Underwater Physiology

PROCEEDINGS OF THE THIRD SYMPOSIUM ON UNDERWATER PHYSIOLOGY

PREVIOUS SYMPOSIA

PROCEEDINGS OF THE UNDERWATER PHYSIOLOGY SYMPOSIUM, January 10 and 11, 1955. Washington, D. C., edited by Loyal G. Goff. Prepared by the Panel on Underwater Swimmers of the Committee on Undersea Warfare, with support from the Office of Naval Research, 1955. Publication 377. $3.00

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C. J. LAMBERTSEN / Editor

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Foreword

The papers contained in this volume were presented at the Third Symposium on Underwater Physiology. The Symposium was held at the State Department, Washington, D. C. on March 23, 24, and 25, 1966, under the sponsorship of the Office of Naval Research and the Committee on Undersea Warfare of the National Academy of Sciences—National Research Council.

Following the pattern set by the two preceding symposia, the aim of this symposium was to emphasize the great importance of Naval medical research in extending man's capabilities under the surface of the sea. The program was chosen to illustrate the status of information available, to indicate areas of research interest and to pinpoint critical items that require further study.

The recent manned operations in the open sea, highly important in their own right, are exploiting the basic physiological findings of the past fifty years. However, the lack of basic information concerning a means for improving decompression from great depths, the effects of gases at extreme pressures, and the effects of interactions of multiple environmental conditions differing radically from those on the surface of the earth, will present serious limitations to the great opportunity for further practical application of human capabilities and engineering skills. The Symposium was designed to encourage the reporting of progress in critical areas of underwater physiology. These proceedings are a documentation of the papers presented as well as the discussion resulting from these papers. It consists of detailed and searching studies of man, animals, tissues and cells, with emphasis upon research required to enable further extension of the maximum diving depth and its duration.

The proceedings are composed of the numerous papers presented at the symposium and the discussions following each session. Authors of these papers were from several foreign countries as well as the United States.

The formal presentations were supplemented by a special evening lecture on "Manned Vehicular and Extra-vehicular Undersea Activities," presented by Dr. John Craven, Chief Scientist, Special Projects Office, U. S. Navy. A visit to the Experimental Diving Unit and a submarine rescue vessel, affording first-hand information regarding special instrumentation and techniques now employed in all phases of underwater research activity, was arranged by Lieutenant R. F. Cunningham, USN.

In addition to Navy and government representatives, the Third Symposium on Underwater Physiology was attended by representatives from universities, industrial research organizations, and foreign representatives from Monaco, Japan, England, Switzerland, Sweden, Germany, Canada, France and Denmark.

The Office of Naval Research and the National Academy of Sciences wishes to acknowledge the excellent organization of the program topics and the careful planning of the details that resulted in the successful three day meeting, and members of the Planning Committee are to be especially commended for their efforts.

Appreciation is expressed to members of the staff of the Committee on Undersea Warfare, Mrs. Helen Ray, Miss Sally Baideme and Mrs. Helen Sanbourn for their time and effort in arranging the details of the meeting, as well as to the officials of the State Department whose advice and cooperation contributed to the successful conduct of the meeting. The Planning Committee and the Editor have urged special acknowledgment of the extensive and dedicated effort by Miss Eleanor Jones of the University of Pennsylvania Laboratory of Pharmacology throughout the editing of this published Proceedings.

K. W. Hannah
Executive Secretary
Committee on Undersea Warfare
National Academy of Sciences
National Research Council

Preface

At this moment in the fulminating evolution of environmental physiology, the youngest investigator may take for granted that in the past few months two unmanned spacecraft, one Russian and one American, effected the first gentle landings on the earth's moon, presaging the landing of men on that forbidding surface. Within this same year man has accomplished two hours of extra-vehicular activity in the vacuum of near space while orbiting the earth, he has accomplished rendezvous of spacecraft in earth orbit, and he has spent increasing periods, extending to two weeks of orbital flight, in the weightless state. Even before this year, noted but less heralded than such spectacular accomplishments in these earliest days of manned space flight, man has passed under the northern polar ice-cap, he has circumnavigated the earth entirely submerged, he has reached the bottom of our deepest ocean, he has effected rendezvous and landing of a small submersible on the deck of a cruising underwater submarine, he has briefly reached a diving depth of 1000 feet in the open sea, and he has lived for one month exposed to sea pressures up to 50 fathoms.

All these extensions of man into extremes of altitude, of depth, and of duration have occurred since the first of this series of conferences on underwater physiology was held in 1955. The first symposium was arranged following nearly a decade of post-World War II effort and failure to arouse either physiologist or engineer to a recognition of the great opportunities that existed even then for extending man's capabilities under the sea. The first symposium, like the many ancillary activities by a cadre of dedicated individuals, was designed to lead and entice investigators and technical specialists into this unexploited field. Then, as now, it was possible to promote close attention to important but neglected theoretical or practical aspects of undersea science by urging particularly qualified individuals to address their peers on these topics. The results have certainly included stimulation of much needed underwater physiological research.

Today the question is: Do we have a different situation than existed a decade ago? Things are indeed different in some ways, but not in all. Time, international prosperity, great technological advance, and a now general desire for practical application of diving methods, have led to rapid and widespread increase of interest in man in the undersea environment. The use of existing physiological knowledge has led to several interesting deep or prolonged operations in the open sea. Success in these relatively simple applications of existing information has generated the two different reactions that have characterized each major stage of expanding manned environments, from aviation, to undersea activity, to space flight.

One reaction is widespread and ill-advised. It is based on the view that awareness of the physiological limits of man is not important, since the real advance will be accomplished through the engineering efforts that will either keep man physiologically comfortable or, eventually, make his presence unnecessary.

The second reaction, which I trust concerns us all, is that our present rapid progress is in fact based upon the detailed basic and applied physiological studies of previous months and years, and that not only further advance but even consolidation of our limited gains, depends ultimately upon the energetic, imaginative and skillful performance of the physiological studies still to be done. Progress will continue to result from the informed and closely cooperative activities of biomedical and engineering sciences. Let me make no pretense: I hope and expect that by this and other symposia it will continue to be possible to excite the interest of many of you in carrying this vital work further.

C. J. Lambertsen

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RECENT NAVAL EXPERIENCES IN EXTENDING USEFUL DIVING DEPTH

1

ROBERT B. BROWN

DIVING RESEARCH AND INTERNATIONAL NAVAL MEDICINE*

It gives me great pleasure to represent naval medicine at the beginning of this Third Symposium on Underwater Physiology. The U. S. Navy has long been aware of the military, commercial, and industrial potential of underwater operations and, within the Navy Medical Department, there has been a small but significant number of medical officers and allied scientists who have been intimately concerned with this area of development. These physicians and scientists have appreciated the need for investigation into the physiologic requirements and demands which are placed upon man during his efforts to exploit the underwater world. They realize that this wet, dense, positive pressure environment would exert a combination of physiological and psychological stresses upon man-- stresses not encountered in any other life situation. Unfortunately, in the face of other high priority items created by the ever changing national and world situations existing for many years, the Navy Department has not been able consistently to provide sufficient support for these research personnel so that they could devote all of their time and energy to this area of investigation.

As the importance of the underwater world, or "inner space" as it has

* The opinions or assertions expressed herein by all members of the U. S. Navy are the private ones of the authors and are not to be construed as official or reflecting the views of the Navy Department or the naval service at large.

been popularly called, has become more generally known, and as national and world situations relaxed somewhat, support for research in all associated scientific disciplines began to blossom. Within the medical family of disciplines, possibly the greatest impetus to this fervor to exploit inner space was provided by the first of the Symposia on Underwater Physiology.

The First Symposium, also initiated by our present chairman and supported by the National Academy of Sciences—National Research Council and the Office of Naval Research, was held eleven years ago. The objectives of this symposium as stated were:

(a) To summarize what is currently known in the field of physiology as applied to the underwater environment;

(b) To direct the attention of those working in physiology to the various problems which exist;

(c) To encourage consideration of these problems in the evaluation of related research;

(d) To formulate proposals for future research and development, leading to increased capabilities of underwater swimmers.

To accomplish these objectives, the program committee for the first symposium invited the foremost authorities in this field of research to participate. The evidence for the enthusiastic response to the invitations of the committee may be found in the comments made by the introductory speaker, Captain O. D. Yarbrough, Medical Corps, U. S. Navy, (now retired), when he referred to his audience as "a hard corps cadre representing the sum total of scientific and practical knowledge, at least within these continental confines, with regard to individual underwater activity."

The successful accomplishment of the objectives of this Symposium by this "distinguished hard corps cadre" is a matter of history and is well known to all who are interested in this field. With the support and guidance of the National Academy of Sciences, the Navy Medical Department had been provided with the means to justify a many-fold increase of in-house research programs. Furthermore, the Office of Naval Research was able to obtain funds from the military budget to provide financial support to universities with capabilities and interest in developing research programs in underwater physiology. Additional funds were also made available for the advanced training of selected medical officers at these universities.

Directing our attention solely to those areas of hyperbaric physiology which are applicable to the military needs, the contributions of the 1955 Symposium and the one which followed it in 1963 are indeed impressive. They have resulted in:

1) An increase in knowledge and understanding of the biochemical mechanisms and physiologic effects of oxygen, carbon dioxide, nitrogen, helium, and other inert gases; inert gas narcosis; prolonged and continuous

exposure to increased ambient pressures, as in the SeaLab I and SeaLab II experiments; neuropharmacology and neurophysiology; respiratory physiology and the etiology of and treatment for the bends.

2) Improved decompression and no-decompression diving tables and diving accident treatment tables.

3) Diving tables for deeper and longer dives and for multi-gas mixtures.

4) The development of decompression computers and computer techniques.

5) The design of improved underwater breathing equipment.

A secondary accomplishment of these Symposia on Underwater Physiology has been their impact on clinical medicine. There has resulted an increased recognition that exposure to positive pressures offers a means of modifying physiological and pathological processes in man. Many laboratory investigators and clinicians rushed to the bandwagon with proposals for hyperbaric treatment of various diseases and conditions, particularly those associated with tissue anoxia. Fortunately, you who have been the leaders in underwater physiology were available for consultation and planning of these clinical studies so that they have been conducted fruitfully and with a minimum of complications.

Now, as in 1955 and in 1963, senior scientists of our Universities and the Navy feel that there is a need to compile and re-evaluate the results of research efforts in the field of underwater physiology. Upon completion of this compilation and re-evaluation, this august body of scientists will undoubtedly formulate a program for future endeavors. Although it would be presumptuous of me to suggest to this conclave specific programs for future research, it is evident that continued effort to increase our knowledge of the biochemical mechanisms and physiologic effects resulting from human exposure to even longer and deeper dives, possibly even to the limits of man's capabilities and endurance, is an essential and reasonable goal.

Thus, the Navy Medical Department anxiously awaits (and will be responsive to) the guidance and direction provided by the National Academy of Sciences - National Research Council and the Office of Naval Research in the further and continued exploitation of inner space. And, the entire medical family will profit by the evaluation and recommendations concerning the past three years of hyperbaric research as they may apply to and prove beneficial to the practice of clinical medicine.

2 | R. D. WORKMAN

Underwater Research Interests of the U. S. Navy

The increasing importance of man's underwater capabilities from a military standpoint has been recognized and supported in the U. S. Navy by an expanded research effort at laboratories under management of the Bureau of Ships and the Bureau of Medicine and Surgery, and by the support of research programs by the Office of Naval Research including its joint sponsorship with the Special Project Office of the Sea Lab I and II experiments. These efforts are directed toward realization of the goals of the Navy's Man-In-The-Sea Program to establish man's ability to work in the open ocean down to continental shelf depth for as long as desired, and to determine the ultimate depth-time limits to man's ability to work on the ocean bottom, provided he has available to him all the ancillary equipment, gas mixtures, pharmacological agents, etc. that can be of help. There are many medical, physiological, psychological and technological problems associated with attaining these objectives. A brief review of the work in progress in the U. S. Navy to meet these goals will be presented here.

An evaluation of the necessary components of the diving system including equipment and procedures was needed, for it was obvious that those used in the past would not be adequate to meet extended requirements. Where the emphasis in the past had been upon short, deep helium-oxygen dives in support of submarine rescue and salvage, extended work periods underwater will now be required with ultimate decompression time significantly increased. The need for a pressurized compartment at the work site with a respirable atmosphere maintained therein for the dive is clearly seen. Two alternate approaches are possible to meet these needs, including

a. An underwater station.

b. A submersible decompression chamber (SDC) - shipboard or deck decompression chamber (DDC) complex.

The capabilities of the two systems complement rather than substitute for each other.

Divers with the necessary breathing apparatus are thus able to be placed at the underwater site to carry out productive work over a period of hours or days. Upon completion of the work, the divers are transferred under pressure to the shipboard decompression chamber from the mated SDC and final decompression carried out. The ascent profile may be by stage, or continuous ascent at a carefully controlled rate, with an atmosphere of helium-oxygen or helium-nitrogen-oxygen maintained in the DDC. A constant safe Po_2 is controlled by a polarographic oxygen electrode sensor-control system, and carbon dioxide removed by alkali absorbent canisters. Atmosphere recirculation, humidity and temperature control is provided by a recirculating chilled water system powering fans magnetically linked to water turbines, thus eliminating electric motors in the pressure chamber.

The submersible decompression chamber was first proposed by Dr. Leonard Hill, a renowned British physiologist, in 1907 in a report of studies on diving to the Admiralty by J. S. Haldane (1). Designed and built by Sir Robert Davis of Siebe Gorman Ltd, the SDC has been in use by the Royal Navy for over 30 years. Only recently has its full capability been realized with a design used by E. Link and C. J. Lambertsen to permit locking on to a deck decompression chamber (DDC) by which the divers can be transferred under pressure at the surface from the SDC (7). Thus, the long exposure to cold during decompression in the water is avoided, and decompression of hours to days duration can be accomplished with comfort in the chamber to greatly extend the scope of diving depth and duration of exposure.

Another important advantage gained in the use of the SDC is the safety provided the diver working at depth by the proximity of a respirable atmosphere in a dry chamber where he can return in the event of equipment failure, injury or impairment of consciousness.

As the use of the SDC is developed, heat can be provided to the divers from the power or heat source at the SDC. Direct observation of the condition of the divers in the SDC and at the work site is possible with use of closed-circuit television. The SDC can be placed near a work site, thus avoiding the drag of current on hoses to the diver from the surface, which has seriously impaired mobility and work efficiency.

Decompression procedures and diving equipment development has therefore been along the lines of utilization of the SDC-DDC complex in diving operations, in that deeper and longer dives with present equipment

and techniques is considered to increase risk to divers in an unacceptable manner.

Attention has been directed to design of breathing apparatus for the diver working from the SDC or underwater station. It was considered that semi-closed mixed gas SCUBA with mass flow of the gas mixture could provide adequate control of the breathing mixture oxygen level, reduce the gas volume use rate required at depth, absorb exhaled CO_2 efficiently and give mobility to the working diver. This apparatus would be particularly adaptable for use from an SDC with gas mixture supplied by hose from supply banks thereon.

Similarly, the diver must be provided an optimum respirable medium that he may work effectively, unimpaired by breathing resistance, CO_2 retention, narcosis and oxygen toxicity. Use of a helium-oxygen mixture, with Po_2 maintained at about one ata. during the work period, has served to accomplish these factors during periods of hard work for two hours (Fig. 1). Decompression may then be carried out with nitrogen-helium-oxygen or nitrogen-oxygen mixtures, which appear to give some decompression advantage over helium-oxygen, at depths at which excessive gas density and narcosis can be avoided.

Studies of breathing resistance in the CO_2 absorbent canister have demonstrated excessive resistance at depth with the cylindrical canister. A flat canister with absorbent space in the form of a frustrum of a rectangular pyramid has been developed at EDU (U. S. Navy Experimental Diving Unit) to decrease the resistance to gas flow through the granular absorbent bed without sacrificing efficiency of CO_2 removal (Fig. 2). This canister has demonstrated acceptable flow resistance to a depth of 400 feet during tests with air (2).

Another equipment requirement developed by EDU personnel is a flow control block for gas mixtures used with the semi-closed mass flow apparatus (Fig. 3). Selection among three different flow settings for use with different gas mixtures can be made quickly and surely by the diver as his requirements vary with the dive and decompression. Gas supply from a manifold inside the SDC can be shifted by the diver as needed. The gas supply pressure is reduced by a regulator to that required for adequate flow at the control block. Gas is supplied by hose directly to the control block, with flow then to the breathing bags.

Thus, the breathing apparatus consists only of the gas flow control block, breathing bags and hoses, mask or mouthpiece, and CO_2 absorbent canister (Fig. 4). No gas cylinders are attached to the apparatus as the gas supply in the SDC is assured and controlled by the dive attendant.

Working dives for 15 minutes actual time at depth have been completed

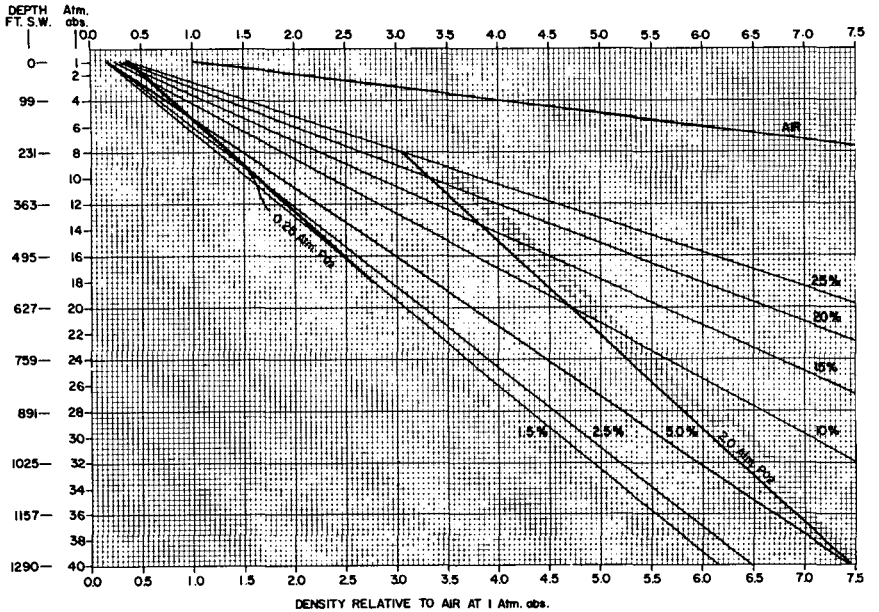

FIG. 1. Comparison of densities of various mixtures of oxygen in helium with air at equivalent depths to 40 atmospheres absolute.

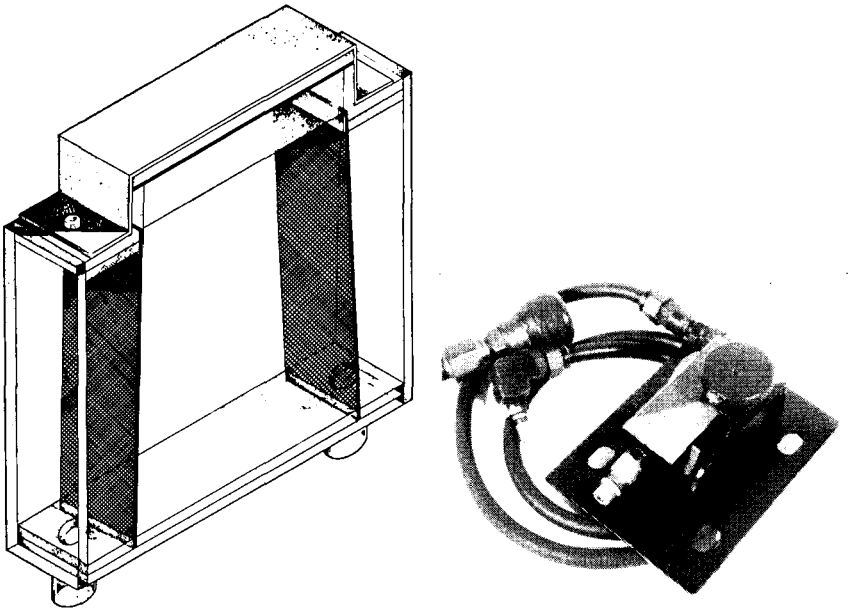

FIG. 2. Generic model of the flat CO_2 absorption canister
Fig. 3. Garrahan mixed gas flow control block

successfully for depths from 300 to 600 feet with the breathing mixtures and equipment described (Fig. 5). The dives were simulated in the wet-dry pressure complex at EDU with the divers transferring to the dry chamber for decompression upon completion of the work period underwater in the wet chamber.

It became apparent that the decompression time required for the diver to breath an enriched oxygen-inert gas mixture by demand mask became

FIG. 4. Prototype of deep dive mixed gas breathing apparatus used at the U. S. Navy Experimental Diving Unit.

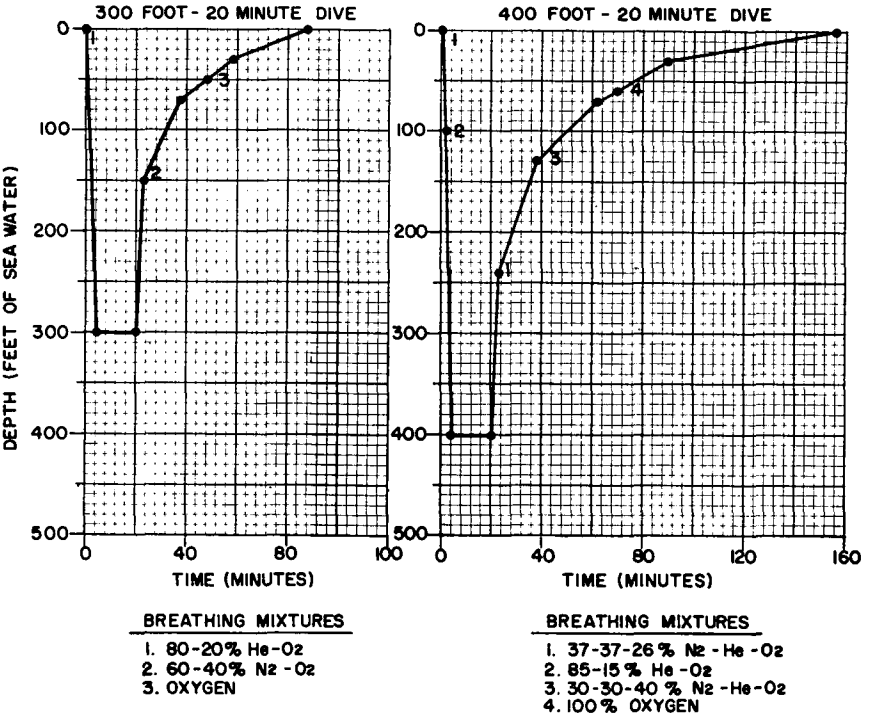

FIG. 5. Helium-Oxygen dive schedules with continuous ascent decompression

excessive as diving depth increased. Thus, a respirable chamber atmosphere would be required for prolonged decompression, and this becomes feasible if productive work time at depth can be increased to several hours.

While there is little information available to indicate work efficiency with exposure time at various depths, cold exposure and types of work, it was decided that working dives of 1 and 2 hours would be needed to accomplish work which would require a considerable number of shorter dives to complete. The significant uptake of inert gas in slowly equilibrating tissues during such long dives obligates a prolonged decompression which can only be considered possible with use of the SDC-DDC technique. Control of the chamber atmosphere to safe levels of Po_2 to avoid pulmonary oxygen toxicity and fire hazard is also readily attained in the closed chamber atmosphere to permit use of helium-oxygen or helium-nitrogen-oxygen mixtures in place of air.

For simplicity, an air atmosphere has been used in the decompression chamber, with divers continuing to breathe a helium-oxygen mixture supplied by demand regulators and masks in the chamber until a depth of 80

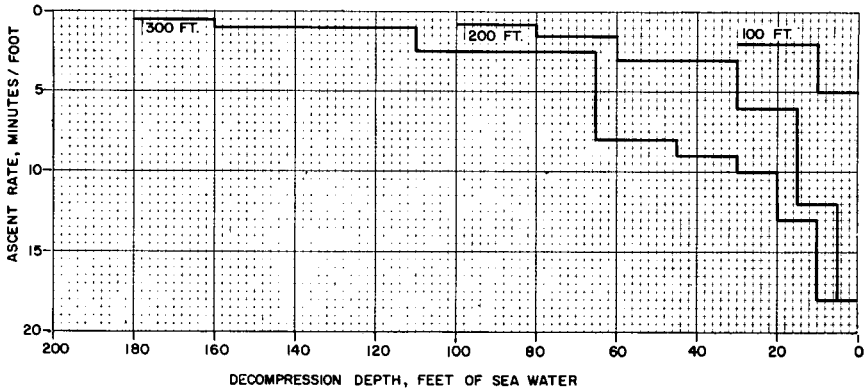

FIG. 7. Comparison of ascent rates for helium-oxygen dives of 100, 200 and 300 feet with 120 minutes bottom time. Breathing mixture: 300 to 100 feet-He-O_2 with P_{O_2} of 1–1.3 atmospheres; 100 to 45 feet-air; 45 to 0 feet-air and oxygen.

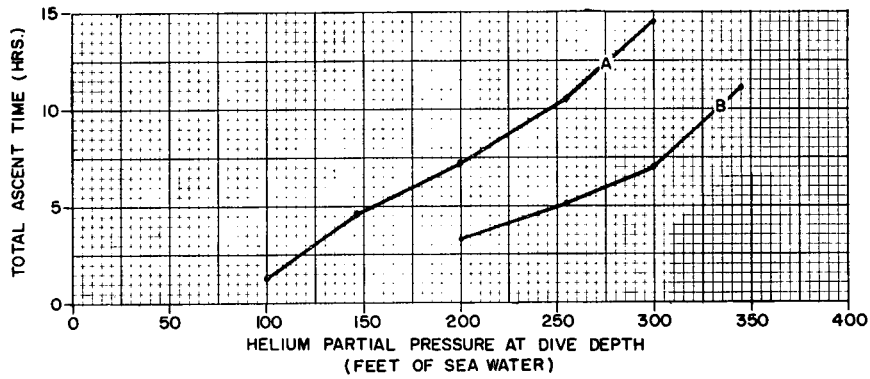

FIG. 8. Total ascent time for helium-oxygen dives of 120 minutes bottom time (Curve A) and 60 minutes bottom time (Curve B).

pression being required following the first 24 hours of exposure to pressure. The SDC-DDC technique makes possible rotation of teams of divers on an underwater site. The ease of atmosphere control and providing for the diver's needs in the DDC has certain advantages. Upon completion of the work, decompression by controlled ascent of the DDC can be carried out over the time required.

Such saturation exposures have been performed successfully by groups of subjects in the Sea Lab I and II experiments (4). In the latter, three successive teams of divers demonstrated the capability to perform useful

work during exposures to helium-oxygen atmospheres at 204 feet for two weeks each in water at a temperature of 46° to 52° F. Two subjects spent one month each in the undersea station. Continuous ascent decompression was employed over a period of 30 hours after transfer to the DDC from the underwater station in the SDC.

At EDU, 24 hour exposures at 300 and 400 feet have been carried out in the wet-dry chamber complex with 0.5 atm. Po_2 in a helium atmosphere breathed by the two subjects on each exposure (5). Work was performed by the divers with Mark VI semi-closed circuit mixed gas apparatus used in the wet chamber during the exposure. Oxygen control of the chamber atmosphere was by means of polarographic oxygen electrode sensors activating solenoid supply valves. CO_2 removal was by means of a fan-driven unit containing canisters of granular Baralyme. Continuous ascent decompression was employed at a rate of 11 minutes/foot (6 hours/atm.) following an initial decrease of 1 atm. pressure. Three watch sections of attending personnel were required for the exposure period and the 49 and 67 hour ascent periods for these dives.

In addition to work with deeper diving systems, a considerable number of dives have been made to evaluate a closed-circuit constant oxygen partial pressure mixed gas SCUBA. Oxygen sensing and control is by means of a temperature-compensated polarographic oxygen electrode with suitable electronic circuitry and battery power supply. Working dives of a range from 300 feet for 20 minutes to 70 feet for 220 minutes have been made to demonstrate depth and duration capabilities. Separate inert gas supply for helium and nitrogen permit switching of the inert gas fraction of the mixture during the dive and decompression (Fig. 9).

A series of minimal decompression dives, and those of duration permitted by 15 minutes decompression time using a nitrogen-helium inert gas mixture with Po_2 of 1.3 to 1.6 atm. abs., are presently being evaluated with this equipment (Tables 1 and 2). Significant extension of dive duration has been observed with this procedure over that possible with helium-oxygen used in semi-closed mixed gas SCUBA.

A decompression procedure using helium-oxygen in the Mark VI mixed gas SCUBA to permit repetitive dives to a depth of 200 feet has been developed (6). A system is provided by which the diver can determine the necessary increase in decompression time for successive dives, based on the amount of excess inert gas in body tissues upon completion of previous dives. The amount of decompression required is decreased by the time interval at the surface between dives. A method utilizing oxygen decompression at 30 and 20 foot water stops is also provided. More than 400 single and repetitive open sea dives at depths to 200 feet have been per-

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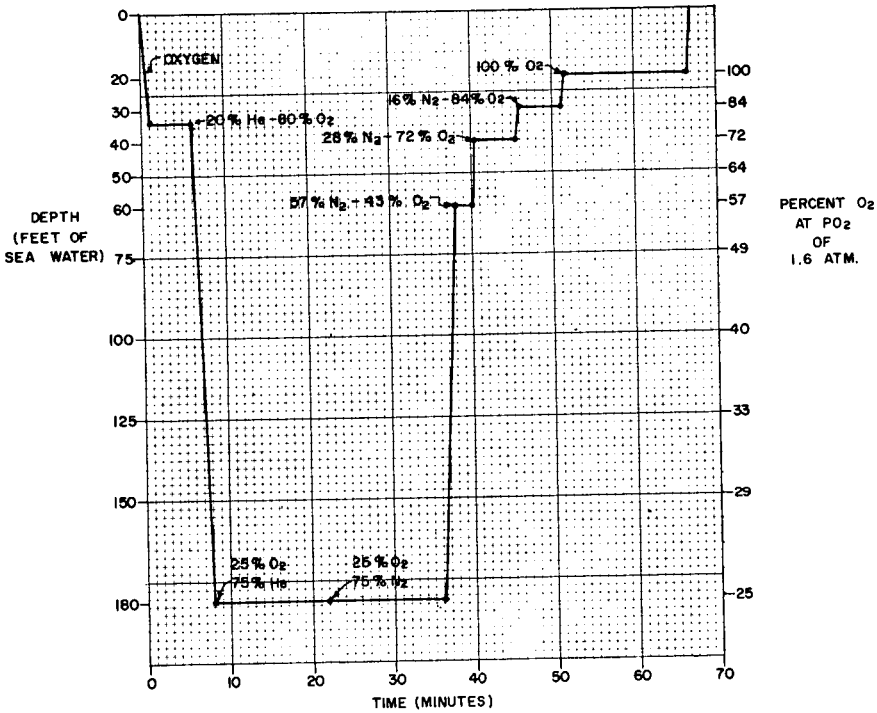

FIG. 9. Profile of a 180 feet-30 minute working dive using closed-circuit mixed gas apparatus. P_{O_2} was maintained at 1.6 atmospheres throughout the dive.

TABLE 1

Comparison of Decompression Required for Dives with 37% He-37% N_2-26% O_2 and 74% He-26% O_2

Depth (ft.)	Exposure Time (min.)	Decompression Time (min.)	
		He-N_2-O_2	He-O_2
80	100	12	46
100	70	14	42
120	60	24	52
150	40	22	52
200	30	35	72

formed without decompression sickness or oxygen toxicity occurring during use by operational personnel.

Several studies vital to the extension of diving in the U. S. Navy are

TABLE 2

Comparison of Dives on He-O_2 and on N_2-He-O_2 with No Decompression and with 15 Minutes Decompression

Depth (ft.)	Bottom Time (minutes) 75-25% Helium-Oxygen			Bottom Time (minutes) Nitrogen-Helium-Oxygen		
	No Decompression	15 Min. Decompression	15 Min. O_2 Decompression	No Decompression 1.3–1.6 Atm. Abs. Po_2	15 Min. Decompression 1.3 Atm. Abs. Po_2	15 Min. Decompression 1.6 Atm. Abs. Po_2
70	85	100	115	240	—	—
80	60	70	80	140	—	—
90	45	60	70	80	130	—
100	35	45	50	50	100	—
110	30	40	50	40	70	—
120	25	35	40	35	60	—
130	20	30	35	30	45	—
140	15	25	30	25	40	—
150	15	25	25	20	—	40
160	10	15	20	15	—	30
170	10	12	20	12	—	25
180	5	10	15	10	—	20
190	—	10	10	9	—	17
200	—	8	—	8	—	15

(1.3 atm. abs. Po_2 / 1.6 atm. abs. Po_2)

reported in other papers of this volume. These include assessment of ventilatory adequacy and performance decrement during working dives, mechanisms of bubble resolution in induced air embolism in animals, improved methods of treating decompression sickness, excursion diving from saturation exposures, decompression for saturation exposure dives and studies of thermal protection during cold water exposure. Even this listing is not inclusive of all the studies in progress for there are many more of a basic and exploratory nature which may well prove vital to advance the state of the art in diving over the coming years.

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Swedish Naval Interests in Diving Research

The Swedish Hydrogen-Oxygen Diving Method Developed by A. Zetterström

Twenty-three years ago the young Swedish engineer, Arne Zetterström, suggested to the Royal Swedish Navy that it "use hydrogen in deep-sea diving in such a way that there would be no risk for explosion" (quoted from ref. 34). The method proposed involved the use of a synthetic gas mixture containing 72 per cent hydrogen, 24 per cent nitrogen, and 4 per cent oxygen. Based on comprehensive physiological studies, including decompression experiments on rats and cats, Professor Y. Zotterman accomplished the important and laborious task of computing hydrogen-oxygen decompression tables applicable for man (10). Two years later, in the summer of 1945, Zetterström broke the then existing, deep-sea diving record as he, in the last of a series of test dives, descended to a depth of 160 meters (525 ft). In this last dive Zetterström breathed a mixture of 96 per cent hydrogen-4 per cent oxygen while on the bottom, and reported that no ill effects from the inhalation of the hydrogen gas mixture were experienced. Thus, no signs of depth narcosis were noticed, and the breathing resistance was appraised as being no greater than with air at 40 meters. Since the voice became nasal and indistinct, the diver had to use the Morse code, and because of the high heat conductivity of hydrogen gas, he felt the low temperature of the water sooner than when diving with ordinary air. In the initial phase of the ascent, the diver was accidentally brought closer to the surface than the decompression schedule of the dive had prescribed, which resulted in the death of Zetterström, due to severe hypoxia and decompression sickness.

Much more basic research is required concerning the physical properties of hydrogen-oxygen mixtures and their physiological effects on man before the hydrogen method can be safely used in routine diving operations. The

work and empirical observations made by Zetterström, however, demonstrate that such gas mixtures provide a respirable atmosphere for man even at very high pressures, and thus, a potential possibility of extending useful diving depth. By its stimulating and encouraging influence on other investigators, the pioneer work of Zetterström has also meant a great deal to the Swedish underwater research activity in general.

In the following pages I will provide a brief review of some of the medical problems which confront man as a diver and, which in recent years, have been studied by Swedish investigators. The topics which will be emphasized will be: performance in high-pressure atmospheres, decompression sickness, free ascent and related problems, and intercommunication problems in deep-sea diving.

Performance in High-Pressure Atmospheres

Mental and Psychological Reactions in Hyperbaric Air

For more than a century it has been known that man may show signs and symptoms of narcosis, such as euphoria, slowed mental activity, confusion, and impairment of performance when exposed to compressed-air atmosphere. According to empirical observations in deep-diving and caisson operations such overt signs of narcosis first appear at pressures equivalent to diving depths of 30 to 50 meters, and then increase gradually with the depth until at a level of about 90 meters the diver is considered incapable of taking care of himself. Although this phenomenon, usually referred to as depth or compressed-air narcosis, is seldom fatal to the heavy helmet diver, it may often result in drowning in the scuba diver because of loss of consciousness, or due to the fact that the diver pulls off the face mask or mouth piece.

Depth narcosis, along with decompression sickness, is not only the most obvious hazard in deep diving operations, but also the vital factor that eventually may determine the limitation of useful diving depth. In recent years therefore, much attention has been directed to the various psychophysiological problems which confront man when exposed to extreme ambient pressures. In Sweden the research activity in this field has been concentrated primarily on studies concerning the effects of raised air pressures on mental and psychomotor functions in order to establish the depth tolerance and limit in ordinary air diving. These studies constitute an integral part of a series of psychological, physiological and technical experiments that are now undertaken by the Swedish Navy with the object of developing methods for routine diving trials down to, and including,

depths of 150 meters, and with exposure times of at least 60 minutes at these depths.

Manual Dexterity and Arithmetic Calculation Capacity: The psychological investigations in this research program have, since 1959, been conducted by Dr. J. Adolfson. In a first pilot study (1), twenty mine clearance divers were tested in a dry compression chamber at a pressure of 7 atmospheres absolute, equivalent to a diving depth of 60 meters (approximately 200 feet). Five types of tests were used, designed to evaluate manual dexterity, manipulative ability, simple and choice reaction times, and arithmetic calculation capacity. When compared with control tests at normal sea level pressure, no significant changes in the first two variables were demonstrated, and only slight impairment of the last three variables was observed. It was therefore considered that well-trained divers, breathing air, should be able to carry out even rather complicated tasks at depths of 60 meters.

In order to further examine the depth tolerance in air diving, tests on manual dexterity and arithmetic calculation capacity were then made on 15 divers and submariners, both officers and enlisted men, at pressures of 1, 4, 7, and 10 atm. abs. (1, 3). In a first test series the subjects were at rest, and in a second series they performed leg exertion on a bicycle ergometer at a work load of 300 kgm/min. In addition, a third test series was made at 13 atm. abs. (approximately 400 feet) on 13 of the 15 subjects under resting conditions. The experiments were carried out in a dry compression chamber at our laboratory. To exclude admixture of expired carbon dioxide, the air inhaled was administered from compressed-air cylinders via a mouth piece and a demand valve system.

As shown in Figure 10, manual dexterity decreased with increasing ambient pressure, both at rest and during leg exertion. As in the pilot study, the performance decrement at rest was very slight at pressures up to and including 7 atm. abs., but it increased markedly with the depth. Of special interest is the observation that, at each test pressure, the decrement was significantly greater in the exercise experiments, in which the impairment in manual dexterity became manifest already at 4 atm. abs. That the leg exertion itself had no apparent adverse effects on manual dexterity is evident from the fact that there was no significant difference between the rest and exercise control values obtained at sea level pressure.

The tests on arithmetic calculation capacity showed similar results, *i.e.*, the capacity decreased with increasing ambient pressure both at rest and during leg exertion, especially in the higher pressure range (Fig. 11). Also in this test the loss of capacity was greater in the exercise experiments. While physical exertion thus seems to aggravate the signs and symptoms of depth narcosis, the causes and mechanisms involved have not yet been established.

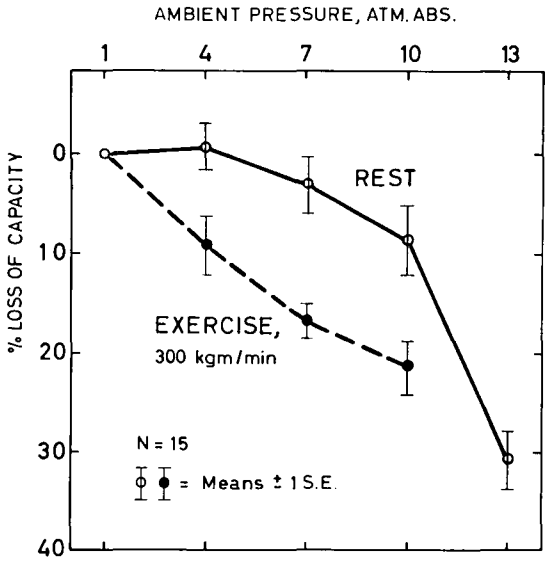

FIG. 10. Effects of raised air pressures on manual dexterity at rest and during leg exertion. [Data from Adolfson (1, 3, 5).]

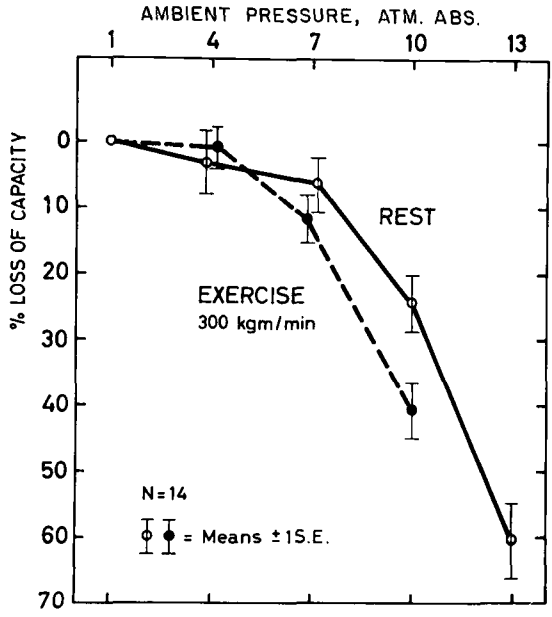

FIG. 11. Effects of raised air pressures on arithmetic calculation capacity at rest and during leg exertion. [Data from Adolfson (1, 3, 5).]

Another interesting observation from these investigations was that the results obtained at rest differed according to the rate of pressure application. Thus, when the test pressures were applied in the order 10, 7, and 4 atm. abs. ("rapid compression"), the decrement of performance was found to be more marked than when applied in the order 4, 7, and 10 atm. abs. ("slow compression"). In the exercise experiments, on the other hand, the rate of compression had no apparent influence on the test results.

Continuous Free Association: In a subsequent investigation (8), tests on continuous free association were made on 9 subjects at pressures of 1, 4, 7, 10, and 13 atm. abs. in a dry pressure chamber. At each pressure level the test subject was presented eight different stimulus words, such as dog, ball, tube, etc., and on each of these stimulus words he was to respond with a series of single words as rapidly as possible. The subject was asked to let each word that he mentioned freely suggest the next in order, as exemplified by the following sequence: "dog - cat - horse - buggy - wheel-tire - rubber - etc." The average number of responses given in 60 seconds on a single stimulus word at each one of the test pressures was calculated for each subject and then estimated in per cent of his control value at ground level. The number of associations became successively reduced with increasing ambient pressure, the mean reduction for the 9 subjects amounting to 22, 32, and 36 per cent at 7, 10, and 13 atm. abs., respectively (Table 3). These results, thus, confirm earlier observations that depth narcosis also shows as an impairment of association ability.

TABLE 3

Percent Decrement of Performance in High Pressure Atmospheres.

[Combined data from Adolfson et al. (1–8).]

Mean values are for 9 to 23 subjects. The reference levels, i.e. 100% performance capacity, relate to control data obtained at sea level pressure.

Condition	Air Breathing									80% He-20% O_2	
	Dry Compression Chamber							Wet Chamber		Dry Chamber	
	Rest				Exercise†			Rest		Rest	Exercise†
Ambient Pressure, atm. abs.	4	7	10	13	4	7	10	7	10	10	10
Manual dexterity	−1	3	9	31**	9**	17**	22**	1	13**	7*	−2
Arithmetic calculation	3	6	24**	61**	1	12**	41**	21*	34**	−5	4
Continuous free association	10	22**	32**	36**	—	—	—	—	—	—	—
Visual choice reaction	1	3	15**	—	—	—	—	—	—	—	—
Hearing discrimination	1	7**	13**	—	—	—	—	—	—	—	—

† Leg exertion, 300 kgm/min, on a bicycle ergometer.

* Significant at the 5% level of probability.

** Significant at the 1% level of probability.

Visual Choice Reaction and Hearing Discrimination: It is an old experience that divers at great depth often show difficulties in conceiving and understanding orders and messages that are delivered over vocal communication systems. Perceptional and psychosensorial disturbances at depth have also been noticed in some of the subjects in the previously mentioned investigations. In an attempt to differentiate and evaluate possible factors and mechanisms responsible for these phenomena, two other series of experiments were carried out (1, 7). The tests used were designed to evaluate visual choice reaction (1) and hearing discrimination (7). Both test series were made in a dry compression chamber at pressures of 1, 4, 7, and 10 atm. abs., the first series on 10 subjects, the second on 23 subjects. In the hearing discrimination test a series of specially selected words were presented to the subject from a tape recorder, and the subject had to repeat the words in the way he understood them. At each test pressure the sound volume was adjusted to a level that was pleasant for the subject and well above the hearing threshold. As can be seen in Table 3, a noticeable impairment of the hearing discrimination ability appeared already at a pressure of 7 atm. abs., whereas visual choice reaction became significantly reduced at 10 atm. abs.

General Behaviour at 13 Atmospheres: The general reactions and facial expressions of the subject and the tester in the pressure chamber were continuously followed on a television monitor screen and, in some instances, also recorded on 16 mm colour film by a remote-controlled film camera. In addition, their conversation and voices were tape recorded.

While no or only slight signs of mental and psychomotor disturbances were noticed at pressures less than 10 atm. abs., marked symptoms were observed in the majority of subjects at 13 atm. abs. Thus, most of the subjects showed alterations in mood and affectivity, which in some cases developed into a manic state with shouting and restlessness. A great variety of perception disturbances, such as micropsia, hallucinatory reverberation of auditory patterns, a general sense of increased intensity of vision and hearing, and illusions of various types were reported by the subjects. No unusual sensations of taste or smell were noted, however. In most cases more or less severe disturbances of consciousness were observed which took different forms, from a general clouding of the awareness of the surroundings with difficulties in concentration to a definite sense of impending blackout. On reducing the ambient pressure, all the symptoms were readily reversible although some of them persisted down to 7 atm. abs. In contrast, on raising the pressure these gross symptoms became first obvious at 13 atm. abs.

Comparison Between Experiments in Wet and Dry Compression Chambers: The object of the next experimental series (4) was to find out whether immersion of the subject would cause any alterations of the ob-

served decrements of performance at raised air pressures. Tests on manual dexterity and arithmetic calculation capacity were therefore carried out on 11 subjects at rest in a wet compression chamber at the Naval Diving Training Center in Stockholm. The pressures used were 1, 7, and 10 atm. abs. It was found that at each single pressure level the test values were 15 to 25 per cent lower than in the dry chamber experiments (Fig. 12). This suggests that although submersion itself made it more difficult to accomplish the tasks presented, it did not have any apparent influence on the performance decrement caused by high air pressures (*cf.* Table 3). It may then also be concluded that studies on depth narcosis which, from a technical point of view, are difficult to perform when submerged, *e.g.*, EEG-studies, may conveniently be carried out in a dry pressure chamber.

Comparison with Helium-Oxygen Breathing: It is well known that the symptoms of depth narcosis become much reduced if helium-oxygen mixtures are substituted for air as breathing medium. However, previous performance tests at depth with such gas mixtures have been restricted to resting conditions, and it was therefore considered of interest to investigate whether muscular exercise might enhance any narcotic effect of helium-

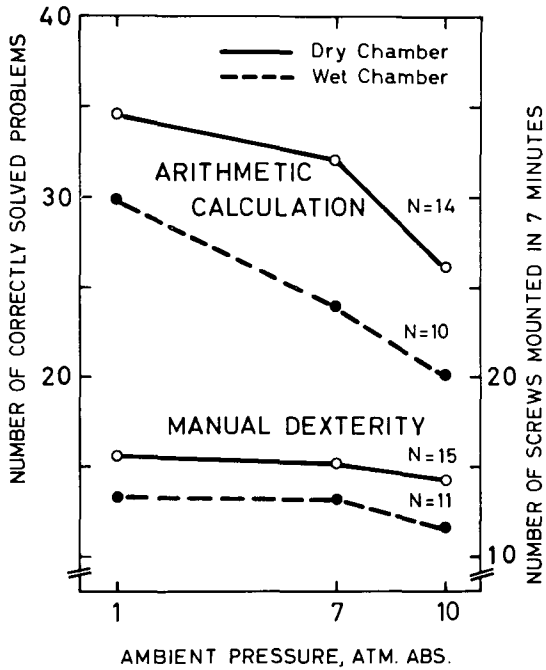

FIG. 12. Comparisons between performance tests at rest in wet and dry compression chambers. [Data from Adolfson (4).]

oxygen mixtures at 10 atm. abs. Tests on manual dexterity and arithmetic calculation capacity were made on 10 subjects at rest and during leg exertion (300 kgm/min) in a dry compression chamber while the subjects were breathing a mixture of 80 per cent helium-20 per cent oxygen (2). No significant changes of the two variables could be demonstrated at 10 atm. abs. either at rest or during exercise, except for a slight impairment of manual dexterity in the rest experiments (Table 3).

Psycho-Physiological Responses to High Oxygen Pressure

A great number of investigations have demonstrated that exposure to high oxygen pressure can provoke convulsive seizures and unconsciousness (30). The nature and site of the neurophysiological disturbances leading up to the convulsive state have not yet been established, however. If, as has been suggested, the cerebral cortex as a whole is the site of motor seizure origin, it would seem reasonable to expect the convulsions to be preceded by a deterioration in performance. Furthermore, if that would be the case, it should also be possible to explain compressed-air narcosis as caused in part by the high oxygen pressure itself.

In order to evaluate these possibilities we have performed a series of experiments in collaboration with Drs. M. Frankenhaeuser and V. Graff-Lonnevig (19). Psychomotor performance of 10 subjects during exposure to oxygen at 3 atm. abs. was compared with performance under normal air breathing at 1 atm. abs. In none of the three tests used (simple and four-choice visual reaction times and mirror drawing) could any significant influence of high oxygen pressure be demonstrated. Nor did performance show any tendency to deteriorate with time within the 30 minutes period employed. Of special interest are the observations made on one of the subjects, who suffered an attack of generalized convulsions and unconsciousness after 17 minutes of oxygen breathing at 3 atm. abs. Even in this case no signs of deterioration were revealed until the moment of onset of the attack, which shows that psychomotor performance can be maintained at a high level up to the critical point, when overt symptoms of oxygen poisoning are noticeable. It may also be concluded that depth narcosis is not, to any significant degree, caused by the high oxygen pressure itself.

The effects of high oxygen pressures on the histology of the central nervous system and certain endocrine cells have been studied by Edström and Röckert (14). Rats were exposed daily to oxygen at 6 atm. abs. for about eight weeks, the exposure times being adjusted so as to give only a low incidence of convulsions and lung symptoms. In some of the animals slight motor symptoms of a paralytic nature developed after about two weeks, but then regressed and eventually disappeared during the continued oxygen treatment. No histological signs of any pathological changes of the lungs,

or degeneration of the central nervous system (hypothalamus, motor cortex, cerebellar cortex and spinal cord) could be observed at autopsy after 7 to 9 weeks. The mode of action of high oxygen pressures on the central nervous system was therefore presumed to be entirely functional. The effects observed on a number of endocrine organs and on the sympathetic nervous system were considered to be characteristic for a non-specific stress reaction, except for the case of the thyroid. Further evidence for a specific effect of high oxygen pressures on the thyroid function has been given by Sjöstrand (32).

