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National Academy of Sciences
National Research Council
2101 Constitution Avenue
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S P A C E S C I E N C E B O A R D

Man in Space Committee

Working Group on Gaseous Environment for Manned Spacecraft

SUMMARY REPORT

The Space Science Board has undertaken, through its Man in Space Committee, to study several topics of importance to the practical realization of space flight. This report describes the results of discussions of the physiological criteria which are important in the selection of the cabin atmosphere in manned spacecraft and discussions, experimental procedures and investigations which should both precede and accompany preparations for the further development of manned space flight.

The membership of the Man in Space Committee and of the Working Group responsible for this paper is given in Appendix C.

In approving this report for distribution, the Space Science Board and the Man in Space Committee gratefully acknowledge the helpful participation of representatives of the National Aeronautics and Space Administration and the Department of Defense.

November 1963

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I. INTRODUCTION

The manned spacecraft must be equipped to maintain its internal economy in complete isolation. Moreover, not only must the crew be kept in satisfactory physical and mental condition under normally expected circumstances, but provision also must be made for survival and recovery in the event of emergencies.

The usual considerations of reliability of function and minimization of weight of equipment must be taken into account during the design of spacecraft - in addition to the purely physiological criteria.

Thus, in the first U. S. manned space flight program - Mercury - and in the face of very severe weight limitations, a cabin atmosphere of pure oxygen at 1/3 atmosphere was adopted. This choice probably represented the greatest simplification which could readily be achieved and, at the same time, it provided protection against some of the risks of rapid decompression. Although the breathing of pure oxygen at higher pressures was known to be attended by some undesirable physiological effects, the short duration of the flights to be undertaken, and the low pressure employed, suggested that no harmful results would accrue in this case. That these expectations were generally borne out is now history. However, preparations for space flights of longer duration - many weeks or months - while presenting similar

problems, require special attention to phenomena which may be either undetectable or of trivial significance on a time scale of a few days.

In this report the principal considerations which appear most likely to be of significance in the selection of the cabin atmosphere for flights of a few weeks or longer are reviewed. While effects on respiratory physiology receive the major emphasis, other factors, such as thermal properties and risk of fire, are important enough to merit attention. Studies which would help to establish the selection of cabin atmosphere on a more rigorous basis are identified in a series of recommendations.

This report is due to the Working Group on Gaseous Environment which, under the chairmanship of A. B. DuBois, conducted a study of these problems for the Man in Space Committee of the Space Science Board. The text was prepared by J. P. T. Pearman in collaboration with the Working Group chairman. Individual contributions by Working Group members formed the basis for a Symposium on Respiratory Physiology in Manned Spacecraft which was held in Atlantic City on April 19, 1963 under the auspices of the American Physiological Society and its Respiration Dinner Group. These papers, on which the present report is also based, are reprinted in Appendix A by kind permission of the Federation of American Societies for Experimental Biology, in whose Proceedings they were first published (Fed. Proc. Vol. 22, No. 4, Part 1, 1022-63, 1963). For more detailed treatment of many of the topics summarized in this report the reader is referred to the papers of Appendix A and their associated references; additional references are given in Appendix B.

II. PHYSIOLOGICAL CRITERIA IN THE CHOICE OF CABIN ATMOSPHERE

If maintenance of normal respiratory physiological function without regard to external circumstances were the only consideration, provision of a cabin atmosphere of about sea level composition and pressure might represent an ideal and straightforward choice for manned spacecraft. This atmosphere has, in fact, been used in the manned space flights conducted by the Soviet Union. No other atmosphere has been shown to be more satisfactory from the physiological point of view and the tedious respiratory studies

which should accompany the use of other atmospheres could then be avoided. Nevertheless, the formidable problems of spacecraft design, and the necessity to take all prudent steps to safeguard the crew from accident, compel consideration of other atmospheric compositions and pressures. For, if a cabin at one atmosphere pressure of ordinary air were decompressed to space suit pressure,* the occupants would develop decompression sickness, i.e., "bends".

Several engineering considerations would seem to argue for low cabin pressures and for a single gas - pure oxygen - composition. Among these are structural weight; design, complexity and weight of atmospheric gas storage and control equipment and the difficulty of contriving pressure suits which allow operation at pressure nearer one atmosphere. Such departures from the normal human gaseous environment, however, require the demonstration of an acceptable level of physiological performance.

The limits between which the composition and pressure of acceptable cabin atmospheres must be sought are then set by: (i) a pure oxygen atmosphere at a pressure which will provide an alveolar oxygen partial pressure equal to that at sea level, and (ii) a mixed gas (oxygen and inert gas) atmosphere of such a pressure and composition as will allow decompression to the highest acceptable pressure suit setting without risk of bends. A numerical value for the lower limit (i) is, approximately, 0.2 atmosphere of pure oxygen. The upper limit (ii) is determined by the operating pressure and composition of the space suit atmosphere and may be of the order of 0.5 atmosphere for a cabin atmosphere of 50% oxygen. Within these bounds it is necessary to ascertain the extent of physiological tolerance under the conditions, and for the durations, of intended use, not only for survival but also for performance of the necessary tasks. Only in this way is it possible to establish with reliability the fitness of any given atmosphere or the limits within which it must be controlled.

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* The normal operating pressure of space suits which are at present in use in this country is about ½ atmosphere.

In the course of its study of the various criteria which are pertinent to decisions on the suitability of spacecraft atmospheres, the Working Group has reviewed the following topics which are directly concerned with respiratory physiology:

(i) atelectasis and pulmonary edema
(ii) oxygen toxicity
(iii) carbon dioxide tolerance
(iv) inert gases
(v) bends

In addition:

(vi) heat exchange
(vii) fire hazards
(viii) acceleration effects on the pulmonary circulation

have also been discussed in view of the marked effects which changes in atmospheric gas composition may produce. In the sections which follow a brief synopsis of the salient points is given under each of the topics listed above. For a more detailed discussion the reader is referred to Appendix A and to the references cited there and in Appendix B.

(i) Atelectasis and Pulmonary Edema

Localized or diffuse collapse of alveoli in the lungs may, if the condition persists, lead to arterial hypoxia. Under the stresses of space flight this may be extremely undesirable. Biophysical considerations lead to the conclusion that the alveoli are probably unstable and when breathing pure oxygen and, especially, at low pressures they tend to collapse if there is blockage of the connecting airways. This collapse tends to occur because each of the gases present in the alveoli (oxygen, water vapor and carbon dioxide) is subject to prompt and complete absorption from the alveoli by the blood. Several mechanisms may produce blockage of the airways; examples are distortion caused by acceleration or obstruction by fluid. Edema may be produced, for example, by accelerations which sufficiently affect the intrapulmonary distribution of blood and by irritation due to respiratory infection.

The alveoli are normally stabilized against collapse by the presence of an abundant proportion of inert and relatively insoluble gas (nitrogen) and an internal coating of lipoprotein substances with low surface tension.

The methods available for detecting and measuring atelectasis include chest x-ray, vital capacity, lung compliance, diffusing capacity, and arterial oxygen tension measurements when breathing 100% oxygen. Further development of these methods for use during simulated missions would facilitate investigation of this phenomenon.

Theoretical and experimental results strongly suggest the desirability of using oxygen-inert gas atmospheres for long missions in order to avoid atelectasis and other gas absorption phenomena, such as retraction of the ear drum, but further experimental evidence is required both to confirm this point and to establish the upper limit of suitability of pure oxygen atmospheres from this point of view.

(ii) Oxygen Toxicity

It has long been known that breathing pure oxygen at normal atmospheric pressure often produces pulmonary irritation and other "toxic" effects both in man and animals. This knowledge has occasioned concern over the use of pure oxygen atmospheres in spacecraft. More recently, experimental exposures of human subjects to oxygen atmospheres at pressures not greatly in excess of the normal sea level partial pressure of oxygen have given equivocal results; particularly in hemolysis and loss of night vision. It therefore appears essential to seek additional experimental evidence to determine what are the toxic effects of pure oxygen on the human respiratory system and other systems at pressures which may be used in manned spacecraft.

In addition to the pulmonary irritant effects which have been noted, it would be desirable also to investigate any effects on the mechanisms of tissue (metabolic) respiratory regulation and enzyme systems (e.g., glucose 6-phosphate dehydrogenase) which may lead to hemolysis. In any event, proposed atmospheres, particularly those which contain relatively high concentrations or high partial pressures of oxygen (or low concentrations of inert gas) should always be checked for evidence of toxic effects under conditions which simulate as closely as possible those of intended use.

(iii) Carbon Dioxide Tolerance

Studies of CO_2 tolerance in submarine crews indicate that no loss of performance is involved if the concentration in air at normal pressure does not exceed 1.5% with exposures of 30-40 days. Biochemical adaptive changes were observed, however, at this concentration. In view of the special conditions which apply in manned spacecraft, it would be desirable to find, in any particular case, how the concentration of CO_2 is likely to change and to find also the maximum concentration which is tolerable under the conditions and for the expected time of exposure.

(iv) Inert Gas Components

If other investigations establish the need for an inert gas in manned spacecraft atmospheres it may be useful to consider, for this purpose, gases other than nitrogen. In particular, the physical properties of helium and neon may offer advantages, compared with nitrogen, with respect to solubility in body fluids, storage weight, thermal properties, etc.

(v) Bends

Decompression, whether accidental (due to damage of the spacecraft), or intentional (as in the use of the pressure suit outside the capsule), carries the risk of bends if the inert gases dissolved in the tissues and body fluids come out of solution. The magnitude of this risk is determined to a very considerable extent by:

(a) individual susceptibility;
(b) the extent to which the nitrogen (or other inert gas) concentrations of tissues and body fluids have been reduced;
(c) the magnitude and rate of the inert gas partial pressure change on decompression.

These effects can be mitigated by:

(a) selection of bends-resistant individuals;
(b) thorough denitrogenation before flight;
(c) limitation of decompressive pressure changes by appropriate choice of cabin atmosphere pressure and composition;

(d) space suit pressure setting.

In some cases, further improvements might be obtained by use, in the cabin atmosphere, of an inert gas component which has a lower solubility in tissue and body fluids or less tendency than nitrogen to form bubbles.

(vi) Heat Exchange

Some spacecraft atmospheres of interest differ significantly from air in the thermal properties which affect heat transfer under forced convection. This in turn will affect the power required to control the crew's heat balance and to cool internal equipment. While such considerations may not be of very great physiological importance in the selection of the atmosphere, they must be taken into account in the final engineering design.

(vii) Fire Hazard

Experience indicates that fires in pure oxygen atmospheres even at low pressures (e.g., 1/3 atmosphere) are extremely difficult to extinguish. While this phenomenon has nothing to do with respiratory physiology, the risk on flights of long duration may be so serious as to demand special measures. Unless effective countermeasures can be devised, the existence of this risk may argue very strongly against the use of such atmospheres in future. Further experimental investigation is required.

(viii) Acceleration Effects on the Lungs and Pulmonary Circulation

Forces produced by high acceleration overdistend one part and compress another part of the lungs. Blood flow diminishes in some parts and increases elsewhere in the lungs. Fluid leaks from the blood into the tissues and into the air sacs in parts of the lungs. These effects cause difficulty in breathing, low arterial oxygen saturation, and impaired consciousness during high sustained acceleration and, to a lesser extent, after its cessation. They enter into a consideration of the best gas to be breathed in that a high partial pressure of oxygen is favorable for consciousness, but a low inert gas concentration during acceleration is unfavorable for rapid lung recovery afterward.

III. RECOMMENDATIONS

On the basis of the considerations outlined above, the Working Group has formulated a number of recommendations for further work in respiratory physiology in support of the developing programs of manned space flight. These recommendations, listed below, are of two kinds: the first include investigations which the Group feels to be necessary for a proper understanding of respiratory physiology in space flight and which will be of increasing importance in the preparations for missions of longer and longer duration. The second group of recommendations specify particular steps which, the Group believes, are essential and minimal prerequisites to any flights of expected duration one week or greater. They fall within the scope of the first set of recommendations but are empirical in nature.

Much of the present uncertainty in this field is due to a lack of systematic knowledge of threshold effects, limiting values and effects with long time constants; it is, therefore, important that work on the first group of studies recommended should not be delayed until the more empirical investigations are finished.

The ultimate criteria for acceptability of a particular environment are survival and performance. However, certain other specific tests have been found to be useful in evaluating the suitability of an environment for human habitation. These are:

1. Physical examination
2. X-ray of the chest
3. Mental performance test
4. Vital capacity test*
5. Arterial oxygen tension and carbon dioxide tension measured while breathing air at sea level and oxygen at altitude or at sea level*
6. Exercise tolerance test, if practical to perform

* Note that tests Nos. 4 and 5 require consultation by an expert respiratory physiologist if accurate results and interpretation are to be obtained.

An acute drop in vital capacity and a low arterial oxygen saturation may be tolerated over brief periods. However, the fact that mental performance may not be perfect during such periods should be recognized. Another criterion of acceptability is that recovery should leave the person within the normal range.

The recommendations advanced in this report are addressed chiefly to matters of immediate concern and to problems which present knowledge indicates will almost certainly be of importance in the near future. As experience accumulates and as the capabilities for extending the duration of flight improve, new problems can be expected to arise and some which now seem to be mainly of long-term interest may well become more immediate. An exhaustive examination of these matters is not attempted here, but the following, at least, suggest themselves:

(a) determination of the suitability of helium, nitrogen, oxygen mixtures with particular reference to missions lasting many weeks or months;
(b) study of the role of pulmonary surface active agents in atelectasis;
(c) study of atmospheric contaminants such as gases (including endogenously produced carbon monoxide), dust, aerosols, ions.

Continued study and review of the relevant aspects of respiratory physiology should keep pace with the developing space flight program.

A. General

Bends

1. Find the effect of changes in the difference between cabin pressure and suit pressure settings on the probability of bends following decompression, i.e., consider providing an alternate suit pressure setting of 5 as well as 3.5 PSI.

2. Determine the rate of change of inert gas concentration in the body fluids as a function of atmospheric composition and time, i.e., measure the family of saturation-desaturation curves.

Atelectasis and Pulmonary Edema (absorptional and accelerational)

3. Investigate the biophysics and biochemistry of atelectasis and pulmonary edema with particular attention to the following:

   (i) techniques of detection and measurement
   (ii) production and reversibility (e.g., breath holding; spontaneous resolution)
   (iii) methods of prevention (including the addition of helium or nitrogen to the inspired oxygen).

Oxygen Toxicity (chemical)

4. Find the upper limit of atmospheric pressure which avoids excessively toxic effects when breathing pure oxygen for different periods of time.

5. Investigate new physiological, neurological, or biochemical methods of finding the incipient appearance or threshold level for toxic effects of oxygen on:

   (i) ears
   (ii) lungs
   (iii) red blood cells
   (iv) central nervous system
   (v) peripheral night vision

Carbon Dioxide

6. Investigate the rate of change of CO_2 concentration in the event that CO_2 absorbing equipment should fail.

7. Find the maximum concentration of CO_2 which is tolerable under steady state conditions and how this is affected by atmospheric composition and pressure.

Respiratory Infections

8. Study the effects of respiratory infections on the production of atelectasis (with pure oxygen, low pressure atmospheres).

9. Study the effects on breathing of sinus drainage during re-entry accelerations.

Therapeutic Agents

10. Pure oxygen breathing may increase the tendency of some drugs to induce methemoglobin formation or hemolysis. Therapeutic agents which astronauts may require in flight (e.g. aspirin) should be studied for these effects under simulated flight conditions. (See Appendix B: Marks, P. A.)

B. Specific Measures: prerequisities to flight

1. All astronaut candidates should be screened for:

   (i) susceptibility to bends
   (ii) absence of hereditary anemias
   (iii) absence of glucose 6-phosphate dehydrogenase deficiency
   (iv) susceptibility to acceleration atelectasis.

2. A minimum of 3 hours must be allowed for denitrogenation.

3. Find the effects of the intended flight profile, in simulation, on the incidence of pulmonary atelectasis, edema and shunt (desaturation for oxygen), as functions of atmospheric composition and pressure.

4. If a pure oxygen atmosphere is contemplated, study its toxic effects for at least the maximum expected duration of flight.

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PHYSIOLOGY SYMPOSIUM

RESPIRATORY PHYSIOLOGY IN MANNED SPACECRAFT

Introductory Remarks

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PHYSIOLOGY SYMPOSIUM

RESPIRATORY PHYSIOLOGY IN MANNED SPACECRAFT[1,2,3]

Introductory Remarks

ARTHUR B. DuBOIS[4]

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THE SCIENTIST OF THE EARLY 1940's was epitomized by Dr. Wallace O. Fenn as a "physiologist on horseback." Today's physiologist is responding not to the beat of drums but to the prospect of accomplishing that which once seemed a dream: manned exploration of space. This symposium appears to be the first major effort to bring into focus the problems and state of the art of respiratory physiology related to manned space flight. That is, it contains the first theoretical and experimental exposition of the effect of acceleration on the lungs and pulmonary circulation, the first complete analysis of factors causing atelectasis, the first studies of the combined effects of acceleration and 2-week exposure to the absence of inert gas, and the first demonstration of the effect of increased oxygen tension on the red cells and blood hemoglobin concentration. Now, let us survey the scope of this subject.

During a trip into space and back, the lungs of a man are exposed to a number of physiological stresses for which they were not originally designed. Before being launched, the man must breathe pure oxygen for several hours to rid the body tissues of physically dissolved nitrogen, which otherwise would come out of solution and form bubbles as the space capsule's pressure became reduced. But breathing oxygen may lead to two new problems: these are the cellular toxicity of oxygen, and the complete absorption of gas from occluded air spaces of the lung.

Then, during the forward acceleration phase of launching, or during the deceleration phase of re-entry into the earth's atmosphere, the lung tissues sag toward the back of the chest, thereby overstretching the lung tissue fibers which surround alveoli in the front, and compressing the air out of the alveoli in the back portions of the lung.

Meanwhile, the pulmonary blood vessels are overdistended in the back part of the lungs and collapsed in the front part because of the extra weight of blood within the pulmonary blood vessels during acceleration. Also, fluid transudation begins in some lung capillaries if the blood pressure inside them exceeds the colloid osmotic pressure of the plasma proteins. These factors cause the arterial blood to become unsaturated with respect to oxygen, making it more difficult for the brain to function properly. These effects, though clearly demonstrated on animals and man, have been reversible and left no aftereffects under the conditions of earth orbital flights to date.

The engineers designing the breathing system in a space vehicle also have to take into account decreased cooling of their electrical instruments in the absence of thermal convection during weightlessness and due to the lowered thermoconductivity of gases under reduced barometric pressure. Also, they must consider fire hazards which become more important when no inert gas is present to dilute the oxygen in the atmosphere.

As faster speeds become necessary in order to escape from and re-enter the earth's field of gravity there may be more compression of the lung tissues and more pulmonary edema and atelectasis at the base of the lungs. And, as the trips become longer in duration, the effects of cellular toxicity of oxygen due to prolonged exposure to slightly increased oxygen tension in the inspired air may begin to make their appearance. These factors have not hampered existing programs, but do require careful study for the future.

Whereas past decisions concerning gas composition

[1] Sponsored by the American Physiological Society and its Respiration Dinner Group.

[2] Presented at the 47th Annual Meeting of the Federation of American Societies for Experimental Biology, Atlantic City, N. J., April 19, 1963.

[3] Speakers at this Symposium have been connected with the Study Group on Gaseous Environments for Spacecraft under the Man in Space Committee of the National Academy of Science's Space Science Board. The Symposium reflects the work and interests of this group and its individual members.

[4] Established Investigator of the American Heart Association and Chairman of the Study Group on Gaseous Environments for Spacecraft, Man in Space Committee, Space Science Board.

and respiratory equipment have been based upon limited information and a reasonable compromise between engineering and medical considerations, the day has now come when panels such as our panel of physiologists are required *1*) to help evaluate the many factors concerned and *2*) to make sure that the acquisition of the physiological information relating to manned space flight is planned sufficiently far in advance of its need so that a minimum amount of extrapolation is required when arriving at future engineering decisions.

Since the physiological questions formulated in this symposium require further work, it is felt that additional thought will have to be devoted to the careful planning of future experiments in the field of respiratory physiology in manned spacecraft.

Influence of acceleration on pulmonary physiology[1]

EARL H. WOOD,[2] A. CLARK NOLAN,
DAVID E. DONALD, AND LUCILLE CRONIN
Mayo Clinic and Mayo Foundation, Rochester, Minnesota

THE PHYSIOLOGIC EFFECTS of acceleration are due to the increase in effective weight which acceleration produces. Since blood is the most mobile organ in the body, circulatory functions are very easily affected by acceleration. This susceptibility is illustrated dramatically by the loss of both vision and consciousness which ensues approximately 4–6 sec after exposure of a healthy man to a positive (headward) acceleration of 4–7 G (9, 19, 23).

These symptoms result from the immediate reduction of systemic arterial pressure to zero at head level at the onset of such an exposure as illustrated by recordings taken from a healthy subject during an exposure to 4.5 G (Fig. 1). Arterial pressure was maintained at normal values at heart level, however, due to the fivefold increase in the weight of the blood, arterial pressure was reduced to zero at head level as soon as 4.5 G was attained, and complete loss of vision, due to stagnant anoxia of the retina, occurred 6 sec later.

The mechanism of this decrease in arterial pressure at head level is indicated in Fig. 2, which shows the hydrostatic distances separating various sites in the circulatory system of a seated subject at 1 G (middle panel) and at 5 G (left panel). At 5 G, a pressure of 125 mm Hg is required to lift the blood from the heart to the head. Consequently, if systolic pressure is maintained at normal values at heart level, arterial pressure at head level is zero while at heel level it is increased to 270 mm Hg.

Considerations such as these dictated the decision that the body position of occupants of spacecraft be oriented transversely to the flight path during the launch and re-entry phases of space flight. The supine seated position selected for the astronauts is well known.

What are the magnitudes and durations of the accelerations which a spacecraft must undergo during the launch and re-entry phases of space flight? These can be calculated easily. Orbital velocity is about 18,000 mph; this is about 26,400 ft/sec. The force of gravity, 1 G, accelerates a body at a rate of 32.2 ft/sec^2. Therefore, 26,400 ÷ 32.2 gives approximately 820 as the total number of G-seconds in excess of the earth's gravitational pull required to accelerate a spacecraft to orbital velocity. The same number of G-seconds—820—is required to decelerate during re-entry. If these accelerative forces could be distributed relatively evenly over these 820 sec, that is during 13⅔ min, the level of acceleration would be in the range of 2 G and no physiologic effects of practical operational import would be expected. However, the characteristics of rocket engines currently in use prevent attainment of such gentle levels of acceleration. Their relatively brief but hard-push characteristics are illustrated by the acceleration profile of the launch phase of John Glenn's orbital flight (Fig. 3).

