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February 10, 1942

Dr. Eugene Du Bois, Chairman
Committee on Aviation Medicine
National Research Council
2101 Constitution Avenue
Washington, D. C.

Dear Dr. DuBois:

Since your visit out here we have continued our preliminary experiments with the labelled inert gases and are herewith submitting to your committee an application for support for the continuation of this work. Before going into more detail as to the types of investigations that we wish to carry out I should like to outline again the reasons for using radioactive argon at the present time.

In view of the importance of aeroembolism to an aviator at high altitudes it seems obvious that if one could use labelled nitrogen important studies on nitrogen distribution and exchange could be carried out. However, there is actually only one radioactive nitrogen isotope available at the present time and this has a half-life of only ten minutes. Consequently, with its use, experiments of long duration cannot be carried out. Nevertheless, we propose to compare, in animals and man, in short-time experiments the metabolism of nitrogen and argon, using the longer-lived argon and the short-lived nitrogen. Experiments of over an hour can certainly be carried out with nitrogen. In this way, comparative curves can be obtained and possibly correction factors can be determined. Since there was no long-lived radioactive nitrogen we looked in the periodic table and found that there were several long-lived isotopes of argon and krypton which both are inert gases and have the same physical and chemical properties as nitrogen. There was a 37-day argon and a 110-minute argon and a 34-hour krypton. Both the 37-day argon and the 110-minute argon are now being explored here in animal and human experiments.

The work which we wish to carry out can be divided into two sections; first, animal and second, human or clinical. Dr. John C. Larkin who is well-trained in both physics and medicine will take charge of the animal work. He graduated from the Massachussetts Institute of Technology, thereby getting a very thorough training in the field of physics and engineering. Then he graduated from the Johns Hopkins Medical School and after completing his internship took three years training with Dr. M. C. Sosman in the x-ray department of the Peter Bent Brigham Hospital in Boston. During the past three years he has been with us and in charge of the neutron therapy. He has also been doing experimental work with the labelled isotopes. He has had considerable experience in gas analysis and already has built a complete set-up for the study of gas exchange in rats, including facilities for studying the rats under varying pressures. He will be able to study oxygen consumption in addition to inert gas metabolism and inert gas exchange. Today he is going to begin doing the first simple rat experiments. In this work he will study the exchange of inert gases under various pressures and will sacrifice animals to determine the percent distribution of the radioactive material in the various tissues of the body. The 37-day argon which has a rather soft irradiation will be used, but he has a set-up for analysing these soft rays by taking the gas directly into the counter tube. It seems certain that we will be able to get important data on the exact distribution of inert gases in different tissues of animals and to study possible methods of influencing this distribution.

The second part of the experiments will concern human subjects. The statement attached to the application summarizes the preliminary work carried out on normal subjects and some patients with pulmonary and circulatory abnormalities. We propose to study immediately, large groups of normal young men between the ages of 18 and 27 to determine standard rates of inert gas exchange and to find out whether or not one might be able to group them according to their speed of gas exchange. It is then proposed to test possible methods of replacing inert gas in the body or possibly speeding up these rates of exchange, using the simple labelled isotope technique for measurement. Using the short-lived isotope of argon one can study individuals in experiments lasting as long as three hours for comparison with others. If long-time experiments are done however, the 37-day argon can be used and experiments run over many hours or several days. Since it is the last few percent of nitrogen which is important in aeroembolism we are aware of the fact that long experiments probably must be carried out. We are also aware, however, of the possibility that rates of exchange of the first 95% of the nitrogen might be related to the rates of exchange of the last few percent of the nitrogen in the body.

We should like to emphasize that we have most of the equipment and we have available or can get the necessary trained men to carry out this work. In other words, there will be no preliminary period of several months to get started. We can start immediately and intensively continue the work for a period of six months, and at the end of this time I am sure that we can have enough results to indicate whether or not these studies are worth continuing. It is our strong belief that in view of the importance of the problems of aeroembolism any lead which has a chance of giving results should be exhaustively investigated at this time.

The program as we have outlined it constitutes the minimum group to accomplish the work at a rapid rate. We hope that you will find it possible to give us support to carry on this work.

Thanking you for your consideration,

Very sincerely yours,

John H. Lawrence, M. D.

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INTRODUCTION

Report number one* under this project X-762 gave an account of the symptoms produced by exposing individuals twice daily to a pressure altitude of 20,000 feet. Inasmuch as symptoms appeared as frequently under control as under experimental conditions it was considered advisable to repeat the investigation. In planning the second experiment particular attention was given to establishing adequate control conditions thus avoiding insofar as possible the factor of suggestion.