Causes and Mechanisms Involved in Depth Narcosis

In spite of a great number of experimental investigations (see ref. 9) the causes and mechanisms involved in depth narcosis are not fully understood. Based primarily on results from comparative studies on the narcotic effects of mixtures of oxygen and the so-called inert gases at increased pressures, the majority of investigators have concluded that depth narcosis can be ascribed to a specific narcotic action of the inert gases under pressure. Other investigators believe, on the other hand, that it is a matter of carbon dioxide narcosis, the CO_2 retention being caused, it is suggested, by interference with the CO_2 elimination in the lungs due to the increased density of the gases breathed.

In an attempt to separate the possible causes and mechanisms involved in compressed-air narcosis, we have compared the effects on psychomotor performance (simple and four-choice visual reaction times and mirror drawing) of inhalation of different nitrogen-oxygen mixtures at rest in hyperbaric environments (20, 24). The gas mixtures and ambient pressures used were chosen in such a way that the effects of 1) increasing the nitrogen pressure with no change in oxygen pressure, and 2) varying the oxygen pressure at a constant high level of nitrogen pressure could be demonstrated. When the oxygen tension was kept constant, either at a low or at a high level, an increase in nitrogen pressure of 3 to 4 atmospheres produced but very slight changes in performance. At a constant high nitrogen pressure (3.9 atm), on the other hand, the simple and choice reaction times showed a tendency to increase with increasing oxygen pressure. Since high oxygen pressures *per se* have no measurable influence on these variables (19), the above results indicate that oxygen excess has a potentiating mechanism on nitrogen narcosis. It was also concluded that excess oxygen acts indirectly by interfering with the elimination of carbon dioxide from the tissues. Evidence for a synergistic narcotic action of high nitrogen and carbon dioxide tensions was first given by Case and Haldane (12).

The observation of Adolfson (1, 3) that exercise potentiates compressed-air narcosis may then be explained in terms of a possible further elevation

of brain tissue P_{CO_2} due to suppression of the normal ventilatory response to exercise. This would be a consequence of a marked rise in resistance of the airway itself and the breathing apparatus at high flow rates and increased air densities. The empirical observation that helmet divers usually become more intoxicated at depth than the scuba diver may possibly be explained in terms of a more pronounced CO_2 retention resulting from the elevated inspired P_{CO_2} due to accumulation of carbon dioxide in the helmet.

Observations on Physiological Reactions in Hyperbaric Environments

Of utmost importance for practical diving operations is to find out why work at depth usually results in exhaustion within a comparatively short period of time. The mechanisms responsible for this phenomenon are as yet poorly understood, but it seems highly probable that a great number of respiratory and circulatory factors are involved.

In collaboration with Dr. B. Holmgren, we have studied the influence of raised air pressures on some respiratory functions at rest (27). With increasing ambient pressure, respiration became progressively slower and deeper (Fig. 13). At 4 atm. abs. the average reductions in respiratory rate and minute volume amounted to 27 and 10 per cent, respectively, and the increase in tidal volume to 33 per cent. Because of a decreased functional

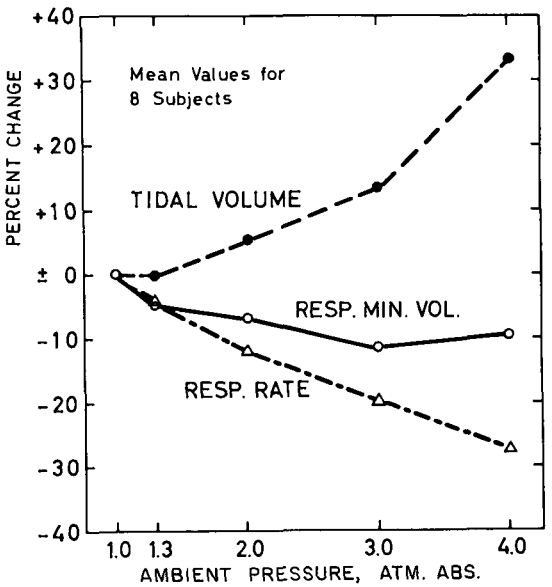

FIG. 13. Effects of hyperbaric air on respiratory functions at rest. [Data from Hesser & Holmgren (27).]

dead space/tidal volume ratio, the alveolar ventilation was somewhat increased despite the reduced respiratory minute volume. In order to separate and evaluate possible factors responsible for these changes, we also studied the effects of inhalation of different nitrogen-oxygen mixtures at various ambient pressures. By comparing the data from different experimental situations, the evidence obtained showed that the respiratory changes observed in hyperbaric air (4 atm. abs.) were caused by the combined effects of increased oxygen pressure and increased breathing resistance due to the increased air density. It was also concluded that nitrogen itself at pressures up to 3.8 atm. exerts little, if any, depressant action on respiration. More information is needed, however, concerning the respiratory responses to air pressures in excess of 4 atm. abs., both at rest and in exercise.

In the earlier mentioned experiments on psychophysiological effects of breathing a mixture of 80 per cent helium-20 per cent oxygen at 10 atm. abs. (2), the respiratory minute volume and heart rate were also measured (25). It was found that, on raising the ambient pressure from 1 atm. abs. to 10 atm. abs. during leg exertion at a work load of 300 kgm/min, the heart rate fell from a mean value of 108 beats/min to 98 beats/min. At 10 atm. abs. the respiratory minute volume averaged 8.8 l/min (ATPS) at rest, and 21.6 l/min during exercise.

In the air breathing experiments at rest, referred to above (8), the heart rate showed a tendency first to decline, and then to rise with increasing ambient pressure. Determination of catecholamine excretion revealed no noticeable changes at raised pressures. A remarkable complication to this study appeared during the collection of urine samples. The intention was to obtain a sample during the first hour at depth. However, most of the subjects were unable to produce any urine during this period even though half a liter of water was consumed at the beginning of the experiment. Not until the pressure was lowered to a level of 3 to 4 atm. abs., could a sample be delivered. In some cases there was a period of complete anuria during more than two hours, after which half a liter of urine was produced in fifteen minutes.

Decompression Sickness

Experiments on Animals

It is generally held that the symptoms of decompression sickness, or the diver's bends, result from the occurrence of gas bubbles in tissues and/or in small blood vessels (13). However, theoretically, it seems quite possible that other than simple physical-mechanical factors might also be involved. To study the bends syndrome from the biochemical point of view, Dr. E.

Kindwall, while working in our laboratory, started a series of experiments, which for the sake of convenience as well as economy were carried out on small animals. It was soon found, however, that small animals react differently to decompression from large animals. As early as 1908 Haldane et al. (11) had observed that small animals are more resistant to bends, and attributed this to their faster circulation being able to remove the excess of nitrogen before symptoms could appear. This explanation seems doubtful, however, because in shorter exposures small animals are also saturated more quickly.

Dr. Kindwall, therefore, made an attempt to analyze, in greater detail, the mechanisms of bends in small animals (28). Rats, guinea pigs, rabbits, and cats were exposed to air at pressures up to and including 11 ata for varying periods of time, and then rapidly decompressed. A goat and a dog were also used for comparison. Except for transient cyanosis or asphyxial death in cases of extremely rapid decompression, none of the small animals showed signs or symptoms comparable to the bends syndrome seen in man and larger animals. By computing nitrogen saturation-desaturation curves of six different half-time tissues in accordance with the animals' different body weights, metabolic rates, and resultant calculated circulation times, evidence was obtained that the tissue nitrogen tensions on surfacing could be extremely high, particularily in the slower tissues, without causing serious ill effects. It thus appears that the shorter circulation time of small animals does not by itself explain their immunity to bends. Similarly, no direct conclusions regarding the efficacy of decompression schedules for man should be drawn from tests on small animals.

In a second investigation, Kindwall et al. (29) found no evidence of histamine and serotonin release in albino rats, which had been rapidly decompressed from 6 ata. Nor were there any changes in the morphological appearance of the mesenteric mast cells.

An entirely different experimental approach to the question concerning the correlation between bends symptoms and tissue gas tensions has been explored by Dr. C. Lundgren, as described elsewhere in this volume.

Observations in Divers

In 1962 the Swedish Navy adopted, with minor modifications, the U. S. Navy standard air decompression tables (33) for routine air dives. In a first test series, which comprised 148 dives to depths of 30 to 60 meters, one case of pain-only bends, and one case with partial paralysis occurred (23). There was a rather high incidence of paresthesia, pruritus and skin rash, usually located in the forearms. Although the causes of such symptoms are as yet not fully established, practical diving experience indicates that they are produced by bubble formation in the skin, and not, as has also been sug-

gested, by functional disturbances of the central nervous system. Evidence supporting the first mentioned explanation was obtained in the following way (23). In order to prevent cooling of the skin, the right forearm of one diver was wrapped with an extra layer of wool, and the left forearm of the second diver. On surfacing, neither of the divers experienced any symptoms in the arm that had been wrapped, whereas paresthesia appeared in the other arm. This suggests that cooling of the skin during decompression results in local vasoconstriction with a consequent reduction of blood flow and nitrogen wash out.

In simulated dives to 90 meters with 80 per cent helium-20 per cent oxygen and exposure times of 30 minutes (25), the U. S. Navy helium-oxygen decompression tables (33) were proved to be safe in 20 dives in which the subjects were at rest throughout the dive. In contrast, when the subjects performed leg exertion at 300 kgm/min during the 30 min exposure time, only two out of ten subjects remained entirely free from bends symptoms during the decompression. In five cases (50 %) the divers had to be recompressed.

Free Ascent and Related Problems

The medical problems associated with methods for emergency ascent in scuba diving and individual escape from disabled submarines are closely related to the physiology of breath-holding. In order to find out whether free ascent can be safely accomplished when preceded by a period of breath-holding, we have conducted a series of experiments in the 20 meter submarine-escape training tank located in the Royal Swedish Navy base at Karlskrona (21). It was interesting to observe that not only the maximum breath-holding time after the inhalation of air increased with the depth of water, but also the symptoms of distress and unpleasantness experienced at the end of the breath-holding period (75–180 sec) vanished completely during the first few meters of the ensuing ascent. While subsequent investigations (22, 26) have shown that the main cause of the increased breath-holding ability at depth is the rise in alveolar oxygen tension, the factors responsible for the second phenomenon have, as yet, not been established. A probable explanation could be, however, that the subjects continued to hold their breath during the first meters of the ascent, which resulted in an increased lung volume and a consequent reduction of the ventilatory stimuli existing at reduced lung volumes (31).

Intercommunication Problems in Deep-Sea Diving

Of great practical importance in deep-sea diving, from the safety as well as efficiency point of view, is the capability of maintaining acoustic communication between the surface and the diver. It is an old experience that

the diver's ability to talk intelligibly and to comprehend speech is much reduced at great depth, but information concerning the causes and mechanisms involved has been limited.

Some experimental studies have been carried out in recent years by Swedish investigators in an attempt to gain improved insight in the physiological and acoustical nature of the above phenomena.

Hearing in Compressed-Air Atmosphere

In order to elucidate the nature of the changes in hearing acuity experienced at increased pressures, Drs. E. Fluur and J. Adolfson (6, 18) have studied the effect of raised air pressures on the hearing thresholds as recorded by air and bone conduction tone audiometry. The experiments were made on 26 experienced divers in a dry compression chamber at pressures of 1, 4, 7, 10, and 11 atm. abs. Earphones were used in the air conduction tests, and the bone conduction tests were carried out with a traditional audiometric bone conductor receiver at the frequency range of 250–6,000 cps. The transmission properties of the earphones used were first analyzed by frequency response measurements at 4, 7, and 11 atm. abs., using an artificial ear of 6 ml cavity. It was found that, according to the frequency and ambient pressure, the transmission changes in the earphones amounted to ±5–10 dB.

As shown in Figure 14 the hearing acuity for air conducted sound decreased in proportion to the rise in ambient pressure. The audiograms

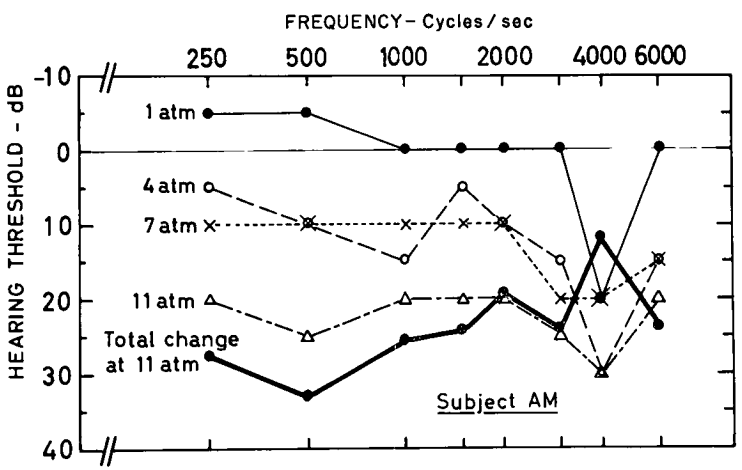

FIG. 14. Air conduction audiograms of Subject AM at normal and at raised ambient pressures. Points connected by heavy lines show the calculated total reduction in decibels (dB) of hearing acuity at indicated frequencies evoked by raising the ambient pressure from 1 atm to 11 atm. [Data from Adolfson & Fluur (6).]

presented in the figure are from one single test subject, but with very small variations similar results were obtained in the other subjects. Points connected by heavy lines show the calculated total elevation of the hearing thresholds at 11 atm. abs., *i.e.*, after allowing for the transmission changes in the earphones. As can be seen, the elevation of the thresholds was most marked in the middle frequency range of hearing, where it amounted to 30 to 40 dB. At the two highest test frequencies the elevation was less marked, and in subjects showing good hearing at these frequencies with normal pressure, only insignificant changes were observed at raised pressures.

The bone conduction thresholds, on the other hand, were found not to be affected by changes in the ambient pressure, indicating that the function of the inner ear perception mechanism remained unaffected. The diver's hearing difficulties at depth may then partially be explained by the fact that the raised air pressure causes disturbances in the sound conduction through the middle ear, whereas there is no loss of sensitivity in the sensory-neural function (6, 18).

Speech in Compressed-Air Atmosphere

As a first part of a research program concerning the causes and mechanisms responsible for the distortion of divers' speech at depth, Drs. G. Fant and B. Sonesson have recently carried out an acoustical analysis of speech sounds at air pressures of 1 atm. abs. and 6 atm. abs. (15–17). Four subjects were told to read out loud a list of nonsense syllables comprising all possible phonetic combinations, and the speech sounds were recorded with a dynamic microphone and tape-recorder. By means of spectrography each single speech sound was then divided into its components, *i.e.*, the fundamental tone (F_0) and the different groups of overtones or formants (F_1, F_2 etc.). Each vowel is characterized by its formants, which have defined frequencies.

The spectrographic analysis showed that, whereas the frequency of the fundamental tone (F_0) remained unchanged on raising the ambient pressure to 6 ata, the frequencies of the first and second formants (F_1 and F_2) tended to increase (Fig. 15). With few exceptions the F_1-shift was greater in magnitude than the shift in F_2, thus bringing the first formant rather close to the second formant. It is this substantial rise in F_1 that accounts for the "nasal quality" of certain vowels at high air pressures.

By means of X-ray studies carried out at 6 atm. abs. it could be shown that the distortion of speech at raised air pressures is not caused by an insufficient velar function. Further analysis, based on a theoretical model developed by Fant, supplied evidence that the observed spectrum distortion was mainly due to a shunting mechanism in vocal transmission, associated with the vibration of the walls of the vocal cavities. Due to the increased

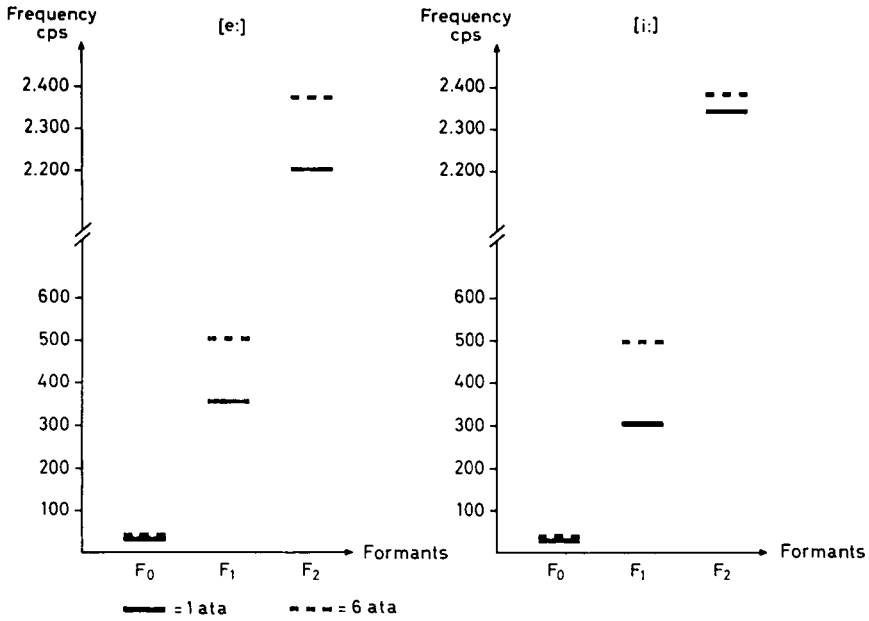

FIG. 15. Graphic representation of spectrograms of the vowels [e] and [i] obtained at normal and at 6 atm abs air pressure. Note that the rise in ambient pressure caused no alteration of the fundamental tone (F_0), whereas the frequencies of the first and second formants (F_1 and F_2) became increased. [From Fant & Sonesson (17).]

gas density at raised pressures the air column of the vocal tract will bring the soft walls of the supraglottal cavities into vibration, which results in leakage of overtones through the walls. Attempts made to reduce the shunting effect by increasing the impedance of the walls of the vocal tract by means of mechanical devices have failed so far, however. The use of teletechnical methods seem more promising, therefore, when trying to reduce or nullify the distortion of divers' speech.

By using the resonance formula of Helmholtz it was calculated that, at 1 ata the resonance frequency of the closed vocal tract for the first formant (F_1) is of the order of 150 cps. The corresponding value at 6 ata was calculated to be 370 cps. This means that, under given conditions, no resonance should be possible in the vocal cavity below these frequencies. These theoretical calculations were supported by the experimental results (Fig. 15).

Studies concerning the effects on speech of inhalation of gas mixtures other than air at normal and at increased ambient pressures are now in progress. Preliminary experiments have shown that the mechanisms responsible for the well-known distortion of speech during inhalation of

helium-oxygen mixtures are quite different from those mentioned above. The main cause is the transposition effect due to a higher velocity of sound in helium atmosphere, whereas changes in the ambient pressure seem to have only minor influence (17).

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4 | L. BARTHELEMY

French Naval Activities in Diving Physiology

Because of the great present interest in deep diving for practical purposes we must extend technological and physiological studies in order to perform diving under proper conditions. Our knowledge of the problems which remain is still very limited.

The purposes of most existing diving development programs are exploration and work on the continental shelf. Two technics for exploring the continental shelves are now being developed. One involves short duration, deep diving for periods ranging from about 10 minutes to 2 hours. The second emphasizes establishment of permanent or semi-permanent submarine bases. These technics are of course not in opposition or competition, but are complementary. During the period from 1963 to the present, the French Navy has devoted much attention to the problems of advancing the ability to perform short duration deep diving, while the civilian group under Cousteau has dealt primarily with practical problems of long duration submarine stations.

This presentation concerning French Naval Research will be a short survey of studies at Groupe d'Etudes et de Recherches Sous-Marines (GERS) during the period since the previous Underwater Physiology Symposium. We have been dealing with decompression schedules and elaborate diving schemes which have presented us with significant and difficult problems. The results are, of course, not conclusive but will be of interest to diving physiologists.

Calculation of Decompression Schedules

We have been using Haldane's method for predicting tissue saturation with inert gas. The method is based on factors which are related to rates of perfusion of the tissues with blood and the solubility of gases in tissue fluids. Despite some deficiencies, this type of calculation is better than

others for many purposes. It appears, however, that Haldane's assumptions are not adequate for very deep diving and especially for long durations (1 hour or more at medium depths (100 meters)).

In determining the tissue half-times by the Haldane method we experiment with different series of tissue half-times such as: 7, 30, 60, 120 and 240 minutes, or 5, 10, 20, 40, 80, 120 and 240 minutes. On the basis of logic it is considered that, when a tissue with a long half-time is saturated, the immediately shorter half-time tissues do not play any part in the calculation of required decompression. In order to have a safe decompression procedure, the schedule must incorporate the slowest necessary tissue. We have, thereby, obtained similar results with different series of tissue half-times.

The critical supersaturation ratios to be used must also be determined. Basic values of these ratios were determined with no-stop dives on air and with mixtures of helium-oxygen, helium-nitrogen-oxygen, and argon-oxygen. The safe values of the ratios were found to be modified by depth, nature of gaseous mixtures, duration of dive, and problems associated with exercise during dives. It is well known that the critical super-saturation ratio is dependent on the exponential factor k:

$$k = \frac{C \times B}{S}$$

where

C is the rate of blood perfusion of the tissue,

S is the solubility of the gas in the tissue, and

B is the solubility of the gas in the blood.

The limiting tissues and supersaturation ratios determined by short no-stop dives cannot be applied to dives where depth, duration and exercise-activity are very important and where breathing mixtures other than air are used.

Another type of decompression schedule for an anatomically definite tissue consists of stabilizing the supersaturation ratio at its beginning value and then making exponential ratio changes which modify the half-time in different experimental conditions.

The breathing gases used in the dives included helium-oxygen mixtures (varied percentage of oxygen), helium-nitrogen-oxygen mixtures (varied percentage of oxygen), nitrogen-oxygen mixtures (varied percentage of oxygen), and pure oxygen. The solubility coefficient in each body tissue (aqueous or fat) varies with the different gases and plays an important part in the determination of different half-times.

Experimental dives during the period from 1964 to 1966 are presented in Tables 4 and 5. It appears from the results that we have to consider

different levels of depth, such as surface to 70 meters, 70 to 120 meters, 120 to 160 meters, and 160 to 210 meters. True parameters in each of these depth ranges cannot be directly applied to another level, but the next stage is based on the preceding one. Duration of stay at the maximum pressure is of principal importance, and a two hour dive at 100 meters involves more difficult calculations than a 10 minute dive at 200 meters.

Our experiments with no-stop decompressions show that, for dives using helium-oxygen mixtures, supersaturation ratios are less than for dives using nitrogen-oxygen mixtures. The results obtained using helium-nitrogen-oxygen are similar to those obtained with air breathing. When several gas mixtures are breathed during a dive, we noted that it is important to use successively gases which do not differ greatly in physical characteristics. Thus, breathing a nitrogen-oxygen mixture below 30 meters after breathing

TABLE 4

Symptoms during Experimental Dives at 100 to 200 Meters (10 to 20 atm.)

Dives were performed in the sea or in a hydropneumatic chamber.

Description of Dives	Number of Dives	Dives with Serious Symptoms	Dives with Bends	Dives with Pain (no recompression)	Dives with No Problems
At rest on the bottom.....	13	1	0	1	11
Light work.....	70	1	4	3	62
Hard work.....	15	0	2	1	12

TABLE 5

Accidents during Experimental Dives as a Function of Duration (A) and Depth (B)

A

Time on the Bottom (min.)	No Accident	Accident	% Accidents
10–15	14	2	12.5
20–30	53	5	8.6
30–60	18	6	25

B

Depth (meters)	No Accident	Accident	% Accidents
80–100	>100	0	0
100–120	65	9	12.2
120–150	17	3	15.0
150–200	8	1	11.1

helium-oxygen is difficult to endure. However between 60 and 30 meters, for example, everything else being equal, N_2-O_2 mixtures can be breathed after N_2-He-O_2 without risk. Above 30 meters, breathing N_2-O_2 after He-O_2 is easily endured and experiments at GERS established that between 30 meters and the surface, work of breathing is nearly the same for He-O_2 as for N_2-O_2 mixtures.

During ascent from a short duration, deep dive we consider that breathing successively He-O_2 (deepest depth), He-N_2-O_2, N_2-O_2 and then pure oxygen is satisfactory, provided that the limits of use are defined for each gas. In regard to oxygen breathing during decompression, it appears from our experiments with ventilatory mechanics that the most efficient depth is about 6 meters. At 12 meters and 9 meters the work of breathing with oxygen is much increased.

From our applied studies of tissue half-times and supersaturation ratios we have arrived at several conclusions:

First, determination of the first stop in decompression is the most important step. The following stops are relatively less important:

Second, we should consider that only two among the entire series of half-time tissues are important in a particular decompression schedule. These are (a) a very short half-time tissue at the beginning of ascent, which can be eliminated from the calculation by choosing the proper rate of ascent, and (b) a long half-time tissue which depends on the type of dive which will control the ascent. It is necessary to be certain about the supersaturation ratio for this tissue.

Next it is considered that tissue half-times and supersaturation ratios are dependent both on blood perfusion of the tissues and the solubility of gases in the tissues. During different phases of the dive many parameters such as depth, duration, exercise, and gas mixture vary. Therefore, for a definite anatomical tissue, the acceptable or safe half-time or ratio can be different on the bottom, during the ascent, and at the surface.

For reasons such as these, it is necessary to define the depths at which the parameters of the decompression calculation must be changed. In such a calculation, it is much more attractive to conceive of using a continuous ascent. Considering the great number and variability of parameters and the numerous and large differences among subjects, it is not possible to assure absolute safety of the decompression schema for a dive complicated by great depth, long time on the bottom, or the performance of work.

Experiments at GERS

Experiments in open sea diving have also recently been performed by GERS with a small Siebe Gorman submersible decompression chamber (SDC). The gas mixtures were stored on the SDC and divers were observed

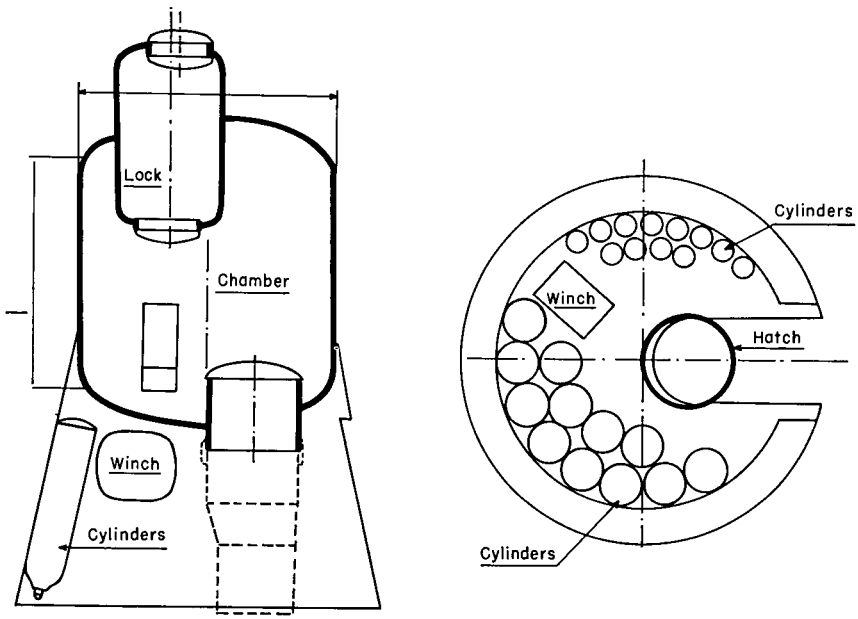


FIG. 15*A*. Diving chamber—type GERS

from the surface by a television camera. At the end of a period at maximum depth, the divers were decompressed inside the SDC which was brought up to the deck of the ship.

In order to improve upon this type of decompression procedure, GERS is procuring a new SDC which is being made at Cherbourg dockyard and will be finished by the end of this year.

The objectives of experiments with the new GERS-SDC will be: to place 3 divers at about 300 meters in the dry, pressurized SDC and then to have 2 of them to go out and work. The divers will be brought to the deck without any lowering of pressure and there will start decompression. The decompression can then be done either in the SDC itself or in a decompression chamber to which the divers can be transferred. In both cases, divers will be dry and comfortable during decompression. Moreover, assistants will be able to go in and out through a lock.

Three diving procedures are foreseen:

One involves diving to a maximum depth of 120 meters for a maximum duration of 1 hour and 30 minutes, with a decompression time of not more than 12 hours. The respired gas mixture to be used in the SDC will be breathed through a "narguile" or breathing apparatus, and the surrounding atmosphere in the SDC is air. Therefore it will be necessary to use a breathing apparatus which can be worn for a long time without disturbances.

A second procedure will be diving to depths of 120 to 300 meters for 30 minutes maximum with a decompression time not much longer than for the 120 meter depth (12 hours). Use of the surface decompression chamber will again be necessary. In this chamber the atmosphere on the bottom must be a gaseous mixture respirable at the surrounding ambient pressure without any apparatus because air breathing at such a pressure is rapidly pathogenic. During the decompression which takes place inside a therapeutic chamber the divers breathe appropriate mixtures through a respiratory apparatus. This decompression technic is practical because the decompression time is short enough.

The next diving procedure will be to depths of 100–300 meters and for a very long duration (from several hours to several days). Long decompression, in some cases for several days, will be required. Under these conditions

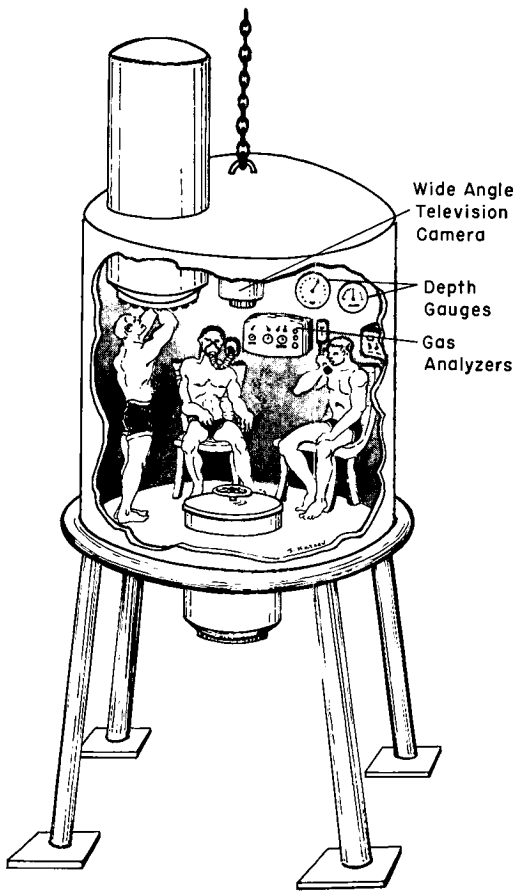


FIG. 15*B*. Diving chamber—type GERS

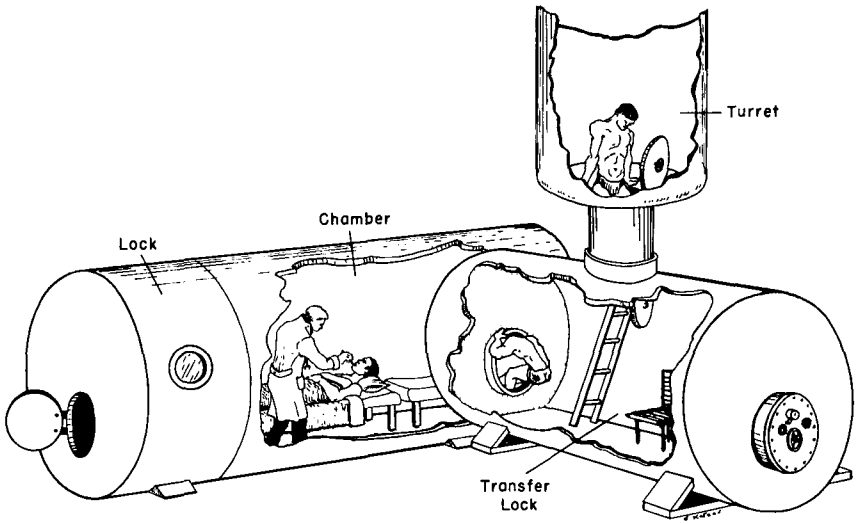


FIG. 15*C*. Adaptation of diving chamber on a decompression chamber

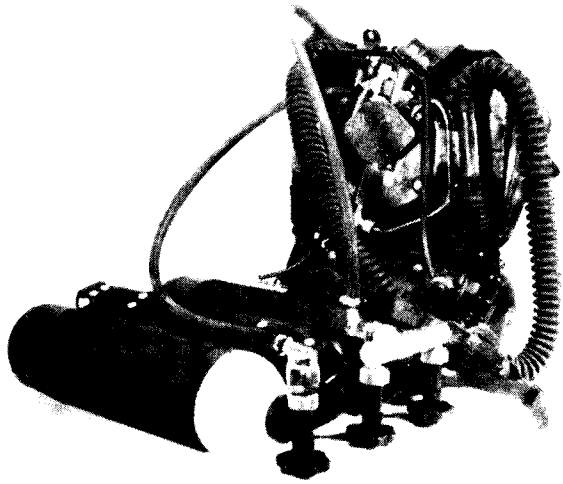


FIG. 15*D*. Breathing apparatus—type OXYMIXGERS

a surface decompression chamber is necessary. The atmosphere in the submersible decompression chamber as well as in the surface chamber must be considered in order to provide at all times gas mixtures that will permit the divers to decompress in comfort without depending for long periods upon breathing masks or other apparatus which might impair their well being, natural activities, and sleep.

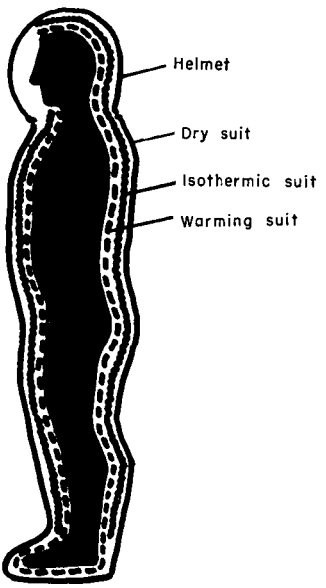


FIG. 15*E*. Design of complete equipment against cold for divers

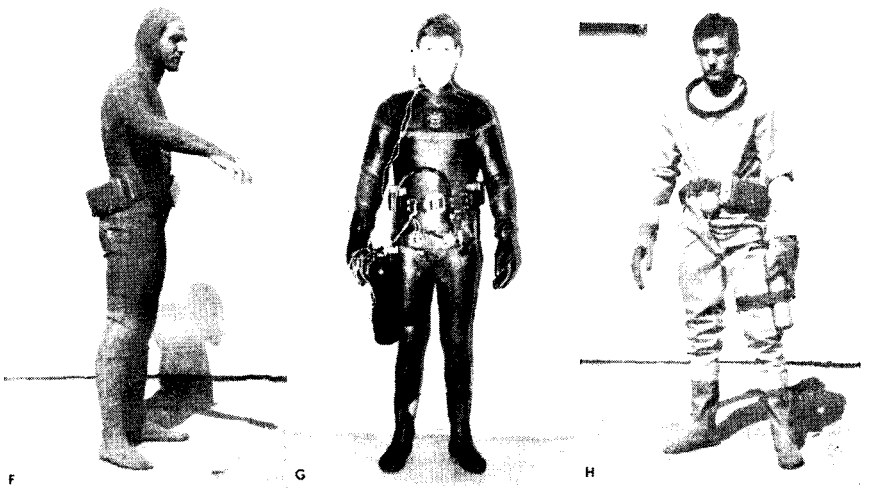


FIG. 15*F*. Warming suit (GERS-SIDEP). The heat generating component is a liquid electrical resistance in a flexible tube. The cadmium-nickel battery acts as a weight.

FIG. 15*G*. Isothermic suit (GERS-SIDEP). The bottle of compressed air compensates for squeeze during a dive.

FIG. 15*H*. Dry suit (GERS-SIDEP). Note the cadmium-nickel battery and the bottle of compressed air.

Development of Equipment

After having experimented with closed and semi-closed breathing apparatus for the past ten years, GERS has developed a SCUBA-unit which can be used either for closed or semi-closed circuit operation. At 100 meters, it is required to provide a gas supply for 2 hours. The decreased weight and bulk are intended to provide advantages over existing apparatus. The basic principle of the apparatus is that oxygen consumption by the diver diminishes the volume of the gas mixtures contained in the breathing bag and the O_2 utilized must be replaced at the end of the following inspiration. A mobile plate on the respiratory bag operates a demand valve which gives new oxygen. Under these conditions the inert gas volume of the breathing system remains the same and the oxygen percentage does not change provided there is no change in the gaseous volume, i.e., the diver remains at the same depth.

We have developed such an apparatus under the name of OXYMIX-GERS, in which the respiratory bag is fixed between two plates and is movable. A smaller bag inside the large bag moves with it. The small inner bag is connected to the large one through a valve such that the small bag empties into the water during every expiration. Since the "leak" of gas is proportional to the volume contained in the large bag, the system provides a gas mixture in stable equilibrium. The ratio between the large and the small bags can be changed with the depth of use and the kind of gases used. The diver chooses the closed or semi-closed system by shutting and opening the exhaust and transfer valves, using an easily-moved operating handle.

The duration of use with its 6 liter cylinder volume is about 3 hours at 25 meters, 2 hours at 55 meters, and 30 minutes to 1 hour at 100 meters. After two years of use, it can be stated that the equilibrium rate is satisfactory in semi-closed use as well as in closed usage, change from semi-closed to closed system operation is easy and during closed circuit breathing at constant depth, the mixture effectively breathed is sufficient.

GERS has also been concerned with developing devices for protection against cold during diving. Earlier devices, especially those developed at Bretigny (France) by Colin, Houdas and Yout, include neoprene suits which give effective protection on the surface. Neoprene thermic conductance is about 4.6 Kgcal/m²/hr/°C/cm, thermic conductance is inversely proportional to the thickness and loss of heat increases with depth because the thickness of the suit decreases due to the increase in pressure.

Considering that the protection against cold with a neoprene suit is in fact very good on the surface, GERS and SIDEP created a diving suit made of synthetic material which has communicating gas cells between two layers of ordinary neoprene. A bottle of compressed air (or other gas)

provides gas to the cellular space and compensation for the squeeze of increased pressure during descent and work on the bottom. A 100 gram calibrated valve prevents ballooning and rupture of the material. During ascent, excess gas contained in the suit is exhausted through a valve which permits a rate of ascent of about 20 meters/minute. A single compressed gas cylinder supplies the suit with a total gaseous volume of six liters. By-passes make possible the inflation of the 3 principal parts, the hood, jacket and trousers.

The study of this new material in experiments at GERS by calorimetric technics and physiological means shows that it has a heat conductance half that of common neoprene. In order to reduce the loss of heat, the gas chosen for inflation must be a poor heat conductor.

In addition to this isothermic suit, we add a warming suit next to the skin, where the heat generating component is a liquid electrical resistance. The power must be chosen according to the kind of suit, dry or wet.

Experiments are being continued at GERS in order to determine exactly the heat losses and also how much energy must be delivered in order to counterbalance the heat losses and to heat the thin water layer near the skin to about 31° C. This is being done for wet and dry suits, for different water temperatures (4° C and 12° C), for different depths, for different gaseous breathing mixtures, and for different levels of exercise.

Finally, in order to determine the nature of ascent curves, GERS is developing an analog computer in which an electrical analog to gas uptake is a capacitor charged through a resistance and the value of ambient pressure is given by a linear integrator. Rate of increase of gas pressure depends on the sign and value of electrical voltage. The calculation of the desired values uses computer time where 1 second of computer time equals 10 minutes of real time. With this analog computer we shall easily be able to calculate decompression schedules, but, primarily, we shall be able to study the modifying effects of the different parameters which influence decompression such as perfusion and solubility of different gases.

This has been a review of some of the experiments carried out at GERS of the French Navy in recent years. The results obtained are encouraging, but they show that there are many still undefined factors in underwater physiology and that research in underwater physiology continues to become more interesting and more demanding.

5 | STANLEY MILES

Underwater Medical Research Experiences of the British Navy

I wish to outline some of the problems which have faced the Royal Navy in recent years in its attempts to increase the depth of its diving capability. Although this volume is directed essentially to underwater physiologists, it must be emphasized that physiological problems are by no means the only important ones in the approach to deeper diving.

Since the last Underwater Symposium, we in Britain have been interested in deeper diving and on the experimental side we have always worked on the assumption that divers may one day be expected to reach 1000 feet or more. Having accepted such a target and bearing in mind the large individual variation between divers, any research work aimed at producing safe universal routines for such depths would have to include a very large safety margin and some would go as far as insisting upon a fifty per cent excess in experimental dives.

Just as depth must always be the major challenge from an emotional and competitive point of view, the important requirement is to achieve a worth while time at depth. This would seem to give two alternative approaches: either to dive to some chosen extreme depth and work up increasing bottom times or to start shallow for a long period and increase the depth by degrees.

Having set a provisional goal, planning became an important requirement. The physiological and medical aspects were considered in the first place by the Underwater Physiology Subcommittee of the Royal Navy Personnel Research Committee (which itself is administered jointly by the Navy and the Medical Research Council) under the Chairmanship of Professor Donald. Later a working group consisting of Professor Donald, Professor Paton and myself was appointed to advise on the physiological

aspects with special attention to safety. For this of course we were in continuous contact with the people who were actually doing the work, in particular Mr. Hempleman, Dr. Mackay and Dr. Barnard. There were moments when it appeared we were putting a brake on their enthusiasm and I feel sure that at times there has been disappointment in the diving teams that progress has not gone on as quickly as they would have wished although current achievements are, I think, quite outstanding.

Our first concern has always been the safety and well-being of the divers and before any sea dives are attempted a series of 10 dives to the same depth in the pressure chamber with double the bottom time must have been completed without even the most minor incident, even a niggle! Also it has been our policy that any routines we adopt should be applicable to any well trained diver. In this respect whatever may have been said to the contrary, we have always been adamant in stating that we are not out to achieve a deep-sea diving record, but to produce safe routines for every day usage. This is the only possible attitude acceptable to a fighting service in peacetime.

The temptation which we have resisted of course was to take a small exclusive group of ace divers and train them through to record-breaking achievements. Had we done this we would no doubt by now have produced some even more encouraging results.

There are some details of technique which cannot be discussed here but which have lead to the recent achievements in our program, including 18 dives to 600 ft. with a bottom time of at least 30 minutes in the sea and dives to 600 ft. for 2 hours in the chamber.

Omission of full detail is not by any means an unreasonable restriction and is made largely in the interests of human safety. For many years most of the great diving achievements have been in the hands of the world's Navies and, certainly in Britain, all deep diving has been exclusively so. We are all well aware, however, that today new techniques which are available are extending the field of diving much wider. It is now not only used in naval practice but is available for recreational purposes and many varieties of under-sea scientific research, much of which is sponsored by University departments. Additionally and recently there is a growing commercial interest, particularly by the major oil companies. They can today see great advantage in an extension of deep diving facilities in their underwater drilling programs and they have plenty of money behind them.

I have already said that in the Naval Service we have an unshakeable obligation to maintain standards of safety of the very highest degree and although many of our divers find the restrictions somewhat irksome and would willingly take personal risks to achieve longer and deeper dives, this

for us is just not acceptable. On the other hand there are individuals outside the Service whose major interest in diving is glamour and record-breaking and who are prepared to take risks. Recent examples have shown how disastrous the results may be and on the commercial side the financial advantages which may be seen in a speedy accomplishment of diving success are considerable and tempting.

It is most important that we should guard against bearing the responsibility for any mishap that might arise from premature disclosure of the details of our experimental diving schedules. In the hands of operators with insufficient technical skill or equipment even well-proved diving schedules can be hazardous, particularly at these great depths. Those of us who have felt dedicated to and proud of our naval accomplishments in diving, must in good faith accept the changing pattern.

We must therefore accept the inevitable truth that non-military organizations may well have a greater need for the exploitation and advancement of deep diving. We are in a stage of transition. For many years we have held pride of place, our men have been the most experienced and our equipment second to none, as for the moment it so remains.

Neither I nor any of my colleagues know at the moment what our future policy will be. We are convinced that diving will remain an important branch of the Navy, we are hopeful that we shall be asked to increase its capability. Whatever the outcome for deep diving, the increasing activity in the shallower depths will keep our specialists busy for many years to come.

Much that has been achieved already has been the result, not so much of scientific reasoning, though of this there has been plenty, but from a careful and considered "trial and error" approach. I know this is a highly technical and scientific Symposium but I hope that the generalization I have given will help to dispel any misunderstanding and present our problems in a frank manner.

Let us look now at the more physiological requirements of very deep diving. I think the physiologists, by and large, know what they want and the burden of imaginative planning is now largely transferred to the engineers. As I see it, our basic technique for very deep diving must be developed on similar lines to that we have already found to be eminently successful. We want the diver at work under-seas or on the sea bed to be relatively flexible and mobile, to be free within the environment, to use his hands for fairly delicate tasks, to be able to swim and move freely over as wide range as possible and to take maximum advantage of his motor and sensory capacity. In other words, we wish to adapt him to the underwater ambient pressure. We would like to maintain the partial pressure of oxygen

in his lungs, within a relatively small range of that of the surface. An upper limit of 2 atmospheres absolute has been suggested; this I think is far too high. I would put it at ¾ atm. abs. Ideally this would mean the introduction of techniques to provide more-or-less constant oxygen partial pressure whatever the depth. We must eliminate the inert gas narcosis hazard and keep the density of the breathing mixture as low as possible; we must ensure adequate ventilation, removal of carbon dioxide and an acceptable environmental temperature. We have gone a long way towards achieving this with adequate clothing, with oxy-helium mixtures and with the practice of lowering the man to his working depth in a submersible decompression chamber. This is the vehicle which takes the diver to his job and lands him there at the pressure of his surroundings, still warm and dry. He can then at the end of his combined life and mixture line do whatever is required of him, returning to the diving bell on completion. He breathes the atmosphere within the chamber and can be maintained at the depth pressure while he is brought back to the parent ship and latched onto the already pressurized working chamber for transfer under pressure to the spacious comfort of large compartments.

Getting the diver to the bottom and out on to the sea bed is possibly the least of our worries. Returning him safely to the freedom of the surface environment is the biggest single problem.

If you read the history of the work which has been done to produce efficient diving schedules, i.e. decompression routines, you will immediately be aware that practically every single worker has been striving to reduce the total decompression time to the absolute minimum, in other words to streamline the timing and just keep the individual within the safety limits. I am not convinced myself that this is the correct approach and particularly in the deep diving where current decompression routines may take days rather than hours, we have to think very carefully about the actual circumstances. The conventional techniques of decompressing divers with a series of stops increasing in length as the surface is approached is perhaps a little crude.

None of us know in detail the processes whereby excess inert gas leaves the tissues and the blood to rejoin the atmosphere. We do not know how man re-adjusts himself to this normal environment after an excessive and prolonged pressurization. In our program so far there have been incidents of decompression sickness, generally speaking mild ones but one at least where evidence of involvement of the central nervous system was present. Fortunately all have made complete recoveries but often they were unexpected and unaccountable. What is a little worrying, however, and perhaps the reason for our extreme caution and unwillingness to claim that we have

the answer, is that although the cases have been mild, so unpredictable is decompression sickness and so uncertain is the site of its development, that we can as yet never be absolutely sure that a major disaster might not occur, however confident we are in our routines.

Therefore, rather than streamline to the brink of safety our decompression schedules, I suggest we should improve and develop the circumstances in which a diver is decompressed so that he is not distressed by any prolongation of time. We have accepted the principle that decompression after deep diving shall be carried out in a decompression chamber in a surface vessel. I think it is important that we should be generous with the time allowance at the various stops and perhaps one day introduce a slow and continuous lowering of pressure along a satisfactory curve so that there remains throughout the whole period of decompression a constant pressure difference between the dissolved inert gas in the various tissues and that of the ambient atmosphere. It is most important therefore that the chamber used for this prolonged decompression should have the absolute maximum of comfort. It must have adequate beds, toilets, washing facilities and arrangements for hot meals and entertainment. It must be a deluxe residence so that the occupant can spend two or three days there completely relaxed, happy and interested. Only when this is achieved will we be able to offer safe and acceptable deep diving.

There is a lot we have to learn concerning bubble formation in man. I think too we must ultimately ascertain the ideal activity for the individual during his long period of decompression. It is for this reason that although we may applaud progress that has been made in achieving the current depths and times under water, we would welcome a breathing space in which we can look more closely, using our present exceptionally worth while facilities, into the whole question of excess gas elimination.

Other parts of this volume describe the exciting developments of man living at the sea bed under pressure. While we in Britain have been concentrating on depths and increasing our time at depth, others have been concentrating on prolonging time first and then increasing the depth. Sooner or later we must meet when both will have achieved increase in time and depth. When we meet we shall have two rather different techniques. On the one hand pressurized establishments will be sited on the sea bed where man will live for weeks under pressure, diving freely as he wishes. On the other will be the surface vessel with its luxury chamber, possibly with similar amenities to the sea-bed one, whose divers, instead of popping out through the hatch to carry out their sea-bed duties, will be travelling to their site of duty in a submersible decompression chamber (SDC) and returned to the parent chamber when the task is completed. These two techniques are complementary and each has its peculiar advan-

tages. The techniques that I have been describing offer a considerable degree of mobility, in other words, whereas from the sea bed establishment the divers activity range is limited to the immediate environment, the surface shipborne chamber and SDC can lower its diver anywhere he may be required. With this facility he can be moved quite freely from one location to another without reduction of pressure.

Here are two techniques. It is quite possible in the not too distant future to visualise a third one in which some form of submarine vessel with similar pressurizable compartments may arise. This is an interesting prospect and we might see a return to middle depth diving from a mobile submarine compartment also submerged to an intermediate depth. This at the moment, however, is a dream, but one which must ultimately be realized.

One thing which is apparent from such thoughts must be that all these techniques need a considerable backing of manpower, expensive equipment and well qualified scientists. Underwater research has, in our country at any rate, always been regarded with a certain amount of suspicion and it is only recently that the potential is being realized. It is too much to ask the Navy to take full responsibility for progress. It is however essential that unauthorized organizations should, in the interests of safety, be discouraged from unrestricted development. It is desirable that some sort of reasoned safety control should be applied to organizations where commercial gain or private enthusiasm might lead to unnecessary risk.

In the United States you have devoted a considerable national effort to the successful exploration in space (though I am intrigued to see that at least one of your spacemen has been lured into the underwater world). Britain has always been a maritime nation and we are proud of our former achievements on the surface. Today we are equally proud of what we are achieving under-water. If we are to maintain our momentum in this direction we will need a greater effort than the Navy alone can provide. My own personal feeling is (and I must emphasize that the whole of this presentation represents my own thoughts and feeling on this subject and is not necessarily an authoritative one) that the only way we can maintain our advantage and progress is by the introduction in our country of a national underwater research authority. This I feel is greatly needed and would include not only diving physiology but many other underwater disciplines.