In general, there are two peaks of acceleration, which occur just prior to burnout of the first- and second-stage rocket engines, respectively. In this instance, the first peak attained a maximum of 7 G and acceleration levels in excess of 5 G were maintained for more than 30 sec. During the second peak, which reached 8 G, the level of acceleration exceeded 5 G for more than 50 sec. The mean levels of acceleration during these two periods were 6.0 and 6.4 G, respectively.

During re-entry there is a single large peak of acceleration that attains a maximal value of about 8 G and during which the level of 5 G is exceeded for a total period of time similar to the sum of the duration of the two peaks of the launch phase of the flight. Since the re-entry acceleration profile entails a longer sustained single period at an acceleration of greater than 4–5 G, it would be expected to produce a somewhat greater physiologic stress than that of the launch phase of the flight. Since the velocity required to escape from the earth's gravitational field is about 25,000 mph, in contrast to 18,000 mph for orbital flight, about one-third more acceleration is required for launch and re-entry for outer space flight than is needed for orbital flight.

What are the physiologic effects of a transverse acceleration of 5 G for 60 sec on a healthy man? The predicted effects on the pulmonary circulation are somewhat devastating, as illustrated in Fig. 4. This figure, which was prepared in cooperation with Dr. H. F. Helmholz, Jr., is based on the assumption that mean pressures in the left atrium and in the pulmonary artery are maintained unchanged at the level of the thoracic

[1] This study was supported in part by Air Force Contract AF 33(657)-8899 and by Research Grant H-3532 from the National Institutes of Health.

[2] Career Investigator, American Heart Association and Member, Study Group on Gaseous Environments for Spacecraft, Man in Space Committee, Space Science Board.

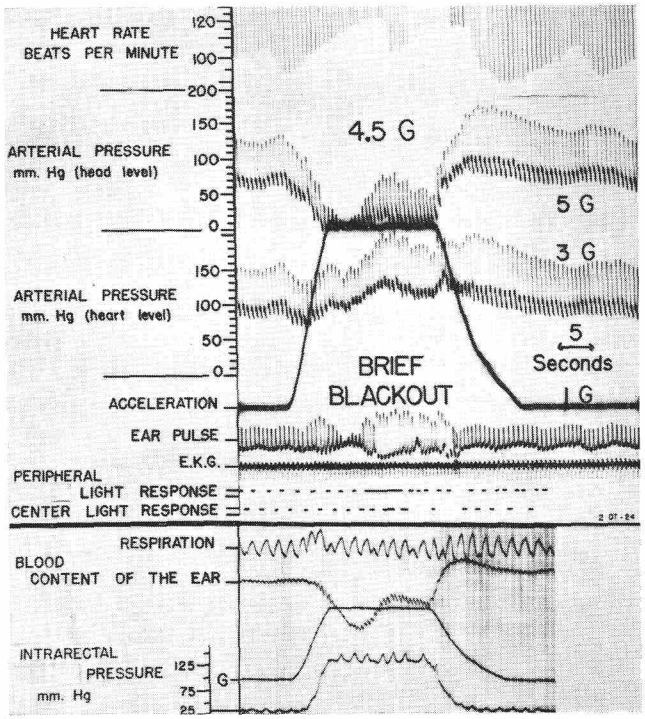

FIG. 1. Sequence of physiologic events during exposure of a normal subject to headward (positive) acceleration of 4.5 G for 15 sec on a human centrifuge. The recordings were made by 2 photokymographic cameras operating simultaneously, 1 mounted in centrifuge cockpit (lower panel) and 1 in recording room adjacent to centrifuge (upper panel). Vertical white lines on lower panel delineate 1-sec intervals. Vertical white lines on upper panel delineate 5-sec intervals and were 15 mm apart before photographic reduction. Black acceleration line indicates the magnitude of headward acceleration in G units. Simultaneous recording of acceleration (indicated as G in lower panel) serves to synchronize the 2 recordings. Length of black lines designated as peripheral and center light response indicates subject's reaction time to light signals in peripheral and central fields of vision, respectively. Note initial period of progressive failure during which there are, in order of occurrence, decrease in blood pressure at head level, increase in heart rate, loss of blood volume in the ear as measured by ear opacity, reduction in amplitude of arterial pulse in the ear, and failure of peripheral vision. Then note a period of compensation during latter half of exposure in which blood pressure at head level increases, ear pulse recovers, blood returns to the ear, heart rate slows, and vision is restored, in spite of the fact that acceleration was continued. (Reproduced from ref. 19 with permission of the authors.)

midcoronal plane during exposures to forward acceleration. The term "forward acceleration" means that the subject is being accelerated in the ventral direction in relation to his body so that the reactive force with which we are concerned is from the front towards the back of the thorax. This is often called "eyeballs-in" acceleration.

In Fig. 4, the panel on the left shows the mean pressures in the pulmonary arteries and veins in the thorax at 0 G. Since the blood, like everything else, would be weightless in this gravity-free state, mean pressures would be essentially equal in all large vessels of the arterial and venous pulmonary vascular system, independent of the position of the vessels in the thorax.

The mean pressure gradients which exist in the pulmonary vasculature of a normal person subjected to the earth's gravitational field of 1 G are shown in the center panel and the fivefold multiplication of these gradients, which would be expected to occur during an exposure to 5 G, are illustrated in the right panel. These simple physical predictions indicate that, during an exposure to a forward acceleration of 5 G, the pulmonary arterial and venous pressure in the dorsal regions of the lung would be increased to 70 and 60 cm H_2O, respectively, while perfusion of the ventral, that is superior, segments

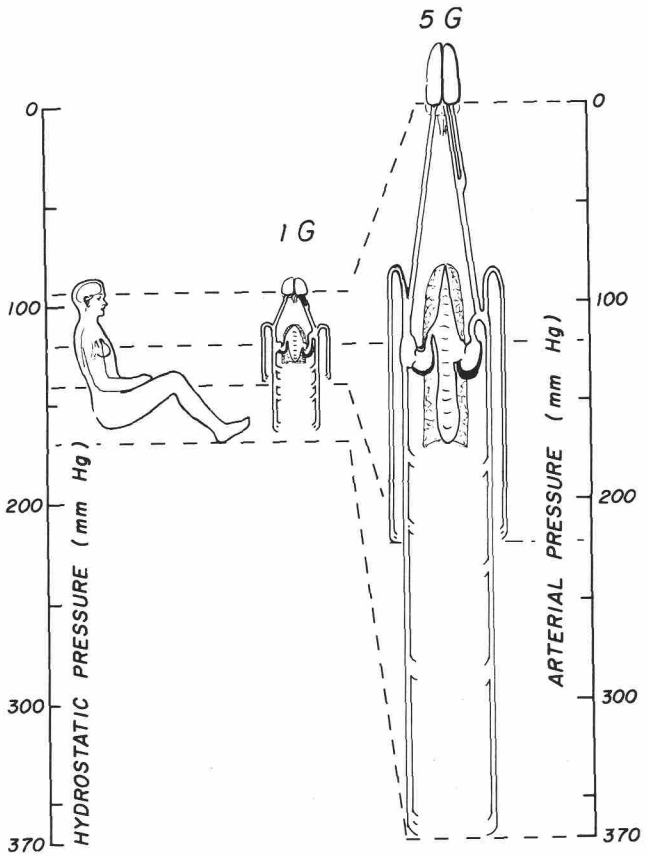

FIG. 2. Diagrammatic representation of hydrostatic pressures in vascular system of a man in upright sitting position at 1 G and during headward acceleration at 5 G. First figure (left) shows average position of pilot in present-day aircraft. Second figure (center) is a diagrammatic representation of vascular system of this pilot at 1 G, indicating that, with an arterial pressure of 120 mm Hg at heart level, arterial pressures at head and foot levels are calculated to be 96 and 170 mm Hg, respectively. Third figure (right) demonstrates the fivefold increase in differences in hydrostatic pressure imposed by 5 G of headward acceleration. Assuming that arterial pressure at heart level was maintained at 120 mm Hg, arterial pressure at base of the brain would be zero, while at the heels it would be 370 mm Hg. Under this circumstance and in the absence of muscular activity, a venous pressure of 250 mm Hg would be required to return blood from the heels to the level of the heart. See Fig. 1 for verification of these differences in arterial pressure at heart and head levels with subject in upright seated position at 1 G and during exposures to headward acceleration. (Reproduced from ref. 19 with permission of the authors.)

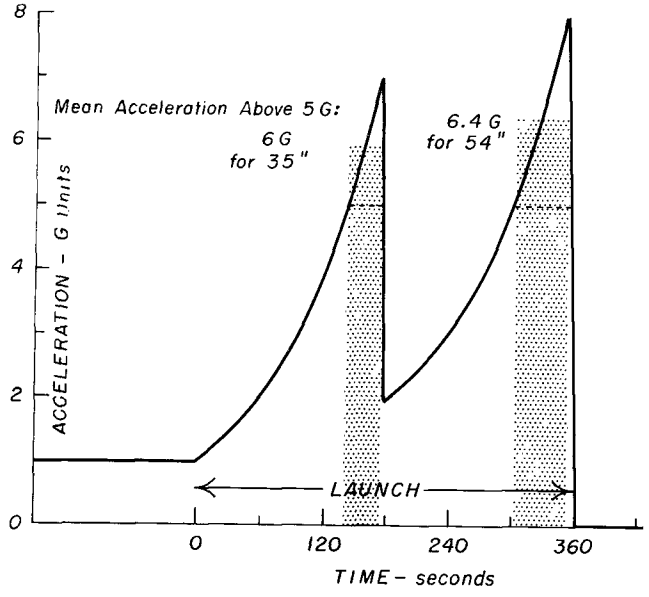

FIG. 3. An approximation of acceleration profile experienced by John Glenn during launch phase of his orbital flight. Stippled areas indicate period during which acceleration exceeded 5 G. Mean accelerations of 6 G and 6.4 G for these 2 periods of 35 and 54 sec, respectively, would be expected to cause a significant decrement in pulmonary function. (Copied from Fig. 9-5 of ref. 20.)

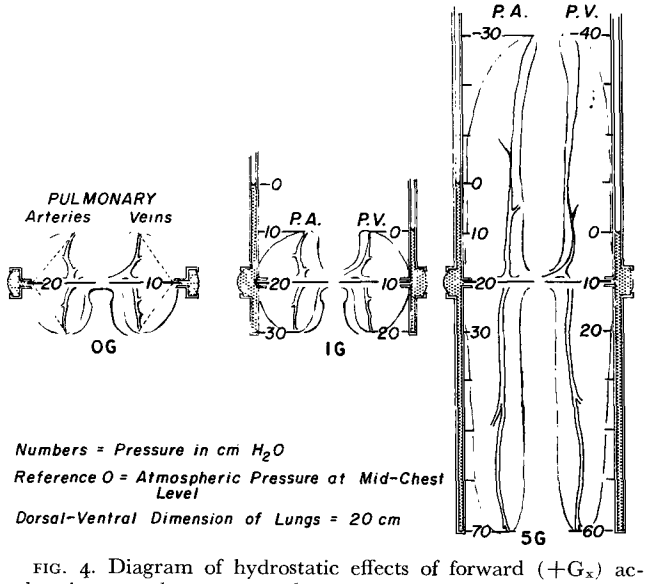

FIG. 4. Diagram of hydrostatic effects of forward ($+G_x$) acceleration on pulmonary circulation. Mean pressures in pulmonary arteries and veins at midchest level are assumed to remain constant at 20 and 10 cm H_2O, respectively, during exposure to 0, 1, and 5 G. Since measurements in dogs and in humans indicate that these pressures actually increase at this level during exposures to forward acceleration, the amount by which pulmonary capillary pressure exceeds pulmonary edema value in the dorsal regions of lungs during an exposure to 5 G would be greater than the value suggested in the diagram.

of the lung would be abolished during the exposure, and. if collapse of the vasculature did not occur, negative vascular pressures in the range of -30 to -40 cm H_2O would be expected at the superior margins of the lungs. The pulmonary capillary pressure in the dependent regions of the lungs would far exceed the colloidal osmotic pressure of the blood so that pulmonary edema would be expected to develop rapidly.

In actual matter of fact, the evidence indicates that the pressures in the right atrium, pulmonary artery, and left atrium are increased at midchest level during exposures to forward acceleration in the horizontal position (17). The average measured changes in these pressures during exposures of four dogs to 6 G are shown in Table 1. Increases of approximately 10 cm H_2O occurred in the pressures in the right and left atria and pulmonary artery when the dogs were in the horizontal or the 15-degree head-down position; a small decrease occurred in atrial pressures in the head-up position. Data are not available on pressures in the left atrium and pulmonary artery in man but measurements of right atrial pressure made during exposures of healthy subjects to acceleration when in the Mercury couch position showed increases of about 5 cm H_2O/G of acceleration (17). It appears probable, therefore, that pressures in the pulmonary artery and left atrium, referred to midchest level, also are increased. If this is the case, increases in vascular pressures in the dependent regions of the lung of man during an exposure to 5 G would be even greater than those indicated in Fig. 4.

It would be expected, therefore, that pulmonary edema would develop rapidly during an exposure of a healthy subject to accelerations of 4–5 G and greater. If this were the case, one should be able to detect evidence of the occurrence of hemoconcentration and of deficient oxygenation of arterial blood during such exposures. There is, in fact, good evidence for the occurrence of both phenomena.

Figure 5 shows the average and range of decreases in arterial oxygen saturation in four healthy men recorded continuously by cuvette oximetry directly on radial artery blood and by ear oximetry, before, during, and after 3-min exposures to accelerations ranging from 2 to 5.4 G. Similar decreases in arterial oxygen saturation also have been observed during exposures to acceleration in the headward (positive) direction—the type

TABLE 1. *Effect of transverse acceleration on intrathoracic vascular pressures*

Recording Site	Intrathoracic Vascular Pressures*			
	Control 1 G	During exposure to 6 G when body tilted		
		15° Head-up	Horizontal	15° Head-down
Right atrium	2	−3	13	12
Left atrium	3	−5	14	12
Pulmonary artery	27	36	33	36

* Pressures are expressed in cm H_2O referred to ambient atmospheric pressure at mid-dorsoventral chest level and values shown are averages of determinations on 4 dogs in supine position.

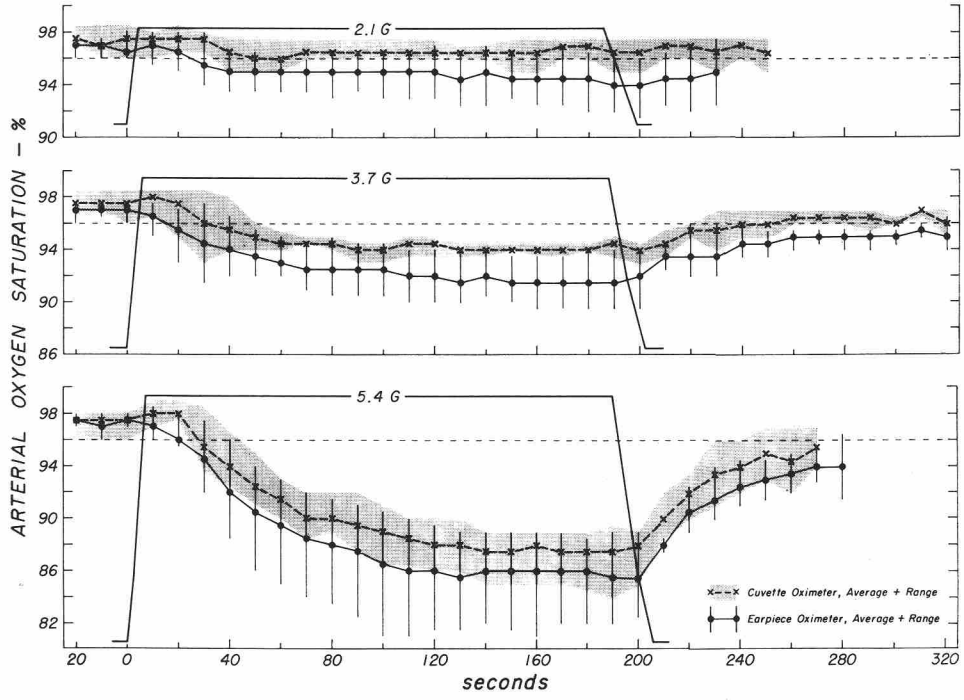

FIG. 5. Average and range of changes in arterial oxygen saturation of 4 healthy men, recorded by cuvette and ear oximeters during 3 min at 2.1–5.4 G, breathing air. (Reproduced from ref. 26 with permission of the authors.)

usually encountered in conventional aircraft—and this effect is exaggerated when an antiblackout suit is used (Table 2) (2, 3, 18). These decreases in arterial oxygen saturation are delayed but *not* prevented when the subjects breathe 99.6% oxygen (Fig. 6) (18, 22, 26). Continuous measurement of the optical density of the blood in the infrared (800 mμ) during such exposures suggest that hemoconcentration, such as might be expected to be associated with edema formation, also occurs.

If a significant decrease in plasma volume did occur, one would expect a detectable decrease in right and left atrial pressures during and following exposures to acceleration. That a decrease in central venous pressure does in fact occur in man subsequent to exposures to forward acceleration is illustrated in Fig. 7, which shows right atrial pressures in six healthy men before, during, and after 10-min exposures to 2, 3.5, and 5 G. Note that the maximal increases in right atrial pressure occur at the onset of the exposure and that a progressive decrease from this maximum occurs during the exposure. After each exposure, right atrial pressures were uniformly less than they were before the exposure, the average decrease being 2 mm Hg. If one assumes that the volume and distensibility of the vascular system was the same at 1 G before and after such exposures and uses Gauer's value for the volume-elasticity coefficient of the vascular system of healthy men, namely 7 cm H_2O change in right atrial pressure per liter of change in blood volume (8), then it is estimated that the decreases in right atrial pressure in these subjects are compatible with a decrease in plasma volume of nearly 400 ml.

Evidence for the rapid occurrence of hemoconcentration during exposures to forward acceleration also has been obtained in dogs. After exposure to 6 G for 60 sec,

TABLE 2. *Minimal values of arterial blood oxygen saturation during first 15 sec of exposure to plateau levels of headward acceleration**

G Suit	Saturation, per cent†			
	Control 1 G	2 G	3 G	4 G
Not inflated	97 96–99‡ (24)	96.5 95.5–97.5 (10)	94.5 92–98.5 (14)	93 91–96 (5)
Inflated to 200 mm Hg	96 95.5–97 (4)	94 92–96 (5)	93 90–96 (5)	89 87–91.5 (4)

* Table reproduced from ref. 18 with permission of authors. † Determined by cuvette oximetry from blood being withdrawn from radial artery in 5 subjects. Number in parentheses is number of individual determinations. ‡ Range of individual determinations.

these dogs usually show a decrease in right and left atrial pressures which averages 1–2 cm H_2O, as shown in Fig. 8. Also, they show a rapid increase in the optical density of the blood measured at 800 mμ, indicating an increase in blood hemoglobin concentration (27), and a decrease in arterial oxygen saturation during the exposures closely similar to those seen in healthy human subjects. These changes apparently are rapidly reversible since the values return to or approach the control values in the 5–10-min intervals between exposures.

It is believed that, in addition to edema, collapse of pulmonary alveoli occurs during exposure to acceleration and this plays an important role in the arterial desaturation which is observed. The simple physical basis for these considerations is illustrated in Fig. 9, which shows

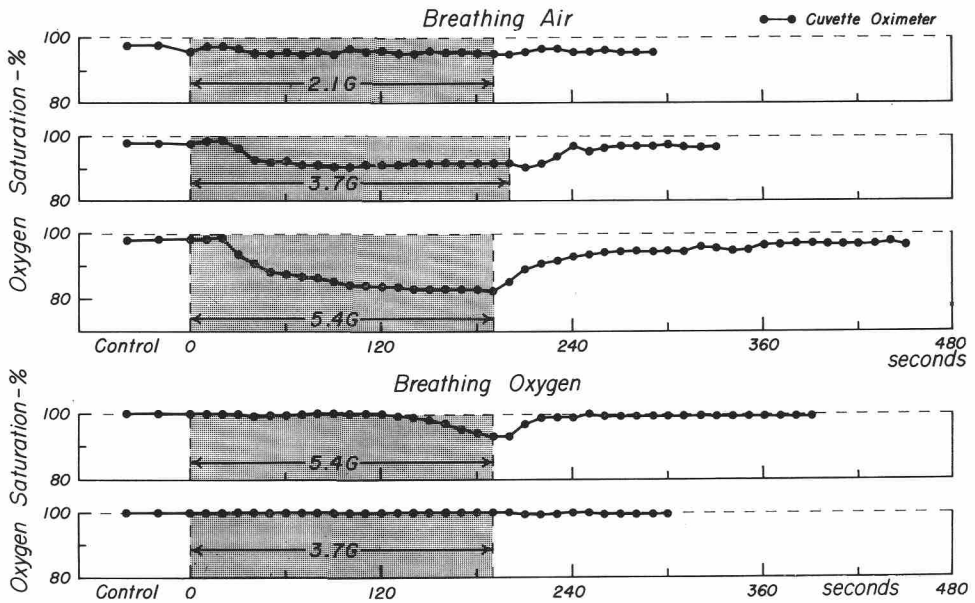

FIG. 6. Comparison of changes in arterial oxygen saturation during 3-min exposures of a healthy man (81 kg, 37 years old) to forward accelerations of 2.1–5.4 G when breathing air and when breathing 99.6% oxygen. Note marked delay in onset and limited extent of decrease in arterial oxygen saturation at 5.4 G and absence of change at 3.7 G while breathing oxygen as compared to similar exposures while breathing air. Stippled area indicates period of constant acceleration. (Reproduced with permission from Nolan, A. C., H. W. Marshall, L. Cronin, W. F. Sutterer, and E. H. Wood. *Aerospace Med.* In press.)