METHODS

Twenty-five healthy men ranging in age from 18 to 25 years served as subjects. As a control procedure, for the first five days these subjects were decompressed twice daily to a pressure altitude of 5,000 feet. The rate of decompression was 2,500 feet per minute. On the following 28 consecutive days the subjects were decompressed to a pressure altitude of 20,000 feet. The rate of decompression on the 20,000 feet exposures was 10,000 feet per minute. Oxygen apparatus, diluter-demand with the A-14 demand mask, was used from sea level to maximum altitude on both the 5,000 feet as well as the 20,000 feet exposure. The temperature inside the decompression chamber varied from 70° to 80°Fahrenheit. During each decompression the subject exercised every five minutes for a period of 30 seconds. The exercise consisted of stepping up alternately with each foot to a height of 18 inches at a rate of one step-up per second. The duration of each exposure to decompression both on the control as well

* See report number one. This second report is an addendum to the previous report.

as the standard exposures was 30 minutes. The subjects were told that all exposures were to 20,000 feet. There was no evidence that any of the subjects were aware of the fact that the control decompressions were any different than those to 20,000 feet.

Two questionnaires were filled out by each subject during and/or following each decompression. The first questionnaire concerned four specific symptoms. These symptoms were headache, changes in visual acui joint pains and palpitation. Two of these symptoms were selected becaus it was felt that they were relatively common complaints of decompression The other two were "control" symptoms having little or no specific relat- ion to decompression illness. A fifth space on this questionnaire was included in order to permit the subject to insert any other symptom or complaint which he might note. A second questionnaire was begun on the second day. It concerned fatigue, need for sleep, changes in appetite ar any variation in the usual interest in outside activities. It further stated that the subject should note any delayed or persistant symptoms which followed the decompression.

RESULTS

A total of 240 man exposures took place at 5,000 feet during the first 5 days of the experiment. This offered an adequate control period. On the sixth day the 20,000 feet decompressions began. A total of 1,039 man exposures occurred during this period from the 6th through the 33rd experimental day.

There were very few complaints of specific symptoms on either the 5,000 feet or 20,000 feet exposures. During the control period there was one post decompression headache, one complaint of paraesthesias, 2 complaints of mild joint distress and 2 instances of headache during the decompression. During the 20,000 feet exposures there were two complaints of mild joint pain during the 1,039 man exposures. Six times paraesthesias were noted. On three occasions mild distress appeared in the knee joint following the decompression. There was one case of transient vertigo.

The majoirity of information gathered during these decompressions centered about the questions concerning the appearance of fatigue, change in appetite and sleep requirements and changes in the usual interest in outside activities. The accompanying table shows the comparative data for the 5,000 feet and the 20,000 feet exposures. It is seen that for the most part little change in the symptoms occurred. However, when changes were reported, there was very little difference in the percent incidence at 5,000 feet and at 20,000 feet. There is some indication that appetites were poorer during the 20,000 feet decompressions. The difference 1.2% of man exposures at 5,000 feet and 4.1% at 20,000 feet is significant. Likewise, the increase in fatigue from 0.8% of man exposures to 3.6% is significant. The remainder of the data show no significant difference in the percent incidence of these complaints.

DISCUSSION

In the previous report on repeated decompression to 20,000 feet it was pointed out that there is considerable difficulty in determining whether certain mild complaints made by subjects exposed to moderate decompression are due to this factor. The type of exercise which was used in the previous experiment consisted of five deep knee bends every 5 minutes. It is felt that perhaps the deep knee bending exercise can i itself produce occasional mild distress. As a result the exercise was altered and a step-up type was used which it was felt would be less like to induce symptoms of its own.

Neither completely naive nor completely sophisticated subjects were used. They were informed of the prupose and nature of the experiment an had only the specific questions on the questionnaires by which to be gui These questionnaires were purposely prepared to avoid improper suggestio and used related as well as unrelated symptoms.

The mildness of the complaints while being repeatedly decompressed to 20,000 feet is again demonstrated. Fatigue again seems to increase with the increase in altitude as shown by the % incidence of 3.6 at 20,00 feet as opposed to only 0.8% at 5,000 feet. Somewhat pporer appetites were seen at 20,000 feet as well. The adaptive trend seen in regards to fatigue in the previous experiment is not apparent this time. However, since there were so few complaints of fatigue each day such a trend would be difficult to demonstrate. There was no trend in respect to the other symptoms as well.

Since so few mild symptoms were demonstrated in this experiment, it is felt that the negative results of the first experiment are verified by the results of this one. It is seen that there are complaints of de-compression at 5,000 feet and that the complaints as the result of re-peated decompression to 20,000 feet brgins forth no further dncrease othe than some greater fatigue.

CONCLUSIONS

1. The repeated frequent decompression of healthy male subjects betwee the ages of 18 - 25 years for an extended period of time results in the production of no serious symptoms of decompression when the exposures are confined to a pressure altitude of 20,000 feet.
2. There is no deterioration in the individual's ability to tolerate such decompressions.
3. Since so few symptoms occurred, no adaptation was demonstrated.