6 | K. UCHIDA

Recent Underwater Physiological Experiences of the Japanese Navy

Since the Japanese Maritime Self Defense Force began its efforts in underwater activity only 10 years ago, we have had few experiences in deep sea exploration. Our work has been mainly concerned with breath-hold diving, diving with self-contained underwater breathing apparatus, and compressed air diving. In this paper I shall emphasize our naval diving and research during the past decade and our studies in the Ama or diving women.

Evolution of Naval Diving

Not much is actually known about the beginning of diving in the Imperial Japanese Navy. Although good work evidently was done at shallow depths in the early days, very little deep sea diving was done. During the second World War the Imperial Japanese Navy, stimulated by its success in disabling ships in harbour, developed a highly efficient organization to cope with all aspects of underwater warfare and the attendant diving problems. For example, underwater demolition teams, salvage groups and varying types of underwater commandos were developed in large numbers. Since then the efforts of our Maritime Defense Force to increase the scope and safety of diving in Japan have continued with the instruction and assistance of the United States Navy. Major steps in the evolution of the Japanese diving program were as follows:

In 1956 the training of underwater swimmers in the Maritime Service School began. There the curriculum was similar to that used by the United States Navy.

In 1960 a Submarine Rescue Vessel (ASR) was commissioned. This

ship employs SCUBA divers and surface-supplied divers using air and helium-oxygen mixtures. It has two double lock recompression chambers for use in decompression treatment and in personnel selection of divers and submariners.

In 1961 EOD (Explosive Ordnance Disposal) groups were organized, each group having about twenty SCUBA divers. Each underwater swimmer works about 30 hours every month at diving depths between 15–35 meters. The work involved is mainly search and recovery but breath-hold diving is also done for inspection or repair. A group of our EOD divers is now attempting to prolong and extend breath-hold diving. These divers are given annual check-ups of cardiopulmonary function, including routine physical examination, chest X-ray, ECG, spirometry, step-up exercise test, and the ventilatory response to 5% carbon dioxide in air. Using data derived from these routine physical and physiological examinations, we have started to study the adaptation to breath-hold diving with particular emphasis on the role of carbon dioxide in terminating the breath-holding period.

In 1963 "Buoyant Ascent" escape training was made available to Japanese submariners at the U. S. Navy Escape Training Tank in Pearl Harbour. About 300 candidates have passed through this training in the last three years.

In 1964 two more recompression chambers were built at the Maritime Service School for training and for treatment of decompression sickness. We have treated over twenty Naval and civilian divers in these chambers.

From 1964 to 1965 we had an opportunity to study the pulmonary function of the Ama-Funado, the breath-holding women divers, at Onjuku in Japan.

Breath-Hold Diving by the Ama

Last year the first detailed and comprehensive scientific discussion of problems of the Ama was published (1). I shall here describe briefly our studies of the adaptation to increased carbon dioxide in the twelve Ama we have used as physiological subjects.

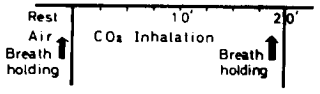
The subjects in these experiments have been diving for 10 to 20 years, usually to depths of 15 meters or more. At Onjuku summer is the diving season. Table 6 lists the experimental procedures used for the measurements which were made on each subject.

The changes in lung volumes observed are shown in Figure 16. Vital capacity and forced expiratory volume decreased during the winter lay-off time but increased during the summer working season.

Figure 17 shows the ventilatory response to carbon dioxide obtained

TABLE 6

Studies on pulmonary function of Ama at Onjuku, Japan

at Laboratory	at Onjuku
1) Spirometry	1) Spirometry
2) F R C. Distribution	2) Exercise Test
3) Exercise Test	3) CO_2 Response
4) CO_2 Response	4) P_{O_2} patterns during diving by micro-electrode
	
5) Breath holding patterns by spirometry	
6) Breaking point	

by exposing subjects for twenty minutes to 5.0% carbon dioxide in air. The respiratory response during the lay-off time is significantly greater than that found during the working period.

Figure 18 shows the change in alveolar P_{O_2} which was measured by means of a micro-electrode attached inside the mouthpiece of the subject. The changes in alveolar P_{O_2} and P_{CO_2} before and after breath-holding at sea level and the relationships of breaking point and P_{O_2} pattern during diving are not significantly different from the control values in a healthy adult.

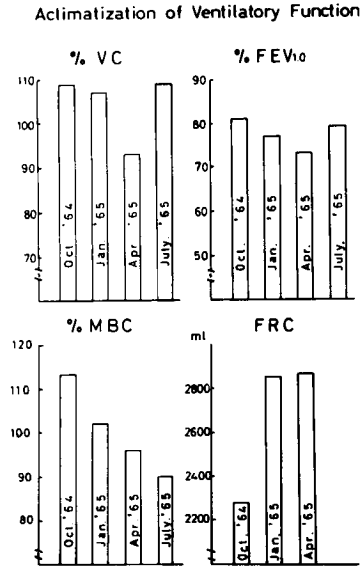


FIG. 16. Average changes in ventilatory functions during a year

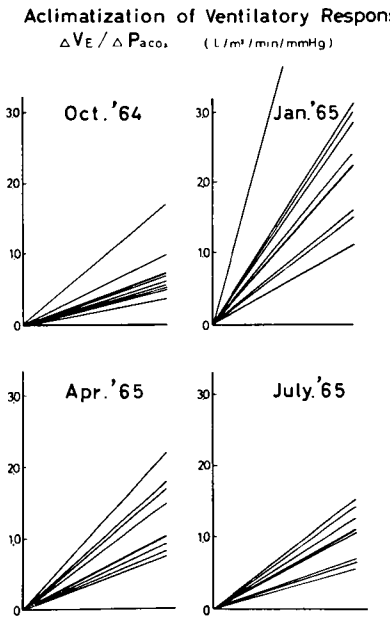


FIG. 17. Change in ventilatory response to administration of 5% CO_2 in air

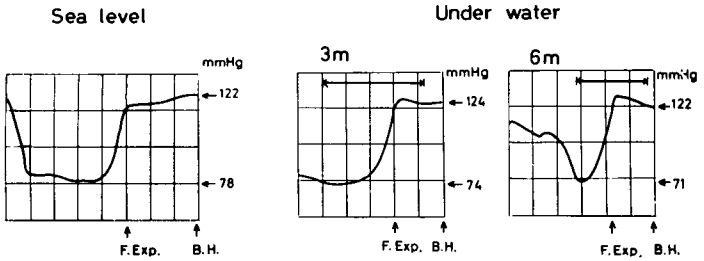


FIG. 18. Po_2 curves during breathholding at sea level and underwater. F. Exp indicates forced expiration. Water temperature measured 19.4° C.

It is interesting to note in this study that adaptative changes seem to occur even in those short durations.

Plans for the Future

Our Navy is of course interested in developing its overall program of diving research. In July of this year a Diving Medical Research Laboratory will be established at the Yokosuka Hospital. The main facility of this laboratory is a chamber with a depth capability of twenty-five atmospheres. The chamber has three rooms, each room large enough for at least three men and the necessary medical instruments for treatment and research.

Up to the present time our Medical Department has performed mainly personnel selection for diving and submarine duty, as well as the treatment of decompression sickness. However, the development of this new facility will certainly put us in a position to contribute materially to decompression research.

Acknowledgement

I would like to express my hearty appreciation to Professor Obuchi, Dr. Umeda and Dr. Suzuki, Tokyo Medical and Dental University, for their valuable suggestions and encouragement.

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Fire at High Pressure

The importance of equipment design for fire prevention in manned chambers under increased pressure became suddenly significant on 16 February 1965 when a fire occurred in a research chamber at the U. S. Navy Experimental Diving Unit with the resultant loss of two Navy research divers. The fact that an increased fire hazard does exist at elevated pressure has been apparent to the community of divers and research workers in the field of hyperbaric endeavors for many years, and chamber fires involving the loss of human lives have occurred at other times in the past.

Most decompression chambers in use by the United States Navy and by commercial diving groups never exceed the maximum depth for treatment of bends using standard U.S. Navy treatment tables (165 feet.) Where these chambers are operated, compressed air is utilized for pressurization. Carbon dioxide, generated by the divers, is eliminated by ventilating the chamber with air at prescribed intervals. Build up of high concentrations of oxygen caused by the use of oxygen inhalators is also prevented by adequate chamber ventilation.

On 22 March 1945, a fire occurred in a recompression chamber aboard a Navy diving ship. Two men subsequently died and one was severely burned. The chamber was at a depth of 40 feet and the subjects were breathing from oxygen inhalators. The cause of the fire was attributed to a spark emanating from a ventilation fan. Some of the changes made in the outfitting of chambers as a result of this fire were: wood grating and electric fans were removed from all Navy chambers, and flame-proof covers were required on mattresses. No known research into the mechanics of fire under pressure was accomplished as a result of this catastrophe. Apparently it was believed that with adequate attention to prescribed safety precautions, fires could be prevented, and since the frequency of fires during the treatment of bends is very low (the above reported fire

is the only one recorded in the U. S. Navy) this appears to be so. It is not uncommon, however, to hear personnel, both Navy and civilian, voicing contempt towards some of the safety precautions, particularly prohibition of smoking in chambers.

The fire that occurred at the U. S. Navy Experimental Diving Unit has special significance, however, due to the presence of an artificial atmosphere in the chamber and the resultant inability to ventilate for carbon dioxide removal without the expenditure of large quantities of mixed gas. Also of significance is the severity of burning involved, and the speed at which the fire propagated. The hazard is further complicated by required research equipment and materials for personal comfort. Investigations following this fire have indicated, however, that fire of this severity can occur in chambers filled with compressed air as well as those filled with atmospheres of mixed gas.

Recent research towards increased depth capabilities has pointed out the need for extended decompression periods in the chamber in lieu of in the water. The need for chambers filled with respirable atmospheres of mixed gas is required because extended periods using an inhalator will cause sore chest muscles and lungs, tired jaws, and general discomfort. Subjects at the Experimental Diving Unit on the average tolerate about two to three hours inhalator time without complaints of discomfort. Since decompression periods of over thirty hours can be expected for some deeper dives, the need for respirable atmospheres and general chamber comfort becomes apparent.

This paper will discuss experiences during a fatal fire and the solutions found to some of the problems associated with fire prevention in decompression and/or hyperbaric research chambers. It is also hoped that those problems that are as yet unsolved will be investigated by others and the solutions found made known to the diving, diving research and hyperbaric medicine community.

Description of the Fire

The dive in progress at the U. S. Navy Experimental Diving Unit on 16 February 1965 was to test the adequacy of a computed decompression for a depth of 250 feet with a bottom time, including descent, of two hours.

The dive procedure utilized a system that has been practiced at the Experimental Diving Unit (EDU) for at least three years as an exercise simulating the use of a submersible decompression chamber with lock-on capability. The dive proceeded as follows: The subjects entered the wet compartment from the "igloo" (Fig. 19) with the appropriate breathing apparatus (MARK VI semi-closed circuit SCUBA that had been modified to function as a hose-supplied apparatus). The doors from the igloo to the upper deck of the building and to the tunnel were closed, and the divers

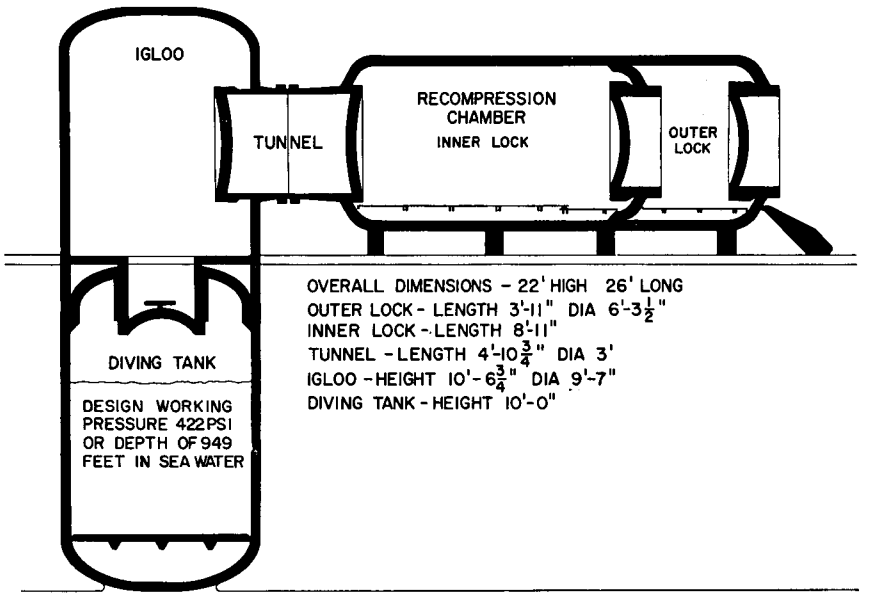

FIG. 19. Facilities for simulating deep diving at U. S. Navy Experimental Diving Unit.

made their descent to 250 feet where they alternated work periods swimming on a trapeze ergometer and lifting a weight. During the working period of the dive, topside personnel filled the decompression chamber with helium and oxygen until the atmosphere was conditioned to a mixture of 28 percent oxygen, 36 percent nitrogen, and 36 percent helium at a pressure of 41 pounds per square inch. A portable absorption canister had been placed in the chamber for removal of carbon dioxide. It was operated for 15 minutes prior to leaving the surface, and continuously while filling the chamber, to assist in obtaining homogeniety of the gas mixture. The carbon dioxide absorption canister (scrubber) was designed for use as an emergency device for submarine atmosphere control and consisted of a tub containing six cylindrical tubes (Fig. 20). One tube, in the center, contained the fan motor. The outer tubes contained four carbon dioxide absorbent canisters and one filter element. The filter element had been manufactured in accordance with military specification Mil-F-5504B for "Filters and Filter Elements Fluid Pressure, Hydraulic Micronic Type".

Ascent commenced with the divers in the water. At 92 feet, they transferred to the decompression chamber and closed the tunnel door. The oxygen percentage in the chamber dropped to 27 percent during the transfer through the tunnel.

Approximately five minutes after the transfer, the carbon dioxide scrubber was again energized, and 2.5 cubic feet of oxygen were admitted to the

FIG. 20. Portable carbon dioxide absorption canister destroyed in fire

chamber over a five minute period. The point of introduction was near the scrubber to provide rapid mixing of the oxygen in the existing atmosphere.

One minute and ten seconds after the oxygen had been reported in the chamber, one of the divers was heard to say "We have a fire in here". Two observers at one of the viewing ports observed a column of flame about "four inches in diameter and two feet high, coming from the carbon dioxide scrubber" (1). Immediately following the observation, the viewers saw a flash which engulfed the entire inner lock.

The pressure gauge on the chamber rose to a reading of 260 feet during the next minute as a rescue was unsuccessfully attempted.

Damage Caused by the Fire

In addition to the deaths involved, considerable damage resulted to materials in the chamber. (Figs. 21*A*, 21*B*, and 21*C*).

Bathrobes, made of untreated cotton terry cloth, were present so the divers could remove their wet bathing suits and complete their decompres-

sion modestly in a comfortable garment. These bathrobes were totally consumed.

Two untreated cotton mattresses, covered with standard Navy submarine-type flame-proof mattress covers, were in the chamber. The mattress covers were manufactured in accordance with the Bureau of Ships Drawing S3306-94306 and Military Specification Mil-C-15104C "Cloth, Coated, Fire Resistant, Berth and Bedding Cover". The covers burned through with holes of about 12 inches in diameter, and the mattress tufting was extensively charred. The localized failure of the mattress covers could have been due to the presence of bare spots in the protective coating as a result of their partially worn condition. No blankets or pillows were present in the chamber.

The air conditioning system contained four flexible ducts of about three feet in length each. These ducts were made of fabric covered spiral wire and the fabric was totally consumed.

The installed chamber electrical system utilized standard shipboard-type armored cables for circuits providing light, communications, power to

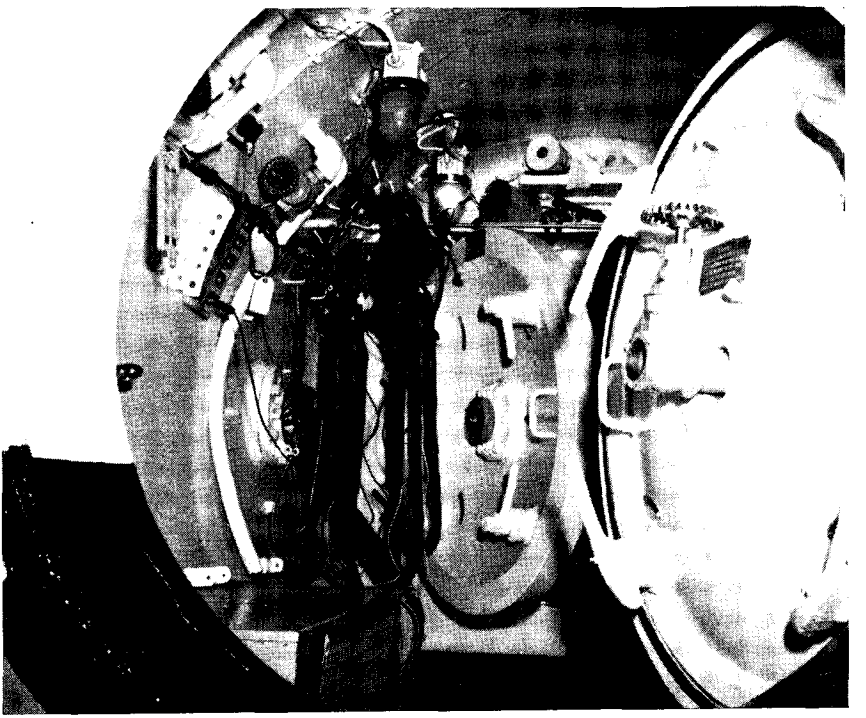

FIG. 21*A*. View of inner lock of decompression chamber number 6 prior to fire

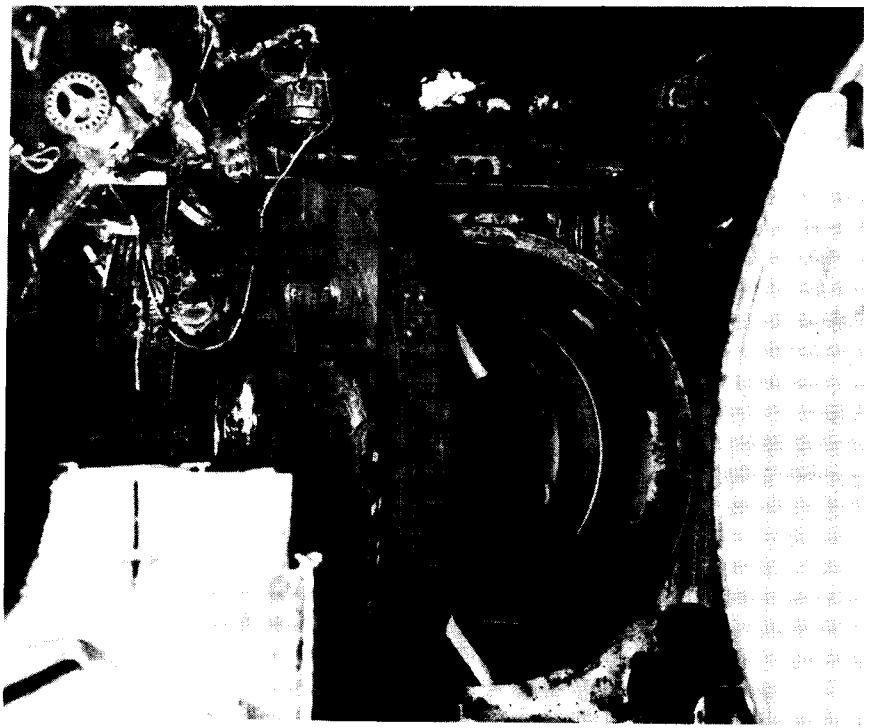

FIG. 21*B*. View of inner lock of decompression chamber number 6 following fire

air conditioning fan motors and receptacles. The portable scrubber had an unarmored rubber cord that burned about five feet of its length. The rubber insulation of the armor-covered cables directly above the carbon dioxide scrubber melted and burned. Damaged insulation was also found on cables removed from the source of the flame.

The interior of the chamber was coated with enamel paint, however, this coating did not burn during the fire. Damage to the painted surface was limited to a patch approximately one foot square above the carbon dioxide scrubber (where the heat was most intense). The reason for noncombustion of the paint and its implications will be discussed at length later in this paper.

Eight oxygen inhalators, consisting of rubber face masks and corrugated rubber tubing with stockingnet covering, were also consumed. They were located on the same side of the chamber as the carbon dioxide scrubber.

A galvanized zinc bucket half full of water was in the chamber for assistance in extinguishing a fire. This bucket was located near the scrubber and was damaged due to melting of the zinc coating above the water level.

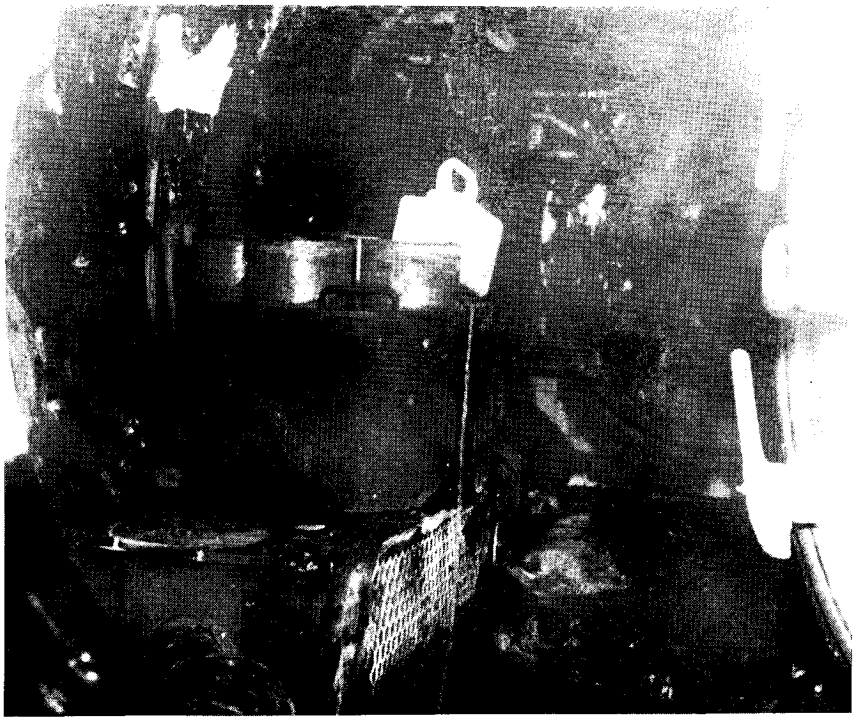

FIG. 21*C*. View of interior decompression chamber number 6 following fire

A stuffing tube for the air conditioning temperature sensing element was located in the chamber wall above the carbon dioxide scrubber. The packing in this tube burned out and allowed the escape of gas.

A regulator, containing plastic inserts, had been placed in one of the chamber exhaust lines for control of constant-rate-of-ascent experiments. These inserts burned out and caused additional release of gas from the chamber.

Reading material and toilet paper also present in the chamber were totally consumed.

Cause of the Fire

The cause of the fire could have been one of the following: open flame ignition, static electricity, adiabatic compression, electric arc, or localized heat source.

Open flame ignition is listed in order to note that supervisory personnel had ascertained that no matches, lighters, or cigarettes were in the chamber prior to the dive. Therefore, this potential cause can be dismissed.

A static spark occurs when the electric potential between two electrically discontinuous bodies becomes sufficient to bridge the gap between them. The gap in this case is the chamber atmosphere and serves as the insulation between the charged bodies. The energy required to bridge the gap varies directly with the relative humidity. In the case of combustible atmospheres, e.g. methane-air mixtures, static energy release can be sufficient for ignition. In a chamber containing an increased partial pressure of oxygen, the ignition temperature of flammable materials is lowered and the energy of an electrostatic spark can cause these materials to burn. The air conditioning system in our chamber maintained a low moisture atmosphere which, with an increased partial pressure of oxygen and flammable materials, could have presented an ignition hazard.

A buildup of static charge would have required movement of the subjects and subsequent friction between electrically discontinuous bodies, such as the bathrobes and the mattress. Upon entering the chamber, one of the subjects lay down on the bunk and the other subject lay down on the mattress on deck. One minute prior to the report of the fire, the subject on the bunk was observed to sit up and pour a glass of water (1). The relative inactivity and time delay between the last reported movement of one of the divers and the fire ignition precludes the buildup of a large static charge as the cause of ignition.

Adiabatic compression or shock-wave compression is considered due to the introduction of oxygen into the chamber just prior to the fire. The explosion of oil or other hydrocarbon material in the reducing or isolation valves of oxygen cylinders is a prime example of ignition by adiabatic compression. Explosions of this nature have been reported (2). It is caused by the heat associated with very rapid compression as the valve is opened and poses as a continuing danger and cause for care in the use of oxygen equipment. With a compression ratio of 100:1 a temperature of 1250° F. can be expected in a valve (3). Ball valves, which allow a very rapid opening, and therefore rapid compression across the valve, should not be used in oxygen systems because of this action. The oxygen had been introduced into the chamber at a slow rate (25 cubic feet in five minutes). Any ignition due to an adiabatic compression would have taken place during the initial opening of the valve and would have had to propagate through the oxygen line into the chamber. In view of the time between start of oxygen introduction and start of the fire, ignition is considered improbable by adiabatic compression.

The four air conditioning fan motors were UL approved, explosion-proof motors. These four motors were not damaged by the fire, however, and none of them were in the vicinity of the carbon dioxide scrubber.

The scrubber motor, on the other hand, was not manufactured to ex-

plosion-proof standards, and therefore could have caused the ignition of surrounding material, particularly in view of the possible high concentration of oxygen in the vicinity of the scrubber due to the previous introduction of oxygen into the chamber.

The Investigating Board determined that the fire was initiated by a localized heat source in the scrubber motor. This determination was made following a bench test of the motor, which revealed that, when energized, it ran at a reduced speed and rapidly overheated. This condition was caused by faulty operation of the centrifugal throw-out switch which resulted in the motor running on the starting windings. A used filter, manufactured to the same specification as the one involved in the fire was tested by the Naval Research Laboratory. An unused filter drawn from stock was also tested. The units were constructed in the form of convoluted cylinders of paper, impregnated with a phenol-formaldehyde (bakelite) like resin for stiffening purposes, and a kerosene-like liquid. Further investigation determined that the primary use for this filter was in hydraulic systems and in the fuel systems of jet aircraft. "It is common practice to test every single filter element by immersion in an organic liquid and, while submerged, blowing air through it to see if flaws exist at the seals of the paper. A hydraulic fluid is commonly used for this purpose which is essentially a heavy kerosene thickened with an acryloid ester polymer and containing other additives" (4).

The filter in the scrubber was in proximity to the motor but separated by a metal shield. The flow of gas through the scrubber was down through the absorbent cans and up and out through the filter unit. In view of the improper operation and overheating of the scrubber motor during testing, the volatility of the filter element, and the observation of the flame coming from the filter prior to total envelopment of the chamber, the most probable cause of fire was an overheated scrubber motor causing spontaneous ignition of the filter element in a high-oxygen atmosphere.

The very rapid propagation of the fire can be termed a "thermal explosion". A thermal explosion has been defined (5) as an explosion in which the material reacts exothermally to produce heat at a faster rate than heat is lost by conduction, convection, and radiation.

A simplified calculation based on adiabatic conditions was accomplished by personnel of the Naval Research Laboratory. It was reported that "in order to reach a depth of 270 feet at the time of the fire, a temperature rise of 405° C. (761° F.) would have occurred. In order to reach such a temperature, only about 500 grams of cellulosic material (i.e. cotton) would have to be burned (6).

Another indicator of the intensity of the heat is given by the condition of the water bucket that was in the chamber. The galvanized zinc coating

above the water line melted off the bucket, and since zinc melts at 787° F. and some heat would have been drawn off by the water, local temperatures must have been considerably above this figure.

The change of the character of the fire from a source to a thermal explosion was too rapid for any fire fighting action to take place by the occupants of the chamber. This rapid propagation was fed by the cotton terry cloth bathrobes, mattresses, electrical insulation and other flammable material in the chamber. It is felt by personnel at the Experimental Diving Unit that time would have been available for one action in response to the fire detection and any hesitancy in decision would have resulted in a fatal fire. Even if one of the occupants had been able to reach the water bucket (which was located next to the scrubber) and throw it on the scrubber, the chances of extinguishment are doubtful. For this reason, an adequate rapid detection and response fire extinguishing system must be developed for use in manned chambers.

Effects of Increased Oxygen Partial Pressures and Varying Inert Gas on Flammability

The effects on flammability associated with increased partial pressures of oxygen and varying inert gas have been only briefly investigated in the past. Intuitively, it is reasonable to expect increased combustion rates with increased oxygen. The effects of increase in inert gas, however, and variation of type of inert gas have not been adequately studied to date. Also the containment of a fire in a chamber causes an effect due to heat reflection from the chamber surfaces, as well as heat absorption by the chamber walls.

In 1931, Naylor and Wheeler (7) found that the ignition temperatures of methane-oxygen mixtures with inert gas were lower in a 440 cc vessel than in a smaller 48 cc vessel. In 1959, Coleman (8) found that the burning time of white unbleached cotton drill specimens in a Perspex pressure vessel 24 inches high and 5.5 inches bore was less than the burning time in free air. The time was slightly less in stationary mixtures than in a current of enriched air. Coleman suggested that the effect is associated with cooling effects of convection currents and the reflection of heat back on the specimen from the surface of the Perspex cylinder. This conclusion would indicate that ignition in a larger vessel should result in higher ignition temperatures and slower burning rates. The apparent contradiction with the work of Naylor and Wheeler exemplifies the state of knowledge today concerning the phenomenon of ignition and combustion in closed atmospheres.

Naylor and Wheeler also found that the heat developed by combustion in a chamber is in part absorbed by the inert gas present and therefore the total amount of heat acquired by the reacting gases depends upon the

thermal properties of the inert gas. They found that replacing nitrogen with helium, of higher thermal conductivity, in nitrogen-methane-air mixtures raises the ignition temperature of the gas, and that replacing the nitrogen with argon which has a low specific heat and a low thermal conductivity, lowers the ignition temperature. The loss of heat to the walls of the reaction vessel in unit-time is considerably greater when helium is present. "The acceleration of the reactions is therefore checked by the presence of helium, and a higher initial temperature is required to enable them to acquire sufficient speed to produce flame" (7). The effects found by Naylor and Wheeler are illustrated in Figures 22 and 23.

Johnson and Woods (9) found that a longer ignition delay resulted when terry-cloth specimens were ignited in atmospheres where nitrogen had been replaced with helium. Another contradiction was noted, however, in their work. They found that although the delay in ignition of both filter paper and terry-cloth was increased when nitrogen had been replaced with helium, the burning rate of the filter paper increased while the burning rate of the terry-cloth decreased.

Union Carbide Research Laboratory, Linde Division, found in a recent study (10) that difficulty was experienced in getting samples to ignite in helium atmospheres, even when the oxygen concentration was as high as 29%. There was a definite increase in combustion rate once ignition had been accomplished in atmospheres containing increased partial pressures of both oxygen and helium.

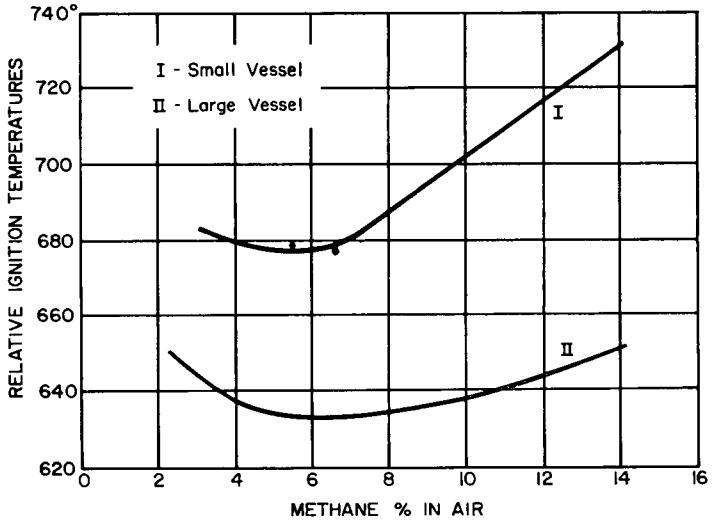

FIG. 22. Ignition temperatures of methane in air mixtures tested in large and small vessels. (After Naylor and Wheeler, et al (7).)

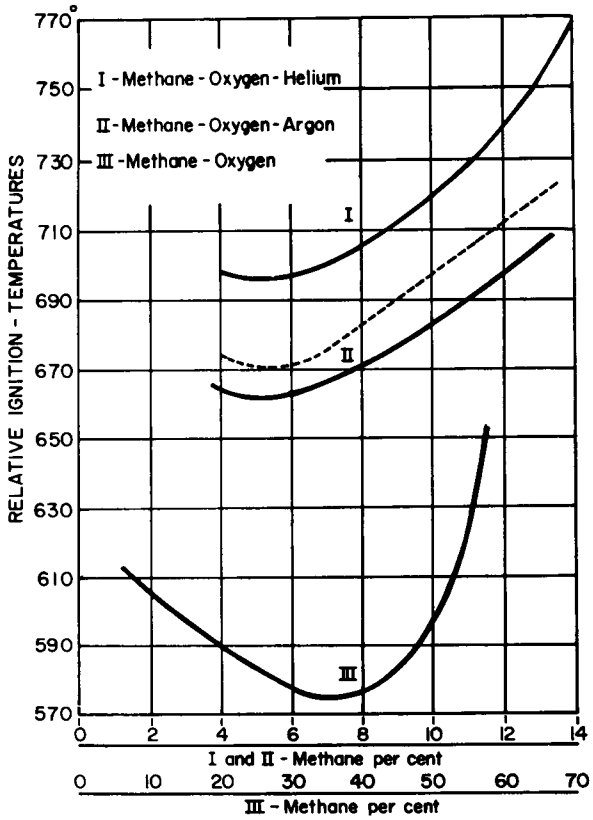

FIG. 23. Ignition temperatures of methane-oxygen and inert gas mixtures. (After Naylor and Wheeler, et al (7).)

The most astonishing phenomenon found to date is shown in Figure 24. The rate of combustion of filter paper increases very rapidly when the pressure is increased and the percentages of oxygen, nitrogen and helium are maintained constant. The rate peaks at a depth of 100 feet, falls off, and begins to rise again at 250 feet. A suggested explanation given by the Laboratory was that the rate of combustion is a different function of the oxygen concentration than the rate of retardation is of the helium concentration. The experiments conducted were only preliminary in nature, have not been repeated, and are therefore unconfirmed.

Coleman found that doubling the oxygen concentration from 21 % to 42 % by enrichment produces a much greater effect than increasing the oxygen by doubling the air depth to two atmospheres. The variation is believed to be caused by the increase in dilution by nitrogen in the case of com-

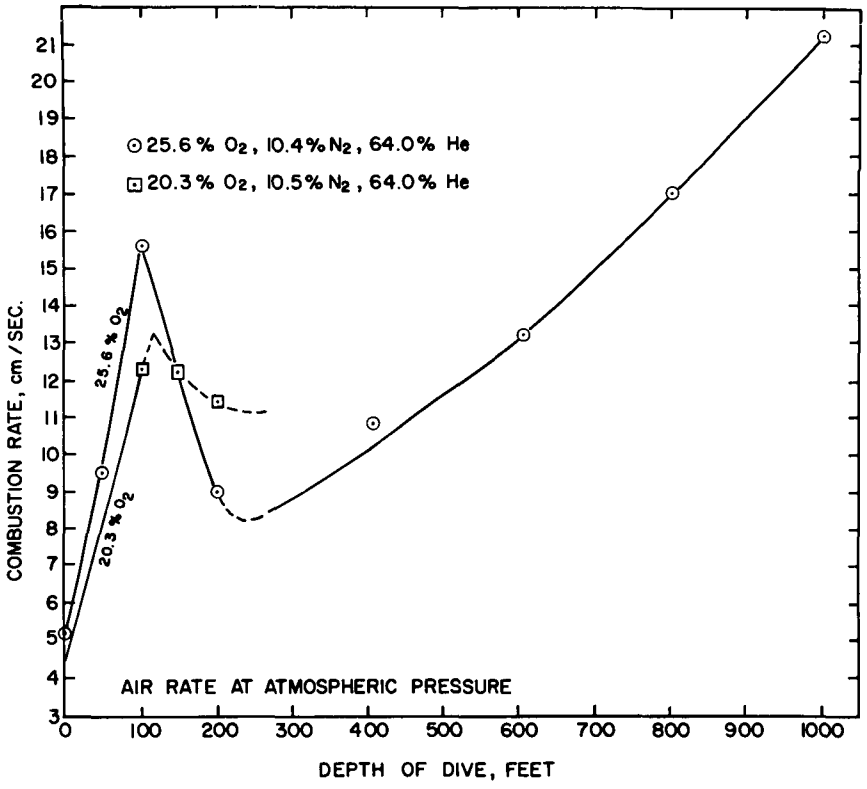

FIG. 24. Preliminary test results (unrepeated) of combustion in a helium-rich atmosphere of filter paper in vertical position, humid atmosphere. (By permission of Linde Research Laboratory (10).)

pressing the air to two atmospheres, and the decrease in nitrogen with oxygen enrichment (See Fig. 25).

These findings lead to the following conclusions:

1) Increasing pressure while maintaining the same percentage of oxygen and inert gas increases the flammability of materials, and that this is due to the affect of increased oxygen being greater than the diluent effect of the inert gas present.

2) Changing the inert gas causes a decrease in ignition delay (lower ignition temperature) with inert gases of lower thermal conductivity and an increase in the ignition delay (higher ignition temperature) with inert gases of higher thermal conductivity.

3) The burning rate of materials is not consistent with the ignition delay.

4) The design of the test chamber will influence the results of ignition and combustion tests.

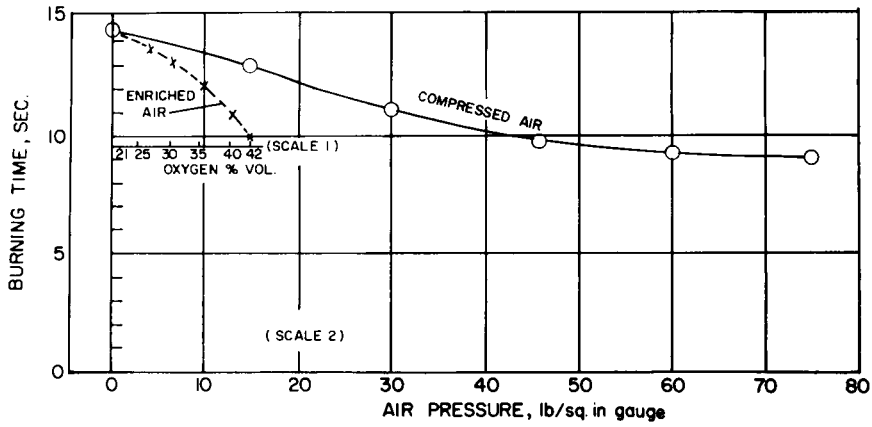

FIG. 25. Burning time of white cotton drill in stationary atmospheres of compressed air and oxygen-enriched air. Horizontal scales 1 and 2 have been adjusted so that vol% O_2 and air pressure represent the same absolute oxygen concentrations. (After Colemen, et al (8).)

5) The composition of artificial atmospheres should be selected with consideration of the fire hazard involved as well as its effect on decompression. An increase in decompression time caused by lowered oxygen partial pressures should be accepted to reduce a dangerous fire hazard.

Resultant Approach to Design of Chamber Components and Operation to Reduce Fire Hazard

As a result of the fire, an approach was established for refitting the chambers that, if completely carried out, would result in a chamber outfitted in such a manner that a fire could not possibly start or propagate. This approach to the chamber outfitting consists of four basic elements:

1) Eliminate all sources of ignition.

2) Eliminate all flammable materials.

3) Utilize reduced oxygen partial pressures in the chamber whenever the experiment in progress permits.

4) Provide adequate fire extinguishment.

It is apparent that if items 1 and 2 are carried to 100% completion, there is no need for items 3 and 4. However, the four elements above cannot be carried to 100% completion, and items 3 and 4 must therefore be utilized as an added safety measure. Where the above criteria cannot be met, due to non-availability of materials or equipment to meet the requirements, or due to particular demands placed on the chamber operations that preclude the use of such materials, the contribution of substitutes to the fire hazard must be weighed in the light of the total chamber system and not as individual components.

Sources of ignition for space cabin applications have been categorized as follows (5):

1) Electrical
   a) electrostatic
   b) induction (break) sparks
2) Hot Surfaces
   a) frictional or impact sparks
   b) heated walls, surfaces or wires
   c) heating by high shear rates
   d) plastic deformation of sharp points
3) Hypergolic Ignition

A detailed description of the physical phenomenon of these ignition sources may be found in the referenced literature and will not be discussed at length here. All of the items listed, except heated gases by shock waves and hypergolic ignition, are causes of ignition applicable to decompression chambers.

Electrical sources are considered the most severe due to the large amount of energy available for conversion to heat in the event of arcing or overheating of electrical machines or circuits. Elimination of all electrical components from the chamber should be accomplished where possible. Where electrical components must be used they should be designed and tested to insure that they are explosion proof in enriched oxygen and high pressure atmospheres. Note however, that this does not guarantee that a machine will not overheat and cause combustion. The scrubber involved in this fire had been used during other dives with no previous malfunction. Had the machine been explosion proof, overheating could just as well resulted.

Hot surface ignition can be prevented by insuring that personnel inside a chamber do not hammer on steel surfaces, unless it is with a spark-proof hammer. Heating by high shear rates and plastic deformation of sharp points could occur in failure of an instrument or machine bearing, or if some other mechanical interference is present in rotating or sliding contact equipment. An example of this would be heat generated by an improperly cooled "prony brake" on a bicycle ergometer or similar device.

Elimination of all flammable material from a chamber is impossible if human subjects or animals are required for the experiment in progress, since animal tissue will burn. The requirement for human subjects is acknowledged, and the problem evolves to choosing a fabric which when made into clothing will be non-combustible and comfortable to wear. In our efforts to find suitable materials, tests of various fire-retardant fabrics have been conducted. Samples of filter paper, untreated cotton terrycloth and terrycloth that had been treated with tetrakis (hydroxmethyl) phosphonium chloride, $(HOCH_2)_4PCl$ were tested by the Naval Research Lab-

oratory in five different atmospheres and at pressures up to 75 psi abs. (9). The samples were originally supported horizontally and ignited by an electrically heated nichrome wire coil in contact with the sample strips. Later tests were also accomplished with the sample strips in a vertical position. The tests were conducted at pressures less than 75 psi abs. due to the limitations of the available pressure vessel. The results are given in Tables 7 and 8. The following generalizations were made from these tests (9):

1) It was more difficult to ignite these materials in helium-oxygen than

TABLE 7

Combustion of Filter Paper and Terry Cloth in Various Atmospheres of Oxygen, Nitrogen and Helium

Atmospheres	Pressure (psi abs)	Material					
		Paper		Terry Cloth		Treated Terry Cloth	
		Ignition Delay (sec.)	Burn Rate (cm./sec.)	Ignition Delay (sec.)	Burn Rate (cm./sec.)	Ignition Delay (sec.)	Burn Rate (cm./sec.)
79% N_2-21% O_2	15	6.5	0.23	8.4	0.20	NI	NI
	30	6.0	0.28	6.6	0.61	NI	NI
	45	7.2	0.28	—	—	NI	NI
	60	6.0	0.35	4.8	1.17	NI	NI
	75	4.8	0.30	4.9	0.89	5.0	0.03*
79% He-21% O_2	15	NI	NI	—	—	—	—
	30	NI	NI	—	—	—	—
	45	NI	NI	—	—	—	—
	60	NI	NI	—	—	—	—
	75	18.0	0.48	18.0	0.40	NI	NI
69% N_2-31% O_2	15	6.0	0.43	8.4	1.67	18.0**	**
	30	5.6	0.45	5.2	1.57	7.2	0.23
69% He-31% O_2	15	17.0	0.76	22.5	1.27	NI	NI
	30	14.3	0.69	27.0	1.02	NI	NI
	60	—	—	—	—	NI	NI
	75	—	—	—	—	**	0.05
34.5% N_2-34.5% He-31% O_2	15	10.2	0.61	10.8	0.94	NI	NI
	30	11.1	0.67	10.2	1.70	NI	NI
	45	—	—	—	—	9.0	0.38

* Flamed momentarily, then smoldered for entire length of cloth strip.

** Did not flame, but smoldered for entire length of cloth strip.

NI Denotes no ignition under the test conditions.

TABLE 8

Combustion of Terry Cloth, Pre-treated for Fire Resistance, when Held Horizontally or Vertically

Atmospheres	Pressure (psi abs)	Treated Terry Cloth			
		Horizontal Position		Vertical Position	
		Ignition Delay (sec.)	Burn Rate (cm./sec.)	Ignition Delay (sec.)	Burn Rate (cm./sec.)
79% N_2-21% O_2	15	NI	NI	NI	NI
	30	NI	NI	9.6	‡
	45	NI	NI	7.2	0.13*
	60	NI	NI	6.6	0.31*
	75	5.0	0.03*	—	—
79% He-21% O_2	75	NI	NI	‡	‡
69% N_2-31% O_2	15	18.0	**	‡	‡
	30	7.2	0.23	6.3	2.61
69% He-31% O_2	15	NI	NI	—	—
	30	NI	NI	—	—
	60	NI	NI	—	—
	75	**	0.05	**	**
34.5% N_2-34.5% He-31% O_2	15	NI	NI	—	—
	30	NI	NI	**	**
	45	9.0	0.38	7.2	2.54

‡ Burned or charred about one-half length of test strip.
* Flamed momentarily, then smoldered for entire length of cloth strip.
** Did not flame, but smoldered for entire length of cloth strip.
NI Denotes no ignition under the test conditions.

in nitrogen/oxygen atmospheres. However, in many cases the burning rate was faster in helium/oxygen.

2) The untreated terrycloth ignited and burned under all conditions listed. Its burning rate was usually much faster than the paper.

3) The treated terrycloth was much more resistant to burning than the untreated cloth. However, it should be noted that even in air at 75 psi abs., the treated terrycloth ignited quickly, flamed up, and then continued to smolder for its entire length. In 31 % oxygen diluted with nitrogen at only 30 psi abs., the treated cloth ignited readily and burned briskly with a flame for its entire length. Dilution with helium increased the resistance to ignition and burning, but 31 % oxygen in the helium/nitrogen mixture

caused the treated terrycloth to ignite and burn readily at a pressure of 45 psi abs.

Furthermore, the following conclusion was made during the study— " . . . the treated terrycloth cannot be recommended for use in atmospheres at pressures higher than atmospheric, or atmospheres enriched in oxygen (i.e. greater than 21% oxygen)" (9). From this and other published data, it appears that attempts to treat cotton cloth to provide fire resistance have not resulted in materials safe for use in atmospheres at higher pressures and/or higher oxygen content.

Later tests were conducted by Johnson and Woods on samples (provided by the Experimental Diving Unit) of materials suggested for use in chambers. The flame resistance of these materials at one atmosphere pressure and 21, 31, and 41 percent oxygen are given in Table 9 (11).

TABLE 9

Flame Resistance of Materials at One Atmosphere Pressure

NRL Sample Number	Material	Form	Combustion in O_2/N_2 Mixture		
			Percent Oxygen		
			21%	31%	41%
FTM-1	Resin impregnated paper	Filter	Burned	—	—
FTM-3	Cotton terry cloth	Robe	Burned	—	—
FTM-4	Roxel-treated cotton terry cloth	Robe	No	No	Burned
FTM-5	Roxel-treated fleece-backed cotton	Sweat pants	Surface only	Burned	Burned
FTM-6	Fire resistant cotton ticking	Mattress cover	No	Burned	—
FTM-7	Fire resistant foam rubber	Mattress padding	No	No	Burned
FTM-8	Viton	Rubber sheeting	No	Burned	—
FTM-9	Nomex nylon	Cloth	No	Burned	—
FTM-10	Teflon	Cloth	No	No	No
FTM-14	Roxel-treated O.D. sateen	Cloth	No	Burned	—
FTM-19	Verel	Cloth	No	Burned	Burned
FTM-22	Vinyl-backed cloth	Mattress cover	No	Burned	Burned
FTM-23	Omni coated Du Pont high temp.	Cloth	No	Burned*	Burned
FTM-24	Omni coated glass	Cloth	No	No	Burned*
FTM-20	Glass	Cloth	No	No	No
FTM-27	Aluminized asbestos, like NASA space suits	Cloth	No	No	Burned

* Burned only over the ignitor.

A glass cloth tested by the Naval Research Laboratory, and fabricated of very small-diameter filaments, has been found to be non-irritating to human skin in wearing tests conducted at the NASA Manned Space Center.

As a result of these tests, we have concluded that materials for use in chambers must be non-combustible, e.g. glass, teflon, or asbestos, and that treatment with fire-retardant chemicals is not satisfactory.

An adequate substitute for rubber is urgently needed. Rubber products are a major source of flammable material in the chamber: electrical insulation, hoses, and door and window gaskets. The hazard of permanently installed electrical insulation can be reduced by shrinking a teflon jacket around the wires and using adequate conduiting. Non-permanent wiring, however, such as instrumentation leads, poses a continuing problem. In a fire at the space simulator at the U. S. Air Force School of Aerospace Medicine, Brooks AFB in 1962, polyvinyl plastic insulation on wiring served as the major source of fuel (5). Another fire in an altitude chamber in 1962 at the Air Crew Equipment Laboratory of the Naval Air Engineering Center, Philadelphia, Pa., also found electrical insulation to be a major fuel. Although these fires did not occur under increased pressures, they occurred in atmospheres of increased oxygen partial pressures and further illustrate the need for nonflammable electrical insulation.

Viton rubber has been considered as a possible substitute for standard insulation. Tests by the Naval Research Laboratory found that Viton will not burn in air, but will burn at atmospheric pressure in 31% oxygen (11). As an interim, it has been suggested by Denison (12) that glass or ceramic fish spine beads be strung over wiring to provide a heat shield.

In the fire at the Experimental Diving Unit, no damage was done to the rubber port seals, except some charring of the edge of the inside gasket. During a recent overhaul of the chambers, the inside gaskets were replaced with an asbestos material, but the outside gasket which actually forms the gas seal was left as neoprene rubber. The design of the port retaining rings is such that no open flame can reach the rubber gasket and the thick chamber walls will conduct heat away from the area. The door gaskets could possibly be reached by an open flame. However, due to the shielding effect of the door and knife edge and the heat conduction of the steel, such a possibility is very remote and would only occur in the event of a completely flaming chamber.