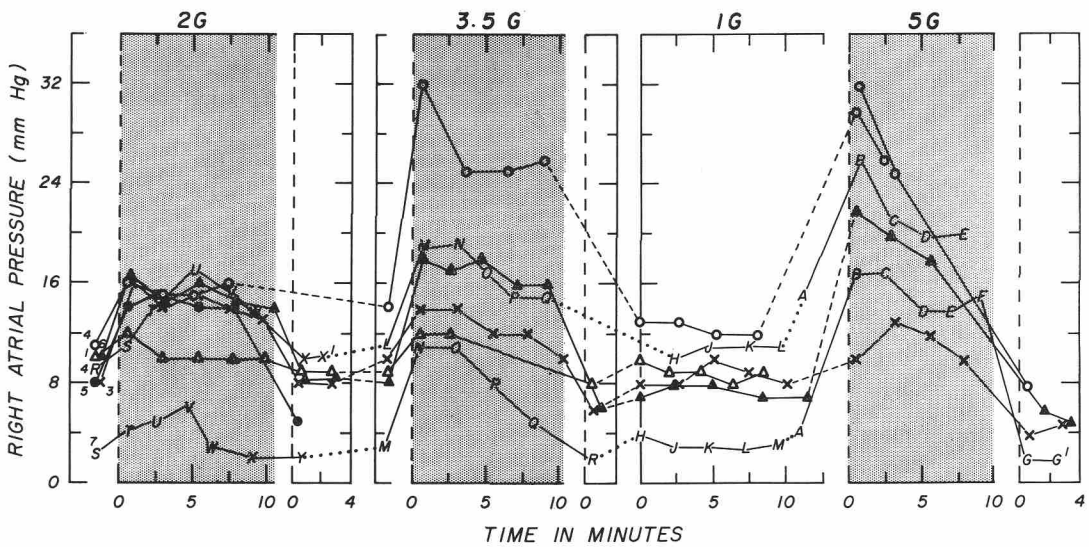

FIG. 7. Effect of forward acceleration on right atrial pressure in 6 healthy subjects. Note *1*) increasing magnitude of increment in atrial pressure with increased levels of acceleration, *2*) progressive decrease in right atrial pressure from maximal level attained at onset of acceleration; and *3*) that in relation to value at 1 G before each exposure there is a systematic decrease in right atrial pressure at 1 G immediately after each exposure. This suggests decrease in circulating blood volume during the exposure, increase in capacity of the vascular bed, or both. (Reproduced from ref. 19 with permission of the authors.)

estimated values for intrapleural and vascular pressures in the thorax at 0, 1, and 5 G. This figure has been constructed, in cooperation with Dr. H. F. Helmholz, Jr., on the basis of a lung with a dorsal-ventral dimension of 20 cm and an average specific gravity of the thoracic contents of 0.5. At 0 G, intrapleural pressure due to the elastic properties of the lungs is estimated to be about -7 cm H_2O, and, due to the weightless state, intrapleural and vascular pressure gradients due to hydrostatic effects would be absent. At 1 G, the negativity of the intrapleural pressure is increased ventrally to -12 cm H_2O and decreased dorsally to -2 cm H_2O, due to the "hydrostatic effects" of the thoracic contents (7). At 5 G, due to the fivefold increase in weight of the thoracic contents, these pressure gradients would be expected to be five times greater so that the pleural pressure in the dependent regions of the thorax would be expected to increase to positive values in the range of 18 cm H_2O while highly negative values would occur ventrally (24). Since the specific gravity of air is essentially zero, when airways are patent, alveolar pressures will be equal throughout the lung, even at 5 G, and closely similar to ambient atmospheric pressure. In this circumstance, collapse of alveoli would be expected in the dependent regions of the lungs and gross overdistention of alveoli would be expected ventrally.

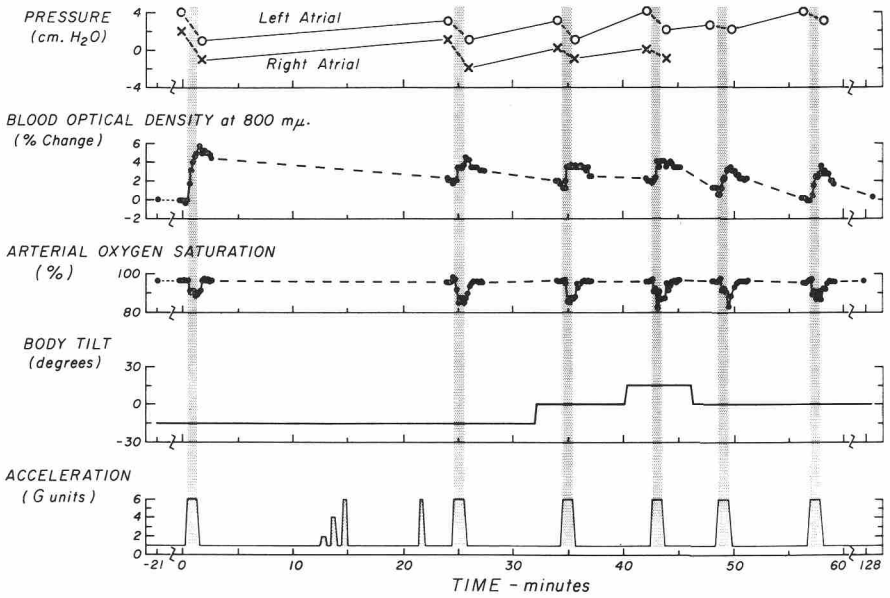

FIG. 8. Decreases in right and left atrial pressures and increases in optical density of arterial blood at 800 mμ in a dog (22 kg, morphine-pentobarbital anesthesia) immediately after exposures to forward accelerations of 6 G. These changes are suggestive of a decrease in circulating blood volume due to hemoconcentration resulting from edema formation in dependent portions of pulmonary and systemic circulations during exposures to acceleration. Note return toward control values during 5–10-min intervals at 1 G between exposures to 6 G, indicating that these changes are rapidly reversible. An increase in concentration of blood hemoglobin of 1.5 g/100 ml of blood is associated with an increase of about 4% in optical density of whole blood at 800 mμ.

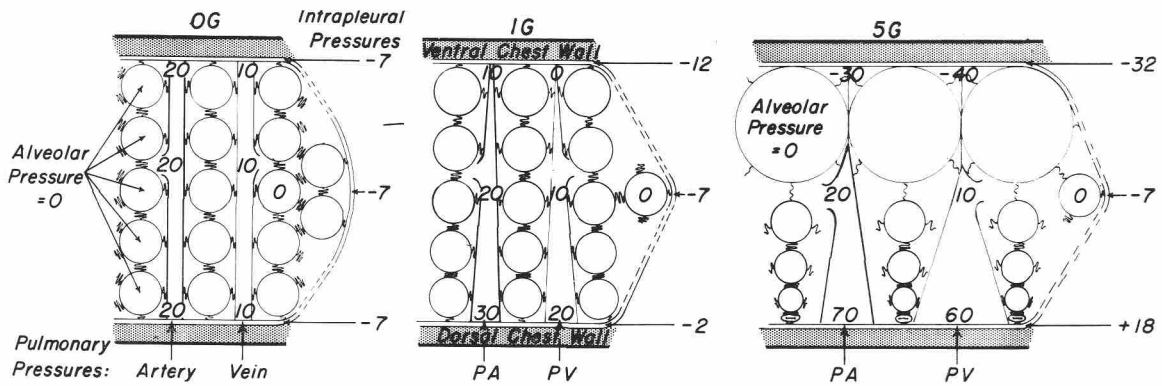

FIG. 9. Diagram of effects of forward ($+G_x$) acceleration on intrathoracic pressures (dorsal-ventral dimension of lung = 20 cm). Numerals indicate pressures as cm H_2O and zero reference level = atmospheric pressure at midthoracic coronal plane. In absence of obstruction of airway, pressure in alveoli (represented as open circles) would be approximately equal to ambient atmospheric pressure and would be the same in all alveoli, independent of level of acceleration or position of alveoli in the thorax. Mean pulmonary arterial, pulmonary venous, and intrapleural pressures at midchest level are assumed to remain constant at 20, 10, and −7 cm H_2O, respectively, during exposure to 0, 1, and 5 G. Intrapleural pressures shown at ventral and dorsal surfaces of the lungs at 1 and 5 G were calculated by assuming that the thoracic contents react to the change in weight caused by acceleration in a manner similar to that of a fluid with a specific gravity of 0.5. These estimated pressure values are closely similar to pressures actually recorded at these sites in dogs exposed to 1 and 5 G in the supine horizontal position.

Data are rapidly accumulating to indicate that the changes shown in this diagram do indeed occur during exposures to acceleration.

The evidence for the occurrence of large pulmonary arteriovenous shunts, both in man and in dogs (2, 3, 18, 22, 26), such as would be associated with atelectasis, has been mentioned. Independent evidence of atelectasis has been obtained from roentgenograms of the thorax of healthy men taken before and after exposure to forward acceleration on the human centrifuge (11, 26) (Fig. 10). Roentgenograms were obtained immediately before and 5 min after a 3-min exposure to 5 G. Both films were taken at maximal inspiration. The elevation of the diaphragm after the exposure and the increase in opacity of the basilar lung segments are evident. Our colleagues in clinical radiology interpret these changes as indicative of the presence of atelectasis in these regions of the lung. Similar or more severe roentgenographic evidence of atelectasis as a consequence of exposures to positive acceleration in jet fighter aircraft, particularly when oxygen was breathed and an antiblackout suit used, has been reported by Green and Burgess (10) of the British Royal Air Force and by others (15, 16).

Since pleural pressure measurements cannot be made safely in healthy men, such measurements have been made in dogs. Fortunately, the dorsal-ventral dimension of dogs in the 20–30-kg body weight range, about 20 cm, is closely similar to the average dorsal-ventral chest thickness of man. Since the dorsal-ventral dimensions of the lungs of dogs and of man are similar, it might

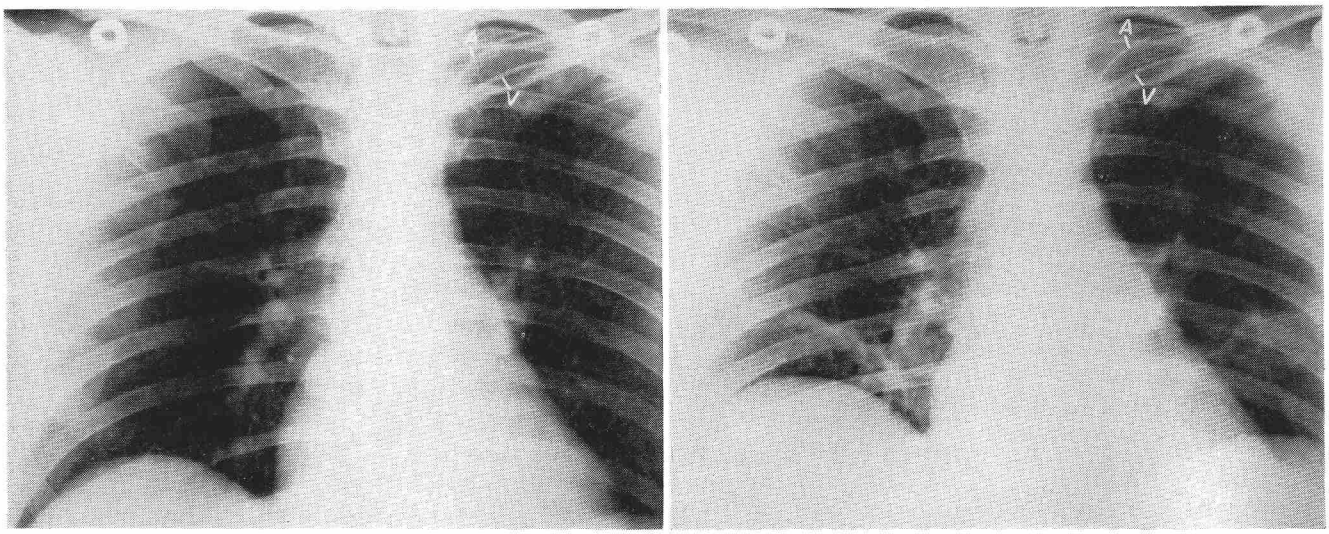

FIG. 10. *Left:* A thoracic roentgenogram of normal appearance, obtained just before the subject was accelerated to 5.5 G for 2⅓ min while breathing 99.6% oxygen. *Right:* A thoracic roentgenogram of the same subject after termination of the 5.5-G exposure. Note focal areas of increased density, indicative of atelectasis bilaterally, with associated diaphragmatic elevation (A = aortic catheter; V = venous catheter high in the right atrium). (Reproduced with permission from Nolan, A. C., H. W. Marshall, L. Cronin, W. F. Sutterer, and E. H. Wood. *Aerospace Med.* In press.)

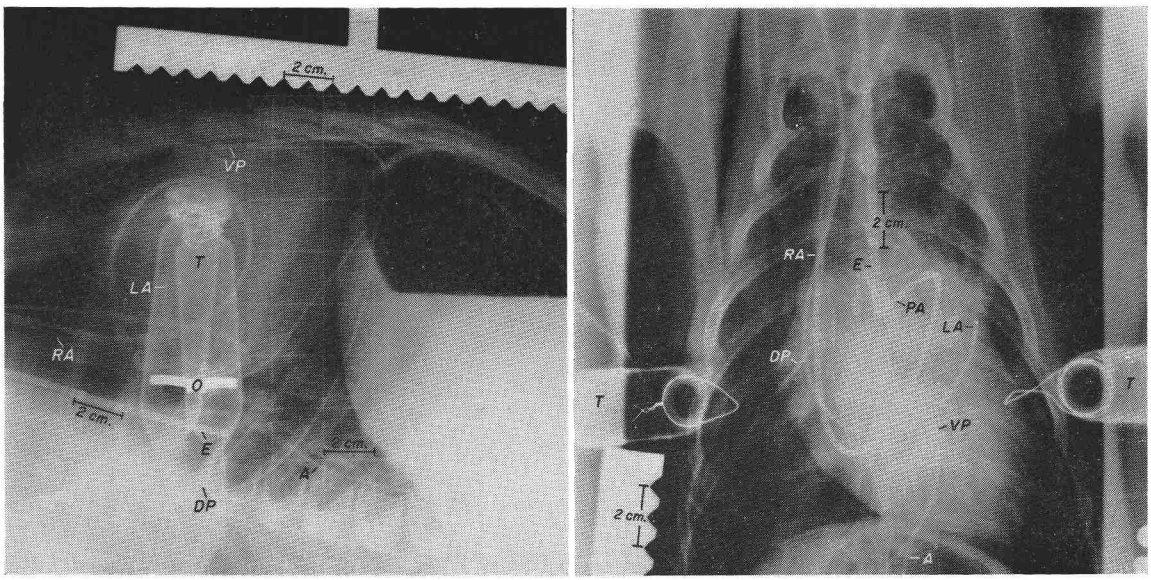

FIG. 11. Lateral (left panel) and anteroposterior (right panel) roentgenograms of the thorax of a dog showing positions of catheter tips at several thoracic sites after a series of exposures to forward acceleration on a centrifuge. Glass thistle tubes (T), fixed by wires to ribs bilaterally and used for determinations of zero pressure reference levels, also are shown. Lead strips (O), which were fastened to thistle tubes (left panel), mark the level of hypothetical coronal plane passing through middle anteroposterior level of the thorax. This plane was used as the zero pressure reference level for all intravascular pressure measurements. Other symbols are: A, tip of catheter in thoracic aorta; DP, tip of catheter in potential intrapleural space in right paravertebral gutter; VP, tip of catheter in potential right retrosternal pleural space; E, esophageal catheter; PA and RA, tips of catheters in pulmonary artery and right atrium, respectively; and LA, tip of catheter in left atrium. The 2-cm marks indicate dimensions of reference grids used to correct, and to verify the accuracy of the corrections, for distortion of measurements of positions of catheter tips made from these roentgenograms which were used to correct intrapleural and esophageal pressure measurements to pressures at the respective catheter tips. (Reproduced from ref. 26 with permission of the authors.)

be expected that the hydrostatic effects of forward acceleration also would be similar. A technique which allows percutaneous introduction of small (1.2-mm diameter) catheters to the desired sites in the thorax without recourse to thoracotomy has been developed (25). Results obtained in studies carried out at 1 G using this technique were reported at recent meetings of the American Physiological Society by Edmundowicz, Kenner, and Donald (6, 7, 13).

Lateral and anteroposterior roentgenograms showing

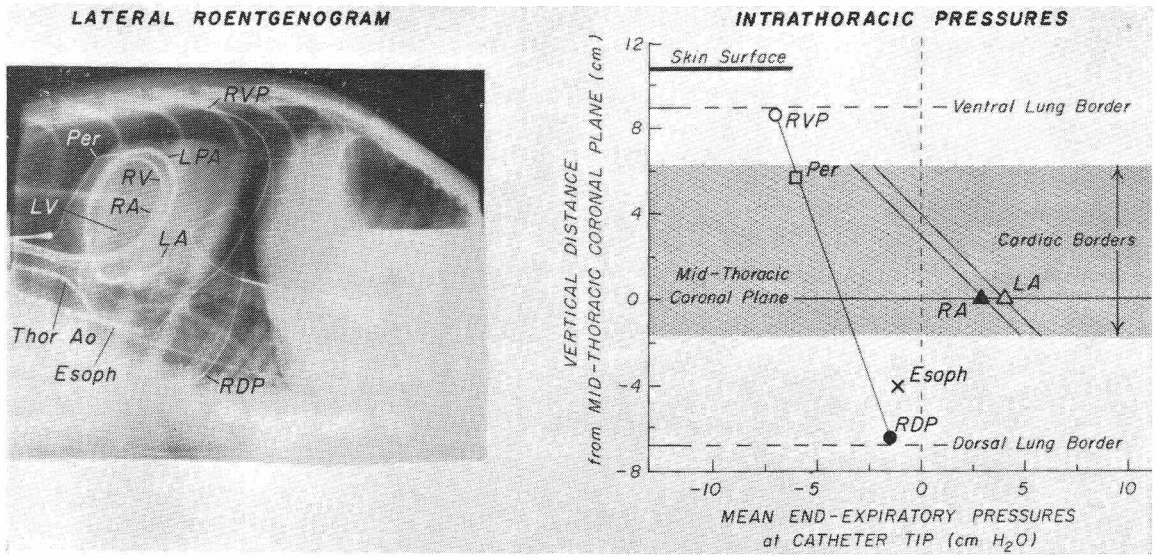

FIG. 12. Lateral roentgenogram (left panel) and graph (right panel), based on this roentgenogram, showing vertical relationship of recording catheters to borders of the heart and lungs and relationship of pressures recorded at these sites to vertical distance from midcoronal plane of the thorax. Note intrapleural pressure gradient of about 0.5 cm H_2O/cm of vertical distance between ventral (RVP) and dorsal (RDP) surfaces of the lung. Pressure in ventral portion of the pericardium falls on this gradient line Vertical gradient for right atrial (RA) and left atrial (LA) pressures of 1 cm H_2O/cm of vertical distance is indicated by slanted lines drawn through the atrial pressure values shown on the midcoronal plane. Esophageal pressure (Esoph) is slightly more positive than intrapleural pressure at the same vertical level in the thorax.

the catheters in place for a typical study are shown in Fig. 11. The tip of the ventral pleural catheter is just below the sternum while the dorsal pleural catheter tip is in the right paravertebral gutter. The 2-cm grid is used for accurate measurement of the position of the catheter tips. The thistle tubes are wired to a rib bilaterally and are filled with fluid to the level of the lead strips that mark the midchest level. This thistle-tube system is used for accurate recording of the zero-pressure reference for vascular pressures at midchest level before, during, and after centrifugation.

The lateral roentgenogram used to locate the vertical position of the recording catheter tips in relation to the position of the heart and lungs is shown in Fig. 12; also shown are the pressures at these sites, in relation to the vertical position in the thorax, in a dog in the supine position at 1 G. The difference in pleural pressure between vertical and dorsal positions in the thorax amounted to a gradient of about 0.5 cm H_2O/cm of vertical distance separating the catheter tips.

The differences in simultaneously recorded dorsal and ventral intrapleural pressures in relation to the vertical distance separating the catheter tips in nine dogs studied by this technique are shown in Fig. 13. The average vertical pressure gradient in these dogs was 0.5 cm H_2O/cm. Krueger and co-workers (14), in a prior study, demonstrated the presence of a gradient in intrapleural pressure in relation to the vertical position in the thorax of dogs studied in the head-up position.

A photokymographic recording of multiple intrathoracic pressures, as well as arterial and mixed venous (pulmonary artery) blood oxygen saturations, during an exposure of a dog to a forward acceleration of 5.9 G is shown in Fig. 14. Studies such as this have been carried out in eight dogs. Pressures and blood oxygen saturations were measured during exposures to 2, 4, and 6 G in the horizontal, 15-degree head-up, and 15-degree head-down positions.

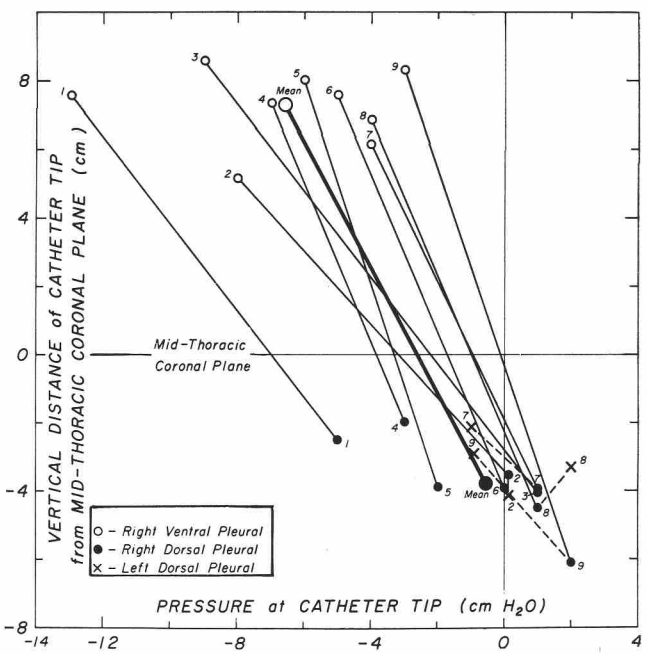

FIG. 13. Variation of intrapleural pressure with vertical position of tip of recording catheter in the thorax of 9 dogs in the supine position. Note that ventral pleural pressure is uniformly more negative than pressure recorded from more dorsal (dependent) sites in the thorax. Heavy line connects the average values for all dogs. Slope of this line, 0.5 cm H_2O/cm of vertical distance, represents average vertical intrapleural pressure gradient in these dogs.

