxia. Such tissue might plausibly be expected to be capable of coping more effectively with the pathophysiological effects of pulmonary hyperoxia than unconditioned lungs of non-acclimatized animals.

In the rabbit a chest window preparation has been adapted which permits close observation of the lung surface for extended periods. This preparation has permitted us to confirm the observation that congestion of the lung is a very early response of that tissue to oxygen at partial pressures capable of producing pulmonary damage.

A prototype model of optical equipment for exploiting the rabbit chest window preparation in the study of oxygen toxicity have been prepared and tested in preliminary runs which demonstrated its suitability for assessing the early vascular responses of the rabbit lung to oxygen at one atmosphere. Equipment has also been assembled for exploitation of the same preparation as a basis for studies of lung blood volume using isotopic tracers, the equipment involved including count rate meter, detector, and recording systems. Paper work to reactivate this laboratory's isotope license will be underway presently. It is hoped that in the near future these preperations can be used for comparing the early effects of HOP on the lung of normal and of altitude acclimatized rabbits to determine whether this early vasomotor response might bear a relation to the protective effect which formed the subject of this investigation.

Publication to date: R. W. Brauer, D. E. Parrish, and R. O. Way, The Protective Effect of Altitude Acclimatization Against Lung Damage From Oxygen [illegible]

Exposure AT P_{O_2} 1800 mb. (sent to the Journal of Applied Phy'siology.)