Inhalators are required in decompression chambers for administration of mixed breathing gases and oxygen for use in decompression and bends treatment. The presently used inhalators are manufactured to Military Specification MIL-I-15379B (SHIPS) "Inhalator, Divers, For Administering Helium Oxygen During Decompression". The inhalators are molded rubber and the respiratory hoses are reinforced corrugated rubber, with a

stockingnet covering. Both will burn in air at atmospheric pressure and are a major source of flammable material in our chambers.

Small bore tubing is required in the chamber for such things as gas sampling and gas injection. Teflon is used for this purpose and is non-combustible. Bearings on air conditioning fans, scrubber blowers, hatch dogs, and divers' stage hoist are lubricated with fluorocarbon oil and greases manufactured by the Hooker Chemical Corp. Some instruments that require a lubricant may also be required in the chamber at various times.

So called "fire-retardant" paint, manufactured in accordance with Military Specifications, will burn in atmospheres of increased oxygen. However, in tests performed at EDU, it was found that while these fire retardant paints would burn when placed on thin sheet metal, they could not be ignited in air at atmospheric pressures even when a butane torch flame was applied to the surface. It is acknowledged that when placed in an oxygen atmosphere this may not be the case. Ignition tests of a painted surface in a chamber, containing increased partial pressures of oxygen will be undertaken. No fire is anticipated, however, since enamel paint did not ignite during the fatal blaze. The reason for this and for the inability to ignite paint in the chamber with a butane torch is that the paint is applied to 2½ inch thick steel. Even localized application of heat is rapidly conducted away from the source, thereby preventing ignition temperatures from being reached. In the case of the thin plate, a large heat sink is not available and the surface of the plate is rapidly heated to ignition temperature.

Denison also found that fireproof paints made to Admiralty specification did not burn in air or 100% oxygen when allowed to dry on ⅜ inch sheet steel. A suggested alternate to painted surfaces is protecting exposed steel with a non-flammable cover, such as zinc spray (12).

Some Problems Already Solved

Protective coating of the chamber interior is being accomplished at EDU using one coat of high-temperature aluminum paint and two thin coats of fire-retardant white paint. The preparation of the surface of the chamber walls to receive the aluminum paint requires careful attention to insure removal of rust prior to its application to preclude any chance of a thermite reaction between iron oxide and aluminum when struck with a metal striker. This potential hazard has been discussed for flammable gases at atmospheric pressure (13). The conclusions in the report indicated that the hazard of sparks with aluminum paint on rusty iron represent a modified degree of the more general hazard which may arise if aluminum metal and iron oxide in close contact are raised in temperature by a sudden blow (similar to thermite welding process).

No more than two thin coats of the fire-retardant white should be placed

over the aluminum paint, since a thick paint film will reduce the rate of heat transfer to the steel.

The installed air conditioning system has been modified to provide operation without the use of electric motors in the chamber, and the carbon dioxide scrubber has been incorporated into the system. This system utilizes chilled (or heated) water from an external refrigeration plant (or hot water heater). The water is piped into the chamber where it exchanges heat with the chamber atmosphere and condenses water vapor on the chilled water cooling coils. Prior to returning to the exterior system, the water passes through five water turbine motors which are magnetically coupled to fans for air circulation. By being magnetically coupled, no shaft penetration is necessary from the water turbine and the chilled water system operates unaffected by chamber pressure. Four of the installed fans are used to circulate the atmosphere across the cooling coils and one fan is used to draw the atmosphere through the carbon dioxide scrubber. This system is used for both heating and cooling the chamber.

A new electrical system is presently being designed for the chambers. It will provide for lighting, 220 volt, and 110 volt power outlets, communications and instrumentation jacks. The lights to be installed were designed for use as navigational side lights on deep diving submarines, and as such, provide a hermetically sealed unit that has been tested to pressures exceeding the test pressure of our chambers. The only permanent wiring will consist of the cabling for the lights and that cabling necessary to reach from the hull penetration to the receptacle box. All installed cabling will have a teflon jacket and will be installed in closed conduit. All power and light circuits will be grounded.

The hull penetration fittings will pass 65 separate wires into the chambers by means of pin connectors. The bulk of these pins will be used for instrumentation outlets. All power and instrument receptacles will be located in a single junction box to eliminate the need for additional permanently installed wiring. Outside the chamber the cabling will divide into two bundles, one for power and one for instrumentation. The power circuits will terminate at a control panel at the chamber operators station. Each separate lighting and power circuit will be fused to lowest amperage possible for proper operation of the equipment on the circuit. External instrumentation, amplifiers, and/or recorders that are monitoring an instrument inside the chamber will receive their power from the same source as the chamber circuits. In the event of a casualty one master switch at the operators panel will isolate all power to the chamber. The instrumentation and power circuits will be available in the inner-lock, igloo and wet pot to allow flexibility in the use of the chamber system when monitoring pulmonary functions, EKG, EEG, pressure, flow, volume or other electrical measurement.

The plug and receptacles inside the chamber will be of explosion-proof

design. The power receptacles are necessary in our chambers for operation of equipment such as the mechanical respirator which is used to test life-support equipment under pressure. It is not expected that electric machines will be operated in the chamber when occupied by subjects. However, in the event that a future requirement makes this necessary, liquid filled or inert-gas filled machines will be investigated and should be utilized if at all possible.

An electric hoist had been present in the igloo for raising and lowering the divers' stage and the wet pot hatch. This hoist has been replaced with a pneumatic hoist lubricated with Flurolube.

Three glass mattresses have been constructed by the Pittsburgh Plate Glass Company for use in the chambers. The construction of all three vary as does their comfort and relative flammability. Tests will be conducted on these mattresses in oxygen enriched atmospheres. At present the submarine-type flame-proof mattress cover is being used in conjunction with these mattresses to prevent skin irritation. A substitute for the submarine-type mattress cover will be developed.

Provision of Adequate Fire Extinguishment

An adequate fire extinguishing system for use in a decompression chamber is one that detects ignition and extinguishes the flame prior to a thermal explosion, and accomplishes this without adding toxic materials to the chamber. Because of the short period of time between ignition and a thermal explosion, an automatic system is considered necessary.

Required fire fighting equipment for use in U. S. Navy decompression chambers consists of one bucket of water and one of sand. Until a more adequate system is available, these agents should continue to be placed in chambers. The limitations of such equipment are obvious.

To provide a system with acceptable response to fire ignition a flame detector with almost instantaneous response is required. Most flame detectors are of the infrared or ultraviolet type (5). The infrared detectors distinguish between the pulsating emission pattern characteristic of a flame and smoother infrared emission patterns associated with other radiation sources. Detection and warning are almost instantaneous with the outbreak of a flame.

An ultraviolet-type fire detector has been developed (14) that distinguishes between the ultraviolet radiation from a flame and random radiation from the sun. It does not respond to overheat conditions, nor is it affected by ambient temperature or residual radiation and is insensitive to infrared and visible light. Other detectors are heat detectors, smoke and carbon monoxide detectors, vapor detectors and pressure detectors. These are used in special locations such as ventilators and would not be applicable to mounting in a chamber. The development and acceptance of an

ultraviolet-type detector for use under increased pressure will result in an adequate detector with almost instantaneous response. This detector can then be used to automatically actuate the fire extinguishing agent and to deactivate all electrical power to the chamber.

Water spray, aqueous foam, dry sodium bicarbonate powder, carbon dioxide, inert gas and volatile organic halides are extinguishing agents in use today. Of these, only the water spray system is known by the author to have been tested in a hyperbaric chamber. These tests were conducted at the Hospital of the Good Samaritan in Los Angeles using an overhead spray installation.

Tests were limited to low chamber air pressures and produced only partially satisfactory results. The use of water spray in atmospheres of increased oxygen partial pressures and depths beyond 150 feet requires study to determine its effectiveness as a fire extinguishing agent.

The use of aqueous foam and dry sodium bicarbonate warrant investigation as chamber fire extinguishing agents. Volatile organic halides produce toxic and corrosive effects that preclude their use in closed atmospheres. The addition of an inert gas to reduce the oxygen content in the chamber below a combustible level is possible but involves large volumes of gas and an extended admission time as well as complications of chamber depth control.

Until an adequate fire extinguishing system is developed, the use of high pressure carbon dioxide extinguishers or portable high pressure water cylinders with nozzles for direct application of water on the flame should be used in conjunction with or in place of the presently required water bucket and sand. High pressure carbon dioxide cylinders are commercially available. Their use must be coupled with the rapid donning of a breathing apparatus to prevent suffocation. Extinguishment of the fire is of primary concern, however, and in event of suffocation a rescue could be made if the fire has been eliminated.

Portable high pressure water cylinders should be installed in chambers as soon as their availability is determined.

Items Under Investigation or to be Investigated

Fire-retardant Roxel treated bathrobes are presently being used during decompression. A glass cloth outer garment is being used by race car drivers for fire protection (15). The National Aeronautics and Space Administration is testing a glass cloth undergarment that reportedly (11) has been used for 30 days with no signs of skin irritation experienced by the wearer. Bathrobes and mattress covers of a similar fabric are being manufactured by the Owens-Corning Fiberglass Company and Fyrepel Company for testing at EDU.

Many problems are still unsolved. Development of lightweight inhalators

and respiratory hoses of fireproof construction is required. A glass fabric covering over the corrugated hoses may prove to be an interim solution. Non-flammable electrical insulation is required for interior wiring including instrumentation leads. Non-flammable hoses of various diameter are required for uses such as sampling atmospheres, injecting gases into an apparatus or channelling expired gas to spirometers. Fire-resistant thermal insulation is required for installed air conditioning piping.

Electrical machinery should be tested to determine its potential hazards. Items such as switches and receptacles should be designed to meet requirements for hazardous locations. Most presently acceptable explosion-proof equipment is very large, and can become unworkable in a research chamber having requirements for many circuits for instrumentation purposes. Refined design is required.

An investigation sponsored by the Office of Naval Research is commencing at a commercial laboratory to study the flammability hazards of atmospheres of a wide spectrum of oxygen partial pressures with selected inert gases. This study will provide basic information of the hazards involved in various atmospheres at depths to 1000 feet, and will provide the knowledge required to choose the safest atmosphere within physiological limitations.

Conclusions

The fire at the Experimental Diving Unit has brought increased emphasis on the fire hazards in hyperbaric chambers and prompted study of this subject, both in the Navy and in civilian institutions.

The information given in this paper clearly points out that the hazard of fire in decompression chambers, both with artificial atmospheres and with compressed air, is increased with increasing pressure, and the flammable effect of increased partial pressures of oxygen predominates over the quenching effect of increased partial pressures of inert gas. Ignition in compressed air is expected to be more rapid than in helium-oxygen atmospheres of the same oxygen partial pressure, but in some cases the burning rate will be greater in the helium atmosphere than in the nitrogen (air) atmosphere.

Adequate fire prevention and protection is a problem that requires research and study to provide the community of divers, researchers, and hyperbaric chamber operators at medical facilities with clear knowledge of the hazards associated with their work and the means to reduce or eliminate them. Material selection to eliminate flammable equipment is at best a grasp at presently available equipment and materials, and is only a prelude to necessary research into the development of nonflammable materials for a variety of applications. A program of selection, testing and

culling of available materials should be undertaken, and where no immediate solution is found, appropriate development should be initiated.

Fire extinguishing systems must be designed for operation at increased pressures. The known fire extinguishing agents should all be selectively tested and the results studied to determine the most effective agent under expected chamber conditions.

Until non-flammable materials and adequate extinguishing systems are available, personnel involved in the operation and use of manned chambers should endeavor to eliminate unnecessary equipment and be knowledgeable of the hazards associated with their particular installation.

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8 | G. F. BOND

Medical Problems of Multi-day Saturation Diving in Open Water

I am to discuss the medical problems of multi-day exposures of man on the bottom of the ocean under conditions such as those obtained in Sealab I and Sealab II. This is intended to concern, not primarily the physiological problems of diving, but the changes which result from long exposure to the cold, wet, high pressure environment. I can summarize the physiological aspects by saying that since 1957, when we first commenced our laboratory work on the physiological problems of prolonged exposures to high pressures of synthetic environments, through all the years of the animal and human experimentation culminating in Sealab I and Sealab II, we have examined almost every imaginable physiological parameter and we have not found any serious deviations from the normal in man or in animals. This is not to say that such data are absolutely reliable when one exposes men in such a fashion. Indeed, we see some trends which would indicate that if the exposure is increased to 60 or 90 days one might possibly get into trouble. In general we see two trends. We see a type of stress response during the first 3 days, which sometimes lasts as long as 5 days of exposure to this new environment. It does not represent a change beyond the normal range, but goes to the limit of normal. After about 5 days all of our human subjects and animals alike tend to come back toward the baseline. However, after 15 days of exposure we now see a drop below the baseline approaching the lower limits of normal. That, I think, is all I will say about physiological data, which you will have a chance to examine later. I will now present a few of the medical problems which we encountered in Sealab II, and sum-

marize some of the general problems which we will face inevitably in the future.

One such problem is visual dark adaptation, which is desirable in deep water with nearly zero visibility. This has been accomplished by the use of red goggles prior to entering the water.

Another prime problem is the requirement for thermal protection against the extremes of cold we find at any point on the continental shelf at 400 feet or lower. Even in operations at 205 feet we were dealing with water temperatures of 46 to 56 degrees. We have used thermo-protective suits, electrically heated, which worked quite well (Fig. 26). However, these suits require an excessive time to don and become a medical problem, in that the man, after struggling for perhaps as long as an hour to get into the suit, is pretty well debilitated and not in very good shape for diving. Furthermore, if he were an inquisitive soul and chose to turn on the suit while he was still standing on the deck, he would get extremely hot. It is necessary to wait until you get into the water before you turn on the suit. Such suits also cause technical problems in medical monitoring.

We have attempted to obtain electrocardiograms and simultaneously to get skin temperature readings on a subject. The operational problem is that, having gotten all the electrodes on a man, he has to put on the bulky suit, and this displaces about half of the electrodes; consequently your data is somewhat confused. I bring this out mostly to point up the fact that during actual operations certain monitoring programs must be cut to the bone because the procedures take up a large amount of time. This man could be outside doing useful work, and it becomes a frustrating affair. Perhaps it is better that we do more of these in the laboratory under controlled conditions rather than to attempt the nearly impossible in open sea operations.

Under conditions of high pressure and in the Sealab atmosphere, the Dwyer instrument for determining carbon dioxide, which costs about $35.00, will function much better than any of the $3,000 CO_2 meters currently available. It is a sad commentary that we are so far behind the times with respect to atmospheric sensing instruments. Many do not function properly in a helium-oxygen atmosphere under pressure. Before we achieve autonomy we will have to have completely reliable gas sensing and monitoring equipment. This is not only true of the atmospheric and physiological monitoring systems; it is true of every piece of hardware equipment inside the living compartment.

Another problem is the need for surface logistic support. If specimens must be transported up to the surface support ship for analysis, it is necessary to have such a system. Massive pressure pots, shown in Figure 27, must be hauled through the water, put in a clumsy elevator, and dragged to the surface. We expect to improve this system, but, as it has been used in

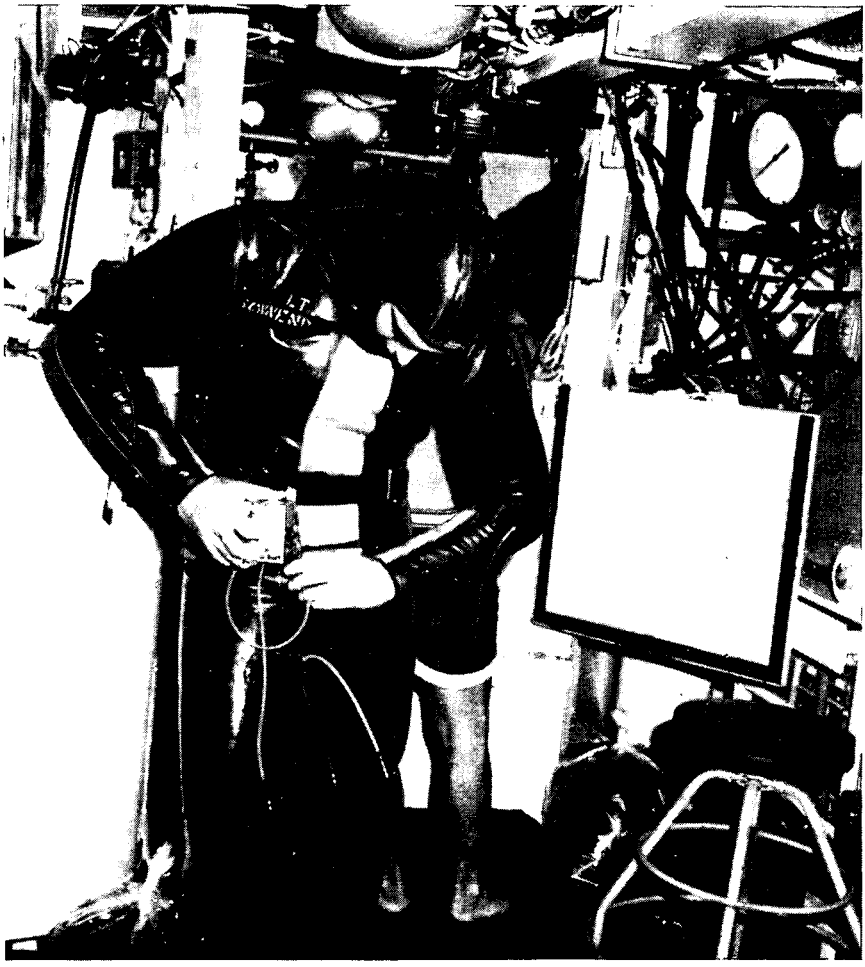

FIG. 26. Aquanaut dressed in thermoprotective suit

operations to date, it has been a very serious problem in that men had to put on their full garments every time just to go out and bring in a pot. Much of the time they felt that we were being whimsical when we asked them to send up the pot or to receive one. This was not the case, but it doesn't make for the best relationship between topside and submerged personnel.

A problem which is not strictly medical but can become critical is the problem of underwater communications. I am sorry to say that today we have absolutely no workable diver-to-diver communications. We have tried

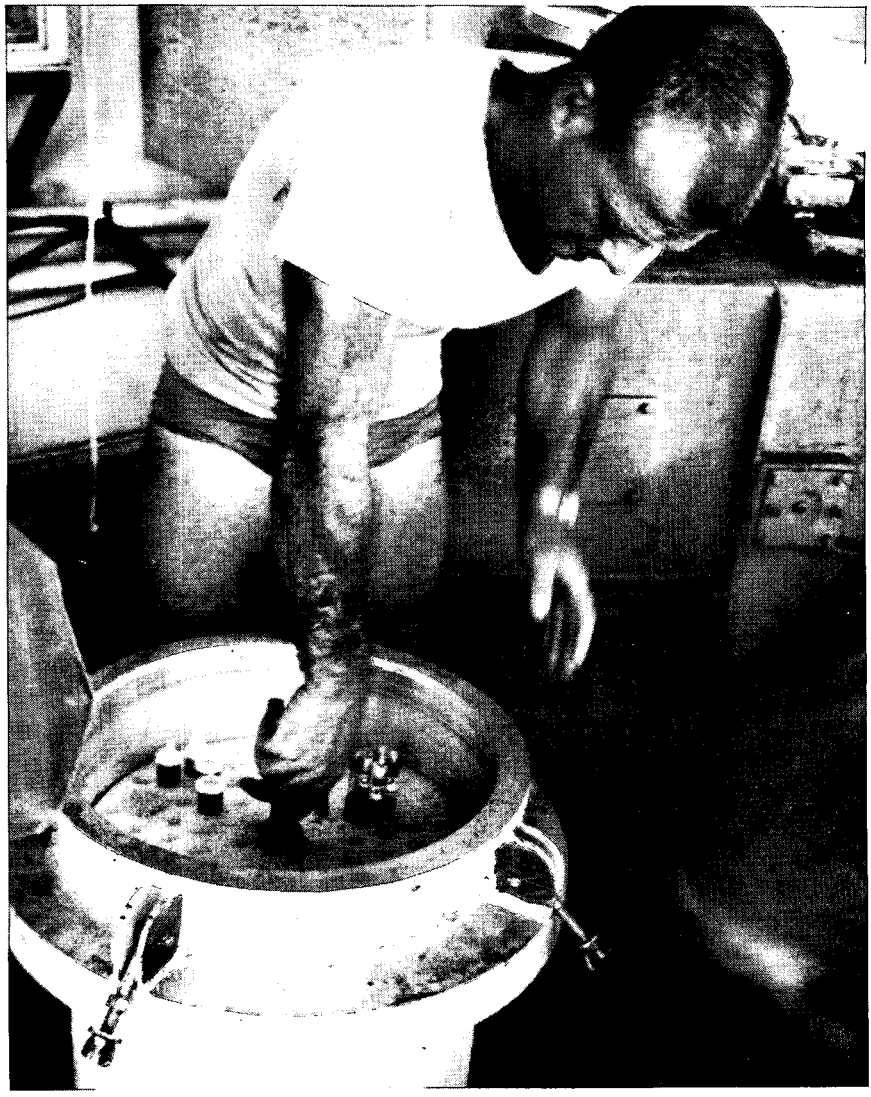

FIG. 27. Aquanaut placing specimen in pressure pot for transport to surface ship

the communications equipment shown in Figure 28 in our Sealab operation. This worked well in the swimming pool, but not at all under the conditions of Sealab. Far too many instruments operate satisfactorily under laboratory conditions but when tested under the extreme environmental conditions of operations, they will not do.

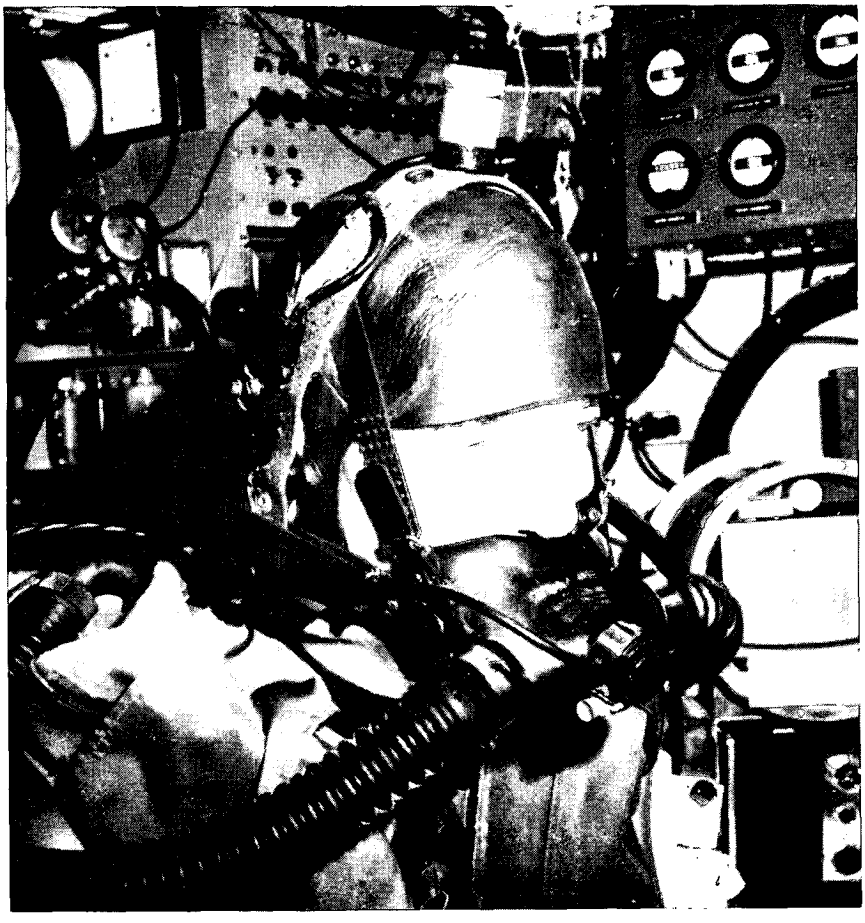

FIG. 28. Aquanaut wearing equipment designed to improve voice communication

Sealab II was built to give a very comfortable and safe habitat for men on the bottom. However, we seem to have overlooked the fact that the purpose of it was to let these people go outside and dive. So, with all the space available for living in the habitat, the entry hatch was only large enough for one diver to get in and out at a time.

A medical problem of considerable proportions concerns the cooking of food. As you might guess, one cannot fry foods in the captive atmosphere because the accidental release of acrolein would necessitate a "bailout" of all personnel. Therefore, frying is taboo. During the Sealab operation the men below asked whether they could have steaks and, without thinking much of it, offhand I said "yes, you may have steaks". Instead of delivering

pre-broiled steaks, someone sent down raw steaks. The men took this as permission to cook and promptly started to broil them. The day must come when we can permit aquanauts more freedom than this, but at the moment our men have to live on boiled or baked foods. In fact, even the question of making toast becomes a hazard, because we found that burning toast produces carbon monoxide.

Medical problems caused by poor human engineering were the result of too much concern on our part for the privacy and comfort of the men. We felt that the aquanauts were entitled to privacy and we gave them draperies which shut off their gas circulation. Consequently, we had CO_2 buildup in the bunk area and unpleasant sleeping conditions. A table was provided which opened for use. However, when it was opened, no one could be in a bunk, and also the food slid off because of the tilt of the Sealab underwater living compartment which was at a 6 degree up angle and a 6 degree port list. This led it to be called the "Tiltin'-Hilton". Figure 29 shows the bunk area of Sealab II.

Some problems, although not strictly medical, were certainly logistic problems. One concerns the lithium hydroxide system which we used for CO_2 removal. While it is an extremely efficient system and we are very pleased with it, it is logistically difficult. We had to stow hundreds of these cannisters inside the living compartment which crowded the people, and then as time went along toward the forty-fifth day we had to re-supply from the surface. It is obvious that we must develop a regenerable CO_2 absorption system, and we must do it quickly.

Now let us look at the many problems which we will face as we go to greater depths for long sojourns. These problems can be broken down quite easily into matters of basic research, of environmental research, and of personnel research. Excluding development of hardware these are our basic considerations.

Under basic studies I think we have two critical things. One is oxygen toxicity and although some progress has been made since 1955, I am not impressed that we are very much nearer the goal of solving this problem. Considerable energy must be devoted to this; the recent emphasis on hyperbaric oxygen therapy will be a boon because many teaching institutions will be working on this problem. Decompression sickness is likewise a basic problem. We have made gains here, but the answer is elusive. We would wish to know, among other things, what is the optimal partial pressure of oxygen to be maintained for people who are going to live in these undersea habitats at a given depth. I do not know what the upper limit of tolerable oxygen is for a 30 or 50 day exposure. I have an instinctive belief that as we go deeper, increase the density of the breathing medium and add to the work of breathing it will be necessary to raise the partial pressure of oxygen slightly to provide for adequate oxygenation. This can be checked in the

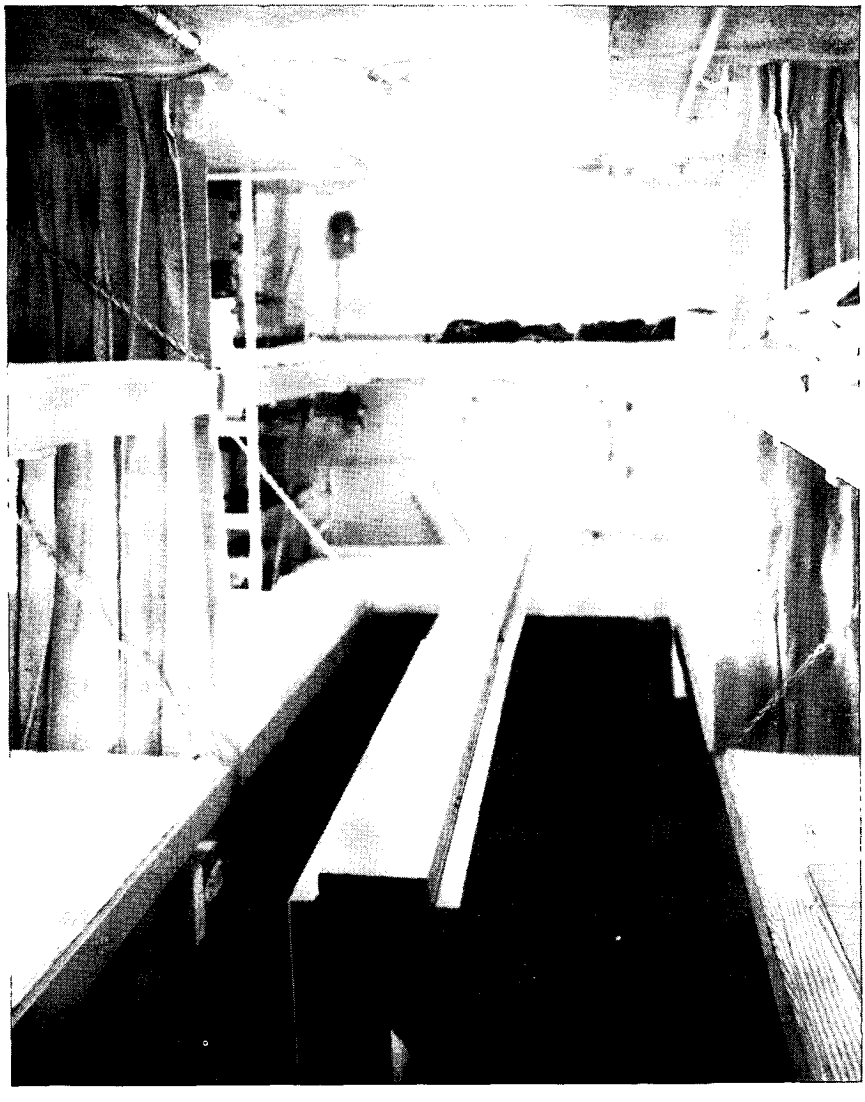

FIG. 29. Sleeping quarters of SeaLab II

laboratory almost immediately. We can utilize laboratory animals and get good arterial Po_2 values to test this hypothesis. If it is not true, we must know it, because we may well have been crowding the upper limits of oxygen exposure during the Sealab II operation. Indeed, there was a fall in red cell count in two people who were exposed for a long period of time.

We need to know a great deal more about direct pressure effects. Very

few of us think there is much to this. On the other hand, all of the prolonged exposure experiences have shown that men do complain of various ill-assorted aches and pains immediately upon pressurization. Many people have their joints lock up when they go under pressure. Why is this? We don't know. We need to know more about direct effects of pressure and what these effects do. We certainly need to know a great deal more about thermo-regulation in a He-O_2 atmosphere, because something must happen to the thermoregulatory centers of the body. We don't even know the comfort zone for an He-O_2 atmosphere under pressure.

Finally, human engineers and psychologists should recognize the fact that when a man is put on the ocean bottom under these conditions, he is deprived of most of his natural senses. He loses his sense of smell, his sense of taste is greatly diminished, his tactile sense is nearly lost in the cold water, his vision is reduced, and he cannot localize sound. An aquanaut is not a whole man. If we can do something to restore these senses or replace them with gadgets we must do so, all the way from image intensifiers to mechanical aids for manual power reinforcement.

In conclusion, there are some additional unsolved medical problems related to environment. We need to know a great deal more about friendly and dangerous marine life. It was obvious to us in Sealab II operations that we did not have a very good awareness of dangerous marine life, although we did work with a useful and friendly dolphin. We must learn to make the oceans work for us. The sea bottom is an unfriendly surrounding for man. We must diminish this hostility and we can only do so by knowing much more about the environment into which we are going to inject our aquanauts. We have a long way to go and we have come a good way. We will occupy the continental shelves of the world, and we will go deeper. However, to do it will take the energy of many people.

9 | JAMES G. DICKSON, JR. and J. B. MACINNIS

Confluence of Physiological, Environmental and Engineering Factors in Prolonged Diving at Extreme Depths

Advances in diving have depended not only upon the evolution of new physiological information but also upon its eventual successful application to actual undersea operation. The success of any manned, undersea, diving operation is based upon the basic and applied research which preceded it. In the course of the continuous blending of physiology and practice, a challenging and important opportunity exists for close and informed collaboration between individuals skilled in physiology and in engineering.

Certain aspects of the need for engineering-physiological collaboration will now be considered, from the point of view of members of the human factors team which carried out life support aspects of an approximately 400 foot, two day saturation dive in the Caribbean area during the summer of 1964. This particular dive represents the deepest, yet perhaps the least complex, open-sea saturation dive to date. The actual depth of the exposure, 432 feet, is of only passing significance; it is hoped and expected that it will be exceeded in the near future. However, as depth of diving is increased and the duration is prolonged, it will become more and more important to recognize the opportunities and vital need for a planned combining of physiological and engineering considerations, long in advance of actual diving operations. This planning is not always evident.

The problems presented by deep saturation diving have been elaborated by others. They include peculiar problems of decompression, inert gas narcosis, difficulties in pulmonary ventilation, limits of oxygen tolerance, temperature, wetness and communication.

Several of these problems had already been studied in relation to the saturation diving method proposed by Bond (10), when, in 1963, Link sought the aid of Lambertsen's laboratory in extending the depth of such diving in the open sea beyond the 200-foot depth his group had accomplished the previous year (3). In the succeeding months there followed the development by Workman (7) of a linear decompression procedure for the elimination of inert gas from the tissues following saturation exposures. It was against this background that an attempt was made to resolve many of the human factors and life support problems that are present in such a dive.

It should be emphasized that the deep, open-sea dive was not in itself a research effort, but rather an application of previously determined physiological and physical principles. The application of these required a high degree of cooperation and coordination among the several types of backgrounds involved. Since my purpose is to emphasize the necessary, desirable, but not inevitable pooling of physiological and engineering skills and judgments, no effort will be made to define sharply the individual contributions to the project.*

At the time the preparations began, humans had not yet been subjected to saturation exposures at a four hundred foot depth. One immediate life support requirement, therefore, was evident. Successful human saturation exposure and decompression must be carried out to this depth in the laboratory before a dive under open sea conditions should be performed. This vital requirement was fulfilled when the U. S. Navy Experimental Diving Unit conducted saturation exposures of subjects to helium-oxygen pressures equivalent to 300 and 400 feet and successfully accomplished decompression using the slowly devised continuous ascent technique.

An important early agreement between the engineering and the human factors groups concerned the scope and manner of approach to this deep, open sea project. Anticipation of the greater physiological stresses to man and the physical stresses upon his supporting equipment resulting from depths significantly greater than has been achieved before, led to the adoption of a "minimal system" philosophy. The number and complexity of mechanical systems and components was deliberately limited. The number of human beings involved was also kept to the minimum necessary to accomplish the primary task, while assuring adequate safety backup for the subjects at sea. The scope of this project was therefore quite different from those of much shallower saturation diving projects then being planned and conducted by others (1, 5). This approach offered distinct advantages from a life support standpoint then and still does. It improves overall managea-

* Engineering group headed by Edwin A. Link. Undersea life support group, from University of Pennsylvania, headed by Christian J. Lambertsen, M.D.

bility and flexibility of the operation, and it tends to reduce to a minimum the sources of potential life-threatening failures, either mechanical or human.

Once the philosophical approach had been established, the remaining human factors evaluation of the entire operation could be completed, with considerations of subject safety paramount.

Major Equipment

Figure 30 indicates diagrammatically some of the major equipment components of the overall diving system. Three major units of the system were in existence as the combined engineering-human factors effort began. These were a surface vessel to serve as the basic support platform with the capacity to provide support for the diving operation, a two-compartment submersible chamber of pressure rating greater than the contemplated bottom pressure, and a unique inflatable structure containing an access trunk to be anchored to the bottom to act as a dwelling during the exposure.

With these three major units provided by the engineering group and the assets of the laboratory most of the requirements for a deep saturation dive were available. However, the submersible decompression chamber,

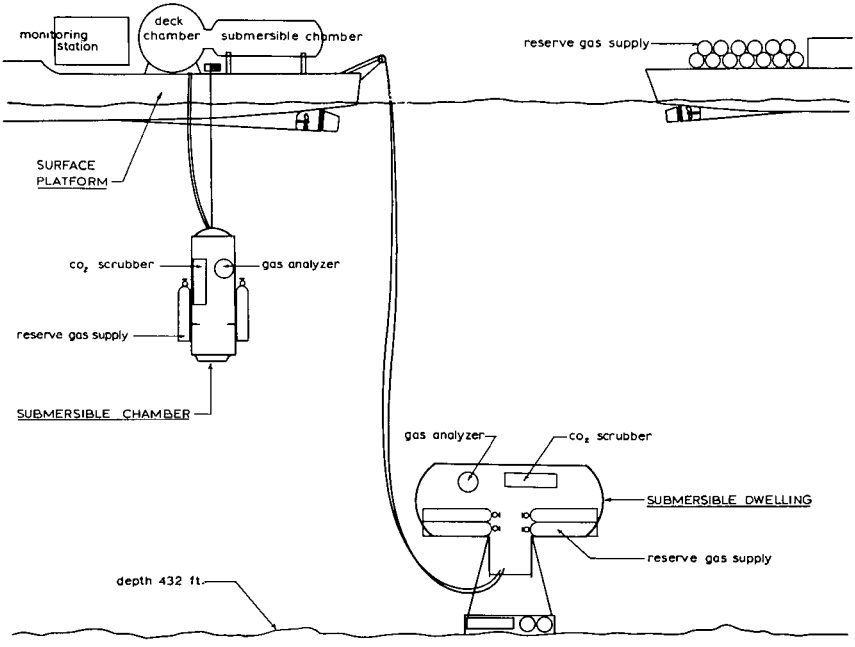

FIG. 30. Diagrammatic representation of basic mechanical components of life support system used in saturation dive to 432 feet.

although suitable for use as an elevator for two men, was quite inadequate in size for the several-day decompression period anticipated. Furthermore, in the event of serious bends in a subject during decompression it would have been impractical for a member of the support team to enter the small submersible chamber to carry out the possibly extensive therapy. Finally it was necessary to provide proper safety backup for supporting divers operating from the surface. For these reasons a chamber on deck was considered essential, and one was designed and incorporated into the life support system. Here, important human factors considerations imposed special features upon this chamber. It had a trunk for mating with the submersible chamber so that subjects raised from the sea could be transferred under pressure into the deck chamber for subsequent controlled decompression. The pressure rating of the deck decompression chamber exceeded bottom pressure such that, if necessary, the entire decompression including therapy of bends occurring at great depth could be accomplished within it. Its size reflected a compromise between subject needs for safety and comfort and the quantities of gas required to fill it. Other human factors considerations in the design of the deck decompression chamber related to controls for compression and decompression, for temperature regulation, for carbon dioxide removal, for gas sampling and monitoring, locks, and provision for the breathing of special gases for therapy and decompression.

An especially important safety problem anticipated for the actual mating operation was the danger to both subjects and deck personnel during the handling of the large mass of the submersible decompression chamber above a rolling deck at sea. This consideration determined that the actual mating should occur with the submersible chamber resting securely in a cradle on deck, thereby minimizing threats to mating surfaces and seals and the gas fittings on both the submersible and deck chambers. This dive appears to represent the first use of such a deck decompression chamber in a saturation exposure at sea and prominently illustrates the scope of life support interests and the multiple merging of human factors and engineering activities and thought.

Gas Environment

Human factors analysis dealt as well with other problems of diving. In order to remain within the boundaries presented by oxygen toxicity, hypoxia and carbon dioxide intoxication, a suitable respirable gas environment had to be selected, and reliable control and monitoring of this environment in the submerged dwelling, the submersible chamber and the deck chamber had to be assured. In determining gas composition for the 400 foot depth, practical choice of the major inert component was limited to helium. However, important further considerations concerned with avoid-

ance of lung damage did influence the selection of the desired range of permissible oxygen pressures. Based largely upon the studies of Helvey (2), the multiday length of the total exposure imposed a ceiling not much greater than about 0.5 atmosphere of oxygen pressure. Likewise, avoidance of hypoxia imposed a floor of about 0.2 atmosphere. Within this safe range, consideration of the effect of an accidental interruption of oxygen control, through failure of either the monitoring or the replenishment systems, upon the relatively small volumes of the dwelling or submersible chamber led to the selection of an oxygen pressure (0.5 atm) near the upper part of this range, thus insuring an oxygen "cushion" of several hours should an interruption of supply occur.

The third gas of major concern was carbon dioxide, and a P_{CO_2} ceiling of 7 mm Hg was established, well below levels which should produce true toxicity even in indefinite exposure (6). Thus at the eventual 432 foot depth of diving the gas mixture supplied was 3.6 % O_2 in helium with a maximum of 0.066 % CO_2.

With the basic gas composition determined, it was decided for reasons of safety that the primary monitoring and control of the gas environment should take place at the surface, with replenishment of oxygen and helium from surface supplies. Carbon dioxide scrubber units which employed granular Baralyme were engineered for each compartment. Again, safety considerations established that the life of the absorbent cartridges in these units should be greater than 12 hours for two subjects, and that spare cartridges be placed at each location.

To provide a readily available safe respirable gas mixture to replace gas losses from the system, supplies of a 3.6 % oxygen in helium mixture were placed at the topside control station, at the submerged dwelling and at the submersible chamber. Prior to open sea activity, the gas analysis system was tested by monitoring the chamber environment during the deep saturation exposures and decompressions conducted at the Experimental Diving Unit. The system employed was also used extensively in monitoring gases to which animals were exposed at a pressure equivalent to 4000 feet of sea water (4). In these exposures the range of control for oxygen was 0.2 to 0.4 percent, for carbon dioxide from 0 to 0.02 %.

Since overall safety considerations necessitated retaining of primary control of the gaseous environment at the surface for the dive, the subjects were dependent for their gas environment upon 400 foot lengths of hose to the surface. This in itself presents the same potential hazard as does the use of hoses in diving. To decrease this dependence upon surface activity, an oxygen supply sufficient for approximately 10 days was integrated with the dwelling, and carbon dioxide and oxygen analyzer units capable of being used at pressure were included in the final system. These gave the

subjects the capability of independently controlling their own breathing environment in event of failure of the more accurate surface control. This placing of pure oxygen at the divers' disposal required tight precautions to guard against inadvertent leakage of this gas into the dwelling, since this could lead rapidly to manifestations of oxygen toxicity.

The joint engineering-human factors approach through detailed consideration of physical and physiological hazards, thus defined the major mechanical components of a minimal system for supporting life in a deep saturation exposure at sea.

Supported from a mobile surface platform, subjects could be lowered to the bottom, work from a dwelling on the ocean floor for an extended period, be returned to the surface under pressure and be decompressed in a suitable chamber at the surface, with assurance of continuous control over both the pressure and composition of their gaseous environment. From a life support standpoint these numerous engineering and life-support components represented, as a group, elements which were of critical importance to the subjects; failure within these systems would present a direct threat to life which could in some cases be measured in minutes.

While component failure should not be expected in systems fit for use at sea, it was logical that such details of structure should receive the greatest attention from the life support as well as the engineering team.

Communications

Scarcely less critical to subject safety and performance, however, are the problems of providing effective and reliable communications. It was known that the serious distortion of the voice produced by the helium in the respirable gas environment would severely impair voice communications between the subjects and from the subjects to surface personnel. The necessity for rapid communications therefore demanded the provision of several alternate methods. These included buzzers at each subject location for the transmission of code messages, and a television system with the camera placed at the underwater dwelling to provide immediate information to the surface monitors of the performance, actions and condition of the subjects. Devices for the direct transmission of handwriting were also introduced into this type of diving as a monitoring and communication measure. These latter devices, serving for the rapid and accurate transmission of written messages, also offer a valuable means for assessing subject performance and state of consciousness.

Provision of such alternate communication routes does not eliminate the need for ultimate improvement of direct voice communications, since of all factors in safety and effective performance this ranks among the most critical. The absence of a satisfactory electronic means of overcoming the

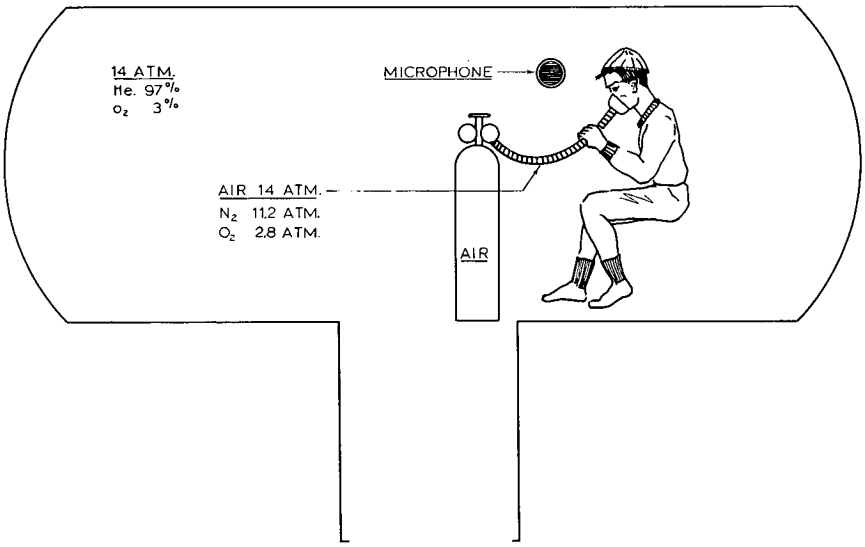

FIG. 31. Method for improving voice communication at extreme depths. Voice distortion resulting from breathing helium is lessened by effecting transient lung washout with air.

helium-induced voice distortion led to a more directly physiological approach to the problem. It was known from field diving experience of others that speech at depths between three and four hundred feet is improved by adding a fraction of nitrogen (about 15 percent) to the helium-oxygen mixture (8). It was therefore proposed by Lambertsen that, if prior to speaking, a subject could temporarily replace a portion of the helium in his lungs by a transient lung washout method using air or a nitrogen-containing mixture, intelligibility of speech should be drastically improved without undue development of narcosis. Figure 31 shows the simple technique by which this was accomplished. Bottles of compressed air and an air-helium mixture were placed at the underwater dwelling, enabling a subject to effect a lung washout prior to speaking. The washout is exponential and the inspired pressures of oxygen and nitrogen, recognized as toxic for long continued exposure at this depth, were judged to be safe for the several breaths of intermittent inspiration required for speech. This lung washout technique did in fact significantly improve voice intelligibility, and was extremely simple in execution.

Temperature

Ranking just behind the critical life-support problems already mentioned is a problem which, while not an immediate threat to subject safety, never-

theless could seriously influence health and performance during a deep saturation dive at sea. This is the problem of maintaining a comfortable temperature for the subject in the deck chamber, submersible chamber, undersea dwelling and particularly in the water, if he is to accomplish effective work on the bottom. Factors which combine to make this difficult are temperature of the water, high thermal conductivity of the helium environment, wetness of the subjects, and the high humidity in the dwelling imposed by the constant water interface present in the trunk. Although considerable efforts were made to develop equipment to overcome these difficulties, this aspect of the task was not satisfactorily accomplished. Decision to conduct the exposure in the Caribbean area, where relatively warm water would impose less of a burden on temperature control, was made in order to lessen the decrement in subject performance in this early dive.

Decompression

The anticipation of physiological problems related to decompression from prolonged diving offers another example of the necessary coordination of physiological and engineering groups. The reliance upon the basic pattern of linear decompression developed by Workman has already been cited. However, the planned addition to this schedule of the principle of intermittent breathing of pure oxygen during the final hours of decompression, in order to increase the outward pressure gradient for helium elimination without inducing oxygen toxicity required the inclusion of a breathing system suitable for this purpose. Further, the use of the additional principle of replacing helium by nitrogen during treatment of decompression sickness was provided for. The case of mild bends which did occur was successfully treated by employing a combination of intermittent oxygen breathing, moderate elevation of pressure, and substitution of inert gases (9).

These remarks have been limited to a consideration of some, but by no means all, of the important human factors problems anticipated or encountered in preparing for one saturation exposure directed at placing man at a then new and great depth in the open sea. Emphasis has been placed upon the very great importance of early, planned and careful coordination between engineering and human factors groups in solving these problems. This particular example of such a collaboration, while effective, was by no means perfect, and many of the problems were less than optimally resolved. Among these persistent problems remain voice communications, temperature and humidity control, decompression and the treatment of decompression sickness. As the depth for saturation exposures in the sea is extended, additional problems related to resistance to pulmonary ventilation, inert gas narcosis and greater distance from surface support will become increas-

ingly troublesome. As man reaches toward new depths in the open sea and places even greater stresses on himself and supporting equipment, the practical solution of these many human factors problems will demand effective collaboration between thoughtful engineers and physiologists.

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10 | C. F. AQUADRO and J. CHOUTEAU

Problems of Extreme Duration in Open Sea Saturation Exposure

At the time of the Second Symposium on Underwater Physiology three years ago, limited and precursory experiments had been performed in the open sea to investigate prolonged durations of exposure by man at depth. Preceding these ventures into the sea, however, came preliminary laboratory experiments to help determine their feasibility.

During the Second Symposium on Underwater Physiology, Bond (1) revealed that personnel of the Naval Medical Research Laboratory at Groton, Connecticut had begun several years previously to explore new approaches to the old problem of effective penetration by man into inner-space. To overcome the two major problems recognized at that time, it was realized that a great deal of basic work remained to be done before man should attempt to apply certain principles to open sea saturation exposures. Bond and his colleagues proceeded to embark on this investigation with animals (2) and later with men, despite much criticism and resistance to their efforts as well as the difficult physical and physiological conditions which they faced. They are to be congratulated for their fortitude and important pioneering work which has helped man to accomplish effective penetration into the sea by use of manned undersea stations.

Since the last Symposium, several generally successful, manned undersea station experiments of various types have been completed. Not all of the problems have been solved, but at least we are gaining experience and confidence that man can thus live and work effectively in the sea without causing damage to his body or mental processes. Some problems may exist which we do not recognize or appreciate yet. Time and further experience will help us to decide and learn what is the best and safest way to continue.

Duffner paraphrased Voltaire by stating that the discovery of what is true and the practice of that which is safe are two important objectives of underwater physiology (3). We shall continue to experiment and with

the aid of an exchange of applicable information on an international and cooperative basis, the future looks bright for our eventually solving most of the problems encountered.

Achievement and survival under the sea depend on mental re-education and perhaps development of new patterns of behavior (4). Once the psychological barrier has been overcome, there remain the exacting demands of physiological adaptation of man's body as well as physical adaptation of material and of mechanical devices to the undersea environment.

The chief responsibility for survival in the foreign environment of inner space lies with the engineer. Physiology remains a second line of defense for the time when the arrangements of the engineer become overtaxed or exhausted. Psychology has its applications throughout the project, but becomes of special importance when the failures of the engineer make the situation particularly stressful and the physiological tolerances become strained (5).