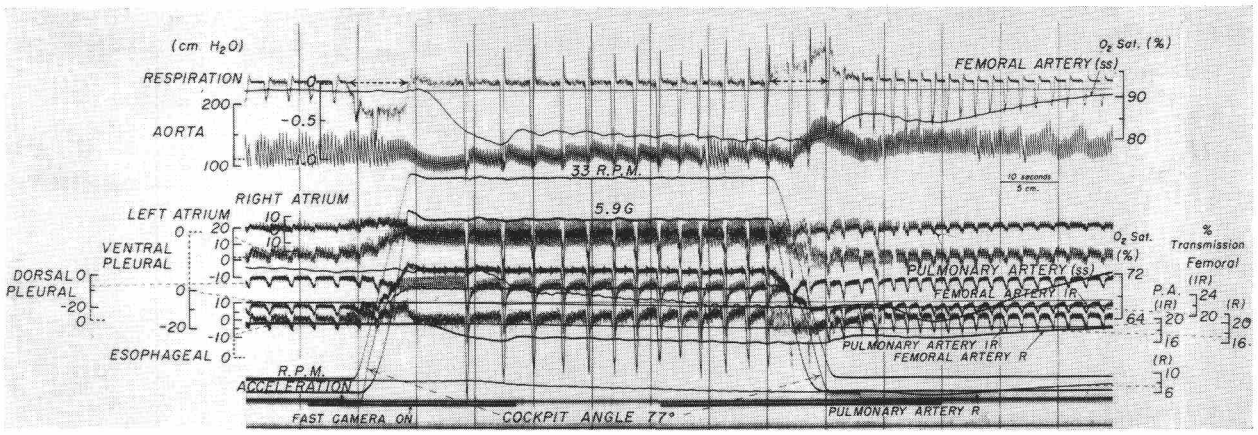

FIG. 14. Simultaneous recording of oxygen saturation and opacity at 800 mμ (hemoglobin concentration) of mixed venous and systemic arterial blood and of circulatory, intrapleural, and related intrathoracic pressures in an anesthetized (morphine-pentobarbital) 20-kg dog during a 1-min exposure to a forward ($+G_x$) acceleration of 5.9 G. Dashed pressure calibrations show zero reference line for the pressure transducer systems when exposed to acceleration. Zero reference level for vascular pressures is midthoracic coronal plane. Pleural and esophageal pressures are referred to ambient pressure at the level of the respective catheter tips, as determined by lateral and anteroposterior thoracic roentgenograms (Fig. 12). Correct zero reference levels for the manometer systems are not given for periods of tangential acceleration associated with starting and stopping the centrifuge, indicated by double-ended dashed arrows. Note *1*) decrease in arterial oxygen saturation during first 20 sec of the exposure, indicative of the presence of a large pulmonary arteriovenous shunt; *2*) progressive decrease, during the exposure, of transmission of infrared light (800 mμ) by systemic and pulmonary artery blood, suggesting the occurrence of hemoconcentration probably due to edema formation in dependent regions of vascular system. A plot of physiologic parameters measured from this recording is shown in left panel of Fig. 15.

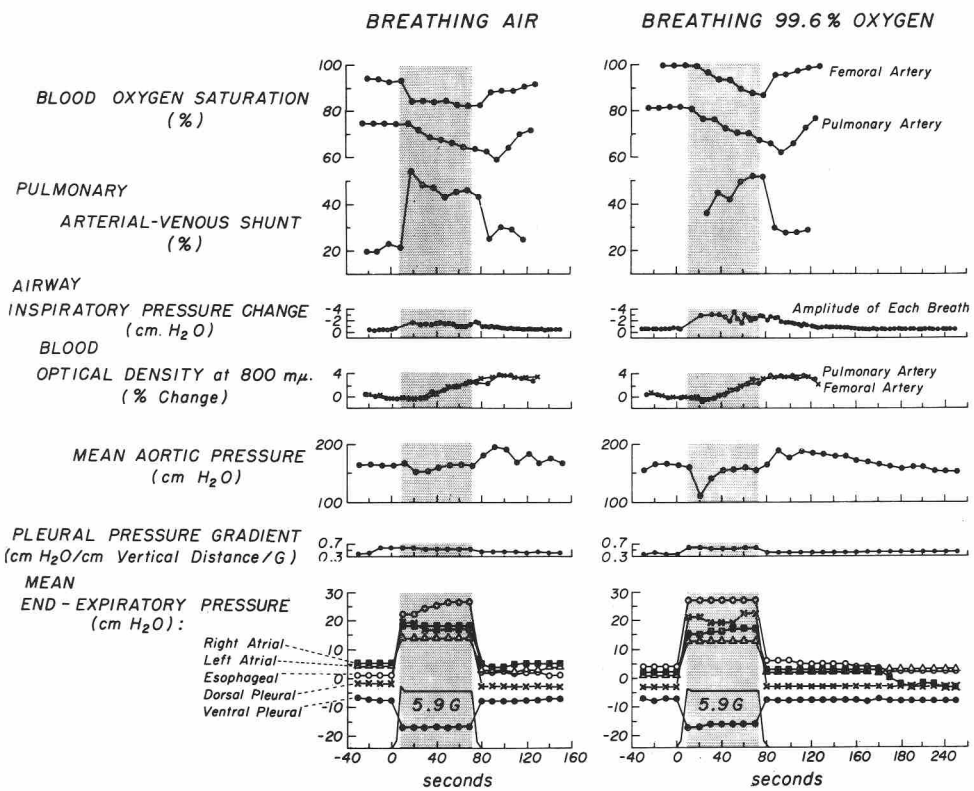

FIG. 15. Changes in simultaneously recorded physiologic variables during exposure of an anesthetized (morphine-pentobarbital) 20-kg dog to forward accelerations of 5.9 G while breathing air (left panel) and oxygen (right panel) at ambient pressure (735 mm Hg).

The pleural and vascular pressure and oxygen saturation values plotted at 10-sec intervals during 1-min exposures of a dog to 5.9 G while breathing air and while breathing 99.6% oxygen are shown in Fig. 15. Note that the dorsal pleural pressure increases to positive values and that highly negative values are obtained ventrally. The estimated pulmonary arteriovenous shunt increased rapidly during the first 30 sec of the exposure and then only slowly for the remainder of the exposure.

Average values for intrapleural pressures obtained

during exposure of four dogs to a forward acceleration of 6 G in three different body positions are shown in Table 3.

Very high negative values are obtained in the ventral pleural region during exposures to 6 G, particularly during inspiration when alveolar-to-pleural pressure gradients of greater than 40 cm H_2O can occur. Alveolar pressure gradients much in excess of this would be expected to cause actual disruption of pulmonary parenchyma (1). That this can occur is indicated by an incident, in our laboratory, of sudden development of acutely incapacitating mediastinal emphysema in a healthy subject during an exposure to 5.5 G while performing maximal voluntary hyperventilation in an unsuccessful effort to prevent a decrease in arterial oxygen saturation. Also it has been demonstrated, in studies carried out in the United States Navy centrifuge, that chimpanzees exposed to very high levels of acceleration when protected by complete immersion in water suffer disruptive emphysematous damage to intrathoracic structures (5).

TABLE 3. *Comparison of mean end-expiratory intrapleural pressures at dorsal and ventral sites in thorax*

Recording Site in Thorax	Intrapleural Pressures*			
	Control, 1 G	During exposure to 6 G when body tilted		
		15° Head-up	Horizontal	15° Head-down
Ventral	−11	−44	−31	−25
Dorsal	−4	7	17	20
Difference† (dorsal-ventral)	7	51	48	45

* Pressures expressed in cm H_2O referred to ambient atmospheric pressure and are shown as average values from 4 dogs in supine position. † Average vertical distance between recording sites, 12 cm.

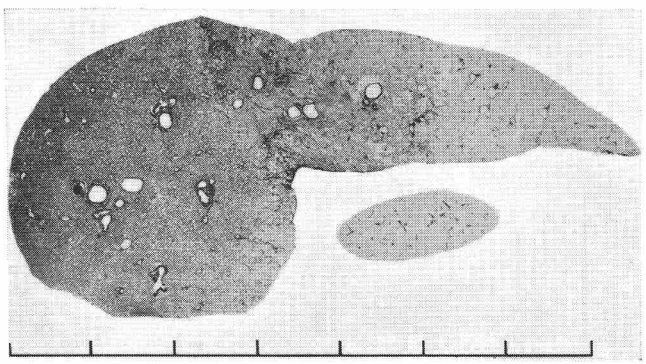

FIG. 16. Histologic section of lung of a dog killed after several exposures, ¼–3 min in duration, to forward accelerations of 2, 4, and 6 G. Total accumulated exposures to 2, 4, and 6 G for this dog were 5, 5, and 20 min, respectively. Large-scale divisions are centimeters. Ventral surface of the lung is on left. Smaller oval section is a coronal section of ventral portion of an apical lobe.

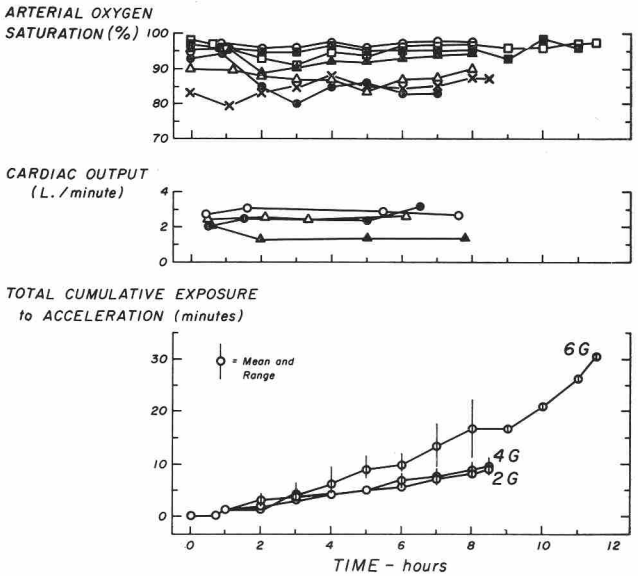

FIG. 17. Variation in physiologic status of dogs with duration of experiments on the centrifuge involving multiple exposures to forward ($+G_x$) accelerations of 2, 4, and 6 G. Duration of individual exposure ranged from ¼ to 3 min. Dogs were anesthetized with morphine and sodium pentobarbital 4.7 hr (4–5⅔) before the zero time shown on this chart. This pre-experimental period was utilized to insert various recording catheters (see Fig. 11) and to set up the animal in the supine position on a special support, with the associated transducers, in centrifuge cockpit. Note that, in spite of the fact that these dogs were maintained on their backs for from 7 to 11 hr and that their accumulative exposures to 6 G ranged from 10 to 30 min, the levels of arterial oxygen saturation and cardiac output at 1 G (that is, control values between exposures) show no evidence of a systematic deterioration of animals' physiologic status with time.

A histologic section of the lung of a dog that had undergone several exposures to forward acceleration prior to being killed is shown in Fig. 16. The grossly overdistended alveoli in the ventral part of the lung are evident as are the collapsed alveoli in the dependent region of this section. Similar findings have been described by Steiner and Mueller (22).

It is of interest that, in spite of the dramatic changes in arterial oxygen saturation and in pulmonary vascular pressures and evidence of occurrence of dependent atelectasis and edema with each exposure to acceleration, the dogs used in these studies withstood periods of 7–11 hr of anesthesia while restrained in the supine position in addition to multiple exposures to accelerations of up to 6 G without apparent evidence of progressive deterioration (Fig. 17).

SUMMARY

This is an outline of only some of the effects of acceleration on respiratory physiology. No attempt has been made to cover the considerable effects of acceleration on pulmonary ventilation and other aspects of lung function which have been well studied (4, 12, 28). If the impression has been created that accelerations in the ranges currently encountered in the launch and re-entry

TABLE 4. *Possible means of protection against pulmonary effects of acceleration*

A: Pressure breathing
Ineffective, due to lack of compensation for vertical pressure gradients in thorax
B: Fluid breathing
Theoretically effective
Practicality unknown
C: Rotation around longitudinal axis
Theoretically beneficial
Practicality unknown
D: Flattening out of acceleration-versus-time profile
275 Sec at 3 G:
Would produce orbital velocity
Would be physiologically acceptable

phases of space flight may have strikingly deleterious effects on lung function, this is correct.

It has been demonstrated, however, that man can tolerate such accelerations on the centrifuge without apparent serious decrement in his ability to perform flight maneuvers, and the excellent performance of Russian and American astronauts during all phases of orbital and suborbital space flight is a matter of record (20). It appears, therefore, that from a practical viewpoint, protection of astronauts against these pulmonary effects of acceleration may not be necessary. This is a fortunate circumstance since effective practical means of affording such protection are not readily apparent.

Some possible proposed methods are shown in Table 4. Of these, fluid breathing, that is filling of the respiratory space with highly oxygenated physiologic fluid of the same specific gravity and colloidal osmotic pressure as blood, theoretically would provide perfect protection. Such a solution probably is not practical, although mammalian respiration of highly oxygenated solutions has been reported (21). A more practical solution is to flatten out the acceleration-versus-time profile. This requires development in rocket booster technology to provide a rocket engine that can deliver a variable controlled degree of thrust for periods of from 5 to 10 min. If this were possible, orbital or escape velocities could be attained without producing acceleration levels high enough to cause physiologic disturbances of sufficient magnitude to be of practical importance.

The authors are indebted to Dr. D. M. Witten, Section of Radiology, and to Dr. G. P. Sayre, Section of Experimental and Anatomic Pathology, of the Mayo Clinic for their interpretations of the significance of the changes in thoracic roentgenograms and in histologic sections of lungs obtained in the course of centrifuge experiments. The technical assistance of Donald Heglund, Julius Zarins, William Hoffman, and Mrs. Jean Frank also is gratefully acknowledged.

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Gaseous environment and atelectasis[1]

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MAN'S CONQUEST OF SPACE, under water or the interplanetary system, will eventually necessitate a change of the gaseous composition of his surrounding atmosphere. As a first step in this exploration it is obviously safe to take the accustomed atmosphere with you such as we find it today in submarines, bathyscaphes, and the Russian manned satellites. However, this does impose certain limits since it confines man to his sealed space. Should he want to leave his ship, in an emergency or particularly to move on his own either on the bottom of the sea or the surface of the moon, he must change the pressure and the composition of his gaseous envelope. However, quick changes in pressure are hazardous and usually require a change in the gaseous composition as well.

Thus, the atmosphere in a satellite is a compromise between *1*) one which can be tolerated for days and weeks in orbit, *2*) one which will allow the astronaut to leave the ship safely and quickly in a pressure suit, and *3*) one which the engineer can easily provide and maintain efficiently. Let us briefly examine considerations which might be advanced for specifying the cabin atmosphere of Project Mercury. The hardware considerations strive to obtain the smallest pressure differential between the cabin atmosphere and the vacuum outside. A one-gas system is easier to control than a multigas system. Both factors contribute enormously to reducing the payload. On the other hand, the astronaut must have an adequate oxygen pressure. It is simple to predict the lowest total cabin pressure which yields a normal O_2 tension. This is approximately 200 mm Hg. With the water vapor tension of 47, the P_{IO2} = (200 − 47) or 153 mm Hg when 100% O_2 is breathed.

The compromise between the best hardware design and the astronaut's mission settled the pressure of Project Mercury at 250 mm Hg (5 psi) with 100% O_2. Should the astronaut have to engage his pressure suit, which operates at a lower pressure, he could quickly decompress without inviting bends as long as he had been breathing pure oxygen. The bends problem will be discussed by Dr. Bond (3). The somewhat greater than normal O_2 pressure of 250 mm Hg and its possible toxic effects will be taken up by Dr. Welch (36). I would now like to look at some additional problems when living not for hours but for days and weeks at a pressure close to that on Mt. Everest and an atmosphere devoid of inert gas.

EFFECTS OF PRESSURE PER SE

The experimental findings of Berg and Cook (2) and Cook and Leon (9) suggest that the O_2 consumption is reduced with decreasing pressure when normal O_2 tensions are maintained. However, in man Houston and Riley (15) found no evidence of this sort nor did the most recent studies of Johnson et al. (17). It would appear that at present there is little evidence which would support such a direct pressure effect in man.

EFFECTS OF ABSENCE OF N_2 GAS ON METABOLIC FUNCTION

The work in this area has been summarized by Cook and Leon (9). When viewed in light of their previous observations of the effects of pressure per se, it is suggested that the normal metabolism of organisms is stabilized by opposing forces, nitrogen tending to suppress metabolism, while total pressure tends to increase it. While it is well recognized that N_2 at higher than normal pressures begins to have a narcotizing effect on synaptic conduction, additional proof must be brought forward to show that the absence of N_2 gas has a metabolic or neural effect. As will be discussed by the speakers to follow, man has recently been subjected for many days to the absence of all inert gases and no untoward metabolic or neural effects have been demonstrated which can be attributed to the absence of N_2 gas. MacHattie and Rahn (23) have maintained mice for nearly 2 months in an atmosphere of pure oxygen at a pressure of 200 mm Hg. These mice conceived and delivered normal offspring.

Before dismissing the possible metabolic effect of N_2 altogether, attention should be directed to the work of Volskii (35), who suggested that fixation of atmospheric N_2 occurs during the development of the chicken egg and showed that in the absence of atmospheric N_2 it does not develop beyond 5 days. Experiments by W. Robertson in our laboratory, however, have shown that normal chick development continues at least for 12 days at 200 mm Hg O_2 in the absence of all inert gases and

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E. P. Hiatt at the Ohio State University (personal communication) has been able to observe normal development up to 18 days by substituting He gas for N_2. A recent note by Boriskin et al. (5) reports 25% hatchability in a O_2: He mixture. While the recent experiments of Schreiner et al. (33) indicate that inert gases, including N_2, exert a very definite effect on the growth rate of *Neurospera* hyphae, the evidence of an interference in normal metabolic processes of higher forms by the absence of N_2 gas is not impressive.

EFFECT OF ABSENCE OF N_2 GAS ON PULMONARY FUNCTION

It is in this area that considerable evidence exists that the lack of inert gas can affect drastically the mechanical behavior and function of alveoli. In 1960 Ernsting (11) described a new postflight syndrome in R.A.F. fighter pilots after flying the high-performance Hawker-Hunter jet aircraft. The symptoms were coughing, chest discomfort, and difficulty in breathing. Frequently patchy areas of increased density in the lower lung fields were revealed in chest radiographs taken immediately after flight. More recent observations by Langdon and Reynolds (19) confirmed these postflight respiratory symptoms. This postflight syndrome is probably best described by the recent observations of Green and Burgess (14). Six pilots were sent on several identical missions during which they were exposed to about 1,300 G-sec. In one case they breathed oxygen either with G-suit protection or without. In the other sorties they repeated these same maneuvers breathing air. Upon landing each pilot was instructed to talk as little as possible, avoid coughing, and to climb out of the cockpit with the least amount of effort. He was then wheeled from the aircraft to the laboratory for chest X rays and pulmonary function tests. From this detailed report I have assembled certain average values in Table 1. To this I have added recent data of vital capacity changes measured by Hyde, Pines, and Saito (16) on pilots in the human centrifuge at Wright Field. There seems little question that these field tests and laboratory experiments complement each other and indicate considerable lung impairment. These changes can be ascribed to lung collapse which is influenced by three factors—acceleration, pressure suit, and oxygen breathing (or absence of N_2).

While the effects of acceleration and pressure suit on pulmonary complications have already been discussed by E. H. Wood (37) in this Symposium, we would like to dwell on the effects of breathing air or oxygen. Each orbital mission is presently preceded and terminated by exposure to large G forces while breathing 100% oxygen. While in orbit the body is in a weightless state but the oxygen is now at a considerably reduced pressure. While our orbital missions are presently a matter of hours they will soon be extended to days and weeks. Naturally there is some concern about the development of atelectasis since exposure of man for many hours or days to a total pressure of 380 [Comroe et al. (8)] and 418 mm Hg

TABLE 1. *Pulmonary changes after exposure to acceleration*

	Breathing Air		Breathing O_2	
	No suit	With suit	No suit	With suit
1. Postflight symptoms Clinical index of coughing, chest pain, limited inspiration. Max. score = 9	1.0	2.1	4.8	7.0
2. Chest X-ray changes Clinical index of density changes Max. score = 4	1.0	1.3	2.0	3.1
3. Loss in vital capacity; ml Average preflight vc = 5,400	349	790	1406	2179
Loss in vital capacity, % 4. + 3 G_z Acceleration	0	0	0	20
5. + 6 G_x Acceleration			40	

Data in rows 1–3 from Green and Burgess (14); rows 5 and 6 from Hyde, Pines, and Saito (16).

[Michel et al. (27)] has demonstrated lung impairment which can be ascribed to atelectasis.

We therefore would like to address ourselves to the question of the potential hazard of pulmonary impairment when breathing 100% oxygen at reduced barometric pressures. In the absence of N_2 gas one would predict that absorption atelectasis will proceed at a very much faster rate, which is further accelerated by reduction of the barometric pressure. Collapse of lung units will not only reduce the pulmonary compliance and initiate various symptoms described by Green and Burgess (14) but will also increase the venous admixture to the pulmonary circulation and result in arterial unsaturation. It seems worthwhile to describe first a general concept of atelectasis before considering specifically the role of oxygen and barometric pressure on this process and, finally, the methods which are available for the early detection of alveolar collapse.

A GENERAL CONCEPT OF ATELECTASIS

The recent work by Radford (29), Clements (7), and Mead (25) has focused on the importance of the surface tension to the alveolar lining in contributing to the stability of alveolar geometry. To maintain an alveolus in a distended condition the retractile force of the elastic network as well as the force of the liquid film lining the alveolar surface must be overcome. Figure 1 has been modeled after these authors and shows the independent pressure-volume relationship of each of these forces. Line A indicates the pressure required to maintain an expanding elastic network as it stretches around the sphere of an alveolus. Line B shows the characteristic pressure maximum which must be overcome to expand a spherical surface film beyond a critical volume. The greater the surface tension, the higher the pressure maxi-

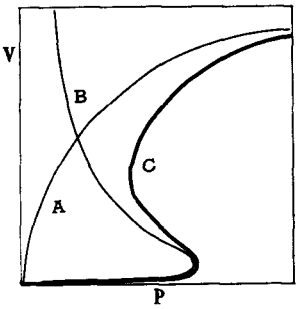

FIG. 1: Pressure-volume characteristics of a spherical elastic network (A) and a liquid film surface lining this sphere (B). Combined characteristics illustrating the theoretical behavior of an alveolus are shown by line C. [Adapted from Mead (25)].

mum. The combined behavior of the surface film and elastic network requires the pressures $P_A + P_B$ and is represented by line C, indicating a region of bistability where the slopes reverse.