Discussions of underwater physiology should not be limited to reflection upon or investigation of physiological aspects of various affected body systems such as those of the cardiovascular, respiratory, musculoskeletal, and nervous systems. Certainly evaluation of these systems and how they are affected by such factors as oxygen toxicity, inert gas narcosis and decompression are vitally important. They present a good base from which an extension of investigations can be conducted. However, various factors which affect or influence psycho-physiological function as a whole (of the total body complex) must be dealt with. Additional problems exist other than those conventionally discussed in volumes such as this. In this presentation, several non-classical problems will be briefly discussed as well as some of the classical problems related to underwater physiology.

A trend was developed in the Second Symposium on Underwater Physiology in which some attention was directed toward extension of diving depth and duration and some effects of prolonged immersion. With the recent advances in applied research and technology, it is encouraging to observe the increased emphasis in this Third Symposium on problems of open sea saturation exposures and prolonged periods at high ambient pressures.

From the varied experiences in open sea saturation exposures to date, it is difficult to attempt to make generalities or to interpret results of experiments by others. Although there is an absence of specific presentations pertaining to the problems of the cardiovascular and respiratory systems in this particular session of the Symposium, we must not deceive ourselves by thinking that therefore no such problems exist.

Peterson (6) previously reported on cardiovascular performance underwater in diving animals and man, and compared observations from the

sparse data available with personal considerations of what might be expected to occur. The observations were confined to dives of short durations as those limited to breath-holding, but interesting analogies occurred which emphasized the need for further study of the cardiovascular response to the underwater environment.

The impression is that there have not been significant circulatory or cardiovascular system problems during manned undersea station (MUST (12)) experiments. This probably reflects effective screening of unsuitable candidates during selection of personnel for the experiments. However, more effort should be devoted to the study of circulatory physiology underwater. One of the problems which have been encountered in attempting to perform some investigations was with electronic ("parasitic") disturbance-interference during application of electrocardiograms to divers in the sea. Likewise similar problems have been encountered in transmitting via cables to the surface control station the registration of electrocardiograms taken in the undersea station.

Some equivocal hematological changes have been observed in man following certain previous undersea station experiments (e.g. Pre-Continent I) (7) and in sheep following the initial physiological experiment in a pressure chamber prior to our most recent open sea exposure. During and following that experiment in the sea, however, the hematological status of the exposed personnel remained stable and within normal limits. In another recent undersea station experiment, Brauer (8) reported that as a result of the exposure there were no changes observed in erythropoiesis in the four men who were evaluated by the U. S. Naval Radiological Defense Laboratory.

In the earlier undersea station experiments previously mentioned, a transient mild anemia occurred which apparently was due to the elevated partial pressure of oxygen in the compressed air atmosphere of the stations which were maintained at an absolute pressure twice that at sea level. Although the initial analysis of the sheep apparently revealed an anemia following their prolonged exposure to high ambient pressures of a helium-oxygen pressure chamber atmosphere, further evaluation disclosed that the apparent anemia was only relative, for their hematological findings remained within the range of normal limits.

In the latter experiment, partial pressures of oxygen in the synthetic atmosphere were maintained at higher levels than were desirable as we sought to perfect operational techniques. Carbon dioxide partial pressures were also greater than desirable, and what effect this had on the animals has not been definitely determined. To complicate matters, the solvent, trichloroethylene, was introduced into the atmosphere regeneration-recirculation system of the caisson. This solvent was used in an attempt to clean from the system some lubricating oil which had leaked from the com-

pressor into the piping of the system thus contaminating it as a result of an accident in the compressor. Perhaps there was a toxic reaction in the sheep caused by the solvent and oil residue which produced the relative anemia. Besides potential effects of elevated CO_2 tensions or other toxic agents, indications are that a partial pressure of oxygen in the atmosphere much above that of normal tensions affects erythropoiesis and can produce a relative or actual anemic condition during or following prolonged exposures.

As for problems related to the respiratory system, we are not yet quite sure of what has occurred during the undersea station experiments. Nevertheless, our general impression, with some reservation, is that there have been no significant disturbances in the respiratory function of persons subjected to these saturation exposures, particularly after they have passed through the initial, about 3 day period of acclimatization to their new environment. There has been no serious or lasting embarrassment of respiration or incidences of respiratory crises as such. There have been incidences in which various persons have noted some breathing-resistance (heavy breathing) and dyspnea (shortness of breath) upon exertion within their habitat or while outside of it on diving sorties during the initial few days of their exposure.

There have also been incidences of transient, febrile illnesses of an influenza-like nature in which some expected, minimal-to-moderate respiratory distress occurred along with other systemic signs and symptoms. Common colds and pharyngitis which may occur in any environment have arisen and caused some minor problems associated with the respiratory system. However, those persons affected have recovered spontaneously or responded favorably to available medication or treatment including temporary suspension of diving activities to prevent occurrence of possible complications.

We do recognize the need to continue investigation in pulmonary and respiratory function, particularly with respect to saturation exposures and work performed at increasingly greater depths and with various gas mixtures. For example, as the result of the limited pulmonary function studies permissible under the circumstances of the most recent MUST experiment, it was concluded that it is necessary to clarify and study further the results which were obtained.

It was not feasible to perform pulmonary function studies down in the station during that experiment. Those which were done were performed on the oceanauts while on surface before and after their exposure. Naturally there would be differences under the realistic circumstances from the results which were obtained. The respiratory function characteristics of the oceanauts noted prior to the experiment had been maintained and compared in general to those observed after their exposure in the undersea station.

In the interpretation of the post-experiment patterns, fatigue of the

oceanauts must be taken into account as possibly contributing to some irregularities of rhythm and amplitude which were observed in certain cases. Generally, some diminution of the minute-volume ventilation was also noted. However, it was felt that the differences registered between pre- and post-experiment studies for the measured parameters were too slight and inconsistent to be significant. Further investigation was recommended including performance of the same studies under increased pressures and with the gas mixtures used.

Perhaps this is an appropriate time to comment more about fatigue of personnel exposed to saturation exposures in the sea. Fatigue is a response to a complexity of factors, depends upon the duration of the exposure to fatigue-producing elements and environmental stresses, and is manifested by individual differences. With variations in one's participation in the experience, his basic state of physical and emotional health, and his manner of work and living, fatigue or absence of it is exhibited in various degrees.

Some factors which may play a part in producing fatigue are the ventilatory effort in breathing compressed air or mixed gases in hyperbaric conditions, repeated exposures to cold water, somber aspects of the deeper depths or turbid waters, and long hours of work with irregular meals and lack of adequate rest depending on the circumstances encountered. However, the resulting fatigue seems to be no different from that observed following prolonged engagement in athletic contests or competitive sports, similar types of industrial or occupational activities, or in persons returning from war patrols on land or at sea. Until manned undersea stations cease to be experiments and become an accepted manner of life and work, the related fatigue is considered to be expected and normal. Even then, one will not always avoid fatigue.

Problems related to the protection against body heat loss during extended immersion are still unresolved. Beckman (9) has previously reported on this subject and additional information appears elsewhere in this volume (Chapt. 14).

In the experiments with which we have been associated, the personnel of the undersea stations used conventional wet suit type of anti-exposure suits with and without various forms of protective under-garments. Material making use of minute glass bubbles as an insulating aid were tried without much success. However, the suit was simply a prototype and needs some modification. This lack of effective anti-exposure clothing has been the most serious problem which has prevented personnel from remaining out on diving sorties for more than an hour or so at a time (depending on sea temperatures and activity). It has also reduced their effective work, not to mention contributing to their associated discomfort from the penetrating cold.

There are some relatively minor problems related to the musculoskeletal system which may or may not be significant. However, the fact that certain signs and symptoms of discomfort in the musculature, ligaments or tendons, and articulations are incompletely explained is justification for further investigation or consideration. Whether or not such affection of the musculoskeletal system has a bearing on the potential problem of the development of aseptic bone necrosis must also be clarified.

Rheumatoid ailments have been observed during some prolonged sojourns in pressure chambers (e.g. during treatment of decompression sickness, air embolism, and during experiments preliminary to undersea stations) as well as in open sea exposures. The etiology has not been definitely determined but has been the subject of conjecture. Because such ailments have been somewhat erratic or transient and only moderately uncomfortable rather than disabling, they have often been overlooked or perhaps forgotten.

More must be known about effects on the musculoskeletal system during saturation exposures by factors such as increased humidity, temperature changes, respiratory (pulmonary ventilation) resistance, and possible altered peripheral circulatory dynamics in such environments. How important are the effects of temperature changes due to coolness in the habitat or to drafts produced by uneven distribution of air currents in the interior ventilation and air-conditioning as well as by repeated exposures to cold water temperatures during diving sorties? Are there peripheral (e.g. osseous system) effects relative to unknown effects of certain gases under pressure or secondary to recognized or unrecognized atmospheric contaminants? May effects occur in the peripheral musculoskeletal system due to potential alterations in pulmonary function which are similar in nature to those sometimes observed in persons suffering from various forms of chronic lung disease? Can these effects along with those of a possible diminished peripheral circulation (secondary to possible increased peripheral resistance) cause inadequate circulation in the muscles and joints of the extremities with resultant chronic changes? These questions must be answered.

The potential problem of aseptic bone necrosis which is sometimes observed in persons who have worked in the increased ambient pressures involved in underwater tunnel construction (10) may not affect personnel who have been exposed to controlled saturation exposures in the sea or in pressure chamber experiments. The necrosis phenomenon seems to be more related to inadequate decompression procedures, with or without evident attacks of decompression sickness, following prolonged or saturation exposures rather than to the exposures to high ambient pressures as such. However, we must keep this problem in mind and seek to prevent its occurrence.

Control of humidity, prevention of atmospheric contamination, and prevention of pollution of the environment by pathogenic microbes (bacteria and fungi in particular) present problems to be taken into consideration. Although not basically a physiological problem, analysis and surveillance of the atmosphere in undersea stations are most important. Questions can arise about the possible relationship of atmospheric components and their maximum allowable concentrations with subjective complaints, medical or physiological disorders, behavior, and performance.

Bacteriological investigations of the undersea habitations which have been conducted in the past have revealed an increase in microbe growth on the skin and in the ear canals of the personnel and within the "air" and on various interior surfaces of the station. Increased humidity within the stations has no doubt been a contributing factor in aiding this growth. Bacteriological investigation of the waters immediately surrounding the undersea station is being undertaken as well, in order to determine what changes, if any, occur which could affect the inhabitants.

Various skin and external auditory canal infections and "irritations" have been observed. In all cases, their etiology has not been definitely determined. Such infections are often of a mixed bacterial and fungal nature and may be secondary to irritation or response to microorganisms or other agents in the sea to which the personnel are exposed.

Seriously handicapping effects from atmospheric components have not been observed or recognized but the sensitivity or accuracy of our measurements may not be satisfactory. Therefore we must continue to seek improvements in this vital aspect of prolonged undersea exposures.

Environmental contaminants other than those of a purely atmospheric or respiratory nature (e.g. paints, varnishes, solvents, lubricating oils, cooking odors and fumes) and other sources of potentially toxic elements in the habitation as well as in the surrounding marine environment must be controlled and avoided where possible. Potential problems are ever present with the collection and disposal of sewage and other waste material such as used food containers, garbage, dirt and dust, and used carbon dioxide absorbant agents which accumulate in the course of housekeeping and living.

Nutrition and problems associated with food storage, revictualing, and food preparation can affect the physiological function and performance of the personnel, particularly during sojourns of prolonged exposure. These are important aspects to consider in providing for the welfare and comfort of those who live and work underwater. In our operations nutriments which provided at least 3000 calories per person per day were provided in variable menus which still allowed for some individual taste or choice.

Besides determining whether or not one's body can accept and tolerate the associated physiological stresses, there are various psychosociological

aspects to be considered in the selection of personnel for participation in prolonged undersea exposures (11). Cousteau (13) has observed that in general an individual having a difficult character in normal conditions may well become more difficult in trying times or circumstances. Or, on the contrary, he may become by necessity an excellent, dependable comrade. We prefer, however, not to run the risk, and we select our personnel from among those who prove daily and spontaneously to be of good team spirit.

Mention should be made regarding security measures for the safe return to the surface of occupants of undersea stations during emergency incidents which necessitate their abandoning the habitation. For example as a result of serious fires, flooding, collapse or other incidents which render the station uninhabitable, provision for the preservation of their well-being or survival must be arranged. Return to the surface under such forced circumstances can cause serious problems with respect to the necessary decompression required. This and other factors can produce greatly increased or overwhelming physiological stresses in those persons involved.

There have been some problems related to communications during open sea exposures, but in general the various forms used have been quite successful. Naturally the primary reason for having effective communications between the undersea station and the surface control center is for establishing and maintaining operational control of the experiments. Television, telephones and other forms of vocal communication, buzzer systems (for sound signal or morse code transmission), tele-writers for transmitting and recording written messages, tape-recorders, photography, voice frequency modulators for helium speech, journals or diaries and personal correspondence, and mechanical means (e.g. watertight pressurized containers) have been effectively utilized in sending information back and forth between the station and the surface. Physiological and clinical data as well as subjective impressions can thus become readily available from the personnel down in the station to aid in the surveillance of their health and welfare as well as their work to be accomplished.

For the vast amount of data which results during the course of a saturation exposure or undersea station experiment, we have made use of a computer system to help with its collection and recording, sending to the surface control center, storage, and evaluation. A questionnaire was devised for use in helping to orient the collection and processing of the symptomatological and clinical information which occurred during the course of the experiment. The questionnaire was arranged so that it could be completed by hand and sent to the surface or replied to by typewriting on a machine in the station which was integrated into the computer system.

Table 10 summarizes the experiments of saturation exposures performed on animals and man within a pressure chamber and by men in the open sea

TABLE 10

Name of Experiment	Description	Subjects	Depth (meters)	Depth (atm. abs.)	Duration (days)	P_{O_2} (mm Hg)	P_{N_2} (mm Hg)	P_{CO_2} (mm Hg)	Specific Mass* (density) (gr. liter)
Conshelf I	14–21 Sept. 1962, Roads of Marseille. Compressed air in open circuit. Decompression: 3 hours with inhalation of O_2 (mask).	2 men	10.5	2.05	7	316	1192	0.4	2.650
Conshelf II	15 June–14 July 1963, Red Sea, Sha'ab Rumi reef. Compressed air in open circuit. Decompression: same as Conshelf I.	6 men	9.5	1.95	30	302	1133	0.4	2.520
	5–13 July, Closed circuit with 50% air-50% helium. Decompression: 3 hrs inhalation (mask) 80% O_2-20% helium at bottom, 20 min at 15 meters, 30 min at 12 meters, overnight (12 hrs) in base house at 9.5 meters, then same as Conshelf I.	2 men	25	3.5	5	270	1030		2.560
Other experiments:									
Merinos	All the other (preliminary) experiments from January to August 1965—High pressure caisson of O.F.R.S., Marseille In these experiments as in Conshelf III, decompression was performed utilizing a continuous ascent following an exponential curve corresponding to desaturation of the 120 minute half-time tissues, with passage from He-O_2 mix to compressed air at 4 atms absolute pressure.	2 sheep	200	21	15	217 ± 29	124	63 ± 15	4.326
Cachemire		2 goats	200	21	14	169 ± 15	124	23 ± 7	4.326
Aliboue		2 goats	120	13	2	478	287	6	3.549
Choutaqua		2 men	120	13	5	177 ± 15	29	10	2.052

* Calculated with regards only for O_2, N_2, and Helium and in STPD for dry air, this value is 1.2923 (density absolute).

TABLE 10—*Continued*

Name of Experiment	Description	Subjects	Depth		Duration (days)	P_{O_2} (mm Hg)	P_{N_2} (mm Hg)	P_{CO_2} (mm Hg)	Specific Mass* (density) (gr. liter)
			(meters)	(atm. abs.)					
Conshelf III	28 Aug.-2 Sept. 1965 —Monaco Harbor Decompression: 8 hr., 5 min., with O_2 (mask)	6 men	25	3.5	4	174	515	4	1.701
	17 Sept-17 Oct. 1965 —off Cap Ferrat Decompression: 84 hrs., with O_2 (mask)	6 men	100	11	29.5	178 ± 24	65	4	2.146

* Calculated with regards only for O_2, N_2, and Helium and in STPD for dry air, this value is 1.2923 (density absolute).

by the group under the direction of Cousteau. Other related data and details of these specific experiments are in preparation and will appear in a separate publication of the Bulletin of the Institut Océanographique of Monaco.

Conclusions

Despite the existing and potential problems which have been recognized in the various experiments of the continuing investigations, it is important to report that no one who has been exposed to saturation exposures in open sea or in the preliminary pressure chamber experiments has had to be removed from them for any reason. Whereas performance of the personnel in earlier undersea station experiments had been somewhat affected during the initial phases of acclimatization, the over-all performance has been remarkably effective. In our most recent experiment, the performance of the oceanauts was far superior to that of the earlier experiments. This probably reflects learning from past experience, better use and control of the station atmosphere of lesser density, and improved equipment and techniques. However there still are many problems to overcome in future experiments and operations.

We must think in terms of what may develop in the future to those who are participating underwater at the present. More is needed than just treating what arises at the time. Having medical-physiological support or control at the surface is not sufficient, at least in these early stages of investigation. If there is no one well trained in examining for and treating maladies or problems which may arise or in conducting essential physiological in-

vestigation down in the undersea habitat, then the situation demands a policy of remote control or remote treatment. This will not suffice, for more is involved in efficient treatment or conducting investigation than the prescribing of medications or recommending advice.

Physiological and medical specialists are learning how to deal with problems just as are the engineers, oceanographers, marine biologists, and other professional and technical specialists. Not enough can be gained or learned from the surface. We must work down in the environment with those persons for whom we are medically or physiologically responsible, and we congratulate the U. S. Navy for the efforts and progress which it has made in this direction.

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11 | ROBERT C. BORNMANN

Decompression after Saturation Diving

In connection with Operation Genesis and Project Sealab of the U. S. Navy the Experimental Diving Unit was asked to formulate and to test decompression schedules for saturation dives to 100, 200, 300, and 400 feet of sea water. Operation Genesis was a laboratory investigation by Bond to test methods and procedures for these saturation dives prior to placing human divers on the actual sea bottom, the Sealab operations of 1964 and 1965. The calculations for the saturation decompressions were originally conceived and carried out by Workman of the Experimental Diving Unit.

In Phase C of Operation Genesis three men were sealed into a pressure chamber of the Naval Medical Research Institute in Bethesda for seven days in November 1962 to examine the physiologic effects of breathing a helium-oxygen atmosphere at sea level pressure. Phase D was conducted at the Experimental Diving Unit in April 1963 when three subjects were pressurized to 100 feet (4 atmospheres absolute), maintained there six days and then decompressed safely. For the final laboratory study, Phase E, the three diver-subjects lived and worked under a pressure of 200 feet (7 atmospheres absolute) for twelve days in the new chamber of the Medical Research Laboratory (Naval Submarine Medical Center) in New London in August of 1964.

For reasons given in the report of an earlier animal study (10) the inert portion of the breathing mixture used in these studies was principally helium. The oxygen proportion or partial pressure was carefully controlled to prevent the manifestation of long term pulmonary oxygen effects. Some nitrogen was present in each study because of the problems raised in any attempt to remove it completely, but in the light of recent information (8) its presence could be beneficial.

Oxygen partial pressure for dives of this type should probably be maintained somewhere between 0.2 and 0.5 atmospheres, although the optimal level within this range has not yet been well defined. The risk of pulmonary toxicity in exceeding the 0.5 atmosphere oxygen limit for long duration dives is a deduction from extrapolation of the results of work done at lower

total pressures. Any effect of dilution with inert gas molecules has not been measured in this respect. Acceptance of this limit for the maximum oxygen pressure does restrict the use of compressed air in saturation dives to a depth of 45 feet gauge or less. Increasing the total pressure beyond that depth by the addition of pure nitrogen seems to have little advantage over the use of helium because of the difficulties involved in breathing the relatively dense compressed nitrogen (7, 10). Proportionate mixtures of helium and nitrogen with oxygen might be used, possibly with advantage, but decompression requirements have not yet been worked out to any extent for such a system.

If one accepts the concepts of perfusion limitation, exponential desaturation, and the symmetry of saturation and desaturation as valid for decompression, then it is a simple, although tedious, task to analyze the inert gas mechanics of a model situation for any dive, projected or accomplished. A modified Haldane method is used for this computation in the U. S. Navy (11). For mathematical analysis the body is assumed to be made up of a number of "half-time tissues" in which the tissue half-saturation time, the time to take up 50 % of the amount of inert gas lacking for complete saturation, ranges from very fast to very slow depending upon the variations of perfusion efficiency to gas solubility. Simultaneous solution for a limited number of half-saturation times is felt to be sufficient to define the range. Figure 32 is taken from the Report of the Admiralty Committee on Deep-Water Diving (1) and shows Haldane's solution for the amount of air dissolved in the 5, 10, 20, 40, and 75 minute "half-time tissue" during a 16½ minute dive to 168 feet and decompression according to his new stage method.

Figure 33 shows a single exponential curve which, so long as the pressure remains constant, represents the inert gas exchange with time in any tissue.

P_T = partial pressure of inert gas in the tissue at any time T
P_0 = original partial pressure of inert gas in the tissue
P = partial pressure of inert gas in the lungs

and

$$P_T = P_0 + F(P - P_0) \tag{1}$$

The time function (F) is defined as

$$F = 1 - \tfrac{1}{2}^U \tag{2}$$

$$U = T/H \tag{3}$$

and is defined as the number of one-half saturation times (H) in the time interval (T). The exponential saturation of a tissue can then be described as

$$P_T = P_0 + (P - P_0)\,(1 - \tfrac{1}{2}^{T/H}) \tag{4}$$

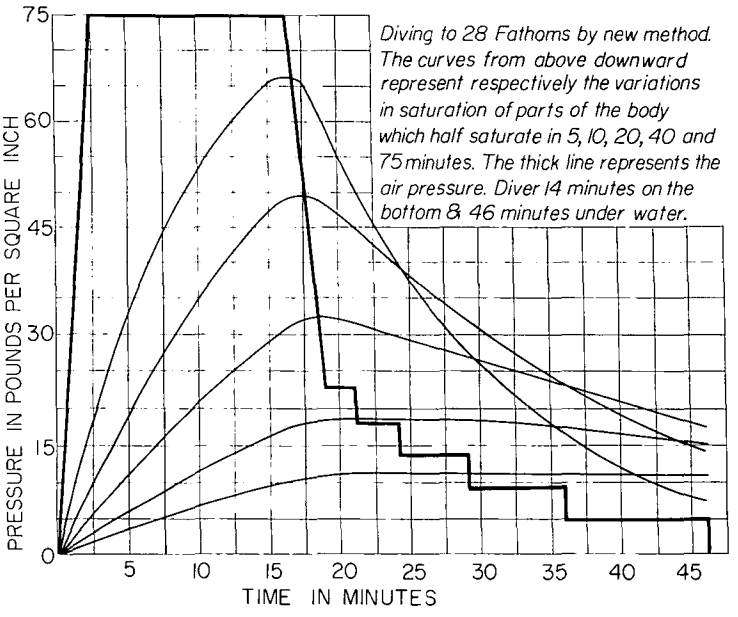

FIG. 32. Haldane solution for air dive to 168 feet with stage decompression. Reproduced from the 1907 Admiralty Committee Report on Deep-Water Diving (1).

A negative value for $(P - P_0)$ indicates the loss of inert gas in desaturation. Table 11 is a tabular definition of this curve from 0 to 98½% within six half-times. Note for future reference that when $F = .278$ then $U = 0.47$.

The object of such analysis, which is to insure the safety of similar dives made in the future or the safety of decompression schedules calculated with the information extrapolated from previous "safe" decompressions, is often frustrated in attainment due to the wide individual variations in susceptibility to decompression sickness from day to day and from situation to situation. Perhaps if enough dives are performed and scored, then computer analysis might make the limits clearer. The diving staff of the Experimental Diving Unit is not now large enough to amass such data quickly.

Haldane's concept of a 2:1 ratio for safe supersaturation in ascent was a brilliant and extremely useful one as it permitted formulation of the first practical and safe decompression tables. However, it is valid only in a limited case and has not proved safe for longer and deeper exposures. Haldane himself states in his first reports (1) that the validity of the ratio for pressures much in excess of six atmospheres was doubtful, as no experimental data existed, and later (3) that for air dives exceeding six atmospheres absolute some reduction of the ratio is required. Later work in the U. S. Navy (4, 6) demonstrated that surfacing ratios increased as the half-

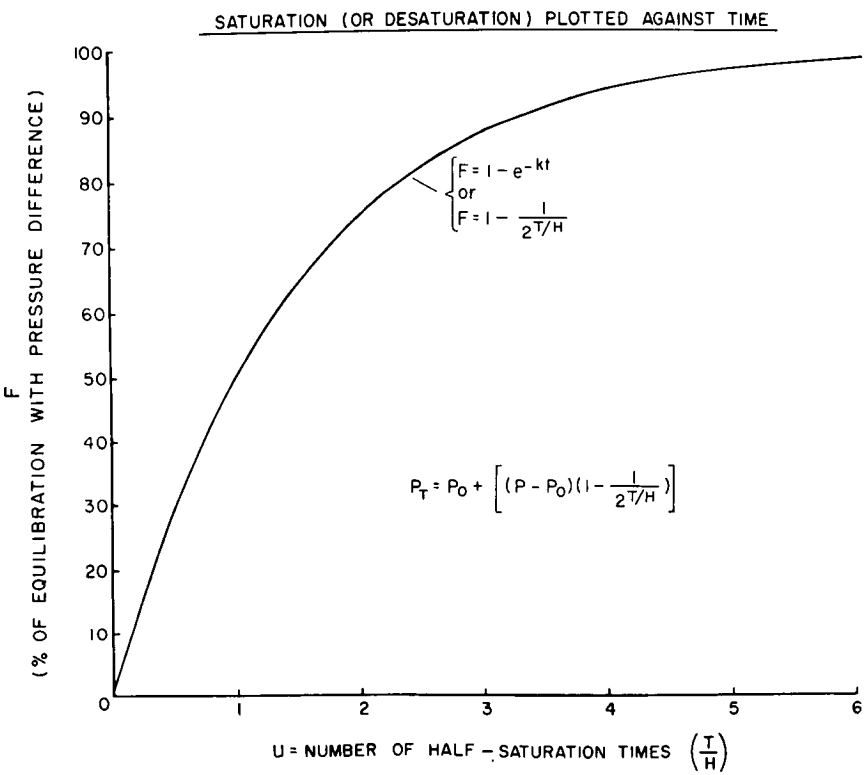

FIG. 33. Saturation (or desaturation) plotted against time

saturation time decreased, to 3.8:1 for the 5 minute half-time tissue, and that permissible ratios also decreased with depth. Development of diving with helium-oxygen mixtures focused attention on the ratio of inert gas partial pressure to ambient pressure rather than the ratio of total pressures. The same mathematical model could be used for air and for helium-oxygen diving, but a different set of ratios and significant half-times would result in different decompression schedules. More recently Workman finds it more convenient to work with maximum tissue pressures (M) rather than ratios (Table 12).

In 1957 Workman reported on the calculation and testing of his Air Saturation Decompression Tables (9). He had considered a number of dives made at the U. S. Navy Experimental Diving Unit between 1937–1945 at depths from 30 to 99 feet for exposures up to 36 hours. Forty-six additional dives were made on air to a depth of 140 feet for times from 90 to 360 minutes. It became apparent during this study that consideration of nitrogen levels in the 160 and 240 minute half-time tissues was necessary for construction of safe decompressions. Although the schedules for the long

TABLE 11

Tabulated Values of Time Function Illustrated in Figure 33 (From Workman (11))

Time Unit (Integer and one decimal place)	Time Unit (second decimal place)										Time Function (Three decimal places)
	0	1	2	3	4	5	6	7	8	9	
0.0	—	.007	.014	.021	.027	.034	.041	.047	.054	.061	
0.1	.067	.073	.081	.086	.092	.099	.105	.111	.117	.123	
0.2	.129	.136	.141	.147	.153	.159	.165	.171	.176	.182	
0.3	.188	.193	.199	.204	.210	.215	.221	.226	.232	.237	
0.4	.242	.247	.253	.258	.263	.268	.273	.278	.283	.288	
0.5	.293	.298	.303	.307	.312	.317	.322	.326	.331	.336	
0.6	.340	.345	.349	.354	.358	.363	.367	.372	.376	.380	
0.7	.384	.389	.393	.397	.401	.405	.410	.414	.418	.422	
0.8	.426	.430	.434	.438	.441	.445	.449	.453	.457	.460	
0.9	.464	.468	.472	.475	.479	.482	.486	.490	.493	.496	
1.0	.500	.503	.507	.510	.514	.517	.520	.524	.527	.530	
1.1	.533	.537	.540	.543	.546	.549	.553	.556	.559	.562	
1.2	.565	.568	.571	.574	.577	.580	.583	.585	.588	.591	
1.3	.594	.597	.600	.602	.605	.608	.610	.613	.616	.618	
1.4	.621	.624	.626	.629	.632	.634	.637	.639	.642	.644	
1.5	.646	.649	.651	.654	.656	.659	.661	.663	.666	.668	
1.6	.670	.627	.675	.677	.679	.681	.684	.686	.688	.690	
1.7	.692	.694	.697	.699	.701	.703	.705	.707	.709	.711	
1.8	.713	.715	.717	.719	.721	.723	.725	.726	.728	.730	
1.9	.732	.734	.736	.738	.739	.741	.743	.745	.747	.748	
2.0	.750	.752	.754	.755	.757	.759	.760	.762	.764	.765	
2.1	.767	.768	.770	.772	.773	.775	.776	.778	.779	.781	
2.2	.782	.784	.785	.787	.788	.790	.791	.793	.794	.796	
2.3	.797	.798	.800	.801	.803	.804	.805	.807	.808	.809	
2.4	.811	.812	.813	.815	.816	.817	.818	.820	.821	.822	
2.5	.823	.824	.826	.827	.828	.829	.830	.832	.833	.834	
2.6	.835	.836	.837	.839	.840	.841	.842	.843	.844	.845	
2.7	.846	.847	.848	.849	.850	.851	.852	.853	.854	.855	
2.8	.856	.857	.858	.859	.860	.861	.862	.863	.864	.865	
2.9	.866	.867	.868	.869	.870	.871	.872	.872	.873	.874	
3.0	.875	.876	.877	.878	.878	.879	.880	.881	.882	.883	
3.1	.883	.884	.885	.886	.887	.887	.888	.889	.890	.890	
3.2	.891	.892	.893	.893	.894	.895	.896	.896	.897	.898	
3.3	.899	.899	.900	.901	.901	.902	.903	.903	.904	.905	
3.4	.905	.906	.907	.907	.908	.909	.909	.910	.910	.911	
3.5	.912	.912	.913	.913	.914	.915	.915	.916	.916	.917	
3.6	.918	.918	.919	.919	.920	.920	.921	.921	.922	.923	
3.7	.923	.924	.924	.925	.925	.926	.926	.927	.927	.928	
3.8	.928	.929	.929	.930	.930	.931	.931	.932	.932	.933	
3.9	.933	.934	.934	.934	.935	.935	.936	.936	.937	.937	
4.0	.938	.938	.938	.939	.939	.940	.940	.941	.941	.941	
4.1	.942	.942	.943	.943	.943	.944	.944	.944	.945	.945	
4.2	.946	.946	.946	.947	.947	.947	.948	.948	.949	.949	
4.3	.949	.950	.950	.950	.951	.951	.951	.952	.952	.952	
4.4	.953	.953	.953	.954	.954	.954	.955	.955	.955	.956	
4.5	.956	.956	.957	.957	.957	.957	.958	.958	.958	.959	
4.6	.959	.959	.959	.960	.960	.960	.960	.961	.961	.961	
4.7	.962	.962	.962	.962	.963	.963	.963	.963	.964	.964	
4.8	.964	.964	.965	.965	.965	.965	.966	.966	.966	.966	
4.9	.967	.967	.967	.967	.967	.968	.968	.968	.968	.969	
5.0	.969	.969	.969	.969	.970	.970	.970	.970	.970	.971	
5.1	.971	.971	.971	.971	.972	.972	.972	.972	.972	.973	
5.2	.973	.973	.973	.973	.974	.974	.974	.974	.974	.974	
5.3	.975	.975	.975	.975	.975	.976	.976	.976	.976	.976	
5.4	.976	.977	.977	.977	.977	.977	.977	.977	.978	.978	
5.5	.978	.978	.978	.978	.979	.979	.979	.979	.979	.979	
5.6	.979	.980	.980	.980	.980	.980	.980	.980	.981	.981	
5.7	.981	.981	.981	.981	.981	.981	.982	.982	.982	.982	
5.8	.982	.982	.982	.982	.983	.983	.983	.983	.883	.983	
5.9	.983	.983	.984	.984	.984	.984	.984	.984	.984	.984	

TABLE 12

Maximum Allowable Tissue Tension (M) of Helium for Various Half-time Tissues to Permit Ascent from Depth Listed (From Workman (11))

	Depth of Decompression Stop									
D (ft)	10	20	30	40	50	60	70	80	90	100
A (ft)	43	53	63	73	83	93	103	113	123	133
	(M) (feet of sea water equivalent)									
H (min)										
5	86	101	116	131	146	161	176	191	206	221
10	74	88	102	116	130	144	158	172	186	200
20	66	79	92	105	118	131	144	157	170	183
40	60	72	84	96	108	120	132	144	156	168
80	56	68	80	92	104	116	128	140	152	164
120	54	66	78	90	102	114	126	138	150	162
160	54	65	76	87	98	109	120	131	142	153
200	53	63	73	83	93	103	113	123	133	143
240	53	63	73	83	93	103	113	123	133	143
	ΔM/Δ10 Feet Depth									
H (min)	5	10	20	40	80	120	160	200	240	
ΔM (ft)	15	14	13	12	12	12	11	10	10	

dives never became completely satisfactory, it was felt that they were adequate for the purposes of this table, which was for emergency use in the case of a diver trapped at depth beyond the times of the standard air tables. It was still believed, however, that for helium-oxygen diving the 150 minute half-time tissue is the slowest which need ever be considered significant in decompression.

In the standard decompression tables as the bottom time increases the obligated decompression increases at an accelerating rate since a controlling amount of inert gas dissolves in the more and more slowly desaturating tissues. Earlier decompression tables expressed a preference for certain schedules which were felt to represent the optimum balance between dive (work) time and decompression (1, 5). The advantage offered through application of the saturation dive technique is that, after some finite interval, the body is completely equilibrated with inert gas at the pressure of the exposure and the decompression obligated is limited by that amount. Further exposure should result in no increase in the decompression requirement, and the ratio of dive time to decompression time again becomes more and more favorable. Since the body is completely saturated with inert gas, the decompression would be regulated by the rate at which the most slowly

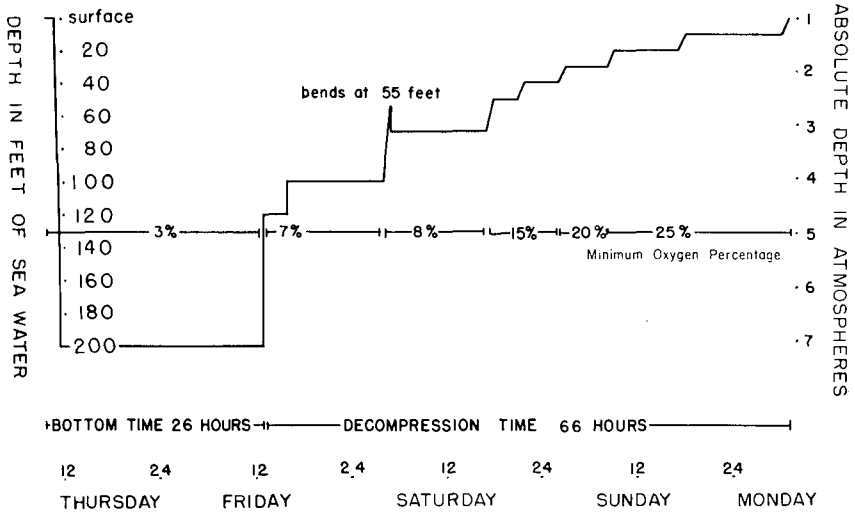

FIG. 34. Stenuit's dive to 200 feet, Villefranche, 6–10 September 1962

desaturating tissue gives up its gas. Since this tissue would control the whole ascent, the technique of a uniform rate of ascent appeared attractive for decompression.

In Stenuit's dive to 200 feet for 24 hours during the Link expedition of 1962 the stage decompression (Fig. 34) used was inadequate and bends was obvious at 55 feet. Decompression subsequent to the return to 70 feet for treatment was much slower and taken in small steps, but still used the stage technique. A stage decompression was used again in Phase D of Operation Genesis for the ascent from 100 feet. Thirty foot ascents with stops of over 12 hours totaled a decompression of 51 hours.

Following the above studies Mazzone decompressed a number of large dogs at the Naval Medical Research Institute to test the concept of constant rate of ascent from saturation exposures. This type of decompression was then successfully carried out in human chamber exposures to 200 feet at the Medical Research Lab for Phase E of Operation Genesis.

The rate of ascent is determined in a manner similar to the following calculation for the 300 foot saturation dives conducted at the Experimental Diving Unit. With a total absolute pressure of 333 feet of sea water, the inert gas pressure P_0 would be 316½ feet allowing for 0.5 atmospheres oxygen pressure. From Table 12 it is seen that the maximum helium tissue tension to permit surfacing is 53 feet in the case of the 240 minute half-time tissue. This is 20 feet more than the absolute pressure of 33 feet at sea level. The allowable maximum increases linearly, foot for foot, with depth and can be expressed as 20 plus Absolute Depth as in Figure 35. To establish

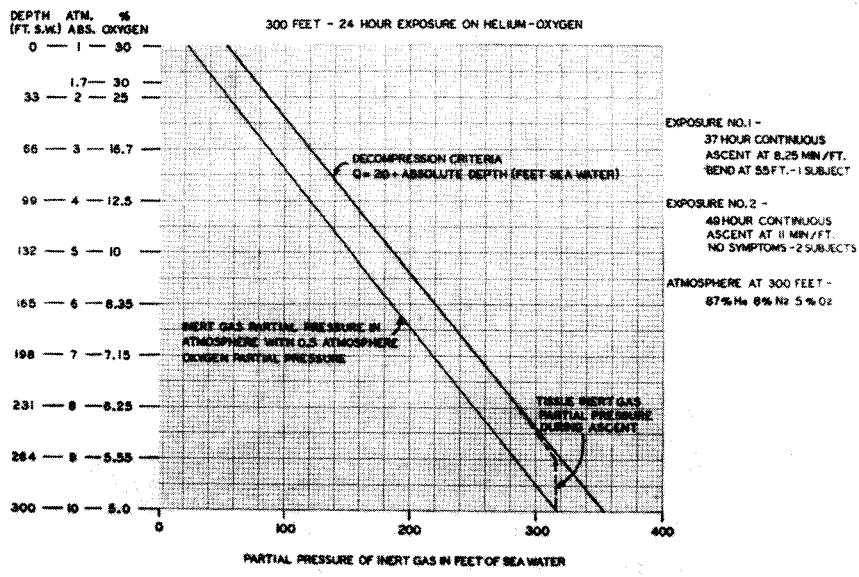

FIG. 35

the maximum safe pressure head for extraction of inert gas an initial rapid ascent is made to a depth which is 20 feet less than the inert gas pressure of the body at the depth of exposure. In this example 317 − 20 = 297 feet absolute or 264 feet gauge depth, which conveniently is 9.0 atmospheres. The oxygen partial pressure is maintained as closely as possible to 0.5 atmospheres. The inert gas partial pressure in the lungs (P) after the initial ascent would be 281 feet. The pressure head for inert gas desaturation would be 317 − 281 or 36 feet. The time required for a tissue to lose 10 feet of inert gas can be determined for this example from equation 1 as follows:

$$P_T = P_0 + (P - P_0)\ (F)$$

where

P_0 = 317 ft. = initial inert gas pressure
P = 281 ft. = inert gas pressure in lungs
P_T = 307 ft. = P_0 − 10 ft.

With a pressure head ($P - P_0$) of 36 feet, a 10 ft. loss of inert gas requires that $F = 0.278$ ($F \times 36 = 10$; $F = 0.278$). From Figure 3, $U = 0.47$ when $F = 0.278$ and T can be determined for various half-time tissues using equation 3.

H	*T*
180	85 minutes/10 feet
240	113 minutes/10 feet
300	141 minutes/10 feet
360	169 minutes/10 feet

An ascent rate of 8½ minutes per foot would result in a one foot desaturation of the 180 minute half-time tissue for each foot of ascent. It is obvious that this calculation is actually for stage decompression with 10 foot ascents. This is used for simplicity and because it is a conservative approximation of the constant rate. The actual ascent rate is being determined empirically.

A similar calculation for the 240 minute half-time tissue would result in an 11 minutes per foot rate of ascent. However, it was stated previously that the 150 minute half-time tissue was considered to be the slowest which would ever need be considered in decompression from a helium-oxygen dive. A rate of ascent which permitted safe desaturation of gas from any possible 180 minute tissue should certainly be safe.

It was nevertheless planned that if symptoms of decompression sickness should be encountered during this ascent, the chamber pressure would be increased by the addition of pure helium to the depth of relief. This procedure permits maintenance of the oxygen partial pressure at the predetermined level. Once relief of symptoms was achieved, the subject would be instructed to exercise the affected part to insure that relief was truly complete, and the pressure would be maintained constant for a period of 60 minutes thereafter. Subsequent decompression would be at the rate of 16.5 minutes per foot (9 hours per atmosphere). This rate would allow sufficient decompression for injured tissues which could require as long as 36 hours to achieve equilibration with inert gas tensions. Should symptoms recur during this ascent, pressure could again be increased to the depth of relief and the above procedures repeated. If necessary, oxygen could be breathed intermittently at depths less than 60 feet to assist in bubble resolution.

During the decompression from the first Experimental Diving Unit exposure of two subjects to 300 feet for 24 hours (Fig. 35) one diver noted the onset of a slight pain in one knee at 75 feet. This was mild and was relieved by the application of warm, wet packs. At 54 feet the pain recurred in that knee and a slight pain began also in his other knee. His companion was free of symptoms throughout. The chamber pressure was increased by the addition of pure helium and at 99 feet his pain was markedly decreased. The pain was completely gone after one hour. After an additional two hours at this depth the divers were brought to the surface at a rate of 16½ minutes per foot.

Another pair of divers completed a similar exposure to 300 feet and were

decompressed without incident at a rate of 11 minutes per foot. A third pair of divers were exposed for 24 hours to a pressure of 400 feet on helium-oxygen and were decompressed at a constant rate of 11 minutes per foot. This decompression was also completed without incident (Fig. 36).

In the sea bottom dive of Sealab I the decompression of the four divers from their eleven day exposure at 193 feet was complicated by operational problems. A constant rate of ascent was programmed for 20 minutes per foot. The large crane of Argus Island lifted the habitat with aquanauts inside slowly to the surface. The sojourn had been slightly shortened by the approach of bad weather and, although the first 20 hours went smoothly, by the evening of the first day of decompression the surge of long swells was being felt in Sealab and the dynamometer on the crane recorded peaks of 15 tons. Several holds on the ascent were necessary and progress at this point was slow. By the time the habitat had reached 80 feet it was decided to evacuate the divers and to transfer them to a topside decompression chamber via a submersible chamber for completion of their decompression. This necessitated a ventilation with compressed air and decompression was completed on air over the next 24 hours. The subjects emerged in good condition. Total decompression time was 55½ hours and was completely successful in respect to absence of decompression sickness.

In the Link-University of Pennsylvania expedition dive of that same summer the decompression was planned to follow more closely the format of the Experimental Diving Unit dives. The divers lived for 49 hours in and out of a dwelling pressurized to 427 feet and were then brought directly to the deck decompression chamber (DDC) via a submersible decompression chamber (SDC). The initial ascent to 396 feet was accomplished during the

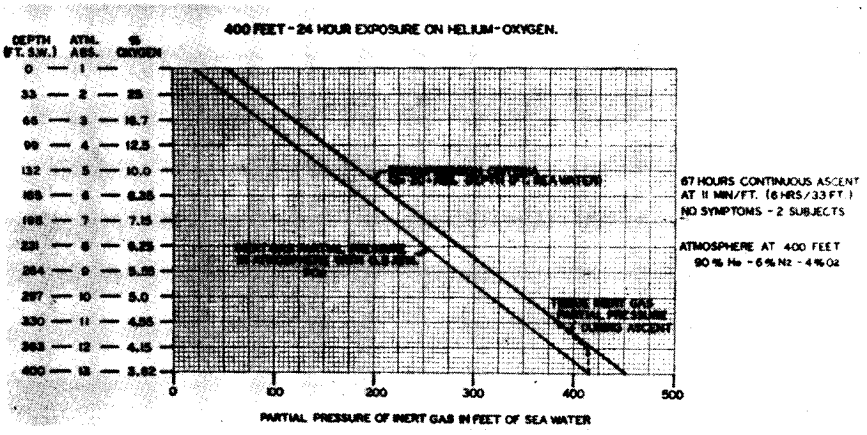

FIG. 36

equalization of the pressure between the SDC and the DDC. Constant ascent decompression thereafter was at the rate of 12 minutes per foot. The oxygen partial pressure was maintained at 0.5 atmosphere in the chamber, but pure oxygen was breathed intermittently, shallow to 30 feet. At 24 feet, just after the termination of one period of oxygen breathing, one of the divers noticed pains in his right knee. The pain disappeared with oxygen breathing, but recurred, and was then relieved by repressurization to 43 feet. After a period at that depth ascent began again at a rate of 15 minutes per foot, also with intermittent oxygen breathing shallow to 30 feet. Perplexing symptoms continued in the same diver, but both subjects reached the surface after a total decompression time of 92 hours (2).

In the Sealab II dive to 204 feet this past year 28 successful decompressions were made at a constant ascent rate of 10 minutes per foot. The length of the dives was 2 weeks except that one subject, Carpenter, stayed down for 4 weeks. Another, Sonnenburg, was with both Team 1 and Team 3 for two dives. One diver who celebrated his 50th birthday during the dive suffered from mild bends pain which began somewhere before the 35 foot level and which was safely treated by return to 60 feet followed by a more leisurely subsequent ascent to the surface.

In summary, a number of saturation dives have been made in recent months and some experience has been gained with decompression at a constant rate of ascent. The method seems practical and is theoretically attractive. That it is not yet completely safe is proved by the several failures to prevent bends.

The occurrence of bends following a period of pure oxygen breathing raises questions about its use as an aid to decompression. Oxygen is a pharmacologically active agent. As Workman has pointed out elsewhere in this volume (Chapt. 2), if we consider only that it displaces inert gas in the lungs to enhance desaturation we are fooling ourselves. What are the dynamics of its effect on blood circulation and perfusion? Can we dissect these effects into local actions and can we remove, sustain, or enhance a particular effect with complementary agents?

What are the factors governing safe supersaturation and bubble initiation? Why do tissue ratios and M values vary? If one plots the decrease of tissue tensions after surfacing, it is seen that in 10 or 15 minutes the pressures have fallen in all tissues to a similar level which may represent a true limit. Perhaps the area under the early portion of the curves (Fig. 37) represents not the limits of safe supersaturation but the limits of the probability of bubble formation under these conditions.

We have attempted in the past to develop schedules which are safe for a large range of decompression susceptibilities. Miles has stated that measures which increase the comfort of the diver: rest, warmth, food, and hydration

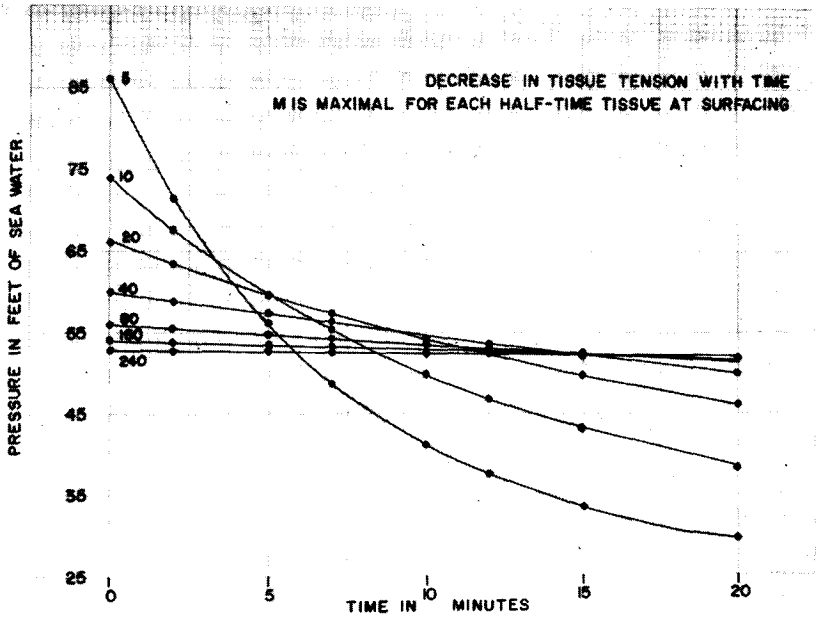

FIG. 37. Decrease in tissue tension with time. M is maximal for each half-time tissue at surfacing.

inside a topside chamber, also increase the safety of his decompression (Chapt. 5). Total time may thus not be a practical problem. But is there any predictability to the bends of the susceptible person, the overage, the overweight, and the diver who gets bends several times in one location? What is the relationship of physical fitness, physiological age, and chronological age? Can we develop tests to eliminate from deep diving the individuals who would be bends-prone in that type of operation and end up with shorter decompressions which are uniformly safe for the divers selected?

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12 | JAMES W. MILLER

Psychophysiological Aspects of Deep Saturation Exposures in the Sea

Most of the participants in this Symposium are familiar with the variables associated with living and working in an underwater environment, such as cold, pressure, visibility, and biological hazards and many have devoted professional lifetimes to investigating the physiological aspects of diving and, more recently, of saturation diving.

Physiological investigations are undertaken to satisfy scientific or intellectual curiosity, to gain a better understanding of those factors associated with increasing the probability of survival, and to determine the effect of such variables upon the performance of man. This section will be addressed to the third category.

Let's ask ourselves why we want to measure performance. Men always have been measuring each other's performance, be it memory, intellectual capacity, motor skills, athletic prowess or business skill. In the underwater world we are interested in performance measurement for several reasons:

1) To determine whether man should be included as a free swimmer
2) To increase the probability of survival
3) To better estimate the probability of man performing successfully
4) To establish safety practices and medical limitations
5) To properly select and plan specific tasks
6) To decide on equipment requirements
7) To assist in the selection of performance aids in the form of equipment, drugs, or training
8) Scientific curiosity

There are, of course, numerous additional reasons. It is obvious that in each case we are concerned with determining how well man can do "something," either that which we are specifically measuring or some task in which man plays a role.

Let's look briefly at some of the environmental and physiological factors

known to influence performance underwater, keeping in mind, in each case, possible methods to improve performance.

The physical effects of cold on the body as well as its cognitive processes have been studied for years, both in the laboratory and in the field. The Sealab II project demonstrated once again that individual differences in cold tolerance are great. According to the divers, less time was spent in the water the first few days due, at least in part, to the cold. There seemed to be general agreement, however, that as the days went on, they were returning to the habitat more because of fatigue or running out of air than because of being cold. This points out, as have previous studies, that there is marked acclimitization to extreme temperatures (1–3), and that it would be advantageous to expose divers to cold for some period just prior to entering a Sealab environment. This would be of particular importance if a high level of performance is required shortly after initial exposure. Although the interaction between personality, motivation and cold tolerance is not understood clearly, a few studies have been performed which illustrate some of the problems. For example, Karstens conducted a study in an operational setting and concluded the following:

> "Under conditions of dry cold with no wind, loss of aircraft maintenance crew effectiveness at temperatures down to 0° F is small; below 0° F, outdoor maintenance falls off until it may reach zero for poorly motivated crews at −30° F; better motivated crews will attain some degree of effectiveness at the lowest temperatures encountered without wind. . . ." (4), cited in reference (1).

Cold water tolerance, including its effect on performance has been determined experimentally in many ways. Various criteria have been used including subjective feelings, time in water, as well as specific test results. Other tests used in dry cold include: visual-motor coordination tasks where optimal temperatures were found at around 70° F (5); pursuit meter and alignment tasks (6); and in a further study, "Five dependent variables were measured: kinesthetic sensitivity, tactile sensitivity, hand-grip strength, free-movement and pressure tracking, and skin temperature. . . . " (7). Needless to say, much work needs to be done to enable us to predict performance on a more realistic basis. Later in this presentation I will attempt to show why it is essential to perform more of this work in an operational or semi-operational setting.

Underwater visibility with its inherent problems associated with working by feel, lack of communication, and bodily orientation, need not be discussed in detail here. In saturation diving a-la-Sealab, however, the problems are greatly magnified as are the consequences of mistakes. Many divers during Sealab II reported that for a substantial part of the time their minds were pre-occupied with thoughts of becoming lost, especially for the first

few days. As the topography was learned, the situation improved. There are available ways of partially alleviating this situation using visual aids. For example, the use of flexible posts that bend when struck, strategically placed on the bottom, could be of considerable value guiding a diver in unfamiliar surroundings. The posts could be painted in keeping with recent data on underwater visibility experiments. In addition, improved underwater lights can be obtained which take better advantage of sea water transmission characteristics. Improved diver-to-diver communication systems will greatly alleviate the general problem of diver orientation. Another visibility aid suggested in a recent report involves the use of "silt stabilizing polymers with associated dispensers to eliminate or reduce turbidity stirred up at bottom work sites." (8). Each of these possibilities should be studied in shallow, dark water prior to any deep water tests.

The psycho-physiological problem of fatigue is familiar to all. Equally familiar is the difficulty in obtaining valid measures of fatigue because of the confounding interactions of motivation, stress, etc. One of the chief difficulties is associated with the lack of ability to objectively assess one's own physical and mental state or the status of a general situation in which one is playing a role. This poses a serious threat to the success of any given venture. Careful studies need to be carried out in which performance and behavior are measured simultaneously both objectively and subjectively. Along these lines, the use of telemetered physiological data is becoming more feasible. For example, Almond has miniaturized a Personal Telemetry Transmitter System developed by the Army Medical Research Laboratories (9). This system transmits seven channels of physiological data on a commercial FM band to a receiver 200 feet away. The package at the present time is roughly 2¼ x 4¼ x ¾ inches, including battery. The system was not designed for use underwater but the employment of such techniques appears quite promising. Although such technological advances in telemetry, miniaturization and data analysis will permit us to obtain data heretofore not available, they will not take the place of a carefully thought-out general approach to the measurement of human performance.

To begin with, we must begin taking a long-range view of an underwater program. Now that a series of underwater studies is foreseeable, a definitive program should be outlined by the various scientific disciplines as well as by the operational Navy for a sequence of manned underwater experiments. As mentioned earlier, those in this room are interested in measuring human performance of one kind or another. Because of motivational factors, however, performance on specially devised tests, whether physiological or psychological, must be interpreted cautiously. As in many field situations, the individual taking the test may adopt the attitude that "This is a test so I will try extra hard." or "This test is interfering with important things,

so let's get it over with." In either case the results must be evaluated carefully.

In order to measure performance in an environment such as that found underwater, we must develop better ways of obtaining valid data while men are performing "regular" tasks. To accomplish this it will be necessary for scientists concerned with physiological and psychological assessment of performance to take an active part in planning underwater experiments. As tasks (salvage, search and rescue, scientific, etc.) are selected, methods of determining how well they are carried out can be developed. Only in this way can a solid body of knowledge be accumulated. Many of us lament the lack of proper controls in the field as compared to those in the laboratory. The challenge is to devise good experimental and observational field techniques for obtaining valid data to augment those data gathered under controlled conditions. Such an effort will require the use of modern telemetry techniques, detailed reporting procedures, and systematic observation. An overall program could accomplish these ends while at the same time demonstrating that useful, practical work can be accomplished.

Performance measurement, however, cannot be done on a non-interference basis, but it *can* be done on "real" jobs if sufficient planning has taken place. Such endeavors must accompany laboratory investigations if we are going to understand truly the limitation of man underwater. We have much to learn from the Space Program in this regard.

Let's look briefly now at some specific tasks, how performance might be assessed and what equipment is available which may improve efficiency.

Although, generally speaking, it is more difficult to perform most tasks in the water than on dry land, there are exceptions. For example, divers found during the recent Conshelf III experiment that it was easier and more efficient to install and repair a 5-ton oil-well head while living on the bottom than as conventionally done from the surface.

Let's suppose we wanted to measure overall performance on a task of this type. Various criteria could be used, e.g., 1) Did they accomplish the end result? 2) How long did it take? 3) Were there any accidents? and 4) Were the tools adequate? If we want to plan longer, more complex tasks in the future, even at the same depths, however, we would want answers to such questions as: Were there near accidents? Were the men approaching their physiological limits? Did performance degrade with time? Were there serious cumulative effects from day-to-day? Could improvements in group composition be obtained? If future projects are to be carried out effectively, such information is imperative. By capitalizing on current technology such a program can in fact be accomplished.

We can think of the environmental variables as falling into two categories. The first is associated with a threat to survival, i.e., cold, pressure,

and the lack of available air. The second is the set of conditions or problems remaining if man suddenly became cold-blooded and water breathing.

With regard to the first category, most of you are familiar with recent work pertaining to life support systems, heated suits, better SCUBA gear, extension of decompression tables, etc. You may not be familiar with developments in the space program which may be relevant to underwater life support. Elkins, in a recent paper (10), described a rigid, constant volume pressure suit developed for the space program. This suit is capable of operating over a range of 3.5 to 7 psi. It is designed for maximum flexibility with relatively constant torque at the joints over the full psi range indicated. Because of its rigid structure, the suit lends itself to an integration of the environmental control system. In the future such a suit could be mated from the waist down with additional life support supplies and/or a self-contained propulsion system. The latter would enable man effectively to become a one-man submersible.

Another product of the space program which shows real promise for underwater use is a recently designed set of torqueless tools (11). Thus far developed are saws, drills, hammers, and ratchet wrenches with various attachments. These zero-reaction tools have been condensed into a kit weighing 38 lbs. which also is equipped with work lights. The total weight can be reduced to 20–25 lbs. with further development. Additional design work, of course, would be required for underwater adaptation. If more sophisticated work is to be attempted underwater we must begin to develop such specialized equipment. It should be mentioned that a variety of new underwater tools were tried out during Sealab II. The results of these tests are contained in a recent report released by the Battelle Institute (8).

As has been said many times, particularly in the past year, we are just beginning to understand the concept and implications of men living in the sea. In conclusion I would like to say simply that we must start now to systematically study man as he enters this environment if we are to understand him as he goes deeper. This is necessary in order to better understand man, to accomplish specific tasks, and to enable us to select and train aquanauts of the future. The joint efforts, *closely coordinated*, of the working Navy and the disciplines represented in this room are essential if we are to accomplish our stated goals.

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13 | WEIANT WATHEN-DUNN

Limitations of Speech at High Pressures in a Helium Environment

It will be instructive to begin by examining the physiological mechanism that produces speech. Figure 38 shows a mid-sagittal section of a human vocal tract. Air is forced upward from the lungs through the trachea and the larynx. The larynx consists of several cartilages and muscles that support and control the vocal cords. When the speech message calls for voicing, as it does most of the time, the vocal cords are brought close together, and the Bernoulli effect in the constricted flow of air between them sets them in vibration. Their motion causes a pulse-like variation in the flow of air and thus imparts an alternating component that acts as a source of sound and is propagated with the speed of sound along the vocal tract. The spectrum of this sound falls with increasing frequency at a rate somewhat more than 12 db/oct. The periodicity of the vocal vibration is not exactly uniform, but it is sufficiently regular so that energy is concentrated in the neighborhood of what would be the harmonics of the average frequency.

The frequencies thus generated are propagated upward through the pharynx and usually out through the oral cavity and the mouth. If the velum is dropped, however, an alternate pathway is provided for the sound to exit through the nasal passages. The nasal sounds are produced by closing off the oral pathway so that the sound must pass outward through the nose. If the velum is opened slightly when the oral passage is open, the sound takes on a nasal quality. If the walls of the vocal tract have an impedance that is comparable to, or less than, that of the direct transmission path, sound will pass through the walls, and this, too, will have the effect of nasalizing the sound being produced.

The study of the acoustical aspects of speech production has been enormously facilitated by the use of electrical analogues. The prevailing view today is that speech production may be likened to the electrical engineer's black box. The black box has a system function, and, when it is excited by a source function, the output is the result of modifying each component of

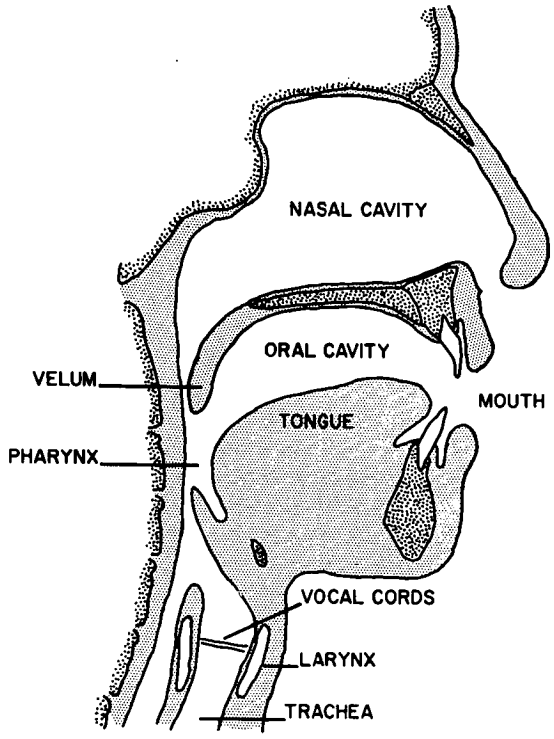


FIG. 38. A mid-sagittal section of the human vocal tract

the source function in amplitude and phase by the effect of the system function on that frequency.

In speech there are two source functions: 1) the voicing provided by the vocal cords, which is the more usual one; and 2) noise produced by constricting or, in some cases, closing and then releasing the oral transmission path. For certain sounds, e.g., voiced fricatives and stops, both sources are present simultaneously.

Let us first consider the system function in some detail. The physical arrangement of the upper vocal tract is pictured in a much simplified form in Figure 39. In Figure 39A we have the situation where the vocal tract is fairly open, i.e., the tongue is low in the oral cavity, and the velum is raised to cut off the nasal cavity. If the mouth is also wide open, we have something very like an organ pipe, closed at one end (the glottal end) and open at the other. The resonant frequencies of such a pipe are given by

$$f = \frac{c}{\lambda} = \frac{c}{4l}(2n - 1) \qquad n = 1,2,3... \tag{1}$$

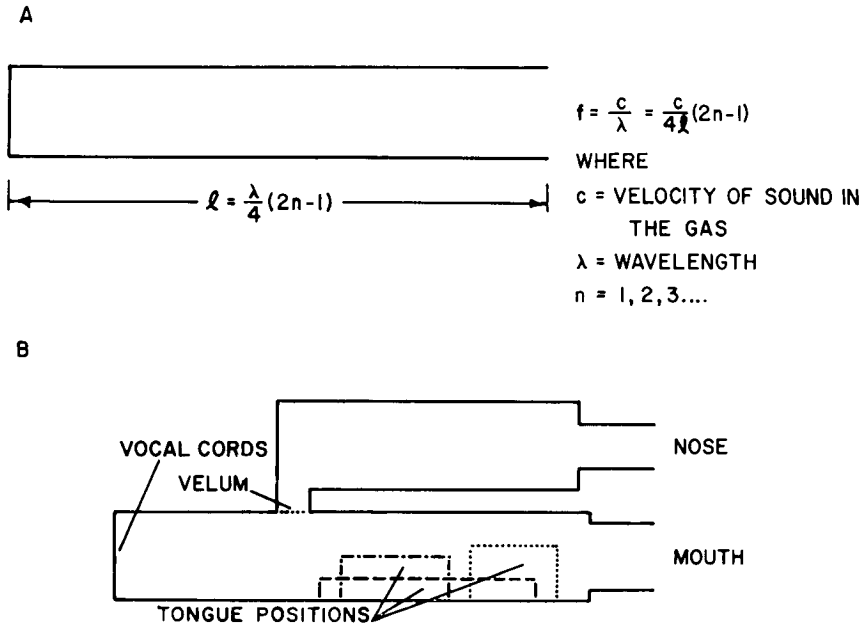
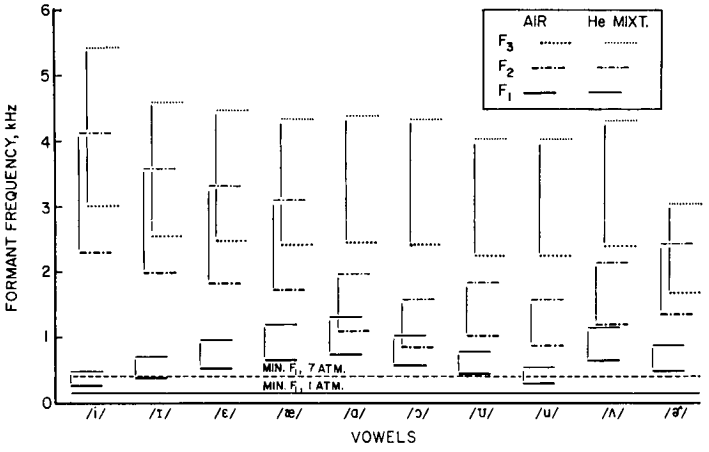


FIG. 39. Simplified representations of the vocal tract. A. Quarter-wave tube model of the oral tract. B. Entire tract, showing elements that control resonant frequencies.

where c is the velocity of sound in the gas, γ is the wave length, and l is the length of the tube. In other words, the tube resonates whenever its length equals an odd multiple of a quarter wave length of the sound. For an adult male vocal tract, where $l \approx 17$ cm, if c be taken as $3.5(10)^4$ cm/sec, the first three resonant frequencies are 515, 1545 and 2575 Hz. Now of course a real vocal tract is curved, not straight, and it does not have a uniform cross section. Nevertheless, for an open vowel like /æ/, the average resonant frequencies for male talkers are 660, 1720 and 2410 Hz (6). These are not too far removed from the resonances of a quarter-wave tube.

The natural frequencies of the vocal tract are called *formants*, and they play an important role in speech perception. Frequencies in the voicing spectrum that are at, or near, a vocal tract resonant frequency are transmitted very strongly, whereas those that are distant from a formant frequency are transmitted only weakly. The transmission properties of the vocal tract thus act to modify the spectrum of the voicing. These transmission properties are controlled by the elements shown in Figure 39B—the mouth opening, the position and height of the tongue hump, and the connection to the nasal cavity. The formant frequencies are therefore representative of the articulatory configuration of the vocal tract and are so interpreted by the listener. The average formant frequencies for a number



AVERAGE MALE FORMANT FREQUENCIES IN AIR AND He MIXTURE

FIG. 40. Average formant frequencies of several vowels for air [after Peterson and Barney (6)] and for the expiratory mixture resulting from breathing 80% He and 20% O_2 . At the bottom, the long horizontal lines give minimum first-formant frequency for both air and the helium mixture at 1 and 7 atmospheres.

of vowels produced by male talkers breathing air are shown by the heavy lines in Figure 40, where the data have again been taken from that of Peterson and Barney (6).

I should emphasize that it is relations among these frequencies, rather than their absolute values, that are the important consideration. If it were otherwise, it would be impossible to understand the speech of different talkers, for example, children. But we do understand children, and women, as well as men, and so it must be relations among these frequencies, though I hasten to add that these relations are not necessarily simple ratios, that form the basis for perception. All variations in these relations that would normally occur as a result of variations in real vocal tract dimensions are allowed by a listener, but if the variations become too large then intelligibility begins to suffer. We can, of course, learn new relations, and Tolhurst (8) has reported that participants in Sealab II managed to do this over periods of a day or so.

As we have already noted, the resonant frequencies in the vocal tract are directly proportional to the velocity of sound in the gas, and the most immediate effect of introducing helium into the vocal tract is to change the formant frequencies, shifting them upward in direct proportion to the upward shift in sound velocity. For the particular case where a mixture of 80 % He and 20 % O_2 was supplied, the velocity of sound in the exhaled gas, *after equilibrium had been established,* was $6.3(10)^4$ cm/sec, which is about

1.8 times the velocity in the exhaled gas when breathing air. Spectrograms of the speech under these two conditions showed a formant shift of 1.8. Sergeant (7) reported calculating a velocity change of 1.8 for an almost identical supply mixture, but his spectrograms indicated the formant frequencies were shifted by a smaller factor. If a shift factor of 1.8 be allowed, this is outside the bounds of normal variation in air, and the intelligibility of helium speech is consequently degraded, which is what Sergeant found. The lighter lines in Figure 40 show the formants shifted by 1.8 for the same set of vowels.

The velocity of sound in any gas is given by

$$c = \sqrt{\gamma p/\rho} \tag{2}$$

where γ is the ratio of the specific heat of the gas at constant pressure to the specific heat at constant volume, p is the gas pressure and ρ is its density. This says that the velocity depends on the product of γ and the ratio of the pressure in the gas to its density, but, since the density is directly proportional to the pressure, this ratio is constant, and any variation in velocity as the pressure changes can only be caused by variation in γ. For air the value of γ changes very little with changes in pressure (3), and I have been forced to assume that the same holds true for other gas mixtures, though it is difficult to find adequate data upon which to base a proper calculation. At any rate, most certainly for the case of air and very likely for the case of a mixture containing helium, the velocity of sound changes very little with increase of pressure. Thus, to the extent that the value of sound velocity controls the formant frequencies, they are essentially unchanged by an increase in pressure.

Now according to this, speech under conditions of high ambient pressure should sound no different from the way it sounds at sea level, and this should apply equally to normal and helium speech. Anyone who has listened to speech under pressure conditions, however, knows that this is not the case. Fant and Sonesson (3) have pointed out one of several possible reasons for this.

For the first formants of several vowels, a Helmholtz resonator is a better model than a simple tube, and the classical picture of such a resonator is shown in Figure 41A. The resonant frequency is given by

$$f = \frac{c}{2\pi}\sqrt{\frac{A}{lV}} \tag{3}$$

where c is the velocity of sound in the gas, A is the area and l the effective length of the neck of the resonator, and V is the volume of the gas inside. This formula indicates that closing the mouth (letting A approach zero) reduces the resonant frequency to zero, but in actuality there is a minimum

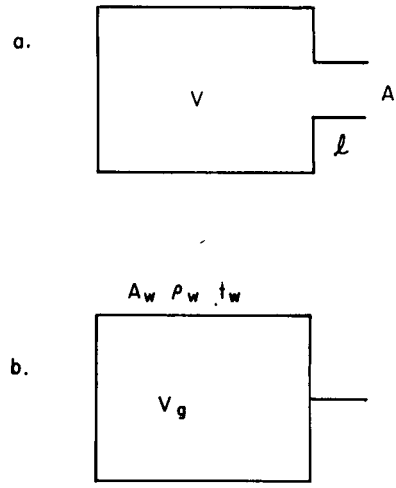


FIG. 41. Helmholtz resonator model for the first formant of vowels produced by constricting the front part of the vocal tract. A. Partial constriction by mouth or tongue. B. Complete closure.

frequency below which the first formant cannot go. This is due to the impedance of the walls of the vocal tract, which provides a fixed mass reactance in parallel with the mass reactance of the air in the neck. So long as this latter is low, as it must be when A is large, the walls have little effect, but when A becomes small, the impedance in the neck increases to a point where the walls provide a shunt path for the sound.

The situation for the case where the mouth is closed completely, which gives the minimum first formant, is shown in Figure 41B. The resonant frequency is given by

$$f = \frac{c}{2\pi}\sqrt{\frac{A_w\rho_g}{\rho_w t_w V_g}} \tag{4}$$

where A_w is the effective area of the vocal tract wall, ρ_w is the density of the wall, t_w is its thickness, ρ_g is the density of the gas, and V_g is the volume of the gas enclosed. If ρ_w be taken equal to 1 gm/cm^3 and t_w equal to 1 cm, this formula reduces to

$$f = \frac{c}{2\pi}\sqrt{\frac{A_w\rho_g}{V_g}} \tag{5}$$

We now have a factor that does indeed change with pressure, namely ρ_g, and, since the density is proportional to the pressure, the density at any pressure other than atmospheric is given by $\rho_g(P)$, where ρ_g is the density at a pressure of 1 atmosphere and P is the pressure in atmospheres. A more

general expression for the minimum formant frequency may be obtained by substituting this product for ρ_g in (5), to wit

$$f_P = \frac{c}{2\pi}\sqrt{\frac{\overline{A_w \rho_g P}}{V_g}} = f_1\sqrt{P} \qquad (6)$$

where f_P is the minimum frequency at a pressure of P atmospheres, and f_1 is the minimum frequency at 1 atmosphere. This says that the minimum frequency at P atmospheres is the minimum frequency at 1 atmosphere times $\sqrt{P}$.

For air, this minimum frequency is about 150 Hz, and, curiously enough, the minimum frequency is almost the same when the vocal tract contains the exhaled gas that results from breathing 80 % He and 20 % O_2. The reason that so little change occurs is that the increase in velocity in equation 5 is almost exactly counterbalanced by the reduction in density. A calculation, using the same vocal tract dimensions as those used for the case of air, gives 160 Hz as the minimum formant frequency. Considering that the dimensions of individual vocal tracts vary over a rather wide range, we can take the minimum frequency to be the same for both air and mixtures containing helium, and in both cases this single value will be subject to the same increase with pressure.

Across the bottom of Figure 40 are two lines. The lower, solid line represents the minimum formant frequency for $P = 1$ atmosphere. This can be seen to be low enough to have very little effect on any natural first formant of speech for either air or helium mixtures. However, the dotted line above represents the case where $P = 7$ atmospheres, i.e., the sea-level value has been multiplied by $\sqrt{7} = 2.65$. It can be seen that this line is above or very near the normal first formant of several vowels that are formed by a constriction (but not a complete closure) of the front part of the vocal tract. Under such conditions, the impedance of the mouth opening and the impedance of the walls operate in parallel, and all of these formants are raised to a point where they have a significantly detrimental effect on the speech of a talker breathing air. For helium speech at 7 atmospheres, the first formants have already been raised, with the possible exception of /i/, well above this minimum frequency. At higher pressures, of course, the first formants of helium speech would begin to be affected, and the resulting frequency shifts, added to those already present due to the helium in the gas, would further reduce intelligibility.

So far we have dealt only with aspects of the system function. Of the two types of excitation, I shall dismiss noise by saying that the only firm fact is the experimental one that fricative sounds in air have less relative energy under pressure, but there is not enough theory to predict what would

happen in the case of helium speech. Conversely, the voicing is increased in level, but again no theoretical prediction is possible for the case of helium.

Actually, the voicing problem is very complicated and the modeling correspondingly inadequate. Figure 42 shows the vocal cords from above when they are relaxed for breathing. The anterior ends of the two ligaments are anchored together on the thyroid cartilage, and their posterior ends are fastened to the vocal processes of the two arytenoid cartilages. To cause voicing, the arytenoids draw the posterior ends of the cords together, thus greatly reducing the glottal area. Air from the lungs is forced through this constricted passage, and the Bernoulli effect causes a pressure reduction in the glottis. This draws the cords together and begins an oscillation that builds up to the point where, for normal vocal effort in the chest register, the cords meet during part of the cycle. For this condition there is considerable wave motion in the tissue surrounding the cords.

Various attempts have been made to deal with voicing on an analytical basis, and I might cite the work of van den Berg (9), Flanagan (4, 5) and a doctoral dissertation just about to be completed by Crystal at MIT. Of these, Crystal's work is the most recent, but not even this is capable of predicting voicing periodicity. It calculates glottal area and volume velocity for a fixed frequency.

At my request, Crystal has put into his formulas the values of velocity and density for exhaled gas from an 80% He-20% O_2 supply. The only significant change is that the instantaneous and average volume velocities are almost doubled, which is what should be expected in view of the fact that volume velocity is controlled by the resistance and the mass reactance

FIG. 42. Top view of vocal cords when they are relaxed for breathing. The anterior ends are towards the top. (Courtesy of P. Lieberman and H. I. Soron, AFCRL).

of the air in the glottis. Both of these depend on the density in such a way that the volume velocity increases when density decreases.

When ambient pressure increases, the density increases and the flow of air is reduced. For air, this reduced flow might account for the roughness of voicing (3). For a helium mixture, there might not be so much roughness, since the density is small to begin with. I know of no experimental evidence one way or the other on this, and I would be glad to be enlightened if someone does.

Since there is no real theoretical foundation the only recourse is to experiment, and I shall end by showing some data on voicing periodicities at atmospheric pressure. Various gas mixtures were supplied to a talker, each for a sufficient time to establish equilibrium, which was determined by using a pulse technique to measure the velocity of sound in the exhaled gas. Measurements of glottal periodicities in the recorded utterances enabled us to plot distribution functions, and the reciprocal of the median periodicity is plotted in Figure 43 against measured velocity for each gas composition. The upper point on the left is for air, and immediately below it is the value for a supply of 80 % N_2 and 20 % O_2 . The succeeding points were obtained with the appropriate amount of nitrogen displaced by 20 %, 40 %, 60 % and 80 % helium. There is a downward trend with increase in helium content, but these data are for only one talker and only a small number of utterances, so that, on the basis of this evidence, it would be hard to argue that a significant change in voicing frequency does indeed occur with changes in gas content. In other words, this corroborates, in general, observations by Bárány (1), Beil (2), Sergeant (7) and undoubtedly others to the effect that helium speech does not change the voicing frequency. As a matter of fact, there would have been little point in doing this experiment

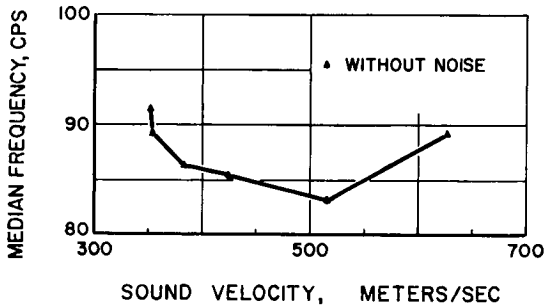


FIG. 43. Median value of vocal-cord frequency as a function of the velocity of sound in the exhaled gas. The points give, from left to right, results (without noise masking the talker's own voice) from the following supply mixtures: Air; 80% N_2—20% O_2 ; 20% He—60% N_2—20% O_2 ; 40% He—40% N_2—20% O_2 ; 60% He—20% N_2—20% O_2 ; and 80% He—20% O_2 .

were it not for the possibility of investigating feedback (another set of measurements was made for the same gas mixtures with noise masking the talker's own speech to make sure there was no feedback control of pitch) and the fact that the experimental conditions were more carefully controlled than anything found in the literature.

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14 | LAWRENCE W. RAYMOND

Temperature Problems in Multiday Exposures to High Pressures in the Sea. Thermal Balance in Hyperbaric Atmospheres

Human thermoregulation in hyperbaric atmospheres introduces many questions of both theoretical interest and practical consequence. It is the purpose of the present report:

1. to apply several conventional heat-transfer relationships to the process of body heat loss under increased pressure;
2. to present preliminary data on changes in the rate of body heat loss by convection due to the use of synthetic atmospheres;
3. to point out areas in which information is lacking and research is needed.

The properties of hyperbaric atmospheres of particular significance to those interested in thermal physiology may be considered in several classes including effects of increased pressure itself, characteristics resulting from the use of synthetic atmospheres, notably helium, and details of environmental construction and equipment. The question of thermal balance in hyperbaric atmospheres may conveniently be analyzed in terms of these categories.

Effects of Pressure Itself

Increased pressure has several inherent effects of theoretical importance in body heat production and dissipation. In addition, many of the *means of measuring* the production and dissipation of body heat are sensitive to increased pressure.

Increased heat production results from the work of breathing at pressures

which increase density and viscosity of the inspired air (1). The extent of this increase in heat production will be modified by the use of artificial breathing mixtures to alter ventilatory resistance or inert-gas uptake (2).

Turning to the matter of loss of body heat, the striking feature of the hyperbaric environment relevant to this process is increased rate of heat transfer through the layer of gas molecules immediately adjacent to the skin. Body heat may still be lost by the routes of radiation, evaporation and conduction, of course, but it is convective heat transfer which will undergo the most marked changes under increased pressure.

The rate of convective heat transfer between the body surface and the enveloping gas may be expressed by the equation

$$\dot{Q}_c = h_c A_c (T_s - T_a)$$

in which $\dot{Q}_c$ is the rate of convective heat transfer (BTU/hr), A_c is the convective surface area (sq ft), and $T_s - T_a$ (° F) is the difference between skin and ambient temperatures. The coefficient h_c, convective conductance (BTU/hr/sq ft/° F), depends upon the physical properties of the gas layer overlying the skin, and upon its movement relative to the skin. If the body is represented by a cylinder six feet tall with a diameter of one foot, the changes in natural (3) and forced (4) convective conductance in air may be plotted as a function of pressure as in Figure 44.

Natural convective conductance, h_c, may be calculated from the equation:

$$h_c = 0.13 \frac{k}{L} (\mathrm{Gr} \cdot \mathrm{Pr})^{0.333}$$

in which k is the thermal conductivity of the gas and L is the length of the surface. Gr, the Grashof group, is calculated from:

$$\mathrm{Gr} = \frac{gBL^3 (T_s - T_a)}{v^2}$$

in which g is the acceleration due to gravity, B is the coefficient of volumetric expansion, L the length, T_s and T_a the surface and ambient temperatures, and v the kinematic viscosity, in compatible units. The Prandtl group, Pr, is equal to the product of absolute viscosity and constant-pressure specific heat, divided by the thermal conductivity.

For *forced* convection, convective conductance, h_c, is calculated according to the equation:

$$h_c = \frac{kC(\mathrm{Re})^n}{D}$$

in which k is the thermal conductivity and D is the diameter of the heat transfer surface. The Reynolds group, Re, is the product of gas density, velocity and surface diameter, divided by absolute gas viscosity. C and n are constants whose values are selected from empirical correlations, as a function of Re.

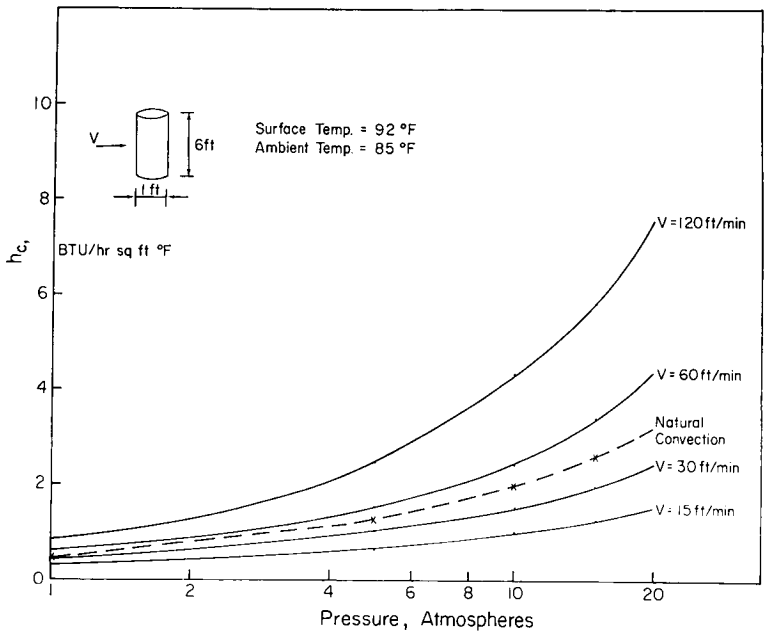

FIG. 44. Convective conductance (h_c) as a function of pressure and velocity in air.

The calculations for convective conductance, h_c, have been extended to pressures at which inert-gas narcosis would prohibit air breathing, only to demonstrate how the convective conductance of any gas will increase with pressure. This example also aims to show that the cooling effects of air movement are magnified under pressure. This may be an important comfort consideration in ventilating hyperbaric enclosures. In deriving Figure 44, thermal conductivity and viscosity are assumed to be independent of pressure (5, 6, 7, 8, 9).

Besides altering the generation and convective transfer of body heat, increased pressure also changes the response of instruments used to assess thermal balance. An obvious example is the mercury-in-glass thermometer, where its use under pressure is not contraindicated on toxicological grounds. To test the accuracy of mercury thermometers under pressure, a spherical thermistor one-eighth inch in diameter was first calibrated against a certified thermometer (National Bureau of Standards) at one atmosphere absolute. The thermistor was then checked for pressure sensitivity by imposing an axial stress of 1,000 psi, which produced no change in the indicated temperature of a constant temperature bath. The bath and thermistor were then placed in a pressure chamber and pressurized to 5.5 atm. abs. Twelve clinical thermometers (USN 6515-299-8263) were checked against

the thermistor, at both 1 atm. abs. and 5.5 atm. abs., and the mean errors under each condition were recorded following a three-minute immersion at a bath temperature of 100° F. At 1 atm. abs., the thermometers read erroneously high by an average of 0.2° F (S.D. = 0.16). At 5.5 atm. abs., the mean error was 0.7° F (S.D. = 0.19), a significant difference ($p < 0.05$). Higher pressures would be expected to produce larger errors, which could be avoided through the use of pressure thermocouples, thermistors or other techniques.

One must also consider the effect of pressure in measuring humidity. If conventional wet and dry bulb thermometers are used, corrections for pressure may be necessary when there is significant wet bulb depression; small errors in temperature may yield errors of 10 to 20 per cent in relative humidity even at normal pressure. The corrected temperatures must then be interpreted with a psychrometric chart corrected for increased pressure (10). Since such a chart multiplies the observed wet bulb depression by the ambient pressure of the measurement, to give a "sea-level equivalent wet bulb depression," any errors in temperature will be magnified by this procedure. With the sea-level equivalent wet bulb depression and the dry bulb temperature, both relative humidity and vapor pressure may be read directly from the chart. Data on the accuracy of this technique are lacking, however; since molecular interactions may cause deviation from ideal-gas behavior under pressures encountered in diving, the degree of inaccuracy should be defined. Aspirating psychrometers are sometimes used in determining wet bulb temperatures, because of their convenience for use in close quarters. It is likely that the increased density of air under pressure will prevent the necessary velocity from being developed across the wet bulb, providing another source of possible error in humidity measurements.

To overcome these difficulties, it is possible to employ hygroscopic salts and polymers whose moisture content, in equilibrium with the ambient vapor pressure, varies the resistance of an electrical circuit which is calibrated to read directly in per cent relative humidity. Atmospheric saturation may damage these instruments. They also require calibration for use at pressures where significant departure from the ideal gas laws is met, about 10 atm. abs. (11). Dew-point hygrometers may prove simpler to use and interpret in many applications.

The influence of air velocity upon convective heat transfer has been shown in Figure 44, and its effect upon evaporative heat loss (12) adds to the need for determining this variable when studying thermal balance. Most velocity measuring devices are sensitive to changes in gas density or convective conductance, and thus require calibration at the pressure of their intended use. The Fleisch or Lilly pneumotachographs are readily calibrated by displacement techniques (13), and they may also be useful

in measuring oxygen consumption. For the latter application, low-resistance displacement meters and vane anemometers (14) are readily tolerated by moderately active subjects at 5.5 atm. abs. Calibration problems with the vane device may outweigh its advantages of portability and low resistance.

Thermal Characteristics of Synthetic Atmospheres Containing Other Inert Gases

Reliable performance involving judgment and fine motor skills at pressure above 4 atm. abs. requires the use of helium in breathing mixtures, for most individuals. Helium's low density and lipid solubility are believed to underlie its low narcotic potency (15). Its heat transfer properties are also of physiologic interest, since habitable atmospheres at pressures above 10 atm. abs. will consist largely of helium. Other inert gases such as argon and neon may be included in breathing mixtures during decompression (2). It is not likely that they will become major constituents of the general atmosphere of hyperbaric environments, however. For thermal balance purposes, their main effect will be on respiratory heat loss.

Although helium's high thermal conductivity, about six times that of air, enables it to transfer heat more rapidly than less conductive gases, the difference in the rate of convective heat transfer in helium versus air is much less than six fold. A number of other physical properties affect this process (3, 4) and the rate of convective heat transfer reflects the interaction of thermal conductivity with the viscosity, density, rate of flow, and other properties of the gas in contact with the body surface, as well as the geometry of that surface. The convective conductance h_c, as defined above, expresses the overall effect of these interacting properties. Its theoretical value may be calculated for any given set of heat transfer conditions. The changes in h_c of a helium atmosphere are shown in Figure 45, as a function of pressure with parameters of velocity. As in Figure 44, convective conductance, h_c, is calculated by representing the body by a cylinder one foot in diameter and six feet in height. Comparison with Figure 44 shows that values of h_c in helium are in all cases greater than the corresponding values in air. Moreover, the *incremental* changes in h_c due to increases in either pressure or velocity are larger for the helium atmosphere than the corresponding changes in air.

Theoretical values of h_c for natural convection, such as those of Figures 44 and 45, can be compared with preliminary measurements made by Goldman and Breckenridge (16) at a pressure of 1 atm. abs. Their technique employs a heated copper manikin to determine the insulating value of the gas layer in contact with the copper skin. Insulation is expressed in "Clo" units, in which 1.0 Clo is defined as that amount of insulation which will transfer 3.09 kilocalories per hour per square meter for each degree Fahren-

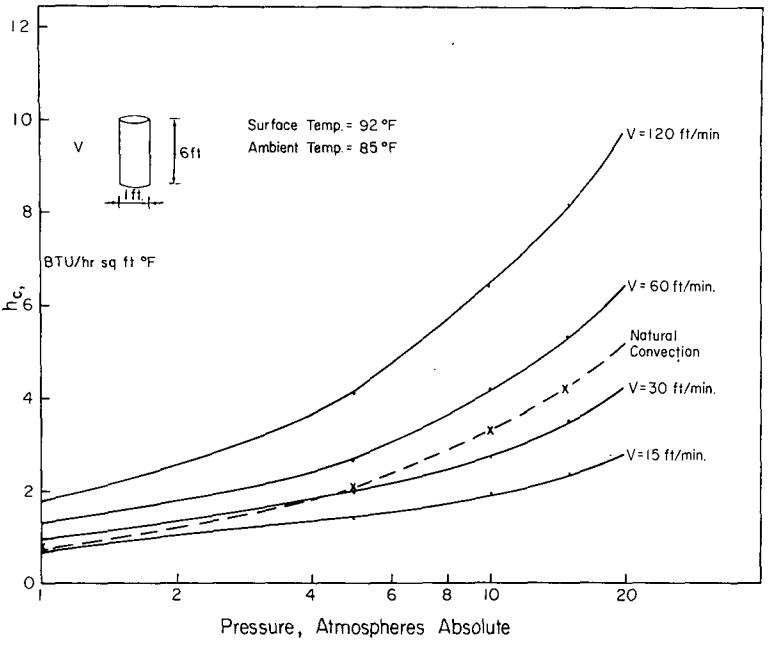

FIG. 45. Convective conductance (h_c) as a function of pressure and velocity in helium atmospheres.

heit of temperature gradient across the insulator, which for the unclothed manikin is the gas interface.

Insulation values of air, helium and carbon dioxide gas atmospheres under quiescent conditions are shown in Table 13, accompanied by thermal conductivity data (17). Helium, with its high conductivity, has a low insulating value as expected. From these observations, about 12 per cent more heat per unit time is transferred in a helium atmosphere than in air or CO_2, under still conditions at 1 atm. abs. A difference between helium and air of 16 per cent is predicted by calculations of natural convective and radiative heat transfer (18). It is pertinent to note that Schreiner (19) has found increases in oxygen consumption of 30 to 50 per cent among mice in an 80 per cent helium and 20 per cent oxygen atmosphere at 1 atm. abs., compared to controls in air. This larger difference may be explained by invoking the possibility that forced convection occurred in the mice environment. The influence of enhanced *conductive* heat transfer as an alternative explanation is suggested by the findings of Hall et al. (20), who observed larger differences in insulation than those shown in Table 13, but whose experimental technique emphasized differences in thermal conductivity *per se*.

TABLE 13

Heat Transfer from Unclothed Copper Manikin to Atmosphere

Gas	Thermal Conductivity, 32° F BTU/hr/sq ft /° F/ft	Insulation Value of Gas Interface, Clo (16)	
		Observed	Calculated
Air	0.014	0.85	0.80
Helium	0.081	0.75	0.67
CO_2	0.008	0.86	0.80

Problems in measurement techniques used to assess thermal balance in helium and other artificial atmospheres are similar to those already described. A psychrometric chart for helium at 15 atm. abs. has been prepared using perfect gas relationships, and a more precise chart could be developed by considering the effect of molecular interactions of helium, oxygen and water vapor (21). Dew point hygrometers or the direct-reading devices discussed above may provide the necessary data for most thermal balance work.

Details of Environmental Construction and Equipment

As discussed in the foregoing, differences in body heat generation and dissipation, and their means of measurement, may occur in hyperbaric atmospheres due to the increased pressure or due to the use of synthetic atmospheric constituents. In practice, both factors will operate and will act in concert with a third factor, the environment itself. Depending on its function and its design, the environment will embody structural details and equipment which may have important influences upon the thermal balance and comfort of its occupants.

The most obvious environmental factor influencing thermal balance is the design of the heating, ventilating and dehumidifying equipment. Engineers skilled in the art are invaluable in this consideration, but may be hampered by the absence of comfort criteria which include the effect of pressure. In addition to the design capacity of heaters, cooking facilities, lighting fixtures and other electrical equipment will add sensible heat to the environment, as will its occupants. They may add moisture as well, as will clothes-drying and bathing facilities, unless separately ventilated. The insulation material, its thickness and its re-expansion characteristics following compression form another environmental feature of thermal balance significance, in combination with the temperature of the outside milieu. Concerning the occupants, it would be erroneous to assume that their activities, clothing, diet, metabolism and possible acclimatization are

independent variables, for these factors will usually reflect their ability to adjust to the particular set of environmental characteristics imposed.

Synthesis of Interacting Effects

An example of the interaction of the hyperbaric atmosphere and its environment in the thermal balance of its occupants is offered by the analysis of Nevins et al., presenting expressions which relate ambient, mean radiant and skin temperatures for air and helium atmospheres at pressures up to 61 atm. abs. (22). Assumed in this analysis are several important variables:

—metabolic rates between 400 and 600 BTU/hr
—convective heat loss by *natural* convection
—no evaporative heat loss, because atmosphere is saturated from free water surface inside vessel

From these assumptions, an expression is developed for an individual's thermal balance which may be written:

$$M - W = 2.5 \times 10^{-8} (T_s^4 - T_{mrt}^4) + A_c C_c (T_s - T_a)^{1.25}$$

in which

$M - W$ = metabolic rate, BTU/hr
T_s = skin temperature, ° Rankine
T_a = ambient temperature, ° Rankine
T_{mrt} = mean radiant temperature, ° Rankine
A_c = convective area, sq ft
C_c = convection coefficient, BTU/hr/(° R)$^{1.25}$
2.5×10^{-8} = radiation coefficient, BTU/hr/(° R)^4, expressing Stefan-Boltzman constant and subjects' area and emissivity

To apply this expression to the thermal balance of an individual in a hypothetical atmosphere of helium at 20 atm. abs., one may employ the values of A_c (19.5 sq ft) and C_c (2.0 BTU/hr/(° R)$^{1.25}$) suggested by Nevins et al. (22) but one must make further assumptions for T_s, T_{mrt}, and T_a. A value of T_a = 88° F (548° R) was found comfortable in the U. S. Navy's Sealab II (23), and a skin temperature of 92° F (552° R) may be assumed arbitrarily. If a mean radiant temperature of 80° F (530° R) is assumed on the basis of insulated walls and abundant internal heat sources, the maximum amount of heat which the body could dissipate under these hypothetical conditions would be about 420 BTU/hr. Additional modes of heat loss such as forced convection and evaporation would be necessary. Since evaporation may be a necessary route of body heat loss, it should be recalled that the skin can lose moisture and thus lose heat even in a saturated atmosphere, as long as the ambient temperature is below skin temperature. Saturation of Sealab and Conshelf atmospheres may take place if the

moisture-generating sources exceed the dehumidifying capability. The low temperature and limited area of the sea water interface would tend to minimize its contribution to the total moisture content of the habitats, as would careful segregation of other moisture sources minimize their humidifying effects on the general habitat atmosphere.

Conclusions

From this brief survey of the effects of hyperbaric atmospheres upon human thermal balance, it can be concluded that

1. Increased pressure inherently tends to increase body heat production and its convective heat transfer, especially in the presence of air motion.
2. Hyperbaric *helium* atmospheres accentuate the increased rate of convective heat transfer, especially in forced convection.
3. Measurement techniques used to assess thermal balance will often require correction or calibration to account for the increased pressure and unusual atmospheric constituents. Corrections based on ideal-gas laws may require refinement for pressures above 10 atm. abs.
4. Observed and predicted rates of natural convection in air and helium at 1 atm. abs. from a heated copper manikin are in good agreement. Extension of such studies to 10–20 atm. abs. will precede attempts to study thermal balance in humans under these conditions.

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15 | ALBERT R. BEHNKE

Special Problems in the Etiology and Treatment of Decompression Sickness

The participants in this Symposium have applied critical evaluation techniques to assess the therapy of decompression sickness and they are providing basic biophysical data which reveal the nature of mechanisms involved. We are in a new era of diving progress featured by saturation exposures in the open sea to depths greater than 400 feet, and in test chambers to simulated depths of 650 feet. The facilities and gas mixtures which are essential in these noteworthy advances, can also be made ready for a type of hyperbaric therapy at high pressures, if required, and which was not feasible even for the moribund patient in a previous generation. Without going into detailed exposition, I will epitomize aspects of some of the problems which still confront us. If these problems cannot be resolved here by those specially qualified to discuss them, we will perhaps elucidate areas of conflicting opinion and outline procedures which eventually may provide the requisite quantitative data.

The Etiology of Bends

So far it has not been possible to demonstrate the manner in which intravascular bubbles produce symptoms, although ischemia, distention of the vascular wall, and other mechanisms have been analyzed. Nor is the relation of extravascular bubbles to symptomatology certain. In some remarkable tests conducted by the Air Force (1), it was found that gas-induced swelling of the ischemic hand at greatly reduced pressures was pain-

less. There is good evidence augmented in recent years by the work of Gersh and Catchpole (2) that under conditions in which men are decompressed, in contrast to abrupt decompression applied to laboratory animals, characteristic manifestations of pain (bends), asphyxia (chokes), and paralysis can be attributed to intravascular bubbles. Even in animals, Gersh and Catchpole state, "Except for fat tissue (where intracellular bubbles may occur in the cytoplasmic fat inclusion and also extravascularly) and for the myelin sheath of nerve fibers, no other extravascular gas bubbles have been noted. . . . Even in these sites gas bubbles may be seen in blood vessels before they appear extravascularly; *in animals decompressed to altitude, only intravascular bubbles occur*".

It is with reference to altitude dysbarism that a question has arisen in regard to discrepancies in the bubble theory. The requirement for use of "overpressure" in the treatment of the serious cases of altitude decompression sickness is apparent from the fatalities which occur in the absence of such treatment (3). Whatever the conjecture as to the etiology of altitude dysbarism, recompression of patients to pressure above one atmosphere invariably has been successful.

Although the preponderance of experimental and clinical data implicate intravascular bubbles as the chief etiologic agent in bends, fat emboli have occurred to confuse the picture. In dogs rapidly decompressed, bone marrow emboli have been found in the lungs. There are also products of tissue breakdown which may contribute to malaise, fever, and shock. Thus partial circulatory obstruction leads to stasis, hemoconcentration, clumping of cells, and decrease in coagulation time. There have been patients with central nervous system involvement who did not respond favorably even with prolonged exposure at high pressure. Venous obstruction and hypoxia predispose to development of edema. One may conclude that bubbles may be regarded as a primary etiologic agent, but there is set in motion a series of progressive deteriorative changes and secondary complications which not only are confusing but which may not respond to recompression therapy. Noteworthy is the fact that except in the spinal cord, chronic lesions are found only in bones. It is this aspect of decompression sickness that confers on ordinary bends which are easily treated, a sinister prognosis if joint surfaces are involved.

Treatment

The prime *modus operandi* is recompression but there are ailments and disabilities such as muscular or ligament injury, appendicitis, and coronary occlusion, clearly not part of the decompression syndrome. Pertinent to the complications attending too rapid decompression is the important matter of proper sedation in patients who are irrational or subject to violent motor

seizures. There is the problem of fluid administration in the treatment of shock and the matter of appropriate drug therapy to relieve pulmonary and bronchiolar spasm. In the paralytic, bladder care is imperative. There is the question as to the advisability of administration of anticoagulants and antifoaming agents in the attempt to restore normal rheology. Hypothermia and drug therapy have been employed to alleviate edema on the assumption that it is present in patients who do not respond to pressure therapy. Even surgical intervention has been suggested to remove frothy blood.

Recompression Therapy

An earlier generation of investigators in the U. S. Navy put into practice two cardinal principles of therapy:

1) The employment of oxygen at relatively low pressures

2) The prolonged residence in compressed air at comparatively low pressures colloquially designated by Yarbrough (4) as the "overnight soak", directed to therapy in the refractive or seriously injured patient. The chief problem in recompression is whether or not one takes the seriously injured patient to high pressures, as in U. S. Navy Treatment Tables 3 and 4. Fortunately, the mild cases (ordinary bends) which may constitute 90 per cent of our problem, have in the past been relieved essentially by oxygen therapy or air at low pressures. As stated by Golding et al. (5), "In the treatment of decompression sickness it appears to be more satisfactory to use the minimum pressure required for relief of symptoms followed by slow decompression with occasional soaks, than to attempt to drive the causative bubbles into solution with higher pressures". The ultimate criterion of success in the treatment of ordinary bends (and in the evaluation of decompression tables) is the absence of aseptic bone necrosis. These bone changes have not been observed in U. S. Navy divers.