This line is redrawn in Fig. 2 to indicate the hypothetical pressure-volume behavior of a typical alveolus. Its normal, stable position is at its FRC volume maintained by a pressure difference of 5 cm H_2O. When its volume is gradually reduced by a fall in pressure, it will follow the heavy line until it reaches the "kink." At this point it becomes unstable and will suddenly collapse to the new volume following the pathway indicated by the dashed arrow. (On reinflation it will follow the heavy line to the right. When it reaches the reversal of slope it will now suddenly pop open following the dashed arrow facing upward.) These are the regions of bistability of a single alveolus reflecting the behavior or surface tension forces as shown in Fig. 1, line B. Should the surface tension forces increase (see below), the pressure-volume behavior would be altered and might be expressed by the dotted line of Fig. 2. On the basis of such a diagram one may explain alveolar collapse in terms of three possible factors.

COMPRESSION ATELECTASIS

It can be seen in Fig. 2 that any force applied to the chest which reduces the distending pressure, P, will move an alveolus from its stable FRC volume toward the unstable point where it will collapse. Negative pressure breathing, underwater snorkeling, and pneumothorax will all reduce ΔP. In the anesthetized dog negative breathing pressures of 10–20 cm H_2O will induce atelectasis as judged by large increases in venous shunting and decreased compliance (21, 34). In man unsaturation of the arterial blood can be obtained by chest binding (6, 24) and possibly by inflation of a pressure suit (22). Finally, compressions of the lung can also be obtained during forward acceleration, but here additional factors contribute to the unsaturation of the arterial blood (37). All of these maneuvers have one thing in common, namely, that the ΔP value is reduced by the application of external pressures. Thus gas is squeezed out of the airway, reducing the gas volume to a point where some of the alveoli collapse and now effectively shunt their capillary blood which contributes to the arterial unsaturation. The large arrow along the abscissa marked

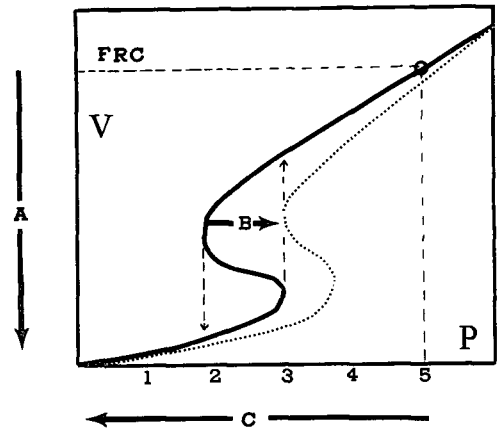

FIG. 2. Hypothetical pressure-volume behavior of an alveolus (line C of Fig. 1). Its normal stable volume is located at its FRC volume supported by a pressure difference of 5 cm H_2O. Heavy arrow, A, indicates the direction of changes which accompany absorption atelectasis; arrow C, the forces which lead to compression atelectasis; while arrow B indicates the consequences of surfactant loss which also leads to atelectasis.

C in Fig. 2 indicates that all forms of compression which reduce ΔP tend to bring the alveolus closer to its unstable collapse point.

LOSS OF SURFACTANT ATELECTASIS

Clements (7) has shown that surfactants are important in reducing the surface tension of an alveolus as its surface area or volume decreases. It can be appreciated from Figs. 1 and 2 that a reduction in surface tension will move the bistability area of the pressure-volume curve to the left. In other words, surfactants protect against collapse in that the critical closing pressure will now occur at a lower volume and distending pressure. In Fig. 2 the heavy pressure-volume curve is supposed to include such a surfactant effect. If, on the other hand, surfactants are not produced or destroyed and consequently the surface tensions are not appreciably reduced when the volume becomes smaller, the pressure-volume behavior of this same alveolus might be represented by the dotted line. The heavy arrow marked B would represent the shift of the bistable region to the right due to surfactant loss. Under such circumstances the alveolus is less stable since its collapse volume and pressure are closer to the normal FRC volume.

The question has been raised whether O_2 breathing will destroy or denature the lipoproteins responsible for the normal surfactant behavior. While this obviously becomes an important consideration in our orbital space missions, the in vivo exposure of rat lungs to 6 atm of oxygen has so far shown little inactivation (4).

ABSORPTION ATELECTASIS

The only other way a gas volume can be lost from an alveolus is by absorption into the blood of the pulmonary circulation. This necessitates first blockage of an airway which may be produced by mucus, edema fluid, or

physical compression of the airways such as may occur during certain types of acceleration. This general behavior is designated by the large arrow marked A along the ordinate of Figure 2. While the clinical literature recognizes various types of atelectasis it would appear that there are three fundamental mechanisms which may lead to the collapse of an alveolus. Either the gas is pressed out of an alveolus by an external force which lowers the distending pressure, ΔP, until the collapse pressure and volume are reached (compression atelectasis) or the gas is absorbed by the pulmonary circulation after blockage of an airway (absorption atelectasis). Finally, an alveolus may collapse because the critical collapse pressure and volume have been moved into the normal FRC volume due to loss of the surfactant (loss of surfactant atelectasis). In practical situations atelectasis may be induced by any one or a combination of any of these factors.

Rates of Absorption Atelectasis

The differences in pulmonary function loss after breathing air and O_2 are well illustrated in Table 1. We must now inquire to what extent a lowered barometric pressure might influence collapse. One can predict the rate of lung collapse after blocking the airway when *1)* air, *2)* oxygen at 1 atm, and *3)* oxygen at .25 atm is breathed. The respective ratios are 1:60:360 (30). Any tendency therefore for occlusion of an airway, be it mucus secretion, edema fluid, or a slight respiratory infection, might lead very rapidly to collapse if O_2 is breathed at reduced pressures. For this reason we must test these predictions by measuring the rate of collapse of a lung under these conditions.

This has been done in animals and man and closely confirms the predictions. Dale and Rahn (10) used bronchospirometry to measure the collapse rate of one lung in the dog while the other lung inspired various gas mixtures. This experiment showed that if both lungs were initially filled with oxygen, then the rate of collapse was indeed about 60 times faster than if the animal had been breathing air. The N_2 gas due to its low solubility acts as a brake and of all naturally occurring inert gases is the best brake (28). To test the effects of barometric pressure (when breathing 100% O_2) upon the rate of lung collapse Robertson and Farhi (32) used anesthetized rats. The animals were placed in a plethysmograph with a tracheal cannula which led to the outside. Thus they were exposed to various pressures from 200 to 1500 mm Hg while breathing oxygen. When the trachea was occluded the change in total body volume could be recorded, which was assumed to be equal to the change in lung volume. Figure 3 shows that at the normal ground level pressure of 750 mm Hg the average time for complete collapse of the FRC volume was 21 sec and 3 sec at 200 mm Hg.

These observations led to a general formulation of time required for complete collapse (after obstruction) of any

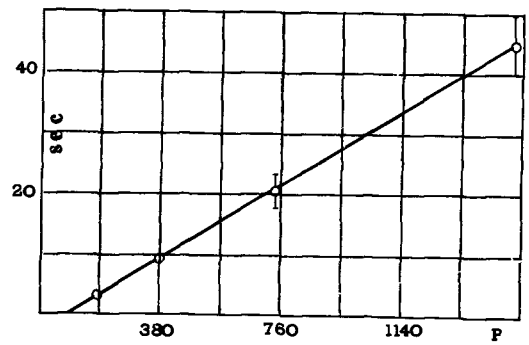

FIG. 3. Absorption atelectasis. Time required for complete collapse of the FRC of rats when trachea is obstructed after breathing oxygen at various barometric pressures, P_B. Vertical bars, SE. At P_B = 200 SE is too small to be indicated. [Robertson and Farhi (32)].

unit of the lung provided it received a pulmonary blood flow proportional to its volume,

$$t = V_L(P_B - P_{H_2O} - P_{CO_2})/\dot{V}_{O_2} \cdot 864 \qquad (1)$$

where t = time in minutes to absorb the oxygen; V_L = lung volume to be occluded, BTPS — ml; $V_L(P_B - P_{H_2O} - P_{CO_2})/864$ = the volume of oxygen in the lung STPD — ml; 864 = constant for conversion of the BTPS volume to STPD volume; and $\dot{V}_{O_2}$ = the rate of oxygen absorption ml/min STPD. It might be pointed out that for total volume collapse one need not consider separately the absorption of CO_2 and water vapor. The former becomes concentrated during the volume shrinkage and will pass into the blood. It is carried "piggyback" along with the oxygen into the blood. The water vapor will condense. Thus for a given lung volume, oxygen uptake, normal alveolar P_{CO_2} of 40, and a pH_2O of 47 *equation 1* can be simplified for general application to the expression that time for collapse is proportional to the

$$\text{(barometric pressure} - 87) \text{ or } t = k(P_B - 87) \qquad (2)$$

It can be seen in Fig. 3 that the intercept was close indeed to 87 mm Hg. The k value of *equation 2* is the slope of the line and is proportional to the ratio of lung volume/oxygen uptake.

In man similar experiments have recently been conducted by the simple procedure of measuring the change in lung volume during breath-holding. Lee (20) had six subjects hold their breath with full inspiration at various simulated altitudes up to 40,000 ft (P_B = 141). Klocke and Rahn (18) conducted similar experiments at ground level. Figure 4 shows the average changes in lung volume with breath-holding time after breathing 100% O_2 at ground level and altitude. All starting volumes are vital capacities. These are converted to STPD volumes to emphasize the decreasing number of gas molecules per unit volume to be absorbed by the circulation as the barometric pressure decreases. It will be noted that the slopes of these four lines are approximately the same; the exact values, $\Delta V/\Delta t$ from ground level to 40,000 ft

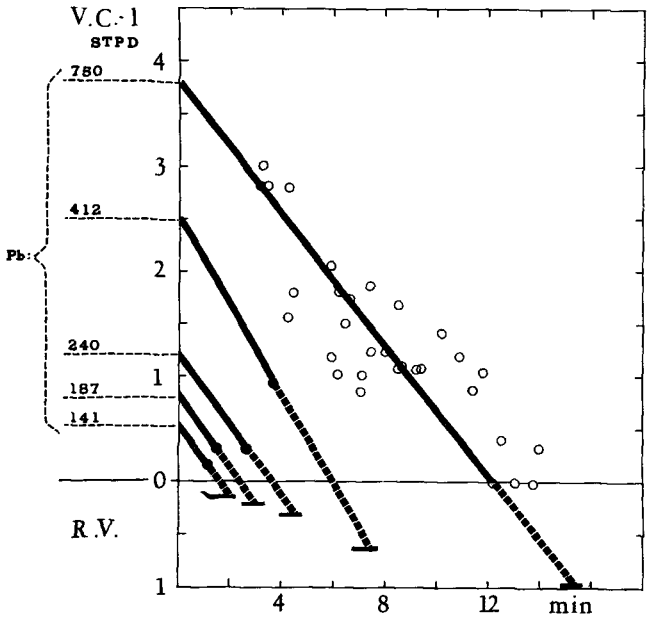

FIG. 4. Changes in lung volume of man when breath is held after maximal inspiration when breathing oxygen at different barometric pressures. All lung volumes are expressed in unconventional standards, namely STPD; time in minutes. Open circles are individual experiments obtained at ground level (18) and top line represents average slope extrapolated to residual volume. Lower 4 lines were reported by Lee (20) and indicate the average lung volume changes of 6 subjects at various altitudes. All lines extrapolated to their zero lung volume (by assuming that residual volume = .25 VC) and indicate predicted time for complete collapse. Note that slope, $\Delta V/\Delta t$, is about the same at each altitude and averages 340 ml STPD/min.

altitude were 313, 420, 324, 335, and 315 ml STPD/min and are close to the predicted resting O_2 uptake. This lends further support for the general application of *equation 1*.

The plethysmographic recordings of the rat (32) show that once the trachea is obstructed $\Delta V/\Delta t$ is constant throughout the whole period of collapse. We have therefore extrapolated the lines of Fig. 4 until they intercept zero lung volume. The residual volume was assumed to be equal to .25 vital capacity and thus varied at each altitude as shown by their individual intercepts. From these intercepts at zero lung volume we have a predicted time for complete collapse of the lung when the initial lung volume is at full inspiration. At ground level this time averages 15.3 min and at 40,000 ft it is just less than 2 min.

These predicted times for complete collapse, that is an airless lung, have been plotted in Fig. 5 against the barometric pressure. They provide a reasonable straight line, A. According to *equation 1*, the slope of this line is proportional to the initial lung volume (BTPS) divided by the oxygen uptake (STPD). If we have an average $\dot{V}O_2$ = 340, then the initial lung volume (BTPS) according to *equation 1* is approximately 7,000 and is a reasonable figure for the experiments of Fig. 4, namely, a VC = 5,600 and an RV = 1,400 ml.

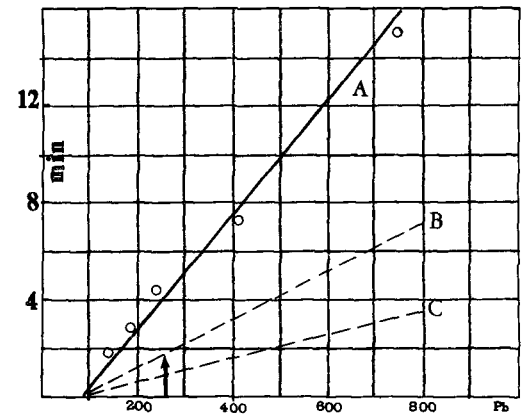

FIG. 5. Time for complete collapse of lung volume after breathing oxygen at various barometric pressures. The 5 circles are taken from extrapolated values of Fig. 4. They are connected by line A, which according to *equation 1* represents a total lung capacity of 7,000 ml BTPS and an average $\dot{V}O_2$ of 340 ml/min. Middle line, B, represents *equation 1* when FRC = 3,000 and $\dot{V}O_2$ = 340. Lower line, C, represents same lung volume but twice the oxygen uptake. Arrow indicates the barometric pressure at 5 psi.

The middle line, B, in Fig. 4, predicts the collapse time for the whole lung or any part of it when the initial volume is at an FRC of 3,000 ml and the $\dot{V}O_2$ = 340 at rest. The bottom line, C, has the same FRC volume but the oxygen consumption is doubled. Lines A, B, and C all intercept at 87 mm Hg. The arrow is the pressure at 5 psi, the pressure of the Mercury capsule. Thus for a normal FRC one would predict an obstructed lung unit to become airless in 1.8 or .9 min depending on the oxygen consumption. An aviator at 40,000 ft, holding his breath at FRC with a normal O_2 uptake, would have an airless lung in 18 sec or at 9 sec if we doubled his oxygen uptake.

DISCUSSION

All we have presented so far are experimental findings in animals and man which support a simple equation which predicts the time required for a lung unit to collapse after obstruction when breathing O_2 at various barometric pressures. Whether these fast collapse rates also imply a potential danger to the astronaut orbiting for days in such cabin atmospheres is difficult to assess. This evaluation must come from pulmonary function tests on subjects kept for many days in simulated space cabin environments and will be discussed later by speakers on this program.

However, we believe there is little doubt that during entry and re-entry from orbit when man is subjected to high G forces the difference between the presence and absence of N_2 gas in the breathing mixture may be important. We remind you again of the striking differences in loss of lung volume shown in Table 1. When similar G forces are applied at reduced atmospheric pressures one might expect such differences to become even greater.

One may describe the 100% oxygen atmosphere at reduced pressure as a potentially hazardous one from

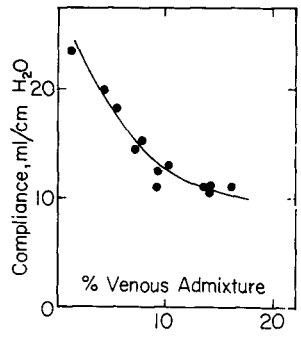

FIG. 6: Changes in compliance and venous admixture with increasing atelectasis in the dog. [Farhi and Velasquez (12)].

the point of view of maintaining all alveoli open during the normal, everyday stresses to which a lung is subjected. There are many questions which still remain to be answered. What are the possible hazards of a slight respiratory infection? Will increased mucous secretion and its temporary blockage of small airways precipitate such rapid collapse that alveoli cannot be easily re-expanded? Would a naturally occurring collapse, in itself, lead to infection? More information must be obtained to show whether or not such atmospheres have any effects upon the normal production of surfactants. Should these be impaired by the oxygen atmosphere, the surface tension will not decrease when the alveolar volume is reduced and thus alveolar collapse will occur more easily. To what extent are naturally occurring deep sighs able to re-expand collapsed units? If collapsing units are normally the trigger for sighing, then we must learn whether this is still sufficient in the new atmosphere or whether repeated deep inspiratory maneuvers must be initiated. Finally, we must not forget that all our previous considerations also apply to another closed but perfused body gas pocket, namely, the middle ear. Experience with these oxygen atmospheres at low pressure has shown that "ear clearing" becomes a problem and that particularly during sleep the Eustachian tubes must be periodically opened to admit new O_2 gas into this collapsing cavity.

Procedures for Testing Atelectasis

It becomes obvious that if we are to explore the potential danger of this gaseous environment on lung function, we must have sensitive tests which not only tell us when large functional losses have occurred but, hopefully, will allow us to detect the initial stages of atelectasis. Neither space nor time allows us to go into detailed appraisal of present day methods.

Chest X ray. While this is a time-honored method, it will unfortunately not detect uniformly distributed small areas of collapse. In addition, it is difficult to quantitate the pulmonary tissue loss.

Vital capacity. While this has, a priori, great appeal, it may only be useful when relatively large volumes are collapsed or obstructed as shown in Table 1. It should be pointed out that this maneuver in itself is a corrective measure and may thus obscure initial collapse. Furthermore, it is more than likely that if the amount of collapse is small and does not open up during a full inspiration, the more compliant areas of the lung may fully compensate for the loss of the collapsed areas. Finally, a word about the standard deviation of a vital capacity measurement. Experience has shown that this is equal to 2–3 % of the vital capacity (31). Thus, changes greater than 100–150 ml are necessary before much reliability can be placed in this method. For these reasons probably only major functional loss can be detected by this method.

Pulmonary blood shunting. If the perfusion to a freshly collapsed area is maintained (1), its pulmonary artery blood will remain unoxygenated and can thus be detected by conventional methods of shunt measurements. This requires arterial blood samples. However, it is extremely sensitive and shunts as small as 0.5 % of the total pulmonary blood flow can be detected when oxygen is breathed. For example, normally anesthetized dogs will indicate a shunt equal to about 5 % of the pulmonary blood flow. When their lungs are briefly inflated above normal value, this shunt is immediately reduced to about 1 % but gradually increases again when they resume spontaneous breathing (13). This large shunt is explained by alveolar collapse which is temporarily opened by re-expansion of the lung.

Pulmonary compliance. Similarly, it has been shown that lung compliance decreases with time in anesthetized dogs but can be quickly restored by temporary re-expansion of the lung only to decrease again when spontaneous breathing is resumed (26). The current explanation is that the reduction in compliance reflects the collapse of alveolar units and thus provides another sensitive measure of minor pulmonary impairment.

Shunt and compliance. Recently Farhi and Velasquez (12) have determined simultaneously the changes in total chest compliance and shunting in dogs with increasing atelectasis. Figure 6 shows the changes in venous admixture and the simultaneous changes in compliance. It will be noted that this is not a 1:1 relationship and that the largest changes in compliance occur during the initial increases in venous admixture. If such a curve could be established for man, it would suggest that changes in total chest compliance might be a very sensitive test for detecting the early changes of lung collapse.

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Inert gas components for space capsule atmospheres

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Of the human environmental factors to be studied in connection with our national program for manned space travel, the atmosphere to be breathed by the astronaut would seem to be an important item. Notwithstanding, it is apparent that less physiological research has been devoted to respirable atmospheres than to any other major component of the man-machine system designed for outer space exploration. To a degree, this neglect is understandable. Since man is an air-breather, an atmospheric environment providing the rough proportions of air should be satisfactory for prolonged exposure. On the other hand, oxygen could surely be employed as a single gas for short journeys and might be acceptable for long-term utilization. Although somewhat lacking in imagination, this approach permitted simplicity of engineering design and seemed to require little or no additional experimental effort. Accordingly, it was established that the respirable atmosphere of Mercury and Gemini orbital flights would consist of 100% oxygen, while that of Apollo, a longer mission, would be approximately 50–50% oxygen–nitrogen.

Following the successful series of manned space probes culminating in the multiorbital mission of Col. Glenn, a reappraisal of this concept was accomplished. The dual-gas proposal for Apollo posed undesirable complexities of stowage, mixing, and delivery, which could largely be overcome with acceptance of a single-gas oxygen system. Since no physiological problems were encountered in the latest Mercury flight, the decision was made to adopt a pure oxygen system for the much longer mission aimed at moon transit.

Despite the logistic convenience of such a single-gas system, however, physiological and operational hazards of an oxygen atmosphere may yet require introduction of one or more inert gases into the proposed breathing medium. From a physiological point of view, pure oxygen—even at reduced partial pressures—has a demonstrated toxicity in several parameters. Apart from the additive effect of high G loads, oxygen is productive of varying degrees of pulmonary atelectasis. At slightly higher than planned operational pressures, the effects of this gas on the central nervous system with chronic exposure could be serious and permanent. Finally, there is evidence that chronic oxygen exposure may have adverse effects on the erythrocyte system of human subjects. Perhaps the most formidable objection to use of pure oxygen, however, is that of fire hazard. Regardless of partial pressure, exposure of organic elements to oxygen for extended periods will result in saturation and possibility of explosive ignition. Considering the opportunity for spark formation in the space capsule, this possibility alone may dictate the requirement for an inert gas in space capsule atmosphere.

A perennial problem of high-altitude exposure is that of bends, or decompression sickness. It is generally believed, however, that adequate denitrogenation will serve as an absolute preventive measure against this pressure accident. Recent experimental data tend to discredit this belief. It now appears that after extended exposure to a pressurized atmosphere of pure oxygen, this gas may take the place of nitrogen as a causative factor in decompression sickness. At present, research effort has not been sufficiently extensive to afford a clear-cut answer to the problem. There is nonetheless good evidence that use of multiple inert gas mixtures will drastically improve bends susceptibility in deep sea divers. Possibly this mixed-gas concept should be incorporated into the space research program, where a broader combination of inert gas could be utilized.

If, as seems probable, a mixed-gas system will be required for space probes, it might be useful to consider possible advantages of using inert gases other than nitrogen for addition to oxygen. Briefly, examination will be made of the physical and biological properties of several inert gases which might be thus employed.