Are High Pressures Required?

This question refers to the therapy in serious cases. In dogs subjected to massive decompression embolism (6, 7) comparatively low pressure (30 psi) combined with oxygen inhalation relieves circulatory and respiratory symptoms. Bubbles observed in blood vessels at atmospheric pressure apparently disappear as a result of this logical therapy. Nervous tissue damage however was not prevented at the low (30 psi) pressure and paralysis frequently supervened. Pressures as high as 65 psi (6 atm) were introduced into recompression practice primarily to protect the central nervous system, especially the spinal cord with its specialized, and from our point of view, poor blood supply. Sufficient animal tests at the time however, were not carried out to prove conclusively that high pressure therapy was justified.

Although it may be pointed out that only a small reduction in diameter of a bubble (e.g., 69.3 to 55.0%) occurs when the pressure is raised from 3 to 6 atmospheres, the volume certainly is halved and this may be the important consideration. At lower pressures between one and three atmospheres relatively small changes in pressure between the range of 5 psi and 18 psi may mean the difference between fitness and unconsciousness as shown during the course of treatment over a period of 9.5 days in the remarkable case reported by Golding et al. (5). Small decrements in pressure during therapy frequently bring about deterioration out of all proportion to increase of diameter size of bubbles. In the case of a tunnel worker, for example, after 1.5 hours at 41–43 psi *recovery was complete* and the pressure was reduced to 13 psi. Improvement was maintained at the lower pressure for approximately 1.5 hours when the patient's condition suddenly deteriorated. The eventual outcome was fatal.

In the case of a paralyzed diver who nevertheless was conscious, talking, and in no respiratory difficulty at 165 feet (6 atm), a decrement on Treatment Table 4 to the 120-foot stop (i.e., in excess of 4 atm) brought about respiratory embarassment and eventually fatal outcome. Bubble evolution apparently exceeded resorption during the course of relatively small decrements in pressure.

The additional overpressure required to treat altitude decompression sickness is a case in point. The five-fold increase in pressure from about 38,000 feet altitude in descent to ground level has not been adequate at times to prevent mortality.

Quantitatively the effect of relatively small pressure changes may be observed in response of respiratory rate of the anesthetized dog to pressure change and to air or oxygen inhalation following tachypnea induced by abrupt decompression from 65 psi (Table 14).

Evaluation of Recompression Therapy

It is not clear what constitutes failure in treatment. If a Hawaiian diver transported hundreds of miles by air, and in whom an elapsed time of many hours may exist between onset of paralysis and initiation of therapy, fails to benefit in accord with a given treatment table, is the table necessarily at fault? There are objective ways of testing the efficacy of therapy. One involves animals, the other man, under circumstances that have proved to be innocuous in the past. The exposure of dogs to a pressure of 65 psi for a period of 105 minutes, followed by abrupt decompression in 5 to 6 seconds, will bring about widely disseminated embolization that is prone to involve the spinal cord. The success of a particular regimen of recompression to bring about complete recovery is *prima facie* an endorsement of the procedure. In the initial tests previously alluded to, insufficient numbers of

TABLE 14

Relationships among Respiratory Rate, Air Pressure, and the Effect of Inhalation of Air, Oxygen and Recompression in an Anesthetized Dog Rapidly Decompressed from 65 psi (6 atm)

Time	Procedure	Respiratory Rate	Remarks
12:22	Exposure to 65 psi	26	105 minutes compression
12:33	Post-decompression	90	In air 1 atm. Circulating bubbles observed in blood vessels
1:04	Oxygen, 30 psi	20	Recompression period
1:10	Oxygen, 10 psi	30	Pressure reduced from 30 psi
1:16	Oxygen, 5 psi	32	
1:32	Oxygen, 1 atmosphere	40	Normal barometric pressure
2:30	Air, 1 atm.	52	
3:00	Oxygen, 1 atm.	40	
3:09	Air, 1 atm.	40	
3:50	Re-exposure to 65 psi	22	Air recompression
4:06	Following second decompression	100	Return to normal pressure

dogs were tested at the higher pressure of 65 psi (air) to establish the success of this procedure. The frequent occurrence, on the other hand, of paralysis as a sequel to low pressure oxygen therapy (30 psi), weighed heavily in favor of employment of higher pressures in the effort to limit or counteract embolization of blood vessels in the spinal cord.

The tests involving man are two-fold:

1a) Saturation air exposures were carried out at the 60-foot level for a period of 12 hours. This was followed by oxygen decompression as enumerated in Table 15. The shift from air to oxygen in this type of test did not involve a change of pressure initially. Freedom from symptoms was the criterion of success for this type of decompression.

1b) This comprised an exposure at a depth of 90 feet for a shorter period of time, 6 hours (about 87 % saturation). During the initial stage of decompression, pressure was reduced in 2 to 5 minutes to a level of 60 feet or less where oxygen inhalation was started. In this type of test, bubble formation and growth could occur prior to and during the early stage of oxygen inhalation. The data in Table 15 point out limitations of oxygen inhalation in prevention of bends.

2) The second procedure was devised by Van Der Aue (8) as a test of recompression tables extant in 1944. Yarbrough and Behnke (4) had reported that 49 out of 50 cases of decompression sickness arising during the course of helium-oxygen dives to deep depths (at the time) of 500 feet responded successfully to therapy in accord with either a long or a short

TABLE 15

Evaluation of Oxygen Decompression following Long Exposures in Air at Relatively Shallow Depths

Exposure	Period of O_2 Decompression	Results
60 ft for 12 hrs	60 ft for 58 min 5 min to surface	Pain in chest. Deep inspiration elicits cough reflex, 2.5 hr following decompression. 4.0 hrs pain in both knees. Recompressed.
60 ft for 12 hrs	60 ft for 75 min 5 min to surface	3.5 hrs, swelling, redness right lumbar area, interscapular dermographia. 5.5 hrs, knee pain. Recompressed.
60 ft for 12 hrs	60 ft for 63 min 6 min to surface	2.5 hrs, substernal soreness on deep inspiration, ECG negative. 5.0 hrs, chest feels better, pain in knee. Recompressed.
60 ft for 12 hrs	60 ft for 30 min 30 ft for 25 min 20 ft for 22 min total time 82 min	3 hrs, pain in both knees (heads of tibiae). Recompressed.
60 ft for 12 hrs	60 ft for 87 min 5 min to surface	Recurrent attacks of nausea while breathing O_2 at 60 ft. 1.5 hrs, shifting pain in right arm, X-ray negative. 3.5 hrs, fatigue, pain in arm, leg. Recompressed.
60 ft for 12 hrs	60 ft for 1 min 50 ft for 2 min 40 ft for 28 min 30 ft for 32 min 20 ft for 40 min 10 ft for 51 min	2.5 hrs, stiffness left knee, paresthesia left leg. 22 hrs, left knee felt "rubbery", some pain felt in quadriceps tendon on standing or coughing but not lying down.
60 ft for 12 hrs	60 ft for 2 min on air 40 ft for 75 min on O_2	No symptoms.
90 ft for 6 hrs	5 min to 40 ft 40 ft for 102 min on O_2 4 min to surface	Oxygen inhaled 135 min at surface. No symptoms.
90 ft for 6 hrs	5 min to 40 ft 40 ft for 116 min on O_2 4 min to surface	Oxygen inhaled 60 min at surface. No symptoms.

oxygen table outlined in Table 16. Van Der Aue's ingenious and innocuous procedure centered in a preliminary one-hour work dive (air) at a simulated depth of 130 feet followed by standard Navy decompression. Normally decompression sickness did not supervene. If in the course of one half to one hour following decompression, a repetitive exposure in the guise of a treatment table was given, then success or failure of the table was evaluated by subsequent absence or occurrence of bends. The results showed con-

TABLE 16

Descriptions of Short O_2 Table and Long O_2 Table with Assessment by Van der Aue's Procedure of the Two Treatment Tables in 1944 at the Experimental Diving Unit for Therapy in Decompression Sickness

	Depth (feet)	165	140	120	100	80	60	50	40	Surface
Short oxygen table	Gas breathed				Air	Air	O_2	O_2	O_2	O_2
	Duration of stay (min)				30	12	30	30	30	5 min to surface
Long oxygen table	Gas breathed	Air	Air	Air	Air	Air	O_2	O_2	O_2	O_2
	Duration of stay (min)	30	12	12	12	12	30	30	30	5 min to surface

Van Der Aue Assessment

	Successful Treatments	Unsuccessful Treatments
Short O_2 table	6	0
Long O_2 table	5	5

clusively the efficacy of the short oxygen table and the ineffectiveness of the long table. Although treatment of helium-oxygen complications, frequently severe and attended by chokes, edema, and shock, was satisfactory in accord with the long oxygen table, it was a failure following air dives.

It is this type of controlled test procedure that is recommended for evaluation of modifications in the U. S. Navy Treatment Tables.

Toxic Partial Pressures of Oxygen

The high partial pressure of oxygen in air at high pressures may not be fully appreciated. At 165 feet (6 atm) Po_2 is 1.26 atmospheres. In one long air treatment table outlined as therapy for critically ill patients, the partial pressure of oxygen in compressed air inhaled over a period of nine hours was equivalent to more than one atmosphere of oxygen.

Various Gas Mixtures In Pressure Therapy

The relative rates of diffusion of several inert gases may be taken advantage of in recompression practice. Apparently air recompression is effective in expediting elimination of helium in the treatment of helium-oxygen bends. It does not follow that the reverse is true and a shift to a

rapidly diffusing gas as helium may actually enlarge nitrogen bubbles. Mention is made of this problem for discussion.

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16 | E. E. P. BARNARD

The Treatment of Decompression Sickness Developing at Extreme Pressures

In 1961, before the resumption of experiments in deep diving by the Royal Navy, the question of what should be done if decompression sickness developed before reaching the surface had been given some attention, since such cases had been reported by the Admiralty Diving Committee (1) following deep dives on air. The rather naive conclusion reached at this time was that if these cases required a similar pressure ratio to that used in treating cases occurring at the surface, it might be necessary to compress to 300 feet. A theoretical treatment schedule was therefore produced which fortunately was never used, since it would have been ineffective, but which for ease of calculation employed 'stops' of equal length with progressively decreasing pressure intervals between the stops. This latter idea is the only fragment which has survived from the early theoretical period into the present era of primitive pragmatism since it has practical virtues for tired timekeepers during long decompressions.

In 1963 during the course of a simulated dive to 500 feet our first case of decompression sickness occurred at depth. The diver concerned had carried out a working dive of eleven minutes at 500 feet and after 5 minutes at the 150 foot stop he complained of severe pain in the right side and loin. Since he had only seven minutes remaining at the 150 foot stop, and was due to change from a 90% He-10% O_2 mixture to a 60% He-40% O_2 mixture on reaching 140 feet, decompression was continued and the diver examined at 140 feet.

On examination he showed a loss of power in all muscle groups in the right leg with brisk reflexes, and he also complained of pain and tingling in the distribution of the right 5th lumbar nerve. After three minutes on 60% He-40% O_2 improvement began and decompression continued on the original schedule, the diver having no symptoms by the time he reached 100 feet, nearly one hour after the time of onset.

The second case occurred nine months later after an exposure of two

hours at 800 feet. One of a pair of divers developed vertigo after nearly an hour at the first stop, which was 490 feet. The symptoms of dizziness, nausea and vomiting were sufficiently unusual to make it difficult to decide whether they were due to decompression sickness or not. It was decided to continue the decompression to 340 feet, the second stop, where after about 30 minutes the first diver developed deafness in one ear and loss of coordination, while the second diver also developed vertigo and began vomiting.

Both divers were recompressed to 400 feet with some improvement and after 2 hours at this pressure decompression on distinctly 'ad hoc' lines was begun. Following a series of attacks of bends pain on the way to the surface both divers emerged with some residual signs 42 hours later.

Depth of Onset

In all, since October 1963 we have had 37 cases of decompression sickness occurring en route to the surface during deep dives on oxy-helium. This however takes no account of the many recurrences following initial treatment, each of which posed the same problems, and helped to lead toward the solutions proposed.

Of the cases being considered, seven managed to continue to the surface either on the original schedule or with the addition of time to the later stops. The remaining 30 cases required recompression.

The depth of onset of symptoms, the depth of relief and the absolute ratio of these depths for the 23 results available is presented in Table 17.

The first point which should be made about these figures is that there does not appear to be a significant alteration in the pressure ratio used for treatment with the depth of onset of symptoms. With one exception all the values lie below a ratio of 2 to 1 and if only cases of bends pain are considered the mean treatment ratio for these is of the order of 1.3 to 1.0. If one prefers to view this in another way the pressure difference (ΔP) required to give relief is usually 60 feet or less.

Treatment Ratio

The low treatment ratio which suffices for cases at raised pressures is a rather curious finding, since when applied to ordinary cases it would predict that most bends should respond to treatment by recompression to 10 feet, while the remainder should be cured by recompression to 33 feet, and neurological cases might only rarely need be treated by reexposure as deep as 165 feet, all of which is quite contrary to experience.

Are the cases which occur at depth in some way different from those which occur at the surface? So far as the clinical findings are concerned there is no difference in their severity, type, or distribution. As far as the

TABLE 17

Recompression Treatment for Cases of Decompression Sickness Occurring at Depth

Depth of onset in feet (gauge) P_2	Depth of relief in feet (gauge) P_1	Ratio $\frac{P_1}{P_2}$ (Abs)	Depth of onset in feet (gauge) P_2	Depth of relief in feet (gauge) P_1	Ratio $\frac{P_1}{P_2}$ (Abs)
8	20	1·28	95	105	1·08
9	40	1·74	125	135	1·06
10	25	1·36	125	165†	1·22
20	40	1·38	150	260	1·60
30	40	1·18	165	200	1·18
40	366†	5·40	170	230	1·30
41	55	1·18	210	450*	1·99
45	70	1·32	220	240	1·08
50	75	1·30	230	450*	1·83
55	70	1·17	260	450*	1·65
55	75	1·23	340	400*	1·16
90	130	1·33			

† Neurological involvement.

* Vertigo.

The initial depth of onset of symptoms, the depth at which relief was observed and the absolute ratio of these two depths is tabulated above.

latter point is concerned, the incidence of bends in the lower limbs following deep dives is some two to three times the incidence in the upper limbs for either group of cases.

In addition to the difference noted regarding the treatment ratio, there is a further remarkable feature of bends developing at high pressure. On many occasions during treatment it has been noticed that even the slight pressure fluctuations due to flushing through the chamber can alter the severity of symptoms. Variations of one foot in 80 have produced noticeable changes and pressure changes of three to five feet almost invariably cause comment.

There is moreover a marked difference in the time course of cases of bends occurring at depth. The pain often comes on immediately and acutely following a pressure drop but may then regress; this in general is not true of bends occurring at the surface which take some time to develop following an initial latent period.

These considerations suggest that there are at least two ways in which

bends pain may arise. While either may occur in a given situation, one is more common at depth and the other at the surface. This is perhaps related to the two different ways in which bubbles are assumed to grow, either by physical expansion according to Boyle's Law or by inflow of gas from tissues at a higher gas potential. Simple expansion seems to be the type of mechanism which would best fit the facts but of course assumes the presence of 'silent' bubbles.

Principles of Treatment

In order to translate these experiences into some sort of guide for treatment it is necessary to explain the assumptions used and the way in which they were employed.

The primary assumption was that pressure cures decompression sickness, that at whatever depth symptoms may occur there is some greater depth which will bring relief.

The second assumption was that, having stayed for some arbitrary time at the pressure of relief, there was some unknown path to the surface which would bring the divers back safely.

Thirdly, that it was possible to find the ideal decompression by the method of seeing what was and what was not safe.

However there are numerous factors which in practice complicate the simple assumptions outlined above. From the point of view of analysing the results, the most frustrating of these is that each case is unique, the history of each exposure is different either in its time-course, the composition of the gas breathed, the amount of work performed at depth or any other variable which one might consider.

Technique of Treatment

When symptoms developed decompression was halted. If the symptoms regressed it was frequently possible to continue the decompression, however if the symptoms persisted then recompression was essential. It was usual to apply the pressure at about 25 feet per minute proceeding to some preselected depth. The pressure would then be held for up to 15 minutes to see whether or not improvement occurred, if it did not or it was only partial then recompression continued to a greater depth. The end-point was reached when the patient said that no trace of his symptoms remained.

The length of time spent at pressure has varied from 15 minutes to 2 hours but in general it seems that 20 to 30 minutes is an adequate stay for bends cases. It is not clear whether a longer stay is necessary for those cases showing neurological involvement, but it has been the practice to use a longer time at pressure as a precautionary measure.

Decompression following treatment has followed various courses, either

stage decompression, a steady pressure-drop or "bleed" or a combination of these methods. Either of the two principal methods is satisfactory. We have found that a useful rough guide is to leave the depth of relief at 20 feet per hour to about 165 feet and then to slow to a decompression rate of 10 feet per hour from 165 feet to the surface.

The recurrence of symptoms is in our experience quite frequent, but even more common perhaps since dives are always carried out by a pair of divers is the development of decompression sickness in the diver who was previously unaffected. As in the initial onset there seem to be two possible outcomes, either the symptoms regress, in which case after about 30 minutes decompression may restart at a slower rate than before; or the symptoms may be severe initially or become worse, in which case one must recompress, again to the point of complete relief.

Learning by Mistakes

While the object of each treatment was to alleviate symptoms, it was obvious that there was much to be learned from mistakes. The eventual hope was to produce a treatment schedule which by its success would preclude the collection of what might be regarded as experimental data, much as the success of the current treatment tables has tended to restrain progress in their improvement.

The method for guiding the progress of the earlier treatments was crude but seemed to work. Each schedule as it developed was plotted on a master graph, with minor mishaps marked in red. On subsequent occasions the decompression was designed to avoid these red zones. The assumption used was that recurrences were due to too rapid a decompression and that therefore they might be avoided if each critical depth was reached at a later time.

When some six treatments had been plotted in this way the graph became so congested with black lines and red marks that the development of some approximate rule became essential.

Inspection of the composite curve showed it to be approximately exponential in form, with a faster rate of pressure-drop at depth than was tolerated nearer to the surface. Over the last part of the curve it was observed that the decompression time for 33 feet to the surface was about 6–12 hours. With this information the following working rule was produced: It should be safe to drop the pressure by an amount corresponding to a 2:1 ratio providing that some six to twelve hours is taken in the process.

The decompression times contained in Table 18 are plotted in Fig. 46 together with the two 'limits' proposed by the working rule to give some idea of the range of decompression rates which might be expected. Since the time spent at maximum depth depended on the whim of the doctor

TABLE 18

Decompression Time for Cases of Decompression Sickness Occurring at Depth

DEPTH OF RELIEF FEET	TIME AT MAXIMUM PRESSURE HOURS	MINUTES	DECOMPRESSION TIME HOURS.	MINUTES	DEPTH OF RELIEF FEET	TIME AT MAXIMUM PRESSURE HOURS.	MINUTES	DECOMPRESSION TIME HOURS.	MINUTES
20	—	30	1	42	135	—	30	27	17
24*	—	30	1	—	165	—	30	26	59
25	—	30	5	11	230	1	—	37	29
40	8	—	4	52	240	2	—	29	29
40*	—	30	1	21	260	2	—	20	—
40	—	30	7	48	366	1	30	29	10
70	1	—	11	33	400	2	—	42	12
70	3	—	9	15	450	2	—	27	23
75*	—	30	14	45	450	—	30	36	55
75	1	—	14	10	450	—	20	29	18
105	2	—	22	12					

* TREATMENT FOLLOWED BY RECURRENCE.

The depth at which recompression produced relief of symptoms, the time spent at this depth, and the subsequent decompression time to the surface is tabulated above and plotted in Figure 46.

concerned, there is a degree of uncertainty which has been represented by plotting the total time also.

Conclusions

In considering the number of cases which we have now treated it is reasonable to try to refine our previous rule-of-thumb method and to see what progress has been made. Two of the most recent treatments are plotted in Figure 47. The first of these began as a severe case of bends at 40 feet which became worse during recompression, with neurological involvement of the right arm. Both divers were symptom-free at 366 feet where they were held for 2 hours. Decompression was completely uneventful on a two-part continuous ascent. The second treatment was for vertigo which began at 210 feet and was cured by recompression to 450 feet. After 20 minutes at this depth a slow ascent was carried out to 420 feet where the pressure was held for one hour. A series of stops was then begun, using a ratio of 1.3

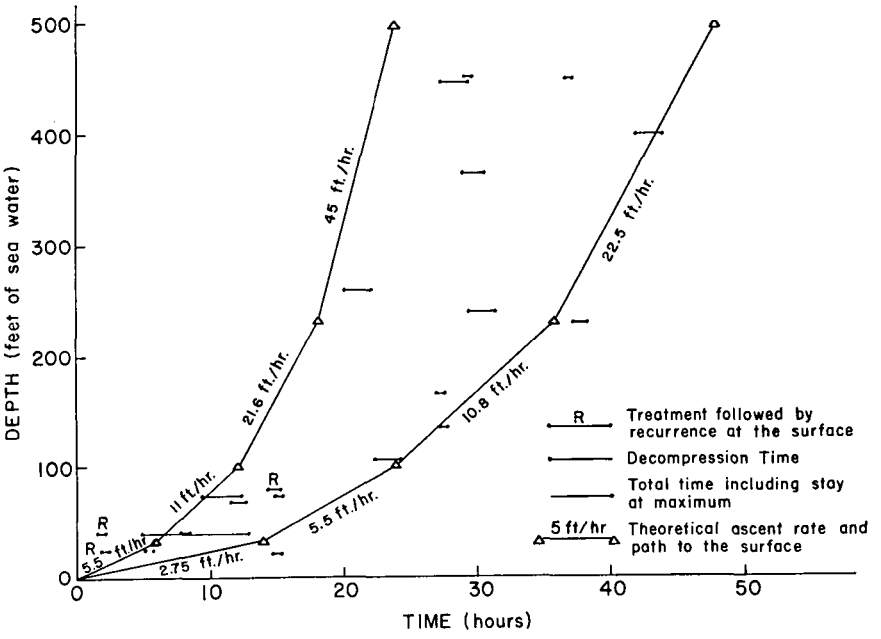

FIG. 46. The information given in Table 18 is plotted as depth of relief against the time required for decompression. Two theoretical decompression curves have been superimposed on the data.

to 1. Reccurrence at 90 feet was treated by recompression to 130 feet and the decompression by continuous ascent. The points to notice about these treatments are firstly that a series of 1.3 to 1 ratio drop can be tolerated over a wide range of pressure, and secondly that the slope of the latter part of the two treatments is the same.

On the scanty evidence presented by some 20 individual recompressions it is suggested that:

a) The tolerable decompression rate after relief is proportional to the absolute pressure.

b) That a safe rate of decompression can be achieved by carrying out a decompression ratio of 1.3 to 1 in 5 hours.

From the first assumption we can derive an expression of practical value which gives an approximation to the suggested ideal curve as follows.

The rate of decompression in time t from a pressure P_1 to a lower pressure P_2 can be expressed as $(P_1 - P_2)/t$. If the relation between P_1 and P_2 is expressed by the pressure ratio r, such that $P_2 = P_1/r$, then by substitution

$$\text{Rate of decompression} = P_1\left[\frac{1 - (1/r)}{t}\right]$$

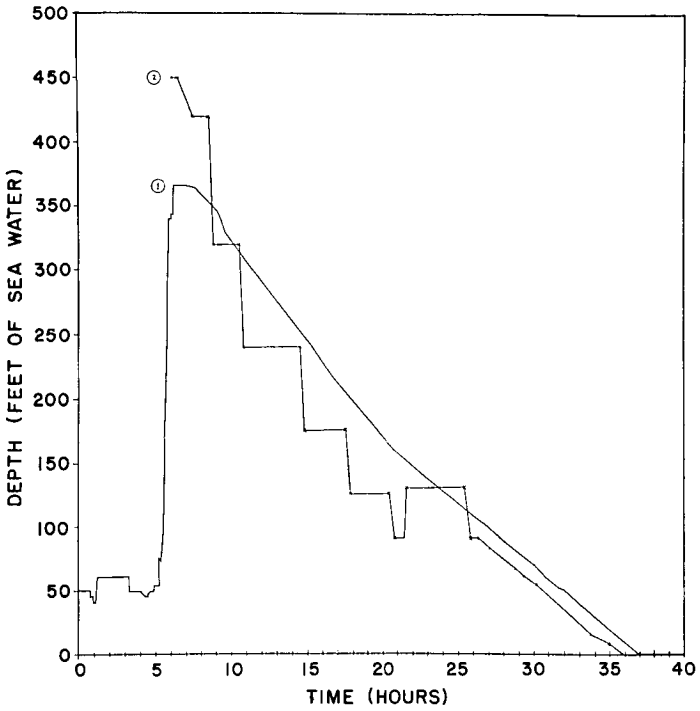

FIG. 47. This represents the time-course of two treatments. The first 1) a bleed from 366 feet, the second 2) which employs stops on a 1.3:1 ratio throughout most of its course, has been plotted so that the time of arrival at the depth of relief coincides with that of treatment 1.

If the numerical values for r and t which have been suggested are incorporated, this becomes:

$$\text{Rate (feet/hour)} = (P_{\text{abs}})\ (0.046) \tag{1}$$

This expression however only allows successive approximations to be made for each five hour period and a more refined approach is to use a decompression curve of the form:

$$P_t = P_0\, e^{-at}$$

where P_0 is the pressure of relief and P_t is the pressure after time t. This becomes

$$P_t = P_0\, e^{-0.052t} \tag{2}$$

when the pressures are measured in absolute units and t is measured in hours.

This gives a time constant of 19.2 hours or a half-time of 13.3 hours.

In practice there are several ways of employing the expression given above:

a) The initial rate from expression (1) may be used until five hours have passed, when the calculation must be repeated to determine the rate for the subsequent five hour period.
b) Decompression rates may be calculated beforehand by generating the curve given by expression (2), and this decompression curve joined at the pressure of relief.
c) Ratio drops of 1.3:1 with 5 hour stops may be used instead.

It should however be made clear that these ideas are tentative and that there has been no opportunity recently to test their validity. They are however relatively flexible and can be modified in the light of experience.

In conclusion it may be remarked that while the disadvantage of pragmatism is that we remain largely ignorant of what we are doing, the advantage is that it works.

Acknowledgment

The author wishes to acknowledge the assistance given in all aspects of this work by Surgeon Lieutenant Commander D. H. Elliott, Royal Navy, who was responsible for several of the treatments, and the skill and patience of the compression chamber operating team of the Royal Naval Physiological Laboratory.

REFERENCE

1. Admiralty Committee on Deep & Ordinary Diving. (1933). Report Oct. 1933. Section VII. Appendix D. "The occurrence & treatment of bends." pp. 120–127.

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Minimal-Recompression, Oxygen-Breathing Method for the Therapy of Decompression Sickness

The Need for an Alternative to Standard Recompression Procedures

A condensation of the epidemiologic framework of this study is provided by Table 19, which has been compiled from hitherto unpublished data and from the reliable repositories of diving casualty information (18, 23, 28, 32, 34–36, 41). In this table and in succeeding paragraphs, attention is directed upon results of initial trials of recompression. Ultimate disposition of persisting morbidity (the "recurrence" and the "residual") has, for the following reasons, been virtually ignored: a) prompt, permanent relief is intrinsically desirable and must be consistently obtainable, and b) initial recompression table results provide a simple and unbiased index of therapeutic satisfaction, susceptible to statistical evaluation and analysis. It is true, of course, that remarkable recoveries have occurred during retreatment following poor or partial responses to immediate recompression. Occasionally the resolution of a catastrophic situation has been substantial and perhaps lifesaving, but real, though proportionately unimportant morbidity has persisted.

One hundred thirty-three casualty experiences in which U. S. Navy recompression treatment tables (40) were used in the management of decompression sickness were reported to the Experimental Diving Unit during 1963–1964. Initial recompression exposure did not produce complete relief in 32 instances (24%), and all but three of these therapeutic failures were encountered in association with recompression according to treatment table 3 or table 4. 62 patients (46%) treated with tables 3 and 4

provided 91% of the clinically unsatisfactory results. The cumulative casualty management experience (from Table 19), amended to include calendar year 1965, is as follows:

Initial recompression:	1120	Initial table 3 and table 4:	318 (28.9%)
Relieved:	959	Relieved:	228
Percent not relieved:	14.4	Percent not relieved:	28.3

Treatment Outcome—Antecedent Exposure Severity

All cases were assigned to one or the other of two categories which are grossly descriptive of casualty precipitating circumstances: cases arising in relation to diving practices not in accordance with those promulgated by the U. S. Navy Diving Manual were termed "non-standard" dives; all others, presumably managed with more uniformly-conservative conduct,

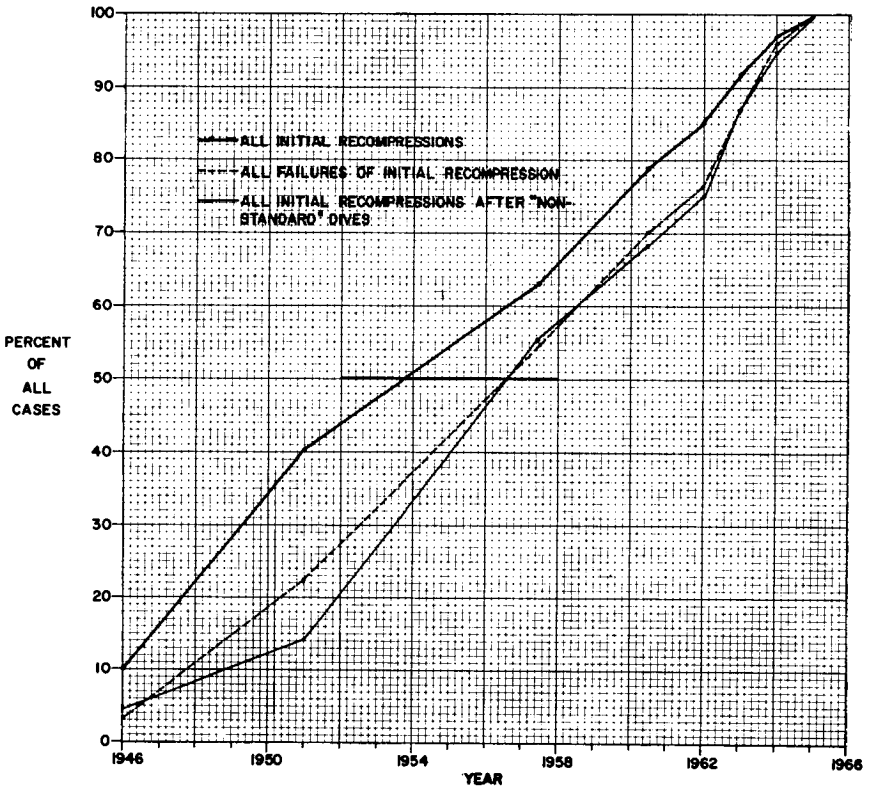

FIG. 48. Cumulative percent curves: cases treated (U. S. Navy tables), cases treated after "non-standard" dives, and results of treatment.

TABLE 19

Decompression Sickness Caseload, Case Severity, Response to Recompression, and Casualty Sources

Part A is data from U. S. Navy sources, B from other sources.

A. Data from U. S. Navy

Year(s)	Initial Recompresions			Percent Failure of Initial Recompression	Initial Tables 3 & 4 Only			Percent Failure of Initial Tables 3 & 4	Number of Cases Following		Percent of Cases Following "Non-standard" Dives
	Total	Relieved	Unrelieved and Recurred		Total	Relieved	Unrelieved and Recurred		"Standard" Dives	"Non-standard" Dives*	
1946	113	107	6	5.3	18	17	1	5.6	96	17	15.0
1947–1955	343	313	30	8.7	62	52	10	16.1	303	40	11.7
1956–1959	256	204	52	26.3	78	51	27	34.6	88	167	65.2
1960–1961	176	151	25	14.2	59	44	15	25.4	124	52	30.8
1962	67	57	10	14.9	23	17	6	26.1	40	27	40.3
1963	73	57	16	21.9	28	15	13	46.4	25	48	65.7
1964	60	44	16	26.7	34	18	16	47.1	28	32	53.4
Totals	1088	933	155	14.3	302	214	88	29.1	705	383	35.2
	Chi square 34; $p < 0.01$ Corr. cont. coefficient 0.21				Chi square 17.9; $p < 0.01$ Corr. cont. coefficient 0.29				Chi square 254; $p < 0.001$ Corr. cont. coefficient 0.51		

* "Non-standard" dive defined as any exposure in which U.S. Navy standard decompression schedules were not employed or any dive performed by a non-graduate of the U.S. Naval School, Deep Sea Divers.

B. Data from other sources

Year(s)	Reference	Initial Recompressions			Percent Failure of Initial Recompression	Total "Serious" Cases	Number Relieved with First Recompression	Per cent Failure with First Recompression
		Total	Relieved	Unrelieved				
1952–1962	Royal Navy—Slark, 1962	134	108	26	19.4	10	8	20.0
1909	East River Tunnels—Keays, 1909	3,680	3,167	513	13.9	402	217	46.2
1948–1950	Tyne Tunnel—Paton, 1954	350	268	82	23.4	14	9	35.7
1957–1959	Dartford Tunnel—Golding, 1960	689	471	218	31.6	35	35	0

were termed "standard". A Spearman rank correlation coefficient (1) computed for percent of cases subsequent to non-standard dives and percent failure of initial recompression was 0.86 (5 *df*, $p < 0.02$). During 1963–1964, for example, this association, for treatment table 3–table 4 results, was 100 percent. Figure 48 traces this relationship of total caseload, casualty source, and therapeutic effectiveness for the entire 19-year reporting period. Table 20 has been derived from Rivera's report (34), to illustrate a particular aspect for therapeutic concern.

It was concluded, in this manner, that current U. S. Navy recompression treatment procedures provide reliable, efficient schedules for those divers stricken subsequent to exposures conducted with reasonable caution and conservatism, and that they are, in general, not adequate for prompt, successful management of severely injured patients following grossly-inadequate decompressions (25).

Important Aspects of Decompression Sickness Treatment Techniques

Among the general considerations or concepts which were consciously employed in evaluating alternative therapeutic approaches were the following: a) at this time there is no effective alternative to prompt recompression; b) in, e.g., explosive decompression, when there are presumptions of massive, disseminated intravascular bubble formation and functional obliteration of both cognate and collateral microvasculature, recompression must be both prompt and substantial, to reduce bubble size (7); c) recompression procedures must be practical, with respect to compatability with deployed facilities, and logistically feasible, with respect to gas mixtures, cylinder inventories; d) final determination of therapeutic efficacy should be adjudicated with chronic, long-term criteria in addition to the acute standard of, "relief-no relief" and the artificial one of, "success-failure". Definitive

TABLE 20

Results of Recompression Therapy with U.S. Navy Treatment Table 4, 1946–1961. (Data from Rivera (34).)

	N	Relieved	% Unrelieved
Initial recompression	57	27	52.6
Second recompression	56	18	50.0
Third recompression	5	1	80.0
Fourth recompression	2	1	50.0
Fifth recompression	1	1	0.0
Total	101	48	52.5

criteria ought to include, e.g., aseptic bone necrosis, pulmonary oxygen toxicity and residual functional impairment or disabilities.

Theoretical Basis of the Therapeutic Schedule

Resolution of Bubbles and the Level of Maximal Re-application of Pressure

An expression to relate the rate of change of the radius of a bubble and time at a given ambient pressure has been derived from the general gas law and Fick's first law of diffusion by Wyman, Scholander, Edwards and Irving (47):

$$\frac{dr}{dt} = RT \cdot \frac{\Delta\alpha}{d} \cdot \frac{P - P_0}{P}$$

in which

r = radius of the bubble
t = time
R = gas constant
T = absolute temperature
Δ = diffusion constant of the gas in water
α = solubility constant of the gas in water
d = thickness of the diffusion shell
P = pressure within the bubble
P_0 = partial pressure of the gas in the fluid surrounding the shell

The bases of this relationship are that the pressure within a spherical bubble depends upon the volume of the bubble, and the quantity of gas which escapes from it by diffusion depends upon the surface area of the bubble. For each value of P, corresponding to any stipulated depth, the bubble radius should decrease in a uniform manner with time. (Pressure due to surface tension is a significant factor only when bubble diameter is less than 0.10–0.09 millimeters.) Wyman's results indicate that the lifetime of an air bubble of given size should not appreciably vary with depth below a limiting depth of 10–15 meters. Recompressions to depths greater than 60–66 feet, therefore, probably provide little advantage in rapidity of bubble resolution except for the additional reduction of bubble diameter (0.693 at 66 feet to 0.550 at 165 feet). However, as ambient depth is increased with compressed air breathing, the uptake of nitrogen into solution in the fluids surrounding a bubble will increase at a rate which is proportional to the increased exchange gradient. The rate of inert gas diffusion out of the bubble diminishes correspondingly. When nitrogen supersaturation occurs, during the subsequent decompression, persistent bubbles will enlarge because both osmotic and dynamic equilibria must be maintained. It is interesting, in this regard, to recall that in their proposal for re-oxy-

genation orientation of decompression sickness management, Behnke and Shaw (7) specified that a mixture of 50% oxygen-50% nitrogen was to be breathed during reapplication of pressure to 75 psi.

Gas Exchange and Tissue Oxygenation

Considerable advantage can be gained in bubble resolution processes by maintenance of the gas exchange gradient from the bubble to the circumjacent fluids ($P - P_0$). This advantage occurs during oxygen breathing and can be exploited at depths where oxygen can be used with safety (10). The time-course of this gas elimination gradient is maintained optimally throughout the entire oxygen-breathing period and, therefore, reductions of ambient pressure are unlikely to permit or facilitate bubble growth through attainment of osmotic equilibrium with supersaturated tissue-fluid inert gases. When air is breathed during therapeutic recompression, bubble growth by such mechanism is feasible.

Of equal or surpassing importance, however, is the tissue oxygenation which occurs and which aids in functional restoration of tissues rendered hypoxic by the ischemic actions of bubble emboli. Collateral channels can supply hyperoxygenated blood to tissue sites affected by emboli impacted within cognate arteriolar vessels. If reflexogenic vasoconstrictive effects of bubble emboli are diminished by re-oxygenation, the tissue perfusion thereby enhanced will favor bubble resolution. Hyperoxia-induced reductions of peripheral blood flow (20, 45) do not significantly influence therapeutic progression, as compared to diving-decompression theory in which the uptake and elimination of gases is computed or integrated through a spectrum of hypothetical, perfusion-rated, inert gas reservoirs or compartments. With reoxygenation of hypoxic tissues, and the patient respiring inert-free gas, rapidity of bubble resolution seems not likely to be of decisive concern.

Sequelae of Impaired Perfusion and Tissue Injuries

Perfusion alterations may result whenever tissues are morphologically distorted by expanding extravascular gas pockets or harmed by vascular occlusions (13, 22). Regardless of mechanism, however, the elimination of inert gas from within bubbles will be compromised because of stagnation of the contactant blood (4, 6). Perhaps the most important pathophysiological consideration in this regard is the unpredictable manner of elimination of dissolved inert gases from injured or convalescent tissues. During the descent and bottom-time stages of compressed-air recompression exposures, inert gas is taken up in solution in tissues. Should supersaturation sufficient for bubble formation occur during the subsequent decompression, and clinical symptoms be thereby generated, the likely (and erroneous)

clinical classification is recurrence. It is important, therefore, to limit uptake of inert gas during recompression treatment in order to avoid both growth of unresolved bubbles and formation of new bubbles within or circumperipheral to areas of disturbed and injured tissues.

Persistence of neurological symptoms, usually indicative of spinal cord injury, can occur subsequent to improper decompression from prolonged or repetitive air dives. Weakness, paresis and paralysis of lower extremity muscle groups, impairment of urinary bladder and bowel functioning have not uncommonly been refractory to treatment with recompression when such treatment has been delayed for several hours. Extracellular edema and hemorrhage, which may reasonably be implicated in the underlying pathophysiology of these subacute clinical stages, cannot be resolved solely with reapplication of pressure. Disordered local perfusion, rather, constitutes a relative contraindication to air saturation recompression. Oxygen breathing at increased pressure is specific therapy because it can provide a high pressure head for diffusion of oxygen outward from capillaries into tissue units. Tissue edema increases diffusion distances, and can close capillary lumena if extravascular pressure increases sufficiently. Capillary dilatation, in response to local tissue hypoxia, does not of itself appreciably alter diffusion path length and, therefore, oxygen peripheral vasoconstriction does not compromise homeostasis.

Empirical Basis of the Therapeutic Schedule

Oxygen Tolerance and the Duration of Therapy

Yarbrough and Behnke (43) treated several stricken divers with a regimen of ninety minutes oxygen breathing at 2.8 atmospheres absolute. Although these individual experiences were not reported, no clinical complications were encountered. For divers at rest in the dry chamber, Behnke (5) stated that oxygen could be inhaled for three hours at a pressure of three atmospheres. One thousand, six hundred and forty nine chamber, oxygen-breathing exposures of resting adults at 2.8 to 3.0 atmospheres absolute are reported (21, 25, 44). Exposure time varied from 21 to 120 minutes, and was limited to 30 minutes in most instances. Fifteen subjects reported symptoms; there were 6 convulsions (0.36 percent). Acceptance of minimal risks of overt CNS oxygen toxicity can be justified. Prudent clinical management of recompression patients is, of course, essential. Exposure to oxygen partial pressure greater than 2.8 to 3.0 atmospheres is patently unrewarding (15). Pulmonary oxygen toxicity has not been encountered within permissible pressure-time dose limits (3, 4). Damage to adult ocular tissues has not been reported in man (2).

Intermittent breathing of oxygen and air (i.e., a low oxygen gas) at

increased pressure results in prolongation of the asymptomatic exposure duration. This phenomenon has been studied by Lambertsen (27, 30) and other workers (12, 26, 33), experimentally verifying earlier conjectural references (3, 8, 9).

Dartford Tunnel Criteria: The Level and Duration of Maximal Reapplication of Pressure

The final fifteen Type 2 cases (patients presenting with serious symptoms other than pain) which were encountered during the construction of the Dartford Tunnel obtained complete, permanent relief during initial treatment according to a schedule devised by Golding, Griffiths, Hempleman, Paton and Walder (23). The level of maximal reapplication of pressure was the tunnel working pressure or the minimal effective pressure to make the patient symptom free, and this pressure was maintained for 30 minutes following resolution of all signs and symptoms. A continuous-bleed, gradual ascent avoided large and abrupt pressure changes between stops. The authors noted, in conclusion, that, "Two general approaches may be made to the problem; in the first (as in the U. S. schedule for therapeutic recompression), one may choose high pressure in the hope of compressing any bubbles present and securing their rapid solution; the second approach is to keep the therapeutic pressure as low as possible, so as to minimize any contribution which absorption of nitrogen during the recompression itself may make to recurrence of the lesion".

Evolution of the Therapeutic Format

Provisional Formats

The original trial schedules (Table 21) provided for a 10 minute test of relief at 33 feet (minimal effective pressure), for a full treatment pressure exposure duration of relief time plus 30 minutes, and for decompression by continuous ascent at the uniform rate of one foot per minute. In provisional format number 3 the continuous ascent was interrupted with a 30 minute stop at 30 feet.

Maximal Recompression Depth and "Adequate" Treatment

With each individual case evaluation, the arithmetic mean value for each of the following parameters was recomputed both for the entire casualty caseload and for the therapeutic failure group: patient age, number of repetitive dives, maximal depth and total bottom time of dives, time to onset of symptoms, elapsed time prior to treatment, total treatment time, time at full treatment depth, and the level of maximal reapplication of pressure. A Fisher t-test (1) was used in analyzing for significance of the

TABLE 21

Evolution of Therapeutic Format

Format		Maximal Recompression Depth (ft.)	Time at Maximum Depth (min.)	Ascent Time (min.)	Oxygen Breathing Time (min.)	Total Time of Treatment (min.)
Provisional	(1)	33	30–40	33	63–73	63–73
	(2)	60	30–40	60	100–110	100–110
Provisional	(3)	60	40	60–90	100–130	100–130
"Minimal-adequate"		60	30	60	90	90
Provisional	(4)	60	40	90	130	130
	(5)	60	75	210	240	285
Current	(1)	60	45	90	120	135
	(2)	60	75	210	240	285

mean differences between these two groups. Thus, it became apparent that both the mean maximum recompression level (60 feet vs. 33 feet) and the mean oxygen breathing time at that level differed significantly between the two groups ($p < 0.001$ and $p < 0.01$, respectively). Time to complete relief correlated significantly with maximal recompression depth ($r = -0.52$, $p < 0.001$). All treatments were thereafter (and retrospectively) called "inadequate" unless the following requirements had been met: full treatment depth 60 feet, 30 minutes oxygen breathing at 60 feet, 90 minutes oxygen-breathing total treatment time.

Definitive Format (Table 21 and Fig. 49)

Along with oxygen-air alternations the therapeutic schedules were empirically extended in duration to one and one-half and three times that of the "least adequate" schedule. Clinical condition and the response to therapy govern treatment time within limits imposed, of course, by oxygen-exposure itself. No symptoms nor clinical entities representative of true oxygen intolerance have been encountered in the patient group or in the panel of normal volunteer subjects first exposed to the 285 minute schedule.

Tender in the Chamber

Adequacy and safety of compressed air exposures and decompressions of the tenders was predicted with modified Haldane computational procedures as described by Dwyer (19) and Workman (46). If the treatment

METHOD USED WHEN RELIEF OF SYMPTOMS IS COMPLETE WITHIN 10 MINUTES AT 60 FEET

DEPTH (FEET)	TIME (MINUTES)	BREATHING MEDIA	TOTAL ELAPSED TIME (MIN)
60	20	O_2	20
60	5	Air	25
60	20	O_2	45
60–30	30	O_2	75
30	5	Air	80
30	20	O_2	100
30	5	Air	105
30–0	30	O_2	135

METHOD USED WHEN RELIEF OF SYMPTOMS IS NOT COMPLETE WITHIN 10 MINUTES AT 60 FEET

60	20	O_2	20
60	5	Air	25
60	20	O_2	45
60	5	Air	50
60	20	O_2	70
60	5	Air	75
60–30	30	O_2	105
30	15	Air	120
30	60	O_2	180
30	15	Air	195
30	60	O_2	255
30–0	30	O_2	285

Commence O_2 breathing prior to compression Depth-time schedules should be followed with care.

Compression: Rapid compression is desirable, but do not exceed rate tolerated by patient. Compression time, usually 1–2 minutes, is not counted as time at 60 feet. Do not halt the compression to verify a report of symptom relief.

Decompression: Decompressions are continuous at uniform 1 f.p.m. Do not compensate for slowing of the rate by subsequent acceleration. Do compensate if the rate is exceeded. If necessary, halt decompression and hold pressure while ventilating the chamber.

Inside Tender: Tender routinely breathes chamber air. If treatment schedule is lengthened (see below), or if the treatment constitutes a repetitive dive for the tender, he must breathe O_2 for the final 30 minutes, from 30 feet to the surface.

Relief of Symptoms: If completeness of relief is at all doubtful after 10 minutes O_2 breathing at 60 feet use the 285 minute schedule. If symptoms recur, fresh symptoms appear, or the patient's condition worsens, return to 60 feet and use the 285 minute method.

If relief is not complete at 60 feet, proceed with the 285 minute schedule, observing closely for any changes of the patient's condition, or lengthen the schedule (see below), or recompress to 165 feet and commit the patient to U.S.N. treatment Table 2A, or Table 4 if symptoms are not relieved within 30 minutes.

A Medical Officer qualified in diving, or the Diving Supervisor (Diving Officer; Master Diver) may extend the 285 minute schdeule with a fourth O_2-air sequence (20 minutes O_2—5 minutes air) at 60 feet, or a third air—O_2 sequence (15 minutes air—60 minutes O_2) at 30 feet, or both.

FIG. 49. Recompression schedules and instructional summary for minimal-pressure, oxygen recompression treatment of decompression sickness in Diving-Manual type full-page format.

recompression constitutes a repetitive diving exposure for the tender, or if the 285 minute schedule is lengthened, the tender is obligated to breathe 100 percent oxygen during the final 30-minute ascent phase. (Other aspects of the training and duties of chamber attendants are discussed in reference 25.)

Results of Treatment

Data Acquisition

The total therapeutic experience of 114 cases of divers' decompression sickness, 3 incidents of altitude chamber or inflight dysbarism not relieved by descent to sea-level, and 10 instances of traumatic gas embolism (5 occurring in association with submarine escape training) represents contributions of eleven reporting agencies and institutions. Stubbs and Kidd (29, 37) have collected the numerically-largest series of cases. "The value to us of using the oxygen treatment table was incalculable—in fact, it was as a result of early delight with the efficacy of the table that we became bolder and extended the trials to provoke bends" (Kidd, D. J., personal communication). EDU/DSDS treated thirty patients. Because direct operational and clinical supervision of these cases has been exercised by nearly 25 individuals, it is concluded that the series represents a satisfactory field trial of the concept.

Tabulations

Nomenclature for Table 22 was introduced in prior paragraphs. The caseload size has been expanded by incorporating, first, ten recompressions of patients stricken with cerebral gas embolic syndromes and, finally, several instances in which minimal-pressure oxygen techniques were utilized but not formally reported to the Experimental Diving Unit.

Caseload Characteristics

The mean age of patients recompressed with minimal-pressure oxygen procedures was 31.3 years ($N = 96$). Fifty-three percent were age 31 or older. Seventy-seven percent ($N = 99$) of the antecedent dives fulfilled the criteria, heretofore listed, of "nonstandard" exposures. Compressed air was the breathing medium in all but 25 percent of the casualty-precipitating exposures. Eleven of the patients were stricken subsequent to, or during decompression from saturation dives. Nearly fifty-eight percent ($N = 56$) of this decompression sickness casualty group presented with serious symptoms, i.e., symptoms other than, or in addition to musculoskeletal, bends pain, or symptoms which occurred during decompression.

TABLE 22

Results of Treatment with the Minimal-Recompression, Oxygen Breathing Method

	Initial Recompressions	Relief Complete	Relief Not Complete	Relief Not Permanent	Percent Failure	Second Recompressions	Relief Complete
Decompression sickness							
All documented cases	107	97	4	6	9.3	9	8
"Adequate" treatment	59	58	1	0	1.7	1	0
"Serious" cases	55	50	2	3	9.1	4	3
"Serious" cases, "adequate" treatment	34	33	1	0	2.9	1	0
All documented recompressions	116	106	4	7	9.5	9	9
All experiences with minimal-recompression oxygen therapy	125	114	4	8	9.6	10	9

Caseload Comparisons

Selected descriptive parameters of casualty populations are compared in Table 23. Incidence levels for casualty group 1946–1961 were computed for the 888 patients recompressed, during that 16-year period, with standard U. S. Navy treatment tables (34). Two hundred and thirty-two treated cases of decompression sickness form casualty group 1962–1965. Both size and composition of this case group have, no doubt, been biased by, respectively, the number of patients submitted to alternative therapy and their preponderently nonconventional antecedent exposures. This is unfortunate because casualty group 1962–1965 is the only concurrent control population in apposition to the minimal-pressure oxygen treated cases. It is clear however, that minimal-pressure oxygen procedures have been tested more rigorously than would have been possible with random selection of patients for treatment.