In space travel, where ambient pressures will range from 5 to 7 psia, it is possible to consider a much wider range of inert gases than in the case of high-pressure exposures. In deep sea diving, one can utilize only those inert gases of lower molecular weight than nitrogen. Such is not the case with space existence, where low partial pressures will obtain, and inert gases of higher weight might be employed with relative freedom from the narcosis and respiratory effects of dense atmospheres.

In examining the inert gases available as space atmosphere components, it is necessary to consider the effects of each gas on metabolism and state of conscious-

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ness, susceptibility to decompression sickness, and the over-all logistic and operational advantages of each gas. For the purpose of simplicity, each inert gas candidate will be treated separately in the discussion.

NITROGEN

As previously described, a 50–50 N_2–O_2 mixture was formerly proposed for the Apollo mission. The stated reasons for the choice of nitrogen in this case, derived from several sources, are as follows: *a*) nitrogen is normally breathed by man; therefore it is the best possible inert gas, and is needed for normal mammalian economy; *b*) the physiological effects of nitrogen are clearly understood, whereas the biologic impact of other inert gases has not been adequately explored; or *c*) nitrogen is plentiful, cheap, and lends itself to cryogenic storage. Of these points, only the latter seems completely valid. There is no scientific evidence that gaseous nitrogen is necessary to man's biologic processes, or that it is preferable, physiologically, to certain other inert gases. The argument that our present state of knowledge of other inert gases is incomplete should be a spur, rather than a bar, to further investigation into possible uses of these elements. Finally, while admitting the economy and logistic simplicity of cryogenic nitrogen, these features need not dictate finally the choice for an environment in which the physiological welfare of the capsule occupants is a major consideration.

HELIUM

Of the handful of inert gases other than nitrogen which might be considered for use in a spacecraft, we have, in general, the greatest familiarity with helium. Over 30 years ago, Barach (1) demonstrated clearly that rodents could survive intact for long periods in an atmosphere composed solely of helium and oxygen. Recently reported work at the Naval Medical Research Laboratory (6) has confirmed Barach's findings, and demonstrated that five species of mammals, including primates, could be maintained in excess of 2 weeks in a nitrogen-free atmosphere made up of helium and oxygen. In this latter work, extensive biochemical, physiological, and histological examination of the experimental animals revealed no abnormalities. Thus, impressive evidence is available to indicate that helium could be utilized as an inert gas component of spacecraft atmosphere without deleterious effects on human occupants.

What advantages might accrue from such a use of helium? From a physiological point of view, it might readily be said that a helium-oxygen atmosphere would be the atmosphere of choice for prolonged space travel. Without elaboration, one might cite recent findings of Workman et al. (5) demonstrating apparent extension of decompression parameters through use of helium and suggesting a factor of protection against altitude bends. Under certain experimental conditions, it has been shown that a helium component offers considerable protection against oxygen atelectasis. Finally, the work of Ebert, Hornsey, and Howard (4) indicates a reduction in sensitivity of growing organisms to radiation in the presence of a helium atmosphere.

Logistically, there is much to be said for the use of helium. Because of its thermodynamic properties, a helium component in cabin atmospheres would significantly prolong the life of electronic elements and permit human tolerance of higher cabin or suit temperatures. Recalling the heat problems which were prominent in the two recent orbital flights, this might be a potent consideration. Again, from the reports of Hitchcock and his group at Ohio State University (3), one finds a compelling logistic argument in favor of helium, in comparison of leak rates versus weights of cryogenic-stored helium and nitrogen. In addition, it must be considered that helium, unlike the heavier inert gases, will not produce radioisotopes of significance under ionizing radiation bombardment of a neutron flux secondary to cosmic-ray impingement on the capsule or its contents.

On the debit side of the ledger, some words are in order relative to use of helium. In the first place, the very thermal conductive properties which make the gas so attractive to the electronic engineer could pose a minor problem to the astronaut. In a helium-oxygen atmosphere, rapid loss of body heat is a significant factor. It is anticipated that a series of planned human exposures in a HeO_2 atmosphere, to be performed a few months hence, will give considerable information on this score. Presumably, higher cabin temperatures and humidity levels, plus body protection at certain periods of space travel, will solve the problem. Obviously, more research is needed in this area.

Second, the problem of communication in the HeO_2 atmosphere must be considered. The octave shift of the human voice in a helium-rich atmosphere is recognized and is a threatening item in deep sea diving communication. Recent research at several laboratories, however, indicates that much of this phonic shift can be corrected electronically, and it is anticipated that research efforts in the coming year will solve the problem.

Finally, the logistic problem of cryogenic stowage of helium deserves attention. The boiling point of liquid helium is -452 F, as opposed to the boiling point of liquid nitrogen at -320 F. On this basis, it is argued that stowage of the latter product is simpler than is the case with helium. In view of the fact that liquid helium can now be transported and stowed with a loss rate of less than 2% per 24 hr, this argument loses a great deal of its force. Add to this the fact that, in the Apollo design, the stowage of liquid gases will be in the service module, exposed to the constant low temperatures of space and shielded from sunlight exposure, and the argument in favor of nitrogen loses much force.

In summary, a potent debate can be made for use of helium as the inert gas component for space capsule atmospheres. From the point of view of breathing resistance, decrease in atelectasis, heat control, and electronic

instrument life, helium has much to offer. The factors of increased cost, difficulties of cryogenic storage and transport, adverse effects on body temperature and voice communication are undeniably real, but probably amenable to projected research efforts.

A final word is in order. Contrary to prevalent belief, the government of the United States is no longer sole custodian of the helium supply of the world. It is now quite certain that all other countries have access to almost unlimited supplies of this important inert gas.

ARGON

The inert gas argon deserves some consideration as a possible atmosphere component for space travel. This gas, which makes up almost 1% of the earth's natural atmosphere, has an assigned atomic weight of 39.9—commonly known as argon 40, as opposed to its radioisotope, argon 41. The "lazy gas," first described by Rayleigh and Ramsay in 1895, has narcotic effects slightly greater than those of nitrogen. It is readily available, relatively cheap, and compares favorably with nitrogen in respect to cryogenic storage, sound velocity characteristics, and general transport properties. In company with other members of the inert gas family, argon demonstrates the feature of reducing radiosensitivity of oxygen-dependent cells. The relative scale of radiation protection values for all of the inert gases has not yet been determined by research, though this would seem to be a critical area for space travel experimentation. It would appear that the scientific world, finding little use for argon, has made no serious effort to consider the total physiological effects of the gas on mammals.

Considering possible use of argon in the capsule atmosphere, many negative values come to mind. In the first place, the gas is so soluble in body waters and lipids that it would surely present a serious casualty problem with rapid reduction of pressure unless combined with several other inert gases. Again, even ignoring the increased narcotic action of the gas, one must consider the density of argon, with respect to the work of breathing. Admittedly, at 7 psia, this would be less than that of breathing air at 1 atm. Nevertheless, this additional energy expenditure could be an item worthy of consideration in the total summary of space travel factors.

Finally, it must be recognized that the gases of the capsule will be exposed to a flux of ionizing radiation. Argon 40 is readily altered, under such circumstances, in partial conversion to argon 41, which could offer a serious toxicological hazard to capsule occupants exposed for a period of days or weeks. In sum, it would appear that argon, as an inert gas component for the atmosphere of a space capsule, offers little promise at this time.

KRYPTON-XENON

These two inert gases are treated together because however fascinating they might be from the point of view of normobaric or hyperbaric effects on man, they are not worthy of consideration as components of respirable atmospheres for space travel. They are unsatisfactory with respect to decompression requirements, breathing medium density, or narcosis capacities. In addition, they are readily productive of assimilable radioisotopes, which in turn are physiologically active. Clathrate formation with certain of the body organic phenol compounds is a distinct, though unproven, possibility. Finally, these gases are expensive, do not lend themselves to cryogenic storage, and would present heat-transfer problems which would negate their use in space travel.

NEON

As a possible inert gas element of respirable atmosphere for man, whether under high or low ambient pressures, neon is a very intriguing gas. Remarkably, almost no biological research has been accomplished with this element. In an over-all estimate of the biological properties of neon, one might estimate that its effects would lie between those of nitrogen and helium, coming somewhat closer to the latter. It must be emphasized, however, that no significant values are available relative to physiological effects of this gas. Importantly, no data are to be found concerning solubility of neon in biological lipids.

Logistically, the gas has much to offer for use in space travel. It is the most compressible of all potentially useful inert gases, adapts to cryogenic manufacture and storage, exhibits properties of heat transfer and sound velocity close to those of nitrogen, and appears to offer a ratio of leak rate to dense weight which gives advantage over any inert gas under consideration.

In view of the attractive potential of this gas for human existence under conditions of both high and low ambient pressures, it would seem imperative that active physiological research should be pursued immediately with neon. If current speculations are partially valid, the benefits of such research must be tremendous.

SUMMARY

In brief narrative, an attempt has been made to survey the potential values of several inert gases for use in space cabin atmospheres. In this consideration, hydrogen has been excluded, since elevated O_2 percentages required in such a breathing mixture would result in a highly explosive mixture. The remaining available inert gases, i.e., helium, argon, neon, krypton, and xenon, have been briefly examined. It is concluded that two of these elements, namely, helium and neon, are worthy of serious consideration for use in space travel. Of the former, considerable information is available and all favorable; of the latter, little of biological significance is known, but this deficit must quickly be satisfied in the interest of proposed manned probes of both inner and outer space.

In conclusion, I wish to quote directly from the excellent publication edited by Gerhard A. Cook, *Argon, Helium, and the Rare Gases* (2):

"Man's need to control his environment under conditions which may euphemistically be called abnormal must include close control of the gaseous composition of his atmosphere for prolonged periods of time. The demands of space-flight, very-high-altitude transport, long-term undersea travel, and exploration of ocean depths may involve such physiological problems as exposure to radiation; the mechanics of pulmonary function in high, low, and rapidly changing gravitational fields; maintenance of function at high pressure; and so on. Helium and other noble gases have been shown to be capable of playing a modifying role in one way or another on the cell or whole organism subjected to these or similar conditions. . . . These, and other questions, remain to be answered by further research."

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Physiological interactions and gaseous environment in manned exploration of space

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In spite of strenuous early objections by some biological scientists to the concept of manned space flight, it is now evident that manned flight will be necessary for the success of detailed scientific explorations of the moon and planets. While many tasks will continue to be carried out by unmanned instrumented vehicles, many aspects of exploration remain which no machines yet conceived can perform. Man has created complex and wonderful forms of mechanical devices and electronic computers; however, it remains true that the only device capable of an integration of all functions such as remembering, recognizing, learning, thinking, reasoning, judging, reacting, communicating, and logically altering a previously programed sequence of events is man himself (8). The question is no longer whether man will have a place in space exploration, but how to assure that he will be able to utilize his priceless superiority over the machine, his ability to exercise judgment in the face of the unexpected (8).

Questions of respiratory physiology loom prominently in the development of spacecraft and propulsive vehicles for truly extended, manned flight. The successes in US and Russian earth-orbital flight, of great technological importance, have depended upon previously existing information concerning respiratory function. Success of future flights such as the nearly 2 weeks' earth-orbiting scheduled for Gemini and for the lunar landings of Apollo will depend on continued physiological study. Flights of such extreme duration that many months of closed-system existence will be involved require studies not yet even planned.

The major reasons for uncertainty regarding the respiratory implications of forthcoming manned space flight relate to the extreme duration of exposure to stresses and to the manner of interaction of different environmental and physiological variables over these prolonged periods of closed-system existence. This presentation will emphasize the relation of these important considerations to the choice of the gaseous environment for various missions in the evolution of manned space flight.

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GASEOUS ENVIRONMENT

Thus far, in the manned space flight programs of the US and the USSR, three distinct choices of an intracapsular gaseous environment have been made. Pure oxygen at a low total pressure (280–260 mm Hg) is being employed for Project Mercury and considered for Project Gemini. The 5-day orbital flights accomplished by the USSR are presumed to have utilized a respirable oxygen-nitrogen atmosphere essentially the same in composition and pressure as air at sea level. The lunar spacecraft for the Apollo program was originally scheduled to use a nitrogen-oxygen mixture. This was to have been 50% O_2 in N_2 at a total pressure of about 390 mm Hg, less than the atmospheric pressure at sea level. However, pure oxygen at a low total pressure is still under consideration for this mission. In each instance it appears that the same atmosphere is intended to be sustained throughout the entire mission, whether in the initial orbiting flights of a few hours or the approximately 14-day flights now in preparation.

It is important to recognize that there are many other possible gaseous environments which could be employed for manned space flight; the choice of a suitable one will be made many times and will depend on engineering as well as biomedical considerations. Unfortunately, while engineering commitments involved in the multiyear task of developing manned spacecraft require that such decisions be made early, our considerable ignorance of physiological tolerance to unnatural gaseous environments makes a rational choice difficult at the early stages necessary for spacecraft development. Studies over the entire duration of the proposed exposure are usually required. However, due to the cost and complexity of such long-duration studies on man, physiological tolerance studies thus far have tended to occur late and to be limited to investigation of a particular gaseous environment already selected on engineering grounds. While this approach has sufficed for previous flights, it has serious limitations for the future. Since it leaves un-

answered many questions such as the basic limits of tolerance and the reversibility of physiological and pathological changes induced by unnatural gaseous environments, we continue to be unable to predict reactions to unusual circumstances.

PROBLEMS IN ATMOSPHERE SELECTION

The problem of selecting a gaseous environment for a particular manned space flight is complicated greatly by the multiplicity of physiological factors which are directly or indirectly related to the gaseous composition of the atmosphere within the capsule (7) and by the difficulties concerned with the physical and engineering aspects of spacecraft mass, design, construction, control, and reliability. These physical considerations lend themselves fairly readily to detailed study, compromise, and solution. The physiological implications are far less adaptable to study and not easily quantitated even when identified.

Table 1 indicates only a few of the fundamental physical considerations involved in selecting a respirable gaseous environment for the closed life-support system of a spacecraft. These may, for present purposes of emphasis on respiratory physiology, be considered as features of the internal environment of the space capsule or as the external gaseous environment of the occupants.

Such features of a capsule atmosphere determine the nature and severity of the stresses encountered by the astronaut. Table 2 indicates that the choice of a gaseous environment involves not only many broad considerations of respiratory physiology but also critically affects the astronaut's judgment, his ability to perform exacting tasks and to communicate. The gaseous environment may also conceivably be responsible for various forms of intoxication, for failure of temperature control, for alterations in water balance, and for severe changes in the blood, skin, and gastrointestinal system. By interfering with the normal patency of gas-filled body spaces, a particular gaseous environment may even predispose the astronaut to infection.

The biomedical and physical factors of Table 2 are related to the characteristics of an intracapsular gaseous environment, not in any simple manner, but in exceedingly complex ways. Table 3 illustrates, if only qualitatively, a number of these interrelationships or interactions to which attention must be given in validating a particular choice of gaseous environment or in

TABLE 1. *Features of gaseous environment*

Duration of exposure
Total pressure
Oxygen pressure
Carbon dioxide pressure
Inert gas pressure
Water vapor pressure
Pressure of gaseous intoxicants
Heat capacity of gas
Velocity of gas movement
Temperature
Leakage rate of capsule

TABLE 2. *Physiological and pathological considerations related to unnatural gaseous environments*

Arousal state
Performance level
Communication
Time of useful consciousness
Explosive or rapid decompression
Bends and aeroembolism
Aerotitis and aerosinusitis
Alveolar collapse
Respiratory activity
Oxygen toxicity { pulmonary, rhinologic, conjunctival }
Anoxia
Radiation sensitivity
Acclimatization { low P_{O_2}, high P_{O_2}, high P_{CO_2}, low temperature, high temperature }
Hemoglobin formation { suppression, stimulation }
Hyperthermia
Infection { middle ear, respiratory, cutaneous, systemic }
Cutaneous desiccation and maceration
Alteration of cutaneous and gastrointestinal flora
Autointoxication
Water balance

TABLE 3

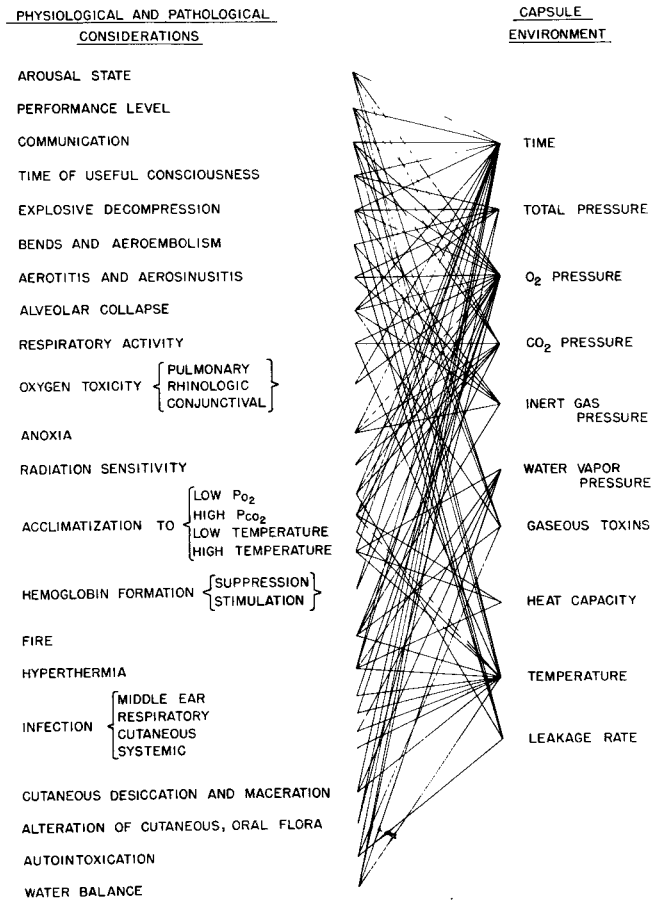

TABLE 4. *Interactions of factors related to gaseous environment*

Physiological Interaction	Findings	References
P_{O_2}, P_{CO_2}, respiration	Decreased alveolar P_{O_2} increases respiratory reactivity to P_{CO_2}, lowers central P_{CO_2}.	4, 6c, 12, 15, 17
	Increased alveolar P_{O_2} leads to decreased respiratory reactivity to P_{CO_2}, raises central P_{CO_2}.	10, 10a, 12
Hyperthermia, P_{CO_2}, P_{O_2}, respiration	Fever increases respiratory response to elevated P_{CO_2}, perhaps to decreased P_{O_2}. Influence in hyperoxygenated state not known.	2, 6a
P_{O_2}, P_{CO_2}, brain circulation	Brain circulation in hyperoxia is a function of arterial P_{CO_2}.	6d, 10b
	Increased brain circulation of arterial hypoxia modifiable by alteration of arterial P_{CO_2}.	5, 6b, 14a, 18
Ambient pressure, respiration, water balance	Hyperventilation dehydration at low ambient pressure.	
P_{O_2}, inert gas, radiation sensitivity	Very low P_{O_2}, high inert gas concentration in tissues reduces radiation sensitivity.	7, 16
P_{O_2}, drugs, intestinal flora	Drugs and hyperoxygenation may alter intestinal flora.	3
P_{O_2}, P_{CO_2}, hemoglobin formation, acid-base state	Decreased P_{O_2} leads to decreased arterial P_{CO_2} and bicarbonate, increased hemoglobin formation.	4, 14
	Increased P_{O_2} may lead to decreased hemoglobin formation, arterial P_{CO_2}, and bicarbonate.	3, 20
Inert gas, pulmonary competence, infection, acceleration.	Absence of inert gas may lead to diffuse atelectasis, infection may alter rate of development and reversibility. Atelectasis may predispose to infection. Acceleration may aggravate all.	1, 3, 7, 9, 11, 13, 19

determining the limits of human tolerance to environmental extremes. Table 4 suggests the nature of certain of the better known physiological interactions.

Lack of information concerning the manner of interaction of such physiological and environmental factors offers an important reason for the understandable uncertainty involved in selecting a particular gaseous environment for manned space flight (7). Some of these interactions may compound the dangers inherent in each of the separate stresses. Other interactions may prove to have practical usefulness. Since few of either the disadvantages or uses of these physiological interactions have been thoroughly explored, developing the ability to predict the reactions of man in truly prolonged space flight will require extensive and strenuous physiological studies. At present, knowledge of these interactions is derived primarily from investigations of acute exposure, but the interest of physiologists in quantitative studies of chronic alterations is continually increasing and promises to improve the awareness of man's responses to interacting changes in his environment.

There is still another, more important, basis for the continued uncertainty in effecting the many compromises between engineering and human factors in choosing a gaseous environment for future spacecraft. This is the lack of quantitative information concerning the extremes of environment which are physiologically tolerable for indefinite periods (9). Even less data exist relating quality of judgment and performance to the degree of physiological stress. This lack of information concerning man is understandable since, except for diving, mountain climbing, and aviation, exposure of man to unusual gaseous environments has, until recently, been brief if a severe stress was involved and has been mild in degree if the duration was to be prolonged. The development of extensive quantitative information defining tolerance limits and the basis for such limits will prove important in a great variety of situations which will be encountered in unusual human endeavors. The national programs involving human extra-atmospheric existence in spacecraft, in prolonged diving, and in submarines provide an opportunity for broadening and strengthening the investigative interest in the tolerance of normal man to chronic environmental stresses. Support must be given to the elaboration of such basic information even though particular studies may not appear to be linked to an existing space flight project.

CONCEPT OF A SINGLE GASEOUS ENVIRONMENT

The necessity for making compromises among these many factors and the problems in selecting gaseous environments for current space flight programs have led to the approach in which a single state of gaseous composition and pressure is selected and then closely controlled during the entire flight. Since the decision regarding gaseous composition is based primarily on the expected maximum total duration of a space flight, it usually involves withdrawal to biomedically familiar ground. However, the most satisfactory compromise for a lengthy flight might well be quite different from the most desirable one for flights of shorter duration or for particular parts of the prolonged flight.

Choice of a single, unnatural, gaseous environment for the entire duration of an extended flight, with the inherent uncertainties related to delayed effects, imposes the necessity for prolonged testing of successions of selected gas mixtures. This will become increasingly important, extremely laborious and perhaps even impractical as the duration of manned flight is inevitably extended to missions lasting many months.

VALUE OF PURPOSEFUL CHANGE AND MODIFICATION OF THE GASEOUS ENVIRONMENT

The latent period required for development of toxicity and for gradual development of a pathological effect

TABLE 5. *Hypothetical illustration of sequence of factors in gaseous environment**

Phase	Day	Composition of Gaseous Environment				Rate of Attainment	Duration of Exposure	Purpose
		Total press.	% Inert gas	% O_2	% CO_2			
Natural environment		760	79	21	0			
Preflight conditioning	1	760	40	60	0	Abrupt	4 hr	Partial denitrogenation without O_2 toxicity if delay occurs. To prevent bends of accidental decompression.
On launch pad	1	250	0	100	0	Abrupt	2 hr	To continue denitrogenation.
Launch phase	1	300	10	90	0	Abrupt	Brief	To prevent O_2 atelectasis during high G stress of launch phase.
Postlaunch	1	250	0	96–100	0–4	At leakage rate	24 hr	To conserve inert gas. To facilitate CO_2 absorption.
In flight condition I	2, 3	400	47–50	50	0–3	Slow	48 hr	To prevent O_2 atelectasis, reduce fire hazard.
In flight condition II	4, 5	250	0	96–100	0–4	At leakage rate	48 hr	To reduce loss of inert gas.
In flight	n, n + 1	Same as condition I						
In flight	n + 2, n + 3	Same as condition II						
Special phases								
Belt penetration		190	0	80	20	At leakage and buildup rate		Increase radiation tolerance by inducing hypoxia.
Lunar landing		500	40	60	0	Abrupt		Facilitate thermal control on surface.
Atmospheric reentry		400	50	50	0	Slow		Facilitate temperature control on reentry, prevent O_2 atelectasis.

* Note that the situations described are intended to illustrate the need for further study. They do not represent established or recommended sequences or durations.

permits man to be subjected safely for brief periods to environmental conditions which, if experienced over protracted periods, would be damaging or fatal. Not only pathological change but even the development of a decrease in performance or a harmless physiological change on exposure to an unnatural gaseous environment is a function of exposure duration. The duration of safe exposure is, in turn, related to the degree of environmental stress. On termination of a period of exposure to an unnatural state, recovery occurs at a rate which also is variable. It is this pattern of periodic exposure to and relief from stress, the occurrence of change and recovery, which characterizes activity, behavior, and life on earth. Nonconstancy of environment or physiological state is evident in such conditions as wakefulness and sleep, physical work and rest, disease and recovery, trauma and healing, altitude acclimatization and recovery from acclimatization, diving and decompression, oxygen breathing in therapy and in aviation and recovery from its effects, brief exposure to and recovery from carbon dioxide breathing in experimental work, in submarine practice, and in diving experience, and exposure to temperature stress with subsequent recovery. In a several-month period of normal life on earth the character of the total environment is continually changing. It is made up of a succession of intermittent stresses of varying degree and duration, with appropriate opportunity for recovery between the exposures to physiologically or biochemically strenuous conditions.

It is likely that the ultimate feasibility of manned extra-atmospheric flight of extreme duration may similarly depend on utilizing intermittent fluctuation or qualitative alternation of particular environmental conditions where maintenance of any single set of conditions would be difficult or would lead to risk of cumulative deterioration. As illustrated in Table 5, this question may even apply to the gaseous environment. The potential advantages of periodic alteration of the gaseous environment make it necessary to emphasize the need for study of the rate of development of either tolerance or dysfunction, and the rate of recovery from particular stresses, in addition to the previously mentioned requirement for determination of tolerance limits and the nature of physiological interactions.

PHYSIOLOGICAL RESEARCH AND FULL EXPLOITATION OF MAN IN SPACE FLIGHT

It is becoming more and more evident that manned flight is necessary to the success of detailed scientific exploration of space. Certainly successful manned space flight requires attention to factors of safety and performance during flight and to factors of health subsequent to space missions. However, the physiological and other risks of many human endeavors, such as mountain climbing, deep diving, submarine operations, and advanced aviation, are also extreme and may lead to fatality or chronic disability. Full opportunity for man to contribute to space exploration requires not only a willingness to accept risk, but also willingness to induce physiological changes. This requires an awareness of the limits of desirable physiological alteration, knowledge of favorable interactions, avoidance of specifically undesirable change, utilization of information concerning rates of development of physiological or pathological effects and of the rates of recovery from them. To approach this idealized state of physiological knowledge and competence and to relate this information to studies of performance will require far more lead time, more breadth of applied research effort, and, above all, more interest in the basic reactions of man than has sufficed for the initial ventures into manned space flight. It is urged that this research be pursued on a broad and continuous basis.

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Future operational and physiological requirements for man in space

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IT IS A PLEASURE to be here and to participate in this discussion of respiratory physiology in manned spacecraft.

I wish to emphatically state that I do not speak for NASA when it comes to policy concerning engineering decisions. The remarks I make this evening are clearly my own and bear no relation to the policies and decisions of NASA.

As you are well aware, all intravehicular atmospheres in manned space vehicles up to this time are 100% oxygen at 5 psi. The reasons for this are many, and I will not get into the pros and cons concerning this decision. Needless to say, we are continuing to investigate the effects of this atmosphere on man and animals under all space flight profile stresses. These studies will continue for some time to come with much of it being carried out on men and animals during actual space flights.

Projects Gemini and Apollo vehicles are presently designed for the 5-psi, 100% oxygen configuration. However, as Gemini is among other things a flying test bed, it may well be that later Gemini vehicles will carry other atmospheres. Should this be the case, and these newer atmospheres prove to be more advantageous, the advanced Apollo vehicles would undoubtedly be reconfigured to carry them.

Looking beyond our approved manned space flight projects, I see in the immediate future long-term orbiting vehicles circling our earth for periods of from 2 or 3 months to several years. Men will live and work in these vehicles for 30 days or longer. Crews will be replaced at regular intervals. Physical and biological experiments will be a large segment of the payload, and scientists will be members of the crew assigned to perform and monitor biological experiments using both man and animals as subjects.

Although orbital laboratory and space station crews can be replaced from time to time, men exploring what we now term "outer space" will be required to spend months and later perhaps years within vehicles and on the surface of distant planets within environments totally alien to ambient conditions. There can be no short-term rotation of duty by "relieving the watch," so to speak.

Let me limit my remaining remarks to the problems involved in the selection of atmospheres. We at NASA are presently engaged in the development, and later the evaluation, of semiclosed and closed environmental systems for long-term multimanned space vehicles. Systems evaluation will soon begin, using 5 men for a 30-day period. This will be followed by a similar 60-day run.

In 1964 a 720-man-day system will be evaluated. This system will permit us to keep four men in a closed system for a period of 180 days. Following this, a full year's test will be run, using prototype systems that are presently labeled "advanced concepts" for flight durations of 1 year or less.

With the increased capability of lifting larger and larger payloads and the advent of virtually leakproof vehicles, the use of higher intravehicular pressures becomes feasible. The use of these higher pressures introduces the problem of deciding which inert gas or gases to use.

The atmospheres for these future vehicles will be decided only after many combinations of gases at various pressures have been thoroughly investigated.

Past work has reasonably defined the lower tolerable partial pressure limits of oxygen; however, upper tolerable limits for prolonged periods of time are not so clearly defined. Thus, it is felt that no matter what total intravehicular pressure is used from 3.5 to 14 psi, the partial pressure of oxygen should remain at or slightly above that of sea level.

Carbon dioxide concentrations at or below 1.5% are considered safe with concentrations of 1% or less reasonable for prolonged periods of time.

A large segment of future respiratory research will be devoted to studying the role of the various inert gases in body metabolism, pulmonary function, and cerebral processes. There is a good basic understanding of the action of nitrogen as related to respiration and tissue physiology, but little is known of the physical action and physiological effects of long-term use of inert gases such as helium, argon, and neon.

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Simultaneously, each of the inert gases must be the object of intense study by the engineering community. Each gas must be evaluated for compatibility to the over-all vehicle system. Factors of availability, handling, storage, and control must be considered. Physical properties such as liquefying, freezing, and vaporizing temperatures must be balanced against weight and diffusion factors before a choice between gases can be made.

Individual inert gases react differently to space radiation energies. Which gas will offer the least hazard of secondary radiation effects is important. The characteristics of individual inert gases during weightlessness in relation to gas transport, selective tissue affinities, saturation and desaturation rates, and cellular-molecular level exchanges must necessarily be the object of serious scientific scrutiny.

The effects of weightlessness on the interface of combinations of gases will more than likely remain an unknown until we are able to carry out experimental studies within orbital laboratories.

I cannot accurately predict the gaseous composition of future long-range space vehicles, but I feel that it will assume a character approximately that which we enjoy here on earth, of course, eliminating our man-made impurities and contaminants.

I am just old-fashioned enough to believe that it will be hard to improve on our natural terrestrial atmosphere for space travel and that we will not be able to alter our physiology to accept even a modest change in atmospheric composition for those long space flights. Man has been acclimated to our environment for centuries. I doubt that we can change it or improve on it within a few short years.

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Time-concentration effects in relation to oxygen toxicity in man

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THE EFFECT OF THE PRESENCE of high or low partial pressures of oxygen in man's inspired gas mixture is an area of research that has received much interest since the original description of dephlogisticated air by Priestly in 1775 (4). In the past, the area of high partial pressures of oxygen (i.e., greater than P_{O_2} = 150 mm Hg)[3] has been the primary interest of the practicing physician (2, 9, 11) and those concerned with decompression from pressures greater than 1 atm to atmospheric pressure (6, 16). The area of low partial pressures of oxygen (i.e., 150 mm Hg P_{O_2} or less) has been, on the other hand, the prime concern of the mountaineer (3, 18) and those interested in aviation physiology (1, 15, 28). The advent of manned space exploration and the possible utilization of atmospheres of pure oxygen at reduced pressure has served as a catalyst to weld these two areas together. This has resulted in a renewed emphasis on the problems of chronic exposure of man to levels of oxygen partial pressures well below the previously established levels for oxygen toxicity, but still in excess of those partial pressures found in normal ambient air. Since much of the research being conducted in this problem area is being done in highly specialized chambers capable of maintaining a given partial pressure of oxygen in either the presence or virtual absence of nitrogen or other inert gases, the words of Priestly (4)—"Who can tell but that, in time, this pure air may become a fashionable article in luxury"—appear to be more appropriate than in the past.

It is not the purpose of this paper, however, to dwell on the social status of this somewhat unique atmosphere, but rather to bring together salient features of research that has been conducted (both at high and low oxygen partial pressure) and, hopefully, to stimulate additional research to fill in the many gaps in man's knowledge and understanding of the essential gas—oxygen.

Man's tolerance to increased oxygen partial pressures has been felt generally to be unlimited at partial pressures below 425 mm Hg inspired oxygen partial pressure ($P_{I_{O_2}}$). Becker-Freyseng and Clamann (5) proposed this relationship (Fig. 1) in which altitude or pressure was plotted against oxygen concentration. No reference was made to time with the exception that those authors noted "In the lower right hand section, the tolerance is additionally determined by the time factor."

In general, oxygen toxicity in man has been characterized by various types of symptoms, primarily involving either a central nervous system response, a cardiopulmonary response, or a hematological response or various combinations of these three. For example (4, 12, 14), one can find oxygen toxicity being described by the following symptoms: *1*) enzyme inhibition; *2*) pulmonary irritation, substernal distress, and reduced vital capacity; *3*) accelerated absorption of gases from closed spaces; *4*) parasthesiae and convulsions; *5*) general malaise and fatigue. The terms by which oxygen toxicity has been defined are dependent primarily on the concentration of oxygen and the time of exposure, and each of the symptoms is not clearly independent of the other. Indeed, all of the descriptions of oxygen toxicity might be correct if exposure (or life) could be sustained long enough to allow the full development of the toxic syndrome.

In considering the toxic effects of oxygen on man and the time-concentration relationships, it would appear advisable to summarize briefly the data available in terms of these categories: *1*) oxygen partial pressure in excess of 760 mm Hg; *2*) oxygen partial pressure approximately equal to 760 mm Hg; *3*) oxygen partial pressure much less than 760 mm Hg.

OXYGEN PARTIAL PRESSURE IN EXCESS OF 760 mm Hg

The toxicity of oxygen at partial pressures greater than 1 atm has been studied by many investigators, among them Behnke et al. (8), Thompson (30), Behnke (6), Haldane (16), Case and Haldane (10), and Lambertsen et al. (19). The oxygen partial pressure range covered by these workers (Table 1) goes from a high of 7,600 mm Hg or 10 atm (10) to a low of 1,520 mm Hg or 2 atm (8, 20). As noted in Table 1, exposure times

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[3] Unless indicated in the text, all values of P_{O_2} refer to ambient partial pressure of oxygen. P_B refers to barometric pressure.

ranged from as short as 5 min to as long as 4 hr. Oxygen toxicity symptoms were not observed in every case, but where they were observed, they were characterized by pallor and syncope or convulsions. Individual variability in terms of time of onset of symptoms at a given P_{O_2} is readily apparent, even in these rather acute experiments. This fact is perhaps best emphasized by the work of Lambertsen et al. (21) in which the time for convulsions at a P_{O_2} of 2,660 mm Hg ranged from 35 to 95 min in a group of six subjects.

OXYGEN PARTIAL PRESSURE APPROXIMATELY EQUAL TO 760 mm Hg

At oxygen concentrations approximately equal to 760 mm Hg, the time of exposure necessary to produce distinct toxic symptoms ranges from approximately 6–7 hr up to approximately 30 hr (Table 2). Maximum reported tolerance times of exposure to this type of atmosphere have been 110 hr (13) and involved two test subjects. Normal voluntary tolerance for exposure to 1 atm partial pressure of oxygen appears to be on the order of 53–75 hr (13, 27), based on data collected on a total of 14 test subjects. The symptoms normally described for oxygen toxicity during this type of exposure include substernal distress, parasthesiae, nausea and vomiting, general malaise and fatigue. With the exception of the report by Becker-Freyseng and Clamann (5), substernal distress appears to be a symptom common to all and should be relied on as a prime index of oxygen toxicity or impending oxygen toxicity.

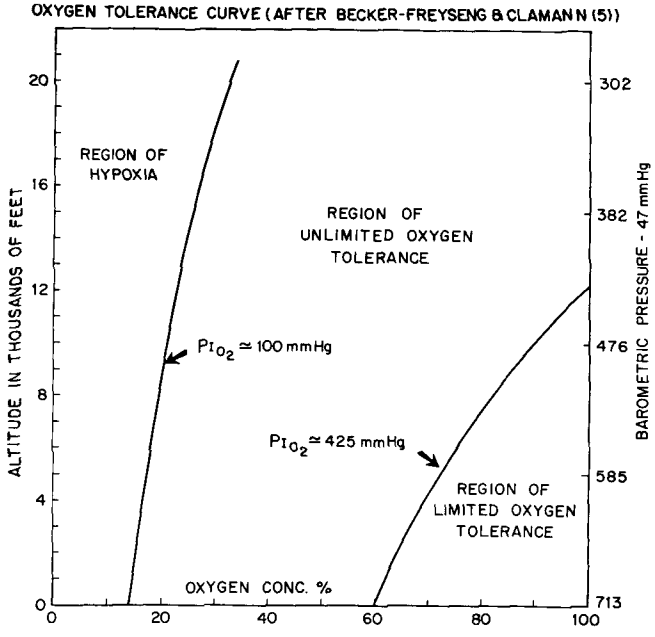

FIG. 1. Diagram of oxygen tolerance taken from Becker-Freyseng and Clamann (5), modified by Mullinax and Beischer (26).

TABLE 1. *Effects on man of breathing oxygen at pressures in excess of 760 mm Hg*

Ref.	P_{O_2}, mm Hg*	No. of Subj.	No. With Symptoms	Time of Exposure, min	Main Symptoms	Time of Symptom Onset, min
10	7,600	1	1	??	Convulsions	??
16	5,320	1	1	5	Convulsions	5
8	3,040	2	2	45	Convulsions, syncope	45
21	2,660	6	6	35–95 (avg. 66)	Convulsions	35–95 (avg. 66)
7	2,280	4	4	240	Dizziness, nausea, impending collapse	ca. 180
8	2,280	4	0	120		
19	2,280	8	0	15–30		
30	2,280	2	2	13–16	Convulsions	13–16
8	1,520	3	0	180		
20	1,520	12	0	23		

* P_B is assumed to equal P_{O_2}.

TABLE 2. *Effects on man of breathing oxygen at pressures approximately equal to 760 mm Hg*

Ref.	P_B, mm Hg	P_{O_2}, mm Hg	No. of Subj.	No. With Symptoms	Time of Exposure, hr	Main Symptoms	Time of Symptom Onset, hr
6	760	750		??	6–7	Substernal distress	6–7
12	760	736	34	28	24	Substernal distress	14
13	760	730	12	12	42–110	Substernal distress	8–14
5	760	684	2	2	65	Parasthesiae, nausea	ca. 30
27	760	630	6	4	53–57	Substernal distress	ca. 20
12	760	546	9	5	24	Substernal distress	ca. 24

OXYGEN CONCENTRATION MUCH LESS THAN 760 mm Hg

As pointed out earlier in this paper, exposure to oxygen partial pressures below approximately 425 mm Hg (PI_{O_2}) has been considered safe for virtually unlimited time periods (5, 12, 23, 27). This limit has some experimental evidence to support it since various investigators have reported the successful nonsymptomatic maintenance of man below that limit. Richards and Barach (29), for example, maintained two normal subjects at atmospheric pressure with a P_{O_2} of 332 mm Hg for 7 days with no toxicity symptoms (Table 3). Comroe et al. (12) exposed two separate groups of six subjects each to approximately 380 mm Hg P_{O_2}. Each exposure lasted for 24 hr with one being conducted at atmospheric pressure and the other at a P_B of 380 mm Hg. Becker-Freyseng and Clamann (5) reported the results of a 70-hr experiment with two people exposed to 189 mm Hg P_{O_2} at a total pressure of 230 mm Hg, again with no evidence of symptoms of oxygen toxicity observed. Further evidence for the validity of the toxicity limit of 425 mm Hg was reported by Michel et al. (23) in an experiment with six men maintained at a total pressure of 523 mm Hg and a P_{O_2} of 418 mm Hg for 7 days.

Substernal distress was observed, but, as noted by the authors: "The successful completion by six men of a seven-day residence in an environment containing oxygen at a partial pressure of 418 mm Hg would, on the surface, seem to indicate that the conditions were within the limits of human tolerance."

TABLE 3. *Effects on man of breathing oxygen at pressures much less than 760 mm Hg*

Ref.	P_B, mm Hg	P_{O_2}, mm Hg	No. of Subj.	No. With Symptoms	Time of Exposure, hr	Main Symptoms	Time of Symptom Onset, hr
23	523	418	6	6	168	Substernal distress	ca. 36
12	760	380	10	0	24		
17	383	378	5	5	336	Hb drop	48–72
12	380	360	6	0	24		
29	760	332	2	0	168		
17	258	250	6	2	336	Substernal distress	48–96
22	267	250	6	6	?	Loss of periph. dark adaptation (blue target)	ca. 144
24	258	242	4	3	336	Substernal distress	ca. 86
17	196	190	5	1	336	Substernal distress	ca. 72
17	196	190	5	4	336	Max. reticulocyte response	216
25	190	174	8	1	408	Substernal distress	216
5	230	189	2	0	70		

More recent data (Table 3) obtained in experiments ranging in duration from 14 to 17 days (17, 22, 24, 25) raise certain questions regarding the previous establishment of finite limits for toxic oxygen partial pressures and indicate the need for consideration of time of exposure, even at the lower partial pressures. For example, in a series of studies conducted at a total pressure of 190 mm Hg, P_{O_2} of 174 mm Hg (25), one subject out of a total of eight experienced a burning substernal pain on the 9th day of the 17-day experiment. This was in addition to the nasal congestion, eye irritation, aural atelectasis, and transient parasthesiae that were noted. In a similar 14-day experiment, Helvey et al. (17) reported substernal distress at the 72-hr mark in one of five subjects and also noted a maximum reticulocyte response at the 9th day in four of five subjects. Subsequent experiments conducted at a total pressure of 258 mm Hg with the P_{O_2} ranging from 242 to 250 mm Hg have revealed substernal distress (17, 24) as well as loss of peripheral dark adaptation to a blue target (22). Finally, in an experiment with five subjects conducted at a total pressure of 383 mm Hg, P_{O_2} of 378 mm Hg (17), a drop in hemoglobin of 2.0–2.5 g/100 ml was noted in the first 48–72 hr of exposure. Concomitant with this hemoglobin drop, there was a rise in bilirubin and urine urobilinogen levels as well as indications of increased erythropoiesis.

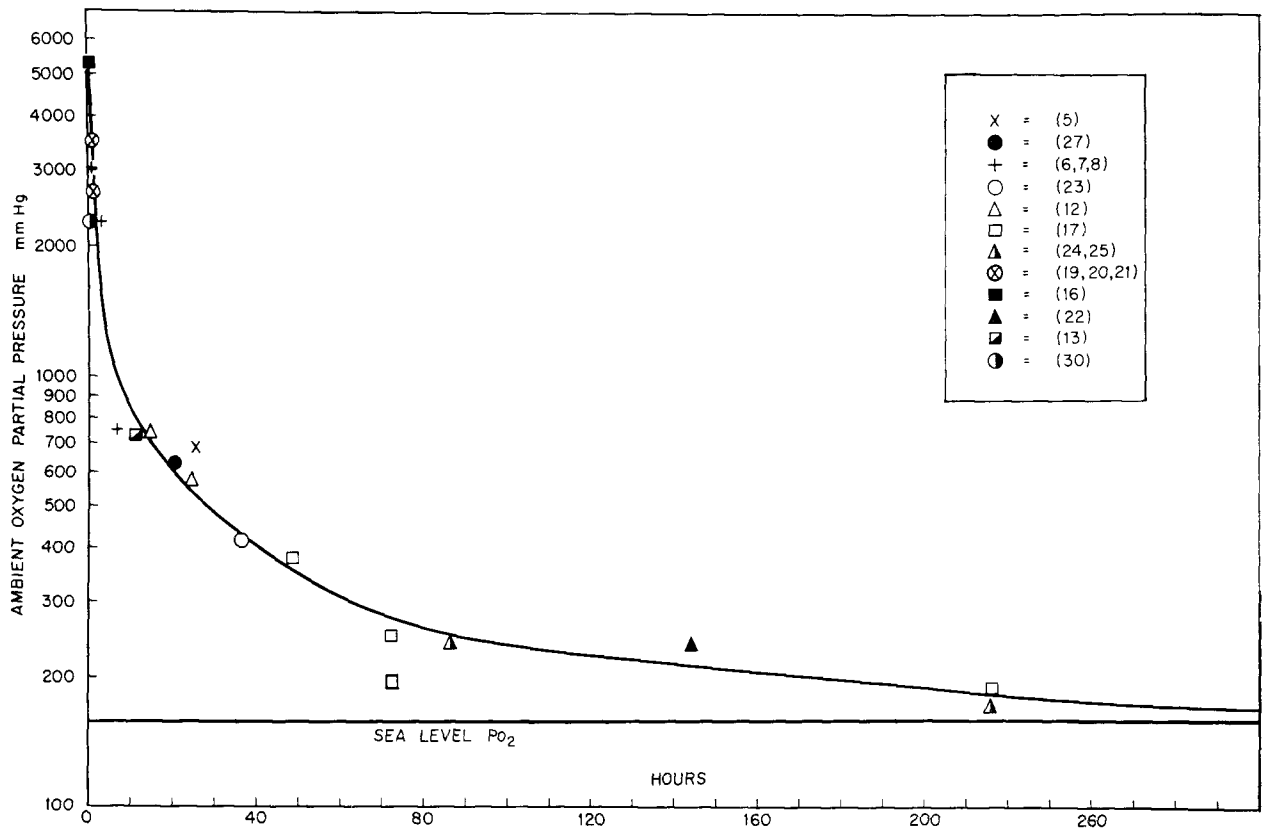

FIG. 2. Average time of onset of oxygen toxicity symptoms as function of ambient oxygen partial pressure.

It would appear advisable, however, to point out some of the differences in these later experiments in comparison to the earlier ones in which negative results were reported. First, the earlier work by Comroe et al. (12) and Becker-Freyseng and Clamann (5) was of comparatively short duration (24 and 70 hr, respectively). Second, with the exception of the data reported by Michel et al. (23), who observed substernal distress, the actual concentration of oxygen utilized in the earlier, prolonged experiments is subject to considerable question due to the mode of administration and the continuity of exposure (11). Third, and perhaps of some importance, the later experiments were conducted at reduced pressures in environments containing a maximum of 5–7 mm Hg P_{N_2}. The earlier prolonged experiments by contrast had P_{N_2} levels ranging from approximately 100 (23) to 420 mm Hg (12).

TIME-CONCENTRATION RELATIONSHIPS

The data shown in Tables 1–3 have been plotted semilogarithmically (Fig. 2) to portray better the relationship between oxygen concentration and time of onset of symptoms indicating oxygen toxicity. It should be noted that the points above 760 mm Hg P_{O_2} generally represent both time of onset and tolerance, whereas those at 760 mm Hg and below represent only time of onset [exception: 6–7-hr tolerance time and symptom onset at P_{O_2} = 752 mm Hg (6)]. The time of onset data represent the average time of onset of symptoms of those subjects showing symptoms. The frequency with which any given symptom occurred can be obtained by reference to Tables 1–3.

The data plotted in Fig. 2 clearly indicate that symptoms similar to those previously described for oxygen toxicity are observed at partial pressure of oxygen well below the level (425 mm Hg) previously established. It does not provide any information regarding man's tolerance to these levels nor does it indicate the impact that continued exposure to such atmospheres would have on man as a functioning entity. It does, however, pose several questions, among which are the following:

1) Does man have unlimited tolerance to ambient partial pressures of oxygen from normal levels up to 425 mm Hg?

2) What is the effect of reduced pressure per se in the development of oxygen toxicity symptoms?

3) What is the effect on tolerance to oxygen of environmental factors, particularly carbon dioxide and temperature?

4) What is the relative role of the presence or absence of nitrogen gas in this over-all toxicity syndrome?

In conclusion, the following quotation from an anonymous source (at least to these authors) seems appropriate: "We have not succeeded in answering all your problems . . . the answers we have found only serve to raise a whole set of new questions. In some ways we feel we are as confused as ever, but we believe we are confused on a higher level, and about more important things."

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A problem of man and milieu: prolonged exposure to pure oxygen

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THE PAST DECADE has witnessed the earth's reluctant surrender to man's persistent struggle to master his planet. The highest mountain and the deepest ocean gorge have been won by the explorer and scientist. The sky has been traversed and the challenge moved from the conquered planet to the reaches of space. Yet man's requirement for a gaseous milieu continues to retard his progress. Although the Trieste has penetrated the ocean to barometric pressures over a thousand times that of man's sea level environment, and Mercury has carried the astronaut to the vacuum of space, human dependence on this barometric breath of life remains the Achilles heel of his achievements.

Although the need for space capsule and submarine cabin are understood, the precise requirements and optimum selection of these artificial environments remains unanswered by the scientist. Although the requirements for man's atmospheric milieu will vary for submarine, terrestrial, and transatmospheric adventures, oxygen will be common to all and is the focus of a space age problem of man and his milieu—prolonged exposure to pure oxygen. The selection of the space capsule atmosphere is one which must meet both medical and engineering constraints. This choice will have a major effect on the design of the vehicle and on the performance of the crew which, in both respects, influences the probability of mission success. Factors which must be weighed in this decision include structural requirements, life-support system complexity, fire hazard, decompression hazards, and crew atmospheric tolerances.

The geometric configuration, strength, weight, and reliability of the cabin are affected by the differential pressure across the hull. Generally the weight will increase and reliability decrease with higher internal pressures. However, additional structural strength required for landing impact, aerodynamic pressures, and meteoroid protection educe this penalty. Increasing the number of gases may increase the complexity and weight and decrease the reliability of the atmospheric control system. The gas loss from leakage and the use of a lock for exit of an astronaut decreases with lower internal pressure although low-pressure gas systems may require greater power for adequate ventilation and thermal control of the cabin.

The effect of the cabin atmosphere on the potential fire hazard is of paramount importance in view of the restricted space and limited escape possible. Vehicle design and material selection should be directed toward reducing the probability of ignition and toxic products of combustion. An atmosphere of pure oxygen is a demonstrated fire hazard.

In the event of an explosive or rapid decompression the time to incapacity of the crew is related to total cabin pressure and the partial pressure of oxygen. This incapacity may be due to sudden gas expansion in air-filled organs with tissue damage or reflex shock, hypoxia, or "bends." Bends appears to be the primary threat if a two-gas (e.g. nitrogen/oxygen) system is utilized, although this can be reduced by minimizing the pressure differential between the cabin and the protective space suit. Haldane has indicated that a reduction in pressure of one-half usually will not precipitate bends. Although there is evidence to the contrary, this appears to be the basis on which the Russian Vostok vehicles have a near sea level atmosphere of nitrogen and oxygen and utilize a space suit with a ½ atm pressure. This provides less mobility of the suit than the American suits using ⅓–¼ atm.

Based on such considerations, and the urgency of the program, a single-gas (oxygen) atmosphere was selected for Project Mercury. This choice created the need for more extensive knowledge of the effects of pure oxygen for prolonged periods on human health and performance. The extension of this choice to Projects Gemini and Apollo, which are designed to maintain a crew for weeks, greatly accentuates this need.

Since its discovery by Priestly there has been an intense interest in the effects of pure oxygen on man and also a great deal of disparity among the investigators. This is characterized by Comroe et al. (1), who stated: "There is no agreement whatever among clinical investigators concerning the harmful effects of oxygen on man." This situation is compounded by the general lack of studies directed specifically toward a determination of the effects of pure oxygen at reduced barometric pressures for prolonged periods. Unfortunately, it is

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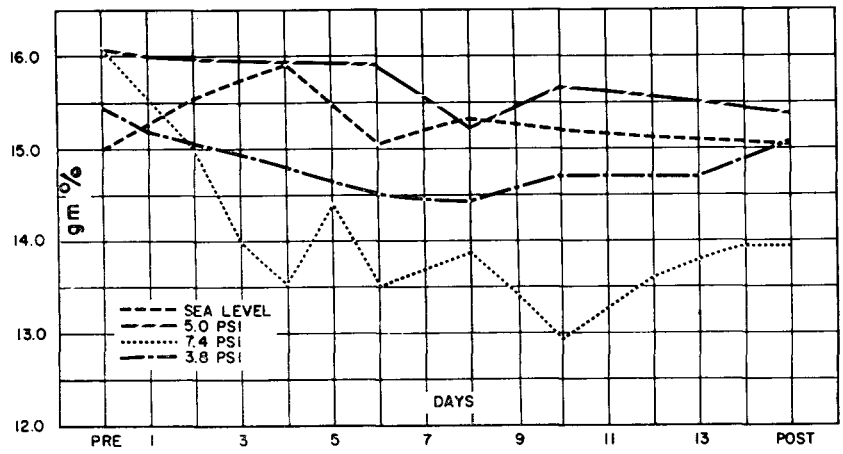

FIG. 2. Average hemoglobin concentration.

role of toxicants in an oxygen-rich environment, the role of nitrogen and other inert gases in man's environment, as well as the potential threat of oxygen toxicity in an oxygen-rich atmosphere of long duration.

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Physiological effects of a simulated space flight profile[1]

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RECENT WORK HAS ESTABLISHED the fact that the combination of breathing high concentrations of oxygen while undergoing prolonged (in contrast to impact) acceleration results in pulmonary atelectasis in man (2-6, 8). Since this combination of conditions, apart from the laboratory, is met almost exclusively in certain aeronautical and astronautical flight situations, pulmonary atelectasis may be viewed as an occupational hazard in these cases. From an operational viewpoint, this hazard is yet another to be added to those already well known which plague pilots of high-performance aircraft and spacecraft. As in the case of all hazards which threaten the successful completion of a mission, it is important that decision-making groups be fully advised of the nature and significance of pulmonary atelectasis and of the penalties to be incurred by alternative methods proposed for its reduction or elimination. We are now at the stage where sufficient evidence has been accumulated to assert that the likelihood of pulmonary atelectasis occurring during presently planned conditions of launch and re-entry is quite high. The practical significance of its occurrence remains to be evaluated. If it is transient and readily reversed by naturally evoked reflex reactions, its practical significance, from an operational viewpoint, is reduced. Penalties of additional weight and equipment complexity should be directed, if such be the case, toward minimizing the threats from those hazards more likely to jeopardize mission accomplishment.

The study about to be described was designed to relate, as closely as possible, to the operational situation. Such factors as the constricting effects of wearing the full pressure suit while breathing 100% oxygen, simultaneous exposure to 100% oxygen and acceleration, and prolonged exposure to an atmosphere of almost 100% oxygen with reduced physical activity were combined in the proper sequence in this study. The subjects used were typical of those already selected as astronaut trainees for future flights. While the limitations of a single study in providing answers to a complex question were well recognized, it was expected that sufficient information would be obtained to guide those responsible for stipulating atmospheric life-support requirements in spacecraft. From the results obtained, it appeared unlikely that any significant or permanent physiological penalty would be paid by astronauts exposed to launch and re-entry acceleration patterns, and to a 2-week exposure to almost pure oxygen at 1/3 atm pressure, under conditions similar to those investigated here. An unanticipated occurrence of fire served to emphasize the ever-present danger of conflagration in living spaces containing high concentrations of oxygen and dramatically demonstrated the difficulties involved with controlling and extinguishing flames under these circumstances.

PROCEDURE

As indicated above, the procedures used in this study were dictated primarily by an attempt to duplicate the most important conditions to be imposed on astronauts during a 2-week orbital flight profile. These conditions are diagramed in Fig. 1 and were based on information obtained from the Manned Spacecraft Center, NASA. No attempt was made to duplicate the condition of weightlessness during phase III. Phases II, IV, and V were carried out at the Aviation Medical Acceleration Laboratory (AMAL), while the remaining phases were conducted at the Air Crew Equipment Laboratory (ACEL). Since these two naval laboratories are separated by a straight-line distance of approximately 25 miles, including the city of Philadelphia and its northern suburbs, it was necessary to transport personnel and equipment from one to the other on a daily basis in a specially outfitted van. The actual route chosen, to avoid traffic congestions and irregular stretches of paving, covered about 60 miles one way. In order to handle the equipment to be described, sizeable cranes and fork-lifts were utilized by engineers and riggers who had carefully planned each step of the procedure to be followed.

The subjects were chosen from a group of highly

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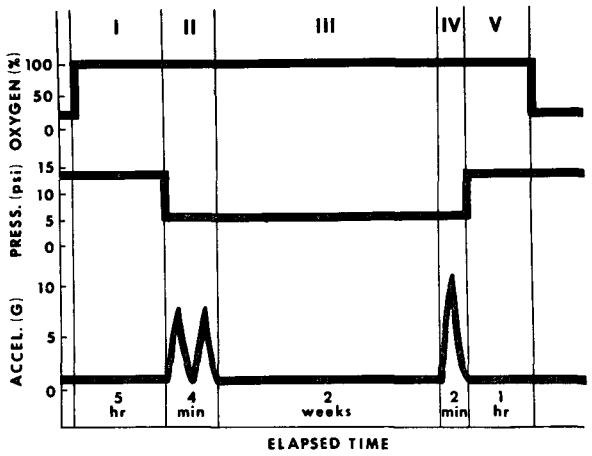

FIG. 1. Diagram of simulated orbital flight conditions. Phases: I—prelaunch; II—launch; III—orbit; IV—re-entry; V—post-re-entry. Actual experimental conditions deviated somewhat for each exposure from those indicated in the diagram. (This figure taken from ref. 1.)

qualified, volunteer naval and marine jet aircraft pilots who were attached to various operational units within the continental U.S. Three subjects were slightly over 30 years old, the other three were about 5 years younger. Two alternates served as controls and as standbys during phases I and II. Prior to initiation of the test sequence in Fig. 1, the subjects and alternates were isolated for a 10-day period during which they were carefully examined and indoctrinated in various procedures pertinent to the forthcoming test.

Before beginning phase I, one subject and his alternate were selected from among those available, and both received similar treatment until the beginning of phase II. In the following description, however, only the subject will be mentioned, for the sake of brevity. Two groups of three ECG electrodes each were attached to the subject so that each group occupied a small area on each side of the torso at about waist level. One electrode on each side served as a ground lead (one active and one standby), while either bilateral set of remaining electrodes could be made to function as standard lead I (one set active and one set standby). The output of these ECG electrodes was amplified and recorded on standard strip chart recorders. The subject then donned long underwear and the full pressure suit. The suits used in this study were similar to those worn by the Project Mercury astronauts and are characterized by forming a single gas-tight compartment around the wearer's body. Thus, the 100% oxygen used to ventilate the subject was also used for breathing; excess oxygen and expired gases were vented to the ambient atmosphere through a port on the helmet. On each of the two lip microphones within the helmet, a small thermistor bead (one active and one standby), was mounted for the purpose of measuring respiratory rate, which was also recorded. Redundancy of bioinstrumentation was necessary to reduce the risk of losing the capability of monitoring physiological reactions during the long periods when the subjects were wearing the full pressure suit. The suit was worn during phases I and II, at the beginning and end of phase III, during phase IV, and at the beginning of phase V.

During the period of preoxygenation (phase I), the subject and alternate were transported from ACEL to AMAL. At AMAL, the subject entered a portable altitude chamber (PAC) mounted on the arm of the large (50-ft-radius) centrifuge. The PAC was equipped with a net couch, into which the subject was secured by lap belt and shoulder harness. Once inside, the PAC was sealed and evacuated by pumps to an altitude equivalent of about 33,000 ft. The subject was supplied with sufficient oxygen to maintain his suit pressure at about a 27,000-ft altitude equivalent. This arrangement insured only outboard leakage from the suit. In addition to direct communication with the subject via the portable suit communication system, an emergency and a response button were located within easy reach of the subject's hands within the PAC. The response button was used to assess the subject's psychomotor performance during acceleration (phases II and IV) by noting button presses in response to experimenter activation of a stimulus light located within the PAC. Simulated launch and re-entry acceleration patterns were applied in phases II and IV so that the accelerative force was directed from the anterior to the posterior surface of the subject's supine body (transverse G). Following phase II, the subject within the PAC was detached from the centrifuge arm, loaded on the van, and transported back to ACEL. The PAC was so connected to a large low-pressure chamber located at ACEL that the subject could leave the former and enter the large chamber which was maintained at an altitude equivalent of 27,000 ft on 100% oxygen. After spending 14 days in this environment, the subject again donned the full pressure suit, was transported back to AMAL within the PAC, and was exposed to the re-entry acceleration pattern (phase IV). The PAC and pressure suit were then recompressed to ambient pressure, and the subject continued to breathe 100% oxygen after leaving the PAC. While the subject held his breath, the pressure suit helmet was removed, an oxygen mask was placed over the subject's nose and mouth, and he continued to breathe 100% oxygen from a portable supply tank while the remainder of the suit was taken off. An arterial sample was obtained, the mask was removed, and 7 min after breathing ambient air another arterial sample was taken. When a final physical examination was completed, the subject was returned to ACEL and observed for a period of days.

The schedule had been arranged so that each of the subjects began the test sequence of Fig. 1 on the next day following his predecessor. After the third subject had completed phase V, a fire prematurely ended the study, as described below. Of the subjects completing the entire sequence, two were examined within 1 day, and one within 2 days, in order to assess the

residual effects of the test conditions on pulmonary mechanics and diffusing capacity (1).

The fire referred to above originated from arcing in an electrical light fixture located in the ACEL low-pressure chamber. Attempts to smother the initial small flame resulted in a very rapid spread of the fire throughout the inhabited spaces. The three subjects remaining in the chamber and a flight surgeon who had been present since the start of the test engaged in efforts to smother flaming clothing and skin. In spite of all attempts to extinguish flames by enclosing them with whatever materials were available (including an asbestos cover), the fire continued to spread. In a matter of minutes, however, the subjects vacated the living spaces, entered a lock, and were recompressed to sea level pressure. The chamber was then rapidly evacuated to a very low pressure and recompressed by flooding it with air. The burned personnel were treated at the U.S. Naval Hospital, Philadelphia, and all have since recovered uneventfully. Approximately 10–20% of the skin area of these individuals received first- or second-degree burns, and, in addition, two of the people also sustained more serious burns. Examination, after the fire, of the chamber contents gave one the impression of a flash fire, with many areas of only superficial charring and melting of combustible materials. It should be mentioned that prior to this study, intensive consideration had been given to procedures to be followed in case of fire, and appropriate instructions had been issued to all chamber-operating personnel. It is only because of the prompt action on the part of all concerned that damage to personnel and material was not greater than that actually sustained.

RESULTS

Detailed results of this study appear elsewhere (7). In general, however, it can be said without qualification that, for those three subjects completing the entire test sequence, no permanent physiological detriment was detectable. This also applies to the remaining three subjects, who had completed phases I and II and 11, 12, and 13 days, respectively, of phase III. Techniques used to determine changes in the lungs consisted of posterior-anterior and left lateral chest X-rays, spirometry, and arterial blood gas analyses. These techniques were applied at intervals during the control period before phase I, immediately on entry into the ACEL low-pressure chamber at the beginning of phase III, at least three additional times during phase III, and during phase V. The sequence of events in obtaining arterial blood samples after completing phase IV has been outlined above. None of these tests in any subject was indicative of decreased pulmonary function, nor did measures of pulmonary mechanics and diffusing capacity performed on the three subjects completing the entire test sequence show any impairment (1).

Chemical analysis and microscopic examination of the blood and urine before, during, and after the test sequence revealed no changes attributable to the test conditions. Similar changes in blood platelets, hemoglobin content, and hematocrit were seen both in the controls as well as the subjects, and these changes were interpreted as reflecting reactions to blood loss induced by the experimental procedures.

An interesting and unexpected finding, now being further investigated, concerns a decrease in scotopic peripheral vision of those exposed to high oxygen concentrations. This visual impairment appeared to be gradually reversible on resumption of air breathing at ambient pressures.

Among the many other examinations done, including electrocardiograms, electroencephalograms, microscopic analyses of smears, and performance measurement, no significant changes were found.

As expected with prolonged exposure to atmospheres containing high oxygen concentrations, several of the low-pressure-chamber inhabitants were afflicted with serous otitis media. Valsalva maneuvers and decongestants were used to counteract this condition.

COMMENT

In this study, no attempt was made to artificially preserve atelectasis which probably occurred during the acceleration periods of phases II and IV. Since testing for this condition was not feasible during and immediately after cessation of the launch and re-entry acceleration patterns, nothing definite can be stated in this regard. However, if atelectasis did occur, it disappeared in a short while, even in an atmosphere of 100% oxygen. Consideration had been given to instructing the subjects to avoid sighing, coughing, or engaging in other respiratory maneuvers conducive to reinflating collapsed lung alveoli, but the difficulty in assuring compliance with such instruction, under the test conditions, was obvious. In addition, it was felt that if the aforementioned techniques for reinflating collapsed alveoli were spontaneously brought about, and that if these techniques were successful, then the same outcome could be expected in the operational situation.

The practical significance of the fire which brought this study to a premature end cannot be overemphasized. The urgent requirement for the development of techniques for preventing or extinguishing fires in space vehicles containing high oxygen concentrations is obvious.

One aspect of the present study deserving comment is the amalgamation of the many special skills and facilities required to successfully accomplish this work. A series of meetings of the Working Group on Gaseous Environments, under the chairmanship of Dr. Arthur B. DuBois, provided the opportunity for all aspects of the problem to be freely discussed and for taking maximum advantage of the experience gained by those other participants of this Symposium who had conducted related studies. Dr. Christian J. Lambertsen, as chairman of the Man in Space Committee, Space Science Board,

National Academy of Sciences, the parent Committee of the Working Group on Gaseous Environments, was most active in the planning phases of this study and provided assistance in training ACEL personnel in the techniques of arterial puncture and polarographic blood gas analysis. As joint collaborators with ACEL, AMAL provided all of the many skills necessary to accomplish the critical phases of launch and re-entry acceleration patterns. The Manned Spacecraft Center, NASA, provided the funding for this study, designed and constructed the PAC, and furnished the dehydrated food eaten by the subjects and alternates during the test period. Considerable assistance was rendered by the U.S. Naval Hospital, Philadelphia, in performing certain blood chemistry tests, interpreting the chest X rays, evaluating nasal and pharyngeal smears, making and interpreting electroencephalograms, conducting renal function tests, and in caring for those burned in the fire. Personnel were temporarily assigned from the Naval Medical Research Institute, Bethesda, Md., and the School of Aviation Medicine, Pensacola, Fla., to assist in this undertaking. Finally, special mention must be made of the volunteer pilots who participated as subjects and alternates. They were exposed to prolonged periods of quite uncomfortable and potentially dangerous conditions and underwent the discomforts of repeated arterial punctures. Three of their number suffered serious burn injuries. Their intelligent and conscientious cooperation was essential to the success of the over-all program.

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APPENDIX B

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APPENDIX C

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