Significance of Treatment Duration

Duration of U. S. Navy Tables

Van Der Aue and associates determined that the treatment schedules promulgated in 1943 (38, 39) could provoke decompression sickness in normal subjects who had been recompressed 30 or 60 minutes after surfacing from a 130 foot, 60 minute bottom time compressed air working dive (42).

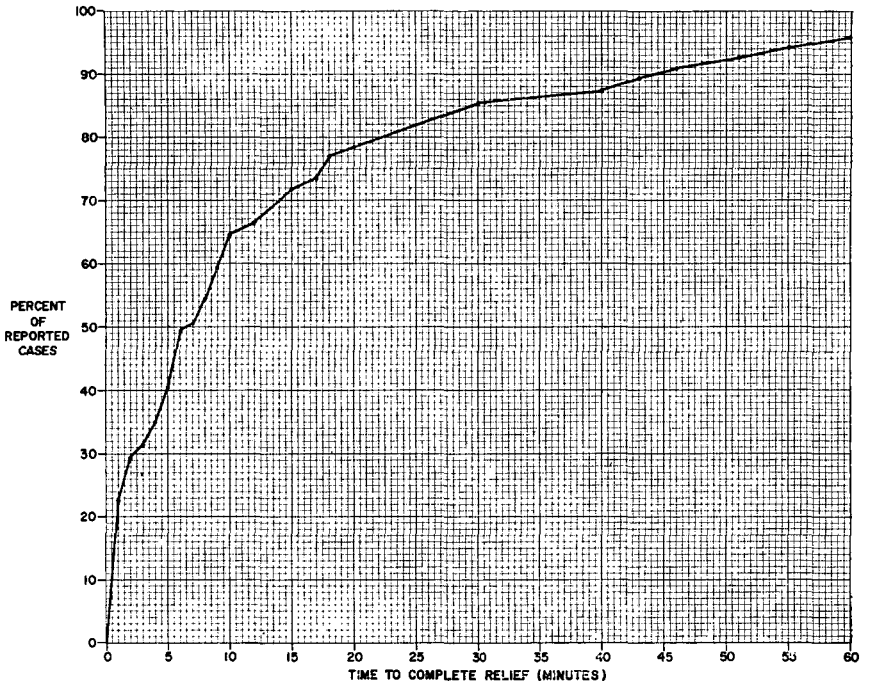

FIG. 50. Cumulative percent curve: elapsed time (minutes) required for symptom remission.

Current Navy treatment tables 2 and 2A were derived from, respectively, the BUMED 165 foot air-oxygen and 165 foot air recompression tables by serial testing and modification. Treatment tables which had been developed by Yarbrough and Behnke (43) were similarly tested, were considered to be satisfactory, and are today known as tables 1 and 1A.

The single progenitor of table 4 was 36.5 hours in duration, 24 of which were to be spent at 60 feet. Two-hour stops were proposed at 165, 50, 40, 30, 20 and 10 feet. The table was tested without a prior 130 foot dive. Four of the six normal subjects contracted decompression sickness from this table. The time under pressure was redistributed into the format of table 4, which did not provoke bends, although the entire panel of six subjects experienced inordinate post dive fatigue.

Thus, decompression adequacy for normal subjects has decisively influenced air treatment table duration.

Treatment duration and manpower employment.

By assuming that average treatment duration with tables 3 and 4 is 28 hours, and that five personnel comprise a treatment duty section it can

TABLE 23

Comparisons of Mean Caseload Characteristics, Case Severity Indices and Results of Initial Therapeutic Recompressions

	Incidence (%) within Each Casualty Group			No. of Cases Compared		Probability for Chi Square	
				O_2 Treatment Cases		O_2 Treatment Cases	
	O_2-treated Cases	1946–1961 Cases	1962–1965 Cases	and 1946–1961 Cases	and 1962–1965 Cases	and 1946–1961 Cases	and 1962–1965 Cases
Age distribution							
36–40	21.6	12.6	25.9	127	75	$P < 0.001$	$P < 0.30$
Over 40	11.4	3.8	10.8	45	35	0.001	0.80
"Non-standard" dives	77.8	31.1	54.7	367	204	0.001	0.001
Dive depth over 8 atm. abs. (231 feet)	42.1	13.7	17.2	164	77	0.001	0.001
Total time on bottom over 120 minutes	30.7	18.9	12.9	204	57	0.001	0.001
Symptoms appearing during decompression	21.6	7.9	3.9	103	28	0.001	0.001
Time between onset and treatment over 360 min	14.0	21.4	25.0	203	77	0.02	0.02
Cases with "serious" symptoms	57.6	24.4	43.5	277	161	0.001	0.02
Relief not complete or not permanent (First recompression)							
All cases	9.3	13.0	20.7	123	58	0.10	0.01
"Serious" cases	9.1	30.9	37.6	58	43	0.01	0.001

be shown that the 56 treatments in which minimal-pressure oxygen procedures supplanted long air tables were conducted by 12 percent of the treatment manpower customarily mobilized for air recompression. The total manpower conservation estimate for initial recompression plus retreatments (1964 retreatment frequency) is 10,600 man hours. Facilities limitations and the priority of treatment obligations have frequently curtailed the pace of research in diving and have influenced the scope and ambition of research projects and the logistics of diving operations. It is, therefore, nonutilization of manpower, not its conservation, which properly deserves attention. The above estimate is useful insofar as it emphasizes this important non-clinical consideration.

Altitude Decompression Sickness

The prognosis in severe subatmospheric decompression sickness which has not resolved prior to touchdown on the runway, or which has appeared

during or subsequent to descent is generally good, although initially the clinical course can be alarming. Neurocirculatory collapse, whether occurring acutely, as the presenting dysbarism syndrome or subacutely, as a supervening complication, can be lethal. With respect to older and overweight aviators the prognosis typically is guarded. Recompression to greater than sea-level pressure, usually as a last-resort maneuver, has been of life-saving significance for such patients (16). When employed as a treatment of choice, minimal-pressure oxygen and minimal-effective pressure air recompression have been impressive (11, 14, 24). There is no *a priori* requirement for the application of specific diver's recompression schedules in altitude cases. This current approach has been used four times; chokes and collapse were present together in three of these cases.

Conclusions

1) U.S.N. recompression procedures are dependable schedules for divers who have been stricken following exposures conducted in accordance with promulgated procedures.

2) Severe decompression sickness, occurring as a result of grossly insufficient decompression after compressed air diving, is often wholly or in-part refractory to conventional therapy.

3) The rising incidence of complicated and difficult recompression experiences can be related to particular segments of the diving-casualty population.

4) The minimal-pressure oxygen approach has consistently afforded prompt, complete and lasting relief in severe decompression sickness following conventional diving, saturation exposures, altitude ascents and repetitive series up to six dives.

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APPENDIX

Case Descriptions

Case No. E4

Dive 240 minutes at 70 feet, compressed air, moderate exertion. Diver age 34, moderately obese. About one hour after reaching the surface nausea, vertigo, malaise and generalized weakness appeared abruptly. During

physical examination, which disclosed pallor, tachycardia and progressing neuromuscular incoordination, the patient became acutely unresponsive and lost consciousness. He was rapidly recompressed to 60 feet, with oxygen breathing. Substantial subjective relief occurred within 4–5 minutes. Shortly afterward he was free of neurological deficits, and vital signs had stabilized. Total treatment time was 98 minutes, after which and throughout the evening hours the patient experienced unusual fatigue.

Case No. P4

Following is a summary of exposure data and the accumulated decompression obligation for a repetitive series of compressed-air SCUBA dives by a 33-year old civilian patient:

Dive No.	Depth (ft.)	Time (min.)	Ascent Time (min.)		Surface Interval (min.)	Residual N_2 Time (min.)
			Required	Actual		
1	60	30	1	1	55	—
2	110	5	5	1	15	16
3	165	20	81	2	15	17
4	165	20	152	2	5	34
5	165	20	152	3	1	35
6	70	15	52	2	—	100
Total			443	11		
Omitted			432			

Nausea and shortness of breath first appeared during the ascent from dive number four, persisted, and gradually increased in severity. Severe left shoulder pain began just after the last dive, followed by generalized muscular weakness and paresis of left leg muscle groups. There was spontaneous micturition. Consciousness was lost just prior to recompression, 75 minutes after completion of the sixth dive. Recovery seemed complete after 30 minutes of the 285 minute treatment.

Case No. P12

Dive 15 minutes at 172 feet, compressed air, deep-sea dress. Diver age 39. Ten minutes after surfacing the patient described generalized blurring of left-eye vision with loss of superior visual fields, and bends pain localized to the left buttock. The left pupil was dilated and unresponsive. Resolution was complete during the initial minutes of the 130 minute long treatment exposure.

18 | CLAES E. G. LUNDGREN

Relations between Bends Symptoms and Tissue Gas Saturation

In defining efficient decompression procedures we continue to place emphasis upon the degree of oversaturation with inert gas which is permissible in tissue phases with faster and slower gas exchange.

When decompression profiles are theoretically considered, an interesting question concerns the extent to which tissues with sub-critical gas content contribute to defining the critical value of that tissue phase which is considered the limiting one at any particular stage of the decompression. Another question relates to whether the nature of the distribution of the oversaturation in the half-time spectrum correlates with the severity or type of the symptoms when decompression sickness is provoked. In order to shed some light on these problems experiments are now being performed on goats in which selective oversaturation of different tissue phases is attempted. For the slow tissue phases this is done by a combined procedure of air breathing at high pressure and depressing the nitrogen content of the fast phases by oxygen breathing for a period preceding the decompression. Selective oversaturation in fast tissues is made in high air pressure after a relatively long period of pre-oxygenation which depresses the basal gas content of the slow tissues.

Following the exposure to a compressed gas atmosphere, provocation of symptoms is attempted by decompressing the animals to 520 mm Hg, or 0.68 atmospheres. The reason for doing so is twofold. By working with the compressed gases at a relatively low average positive pressure level we hope to reduce the risk of oxygen toxicity and when decompression sickness occurs it is possible to carry out the treatment at a comparatively moderate pressure level.

Methods

The goats are trained to wear a breathing mask for several hours. The mask which has a dead space of about 30 ml is sealed around the shaved

nose of the animal by an inflatable cuff. The pressure in the cuff is kept constant irrespective of variations in chamber pressure by means of a small but continuous flow of gas to the cuff, letting excess gas bubble out through a water bottle against a resistance of 30 cm of water.

The animals breathe from a demand valve which is supplied with different breathing mixtures through control valves on the outside of the pressure chamber. On the expiration side of the mask a gas sample is continuously collected for analysis of the nitrogen content by an electronic nitrogen meter. In this way the tightness of the mask, which is very important in the oxygen breathing periods, can be verified. It should be added that the tightness is often so good that it permits quantitative studies of the inert gas elimination.

Compression is made at a rate of 1.0 atmosphere per minute, decompression at 1.5 atmospheres per minute except when going from surface to altitude when it is made in one minute (0.32 atmosphere/minute). During the whole time of exposure and observation the animal is restrained by a loosely fitting wooden collar. The animals are recompressed as soon as unmistakable symptoms of decompression sickness appear or otherwise after one hour of observation. They are allowed at least 7 days off between experiments.

Figure 51 shows how the sums of gas tensions compare with the ambient pressure of 520 mm Hg (ordinate) in different tissue fractions defined by their half-saturation times (abscissa). Seven different types of exposures, designed to give oversaturation peaks in different parts of the half-time spectrum, have been tried so far. To calculate the gas tensions in different half-time fractions the nitrogen elimination or uptake was conveniently derived from a semilogarithmic graph of saturation percentage versus time on which exponential patterns of different half-time phases appear as straight lines. The gas tensions include both nitrogen, which is the variable, and an additional 135 mm Hg for the "physiological" gases (oxygen, carbon dioxide and water vapour). In the calculations it is assumed that the gas uptake and elimination follow exponential courses, that the half-times of various tissues remain constant and also that the tensions of the physiological gases stay within their normal limits. The time spent in compression and decompression is not taken into account in the calculations. The nature of the special exposure and decompression procedures used, leading to the oversaturation/saturation profile curves shown in Figure 51, was as follows:

Curve I describes exposing the animal to air breathing at 3.5 atmospheres for 120 minutes and decompression to 520 mm Hg.

Curve II is obtained when decompression is made after air breathing at 4.2 atmospheres for 120 minutes followed by oxygen breathing during pressure reduction from 2.8 to 1.5 atmospheres in 30 minutes.

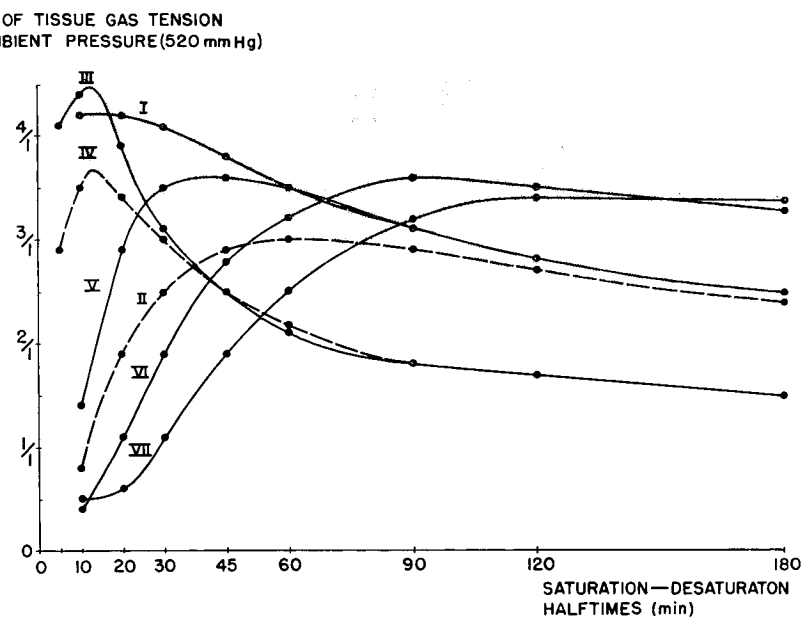

FIG. 51. The curves labelled I to VII illustrate the patterns of oversaturation with inert gas in relation to ambient pressure (ordinate) as distributed in the spectrum of half-time tissue phases (abscissa) after decompression from the different exposures to oxygen and high air pressures described in Table 24. The interrupted lines indicate no occurrence of decompression sickness; the solid lines indicate that decompression sickness occurred. The shaded area represents levels of over-saturation likely to cause symptoms. For details of exposure programs and results, see text and Table 24.

The pattern of Curve III results from pre-oxygenation at 1.0 atmosphere for 120 minutes followed by air at 5.0 atmospheres for 30 minutes and another 5 minutes of air at 2.0 atmospheres to avoid very high oversaturation in the blood and very fast tissues.

The oversaturation profile shown by Curve IV is essentially the same as that of III, except that its peak is further reduced by extending the final stage of air breathing at 2.0 atmospheres to 15 minutes.

Curve V results from air breathing at 6.0 atmospheres for 70 minutes and oxygen breathing as the pressure is reduced from 2.5 to 1.3 atmospheres in 25 minutes, followed by decompression.

Profile VI describes the probable effects of air breathing at 6.0 atmospheres for 160 minutes, followed first by oxygen inhalation while the pressure is reduced from 3.7 to 1.9 atmospheres in 60 minutes and then by the standard decompression to 520 mm Hg.

Curve VII is the result of air breathing at 6.4 atmospheres for 200 minutes followed by oxygen administration while the pressure is reduced from

4.0 to 2.8 atmospheres in 25 minutes, then by air breathing for 10 minutes at 2.5 atmospheres to reduce the risk of oxygen intoxication and finally oxygen breathing at the same pressure for 65 minutes before decompression.

Results

Exposure of goats to the conditions upon which the curves of Figure 51 were based provided the following results:

The exposures related to Curve I resulted in bends in a total of 9 experiments and freedom from symptoms in one. It is therefore considered a "bend-profile."

Fourteen exposures on 6 goats according to Curve II produced no symptoms in 12 cases, whereas 2 developed bends. However, these two cases are not representative since a leak in the breathing mask gave a fluctuating nitrogen admixture of about 10 percent during the oxygen breathing. Accordingly Curve II is considered a no-bend curve (marked by an interrupted line in Figure 51).

A dangerous pattern is shown by Curve III as 5 experiments out of 9 in 5 animals resulted in bends.

Curve IV with much the same form as Curve III but a lower peak, was tried in 7 experiments on 7 goats. No symptoms occurred in 5 cases and bends in 2 cases. One of the bends cases, however, fell outside the curve pattern due to considerable mask leakage. We have chosen to call this (Curve IV) a no-bend curve as compared to the others, not on the basis of statistics but of philosophy.

In 4 animals in which oversaturation was produced according to Curve V, 4 experiments ended with bends. This was a dangerous pattern even though one of the results should probably be omitted due to mask leakage.

When tried in 5 goats, Curve VI resulted in bends in 5 cases and no symptoms in 2. This makes it a "bend profile" as well.

With the saturation program related to Curve VII one experiment was symptom-free and 3 gave bends in 4 animals. Therefore this is also a dangerous saturation pattern.

From Table 24 it is evident that the results obtained on goats 2, 5 and 6, which were used through all the different exposures, are confirmed by those on the other animals as long as the results are only used to judge whether an exposure may produce bends or not.

Discussion

One of the most important questions to be considered in interpreting this study is the degree of reliability of the calculated values upon which

TABLE 24

Description and Results of Decompression of Goats to 520 mm Hg following Various Exposures to Oxygen and Air at High Pressures

Figures within brackets should be disregarded due to mask leakage.

Curve	I		II		III		IV		V		VI		VII	
Exposure before decompression to 520 mm Hg	Air at 3.5 atm for 120 min.		Air at 4.2 atm for 120 min, then O_2 at 2.8–1.5 atm for 30 min.		O_2 at 1.0 atm for 120 min, then Air at 5.0 atm for 30 min, then Air at 2.0 atm for 5 min.		O_2 at 1.0 atm for 120 min, then Air at 5.0 atm for 30 min, then Air at 2.0 atm for 15 min.		Air at 6.0 for 70 min, then O_2 at 2.5–1.3 atm for 25 min.		Air at 6.0 for 160 min, then O_2 at 3.7–1.9 atm for 60 min.		Air at 6.4 atm for 200 min, then O_2 at 4.0–2.8 atm for 25 min, then Air at 2.5 atm for 10 min, then O_2 at 2.5 atm for 65 min.	
Total number of goats	6		6		5		7		4		5		4	
	Number of Experiments with		Number of Experiments with		Number of Experiments with		Number of Experiments with		Number of Experiments with		Number of Experiments with		Number of Experiments with	
	No Symptoms	Symptoms	No Symptoms	Symptoms	No Symptoms	Symptoms	No Symptoms	Symptoms	No Symptoms	Symptoms	No Symptoms	Symptoms	No Symptoms	Symptoms
Goat #:														
2		3	3		2	2	1			1	2		1	
5		2	2	(2)	1		1			(1)		2		1
6		1	4		1	1	1			1		1		1
13	—	—	—	—	—	—		(1)		1		1		1
18	1	1	1		—	—	1		—	—		1	—	—
21		1	1			1	1		—	—	—	—	—	—
22		1	1			1		1	—	—	—	—	—	—
Total number of experiments	1	9	12	(2)	4	5	5	1 (1)	0	3 (1)	2	5	1	3

the curves in Figure 51 are based. The position of their maxima along the horizontal axis is somewhat uncertain. High inspired oxygen pressures lead to a lowering of the rate of blood flow through the brain, and the reduction of flow in resting skeletal muscle at 2 atmospheres of oxygen is known to amount to about 28 percent (1). While an effect of oxygen upon blood flow does not seriously limit the oxygen treatment of bends (2), quantitative knowledge of the possible changes that oxygen may induce in all the different half-time tissue fractions is too sparse to provide for adjustment of calculated rates of uptake and elimination of inert gas in various tissue compartments. The fact that blood flow is altered by high oxygen pressures should probably not influence the experiments related to Curves I, III and IV in which hyperbaric oxygen has not been extensively used.

Another serious question is the possibility that oxygen is a contributing factor in bubble formation. Such an effect of oxygen in combination with nitrogen in the inhaled gas has been shown to exist in goats by Donald (3) and Hempleman (4). However, from experience in both diving and aviation physiology it is known that the administration of oxygen is an excellent method of rendering the subject insensitive even to very rapid decompressions. During decompression the elimination of high oxygen tensions in tissue fractions with short half-times can obviously be effected both by wash out and metabolic elimination.

The empirical fact that high oxygen tensions in long half-time areas do not usually give rise to bends is suggested by Hempleman (4) to depend on diffusion from slowly perfused tissue phases to more vascular ones. In this connection the possibility should also be remembered that bubbles formed in the fast or slow tissues do not necessarily give rise to symptoms (so-called silent bubbles). Development of high oxygen tensions in the tissues is not likely to be a problem in connection with exposures of Types I, III and IV, since high oxygen pressures are not inhaled. With the oversaturation patterns of Curves II, V, VI and VII the oxygen pressure in the fractions with short half-times would probably still not add much to the tissue gas tensions, in spite of oxygen administration. In a resting muscle, for instance, with a perfusion of 30 ml of blood per kg of tissue and an oxygen consumption of 1.6 ml per minute the physically dissolved oxygen at 2.5 atmospheres will barely be enough for the metabolic requirements, leaving a tissue oxygen tension well below 100 mm Hg.

In the right-hand parts of Curves II, V, VI and VII representing the slow tissue fractions, the conditions necessary to build up high oxygen tensions are more likely to exist. The levels of oversaturation indicated in these parts of the curves are not entirely certain. However, the shaded area in Figure 51 indicates what seem to be dangerous levels of oversaturation

under the conditions of the present study. It is to be hoped that more tests and other curve patterns will confirm this.

The fact that the lower boundary zone of the shaded area is sloping is only to be expected, although the exact angle is not yet known. Judging from diving experience it is probably a bit surprising that such degrees of oversaturation as it indicates are tolerated in the slow phases (up to 3:1 in Curve II for instance). It may be that these experiments demonstrate a higher overall decompression tolerance at the average pressure levels studied than is found under genuine diving conditions. There is some support for such a view in high altitude research but it should be remembered, on the other hand, that experience from saturation dives indicates a higher tolerance for oversaturation when one is working at high average pressure levels.

One thing seems to emerge rather clearly from these experiments. It appears that decompression sickness may originate from oversaturation in a wide spectrum of half-time tissue phases and also when fractions adjacent to the critical one are rather low in gas tension. Furthermore, it appears that the amount of nitrogen available in the phase with oversaturation may not *per se* determine whether symptoms will appear or not. Though the nitrogen volumes related to Profiles II and III have not been measured, it seems reasonable to assume that Curve II which does not produce symptoms is the more rich in gas of the two.

When the threshold of permissible oversaturation is exceeded in a tissue phase, its half-time and/or nitrogen content will probably determine the type of symptoms that appear. With the oversaturation patterns of Curves I, III and V, there have always occurred clearcut joint bends which do not seem to influence the animals' general condition seriously, and they gladly accept food. With Curves VI and VII the animals usually rapidly lose interest even in their favorite food and, besides bends, they often show restlessness, very high breathing frequencies, weakness in the legs or fully developed paraplegia, and a number of other symptoms which we do not yet understand.

It is possible that the pain sensitive nerves affected by bends are located in structures with such varying half-times as are indicated here. The diffusion dependent intra-articular cartilages discussed by Hempleman (4) are one example. It is also conceivable that the joint region is particularly likely to trap emboli which then grow to a size which produces symptoms. Finally, as found when the oversaturation pattern approaches that of Curves VI and VII, oversaturation in slow tissue phases with high storage capacity for inert gas and for oxygen may be the source of more massive embolism, resulting in the much poorer condition of the animals and in the symptoms from the central nervous system.

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19 | HUGH D. VAN LIEW

Factors in the Resolution of Tissue Gas Bubbles

Diffusion, the spontaneous movement of a gas from a region of high partial pressure to regions of lower partial pressure, is the fundamental process by which gas leaves the gas bubbles of decompression sickness and air embolism.

It is therefore reasonable to approach the problem of bubble resolution by attempting to extend the basic theory of diffusion so that it applies to decompression bubbles. Background for this approach has come from studies of gas diffusion into and out of subcutaneous pockets in rats (Fig. 52).

Let us visualize a thin unstirred layer or shell of fluid surrounding a gas bubble. The partial pressure of a particular gas, x, dissolved on the gas interface side of this shell is P_{i_x}, the same as the partial pressure inside the bubble. The partial pressure of dissolved gas in the bulk of the fluid outside the shell is P_{o_x}. Flux of gas by diffusion, expressed as the volume of the gas (corrected to standard conditions) which crosses the shell per unit of time, $dV_{x(s)}/dt$, is inversely proportional to L, the thickness of the shell. Flux is directly proportional to α_x, the solubility of gas x in the shell, to A, area of the shell, which approximates surface area of the bubble, and to the concentration difference of gas from one side of the shell to the other. Since concentration equals $\alpha_x P_x$, concentrations can be expressed as partial pressures. In a steady state in which partial pressures inside and outside do not change, flux across the shell equals flux out of the bubble, therefore equation 1 gives the rate of exit of gas x from the bubble, with volume of x expressed at standard conditions.

$$\frac{dV_{x(s)}}{dt} = \frac{(-K'_x)\ (\alpha_x)\ (A)\ (P_{i_x} - P_{o_x})}{L} \qquad (1)$$

The negative sign of the right of equation 1 signifies that the volume of gas x inside the bubble decreases when pressure inside, P_{i_x}, exceeds pressure outside, P_{o_x}.

The coefficient K'_x in equation 1 is a "true" diffusion coefficient with units

FIG. 52. Rat with gas pocket formed by injecting 30 ml of air into the subcutaneous tissue on the back. This preparation can be used to measure rate of diffusion from the gas phase into the tissue (7, 9), and therefore can be considered a model for study of decompression sickness bubbles (11).

of cm^2/min (2). Units of the solubility coefficient, α_x, are ml of gas (STPD) per ml of fluid per atmosphere of partial pressure of gas x (2).

Probably the most significant information about a decompression bubble is its diameter. The diameter will determine whether or not the bubble blocks a blood vessel, and it should determine the amount of tissue distortion or damage due to an extravascular bubble. Fortunately, restatement of the gas diffusion law, equation 1, in terms of bubble diameter leads to relatively simple equations. These equations provide a theoretical basis for consideration of bubble resolution in terms of the anticipated pressure differences responsible for diffusion. The validity of the theory depends on how nearly the diffusion of gases in a decompression bubble can be described by equation 1, which assumes a nonstirred diffusion barrier with perfect stirring beyond.

The major advantage of the present approach over previous mathematical theories concerning decompression bubbles (5, 6) is that these equations concentrate on diffusion of N_2, the major component of bubbles in an air-breathing subject. This allows the equations to account for the gradual resolution of a bubble due to the N_2 partial pressure difference between the

bubble and the tissue which can be expected at any specific environmental pressure (3, 11). With appropriate substitutions, the equations could apply to other gases such as He.

In any situation where measurements are possible, gases in depots or pockets within the body have been found to come to a steady state or state of constant composition where each gas remains at the same gas tension even though the total volume of gas decreases (3, 10). The final equations presented here can be applied most easily in this steady state when pressures in the bubble, tissue and blood are not changing. Two situations in which a steady state does not exist are dealt with only qualitatively: a) when the tissue is becoming saturated with inert gas immediately after recompression, and b) when bubble diameter is so small that surface tension increases the pressure inside the bubble, thereby facilitating outward diffusion.

Derivation

The discussion is limited to air-breathing or to O_2-breathing subjects. The major assumption is that equation 1 is applicable. In addition, it is necessary to assume a) that since N_2 is the major gas in the tissue and in bubbles in the body of air-breathing subjects, consideration of N_2 alone gives an adequate description of the total bubble, which in fact must contain O_2 and CO_2 at levels near those found in nearby tissues (11); and b) that the bubble is spherical so that volume, V, equals $\pi D^3/6$, where D is diameter, and area, A, equals πD^2. Absorption predictions based on a spherical bubble are always conservative since absorption will be faster in other configurations which all have larger surface areas per unit of volume.

The first steps are to restate equation 1 in terms of N_2 and then to obtain volume in terms of total volume, rather than N_2 volume. Let F_{N_2} be the fraction of the total volume, $V_{(s)}$, that is N_2. The identity

$$V_{N_2(s)} = [F_{N_2}]\,[V_{(s)}]$$

can be differentiated to give

$$dV_{N_2(s)}/dt = F_{N_2}\, dV_{(s)}/dt.$$

The implicit assumption that F_{N_2} does not change with time appears to be valid for practical purposes; data with subcutaneous gas pockets showed N_2 fraction or partial pressure to be stable following an adjustment of a few per cent which was completed approximately ½ hour after change of environmental pressure (11). Substitute the derivative into equation 1 to obtain

$$\frac{dV_{(s)}}{dt} = \frac{(-K'_{N_2})\ (\alpha_{N_2})\ (A)\ (P_{i_{N_2}} - P_{o_{N_2}})}{(L)\ (F_{N_2})} \qquad (2)$$

Next, $V_{(s)}$ is replaced by ambient volume V with the Boyle's law relation $V_{(s)} = PV/P_s$, where P is total pressure inside the bubble (which is close to ambient pressure in soft tissues) and P_s is standard pressure. Differentiation gives

$$\frac{dV_{(s)}}{dt} = \frac{P}{P_s}\frac{dV}{dt}$$

which assumes that P is constant. Thus the equations which follow apply only at a given degree of compression, not to situations in which total pressure inside the bubble changes with time. The new equation is then

$$\frac{dV}{dt} = \frac{(-K'_{N_2})\,(\alpha_{N_2})\,(P_s)\,(A)\,(P_{i_{N_2}} - P_{o_{N_2}})}{(L)\,(F_{N_2})\,(P)} \tag{3}$$

Finally, P is replaced by $P_{i_{N_2}}/F_{N_2}$ (total pressure inside equals N_2 pressure divided by fraction of N_2). The F_{N_2} terms cancel leaving:

$$\frac{dV}{dt} = \frac{(-K'_{N_2})\,(\alpha_{N_2})\,(P_s)\,(A)\,(P_{i_{N_2}} - P_{o_{N_2}})}{(L)\,(P_{i_{N_2}})} \tag{4}$$

Equation 4 expresses the rate of volume change of a bubble of any configuration and at any pressure as a function of seven items. All are independent of the size of the bubble except area, which of course changes with volume. It is desirable to have an equation in which a term related to the size of the bubble appears only once. This is done by introducing the equations for volume and area of a sphere, and thereby restricting the applicability of the equations to a spherical bubble.

Differentiate the equation for volume of a sphere:

$$dV/dt = (\tfrac{1}{2})\pi D^2 dD/dt. \tag{5}$$

Substitute equation 5 and the equation for area of a sphere into equation 4. The result can be simplified considerably because πD^2 terms cancel.

$$\frac{dD}{dt} = \frac{-2K'_{N_2}(\alpha_{N_2})\,(P_s)\,(P_{i_{N_2}} - P_{o_{N_2}})}{(L)\,(P_{i_{N_2}})} \tag{6}$$

The difference of P_{N_2} between inside and outside of the bubble, $(P_{i_{N_2}} - P_{o_{N_2}})$, will be termed ΔP_{N_2}, or in the steady state, $\Delta P'_{N_2}$.

Equation 6 still has seven items on the right, but all are independent of bubble size. The equation contains gas partial pressure terms and constants of two kinds: Those that are always constant by definition (2, K'_{N_2}, and P_s), and those that may vary from one situation to another depending on the location and condition of the bubble (α_{N_2} and L). For simplicity all the constants can be combined to give a new constant, K_{N_2}, which can be called the coefficient for diameter rate change.

$$K_{N_2} = \frac{2(K'_{N_2})\ (\alpha_{N_2})\ (P_s)}{L} \tag{7}$$

With use of equation 7, the diameter rate equation becomes

$$\frac{dD}{dt} = \frac{-K_{N_2}(P_{i_{N_2}} - P_{o_{N_2}})}{P_{i_{N_2}}}$$

or

$$\frac{dD}{dt} = \frac{(-K_{N_2})\ (\Delta P_{N_2})}{P_{i_{N_2}}} \tag{8}$$

Thus rate of change of diameter is proportional to ΔP_{N_2} divided by $P_{i_{N_2}}$. The coefficient K_{N_2} does not change with pressure.

Significance of the Diameter Rate Equation

There are three very important points regarding equation 8. First, where the P_{N_2} values do not change with time—the steady state—the bubble decreases in a simple linear fashion with time and equation 8 can be integrated to give:

$$D = D_0 - K_{N_2} \frac{P_{i_{N_2}} - P_{o_{N_2}}}{P_{i_{N_2}}}\ (t)$$

or

$$D = D_0 - K_{N_2}\ [(\Delta P_{N_2})/P_{i_{N_2}}](t) \tag{9}$$

where D_0 is diameter of the bubble at time zero.

Second, the rate of change of diameter has a simple relation to the N_2 partial pressures under all conditions: The rate is directly proportional to the difference of partial pressure, ΔP_{N_2}, between the inside and outside of the bubble (because the greater the driving pressure for N_2 diffusion, the more will exit from the bubble), and the rate is inversely proportional to the N_2 partial pressure inside (because the greater the pressure inside the bubble, the less the bubble diameter will change for a given number of molecules of gas that diffuse out). We have maintained (11) that in an animal or man the ΔP_{N_2} in the steady state, or $\Delta P'_{N_2}$, is mainly a function of arterio-venous, or arterio-tissue oxygen difference, and Figure 53 shows predictions of $\Delta P'_{N_2}$ values for various ambient pressures. With predictions of $\Delta P'_{N_2}$ and equation 8, one can predict relative rates of bubble resolution in the steady state under different pressures without knowing most of the factors about the bubble—its original size, where it is in the body, the length of the diffusion path from bubble to blood, the solubility of the gas in the particular tissue, etc. Thus, when discussion is confined to the relative ef-

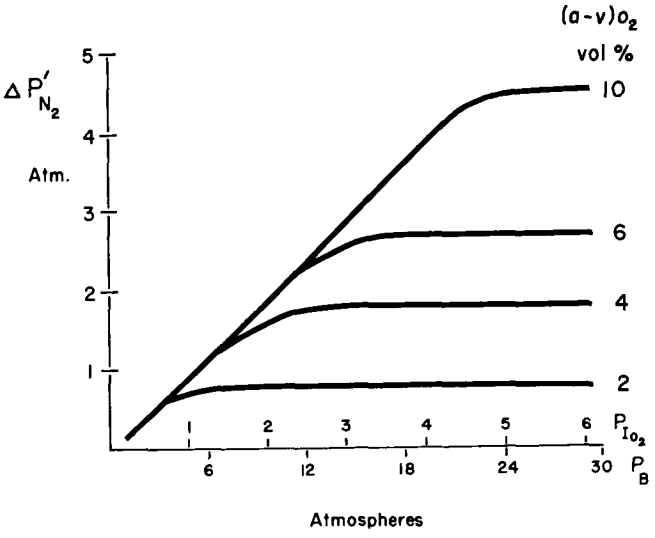

FIG. 53. Theoretical predictions of $\Delta P'_{N_2}$, the steady-state P_{N_2} difference between the inside and outside of a decompression bubble (adapted from (11)). The $\Delta P'_{N_2}$ is plotted against atmospheres during compression with air (lower abscissa), or atmospheres of O_2 during hyperbaric oxygen treatment (upper abscissa). The $\Delta P'_{N_2}$ depends mainly on arteriovenous O_2 difference, which increases with an increase of inspired O_2 brought about either by pressurization with air or by O_2 at high pressures. Therefore ΔP_{N_2} increases with pressure or O_2 until it reaches a maximum which is greater in tissues with a high arteriovenous O_2 difference than in tissues with less O_2 extraction. The curve is level when hemoglobin of venous blood is saturated, that is, when tissue O_2 needs are met by dissolved O_2.

fects of pressures and pressure changes under conditions otherwise constant, the absolute value of K_{N_2} is unimportant.

For example, the rate in an air-breathing subject at 1 and 4 atmospheres can be compared. Nitrogen partial pressure in the bubble approximates barometric pressure minus the pressures of the other gases present, which in turn approximate tissue gas tensions (11). If we assume that tissue P_{O_2}, P_{CO_2} and P_{H_2O} are 46, 53, and 47 mm Hg respectively, then their total is 146 mm Hg and bubble P_{N_2} at 1 atm will be 760 − 146 = 614 mm Hg, or 614/760 = 0.81 atm. Tissue nitrogen pressure, assuming equilibrium with blood P_{N_2}, will be equal to alveolar P_{N_2}, which in turn will be the barometric pressure minus alveolar P_{O_2}, P_{CO_2} and P_{H_2O}. Assuming values of 100, 38, and 47 mm Hg, we find 760 − 185 = 575 mm Hg, or 575/760 = 0.76 atm. Thus ΔP_{N_2} = 0.81 − 0.76 = .05 atm, and the fraction in equation 8 is .05/.81 = .062.

When breathing air at 4 atm, the only significant change expected in gases other than N_2 will be elevation of alveolar P_{O_2} by approximately 500

mm Hg or 0.66 atm. The ΔP will thus increase from .05 to 0.71 (Fig. 53), while $P_{i_{N_2}}$ reflects the 3 atm elevation of ambient pressure and becomes 3.81. The fraction is thus 0.71/3.81 = .186. Thus the rate at 4 atm will be .186/.062 = 3 times greater than the rate at 1 atmosphere.

Maximal Rate

The third point about equation 8 is that in any situation where partial pressure of N_2 outside the bubble, $P_{o_{N_2}}$, is very small compared to partial pressure inside, $P_{i_{N_2}}$, the rate of diameter change becomes constant and essentially independent of the N_2 partial pressures. When $P_{o_{N_2}}$ is zero, as will occur eventually with oxygen-breathing, ΔP_{N_2} becomes equal to $P_{i_{N_2}}$, so the fraction is equal to 1, and the rate of diameter change becomes a function of K_{N_2} alone, and therefore constant.

Actually there are two ways in which the maximal rate may occur. Restate equation 8 as

$$\frac{dD}{dt} = -K_{N_2}\left[1 - \frac{P_{o_{N_2}}}{P_{i_{N_2}}}\right] \tag{10}$$

When the P_{N_2} ratio at the right of equation 10 approaches zero, the rate dD/dt approaches $-K_{N_2}$, where K_{N_2} is a constant, defined by equation 7. There are two different situations in which the P_{N_2} ratio approaches zero: a) if $P_{o_{N_2}}$ falls close to zero during O_2-breathing and b) when $P_{i_{N_2}}$ becomes very large during the "surface tension squeeze."

The concept of a maximal rate which is a constant and independent of the degree of compression can be explained as follows: When the effect of N_2 pressure outside is minimized, N_2 pressure inside increases in direct proportion to the total pressure or level of compression. Since the diameter rate is inversely proportional to pressure inside as well as directly proportional to the driving force for N_2, the two effects cancel each other. In other words, an increase of driving force under compression increases N_2 diffusion but the effect is exactly balanced by the fact that under pressure it takes a greater flux of gas molecules to produce a given change of diameter.

Equations 8 and 9 apply very well to work of Wyman, Scholander, Edwards and Irving in a study of air bubbles perfused by sea water (12). Their experimental data show all three points predicted from the equations. At any depth the bubble diameter decreased linearly with time after an initial adjustment period in which O_2 exit caused a slight increase in rate, and the rate of decrease at various depths was proportional to the difference (P_{N_2} in the bubble minus P_{N_2} in the water) and inversely proportional to P_{N_2} in the bubble. Finally, the rate approached a maximal rate at high pressures when P_{N_2} outside was small compared to P_{N_2} inside.

Actual values for the maximal rate are available in experimental situa-

tions. A bubble in well-stirred water probably has a relatively high potential for rapid resolution. Data of Wyman et al (12) show the maximal rate to be 100 micra per minute. A much slower rate of bubble decrease can be predicted from measured rates of gas efflux from permanently-maintained subcutaneous gas pockets of known surface area, 4.5 μ/min (9). The reason why the value from subcutaneous pockets was $\frac{1}{20}$ the value of the water may be that the subcutaneous pockets have a much larger effective diffusion distance than the water.

These values mean that in an O_2-breathing subject, a bubble of 200 micra diameter might disappear in two minutes or 44 minutes depending on whether it was in a well-stirred fluid or in a location analogous to the subcutaneous gas pockets.

Rate with Air vs Maximal Rate

In connection with equation 10, one can think of the rate of diameter change under any steady-state condition as being equal to a fraction of its maximal rate, the fraction being $(1 - P_{o_{N_2}}/P_{i_{N_2}})$ or $(P_{i_{N_2}} - P_{o_{N_2}})/P_{i_{N_2}}$. For example, at 6 atmospheres breathing air $(1 - P_{o_{N_2}}/P_{i_{N_2}})$ might be $1 - 4.8/5.8 = 1 - 0.83$, so $dD/dt = -0.17\ K_{N_2}$ or 17 % of the maximal rate.

Since the maximum rate equals the diameter-rate coefficient K, which is directly proportional to the diffusion coefficient and solubility of the gas (see equation 7), a bubble of a gas with high product of K times α, such as helium, would have a higher maximal rate.

Figure 54 shows how the rate of diameter change, expressed as fraction of its maximal value, varies with increasing compression in an air-breathing subject. The values are obtained by dividing predictions of $\Delta P'_{N_2}$ for (a-v)O_2 of 6 vol % and 4 vol % (Fig. 53) by appropriate estimates of $P_{i_{N_2}}$. The rate increases sharply up to about 3 atm, then declines slowly until ΔP_{N_2} reaches its maximum (at about 15 atm in the 6 vol % example and 8 atm in the 4 vol % example), then descends along a hyperbolic course. The highest value of the fraction in Figure 54 is only about 0.2 or 20 % of the possible maximal rate which is obtained when the subject breathes oxygen. Since the $\Delta P'_{N_2}$ curves of Figure 53 become level at higher values and to the right of the figure, when (a-v)O_2 values are greater, the fall from the plateau of the fraction curve of Figure 54 will be higher and to the right also. For example the fall for 10 vol % (a-v)O_2 does not occur until 24 atm.

Phases of Bubble Resolution

A complicating factor that occurs in recompression treatment of decompression sickness is that with air-breathing the dissolved N_2 pressure outside the bubble is not constant; it rises at first as the tissues saturate with N_2

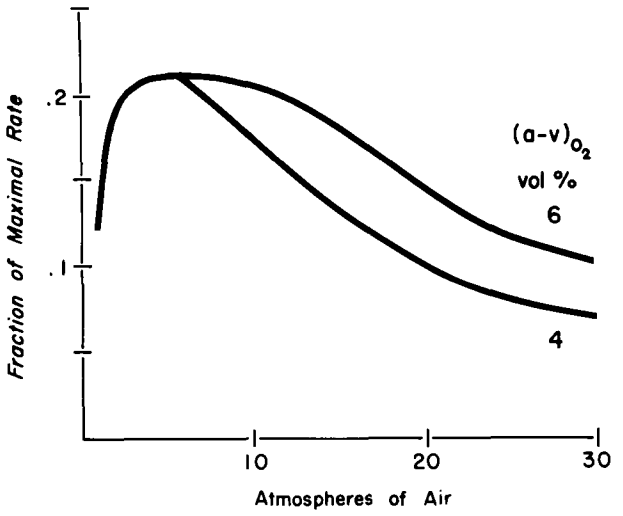

FIG. 54. In an air-breathing subject, predicted rate of change of diameter of a decompression bubble vs pressure. The rate is expressed as fraction of the maximal rate that could be obtained if N_2 in the tissue were zero, as is the case after a period of O_2 breathing. Curves are shown for tissues having two different arteriovenous O_2 differences. The curves were obtained by dividing $\Delta P'_{N_2}$ values from Figure 53 by estimates of $P_{i_{N_2}}$. The rate here is only 10% to 20% of the maximal rate. A fraction of only 0.06 at 1 atmosphere was obtained in a text example by use of slightly different assumptions.

at the new level, but eventually a new steady state is reached. This is illustrated in Figure 55. Of course a true case of bends may be more complicated because the tissue may still contain gas from the initial compression.

The process of resolving a decompression bubble in an air-breathing subject can be divided into four phases. Figure 56 is a sample curve showing time vs diameter of a hypothetical bubble in an air-breathing subject. In phase I, the subject is compressed to 4 atm abs and bubble diameter decreases because of simple physical compression of the gas. In phase II, absorption occurs at a rate which decreases with time as the tissue around the bubble saturates with N_2. In phase III, the steady state, the diameter continues to decrease under the influence of ΔP_{N_2}, but since tissue P_{N_2} has stabilized (ΔP_{N_2} equals $\Delta P'_{N_2}$) the rate is linear with time. The last phase, where surface tension becomes important, is indicated by the dashed curve at the right in Figure 5.

Details of the four phases will be taken up in reverse of the order in which they occur. The effect of surface tension is to increase the N_2 partial pressure inside the bubble, $P_{i_{N_2}}$. As mentioned in connection with equation 10, the rate approaches a constant value which is independent of the N_2 pres-

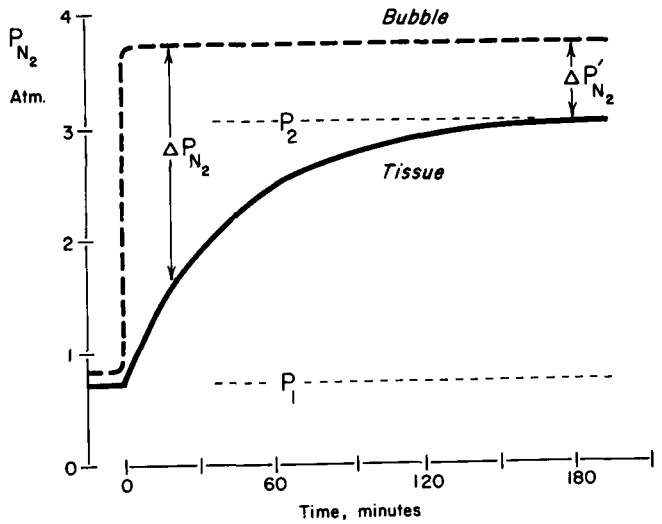

FIG. 55. Saturation of tissue with N_2 and effect on N_2 diffusion (adapted from (11)). After compression with air, tissue P_{N_2} (solid curve) is expected to rise exponentially from P_1, the initial value, to P_2, the saturation level at the new pressure. In contrast, bubble P_{N_2} (dashed), which depends on local tissue P_{O_2} and P_{CO_2}, rises almost immediately to near its steady-state value. The difference between the two curves is the pressure difference, ΔP_{N_2}, which causes N_2 to diffuse out of the bubble. When tissue P_{N_2} is in a steady state the difference is denoted $\Delta P'_{N_2}$; it is greater after compression (right of the diagram) than in the uncompressed state (at extreme left). Time course of the tissue P_{N_2} depends on the tissue in which the bubble is located and is thought to be mainly a function of local blood flow. The example here has a half-saturation time of 30 minutes.

sures when the inside pressure is very large. The maximum rate equals K_{N_2} and is most nearly approached when the diameter is smallest, that is, just before the bubble ceases to exist. Thus independent of its early history and the diffusion driving pressures, all bubbles containing N_2 have a similar ending. It is interesting that the limiting rate during the surface tension effect equals the maximum for O_2-breathing. Figure 54 shows this may be 5 to 10 times greater than the rate at normal pressure breathing air, but it is finite.

The overall result of the delay in tissue saturation in phase II is to reduce the bubble diameter by a given amount, shown on Figure 56 as ΔD. This step change of diameter, which takes a variable time depending on the rate of tissue desaturation, is somewhat analogous to the step change of phase I, which of course takes only as long as the compression time.

During O_2-breathing, phase II is concave downward because the ΔP_{N_2} increases with time instead of decreasing. In Figure 55, if the subject started breathing O_2 at the time of compression his tissue N_2 would decrease to zero,

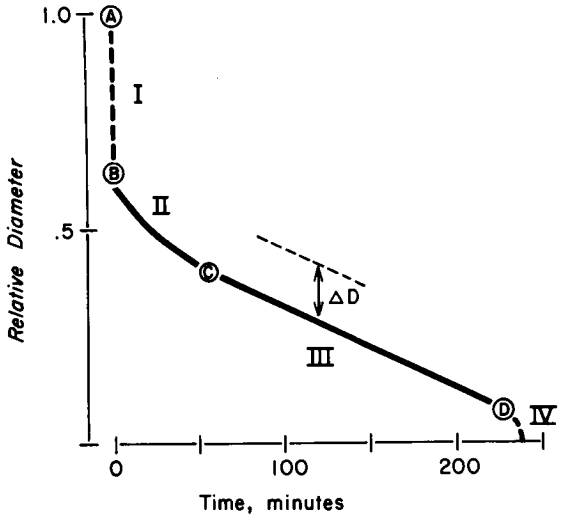

FIG. 56. Phases in bubble resolution in an air-breathing subject. Physical compression, phase I, is drawn here as if it were instantaneous. Compression decreases the diameter of a hypothetical decompression bubble from A to B; symptoms are often relieved during this phase. In phase II, B to C, N_2 diffuses out of the bubble but the rate of diffusion decreases as the tissue becomes resaturated with N_2 . The net result of phase II can be considered a step decrease of diameter, ΔD. Phase III, C to D, is the steady state where the tissue is saturated with N_2 at the new pressure, but the bubble continues to decrease linearly with time because of the steady-state N_2 difference $\Delta P'_{N_2}$. Phase IV represents the "surface tension squeeze"; when bubble diameter is small, surface tension adds to the hydrostatic pressure so that gas diffuses more rapidly out of the bubble. The duration and relative importance of the four phases for a real bubble depends on the specific environment in which the bubble exists.

presumably along a curve with the same half time as the one shown for increase of tissue N_2 in the air-breathing subject.

Compression

When a victim of decompression sickness is recompressed as in phase I of Figure 56 there is often, but not always, dramatic relief from symptoms. However, compression is relatively ineffective in changing the diameter of a spherical gas bubble. Because volume is inversely proportional to the pressure, diameter is proportional to the cube root of the volume, and is therefore inversely proportional to the cube root of the pressure. This is illustrated in Figure 57. For example, compression to 6 atmospheres absolute only decreases the bubble diameter to 55 % of its 1 atmosphere diameter although the volume is down to 17 %. Doubling the pressure decreases the diameter to approximately 80 % of its original value.

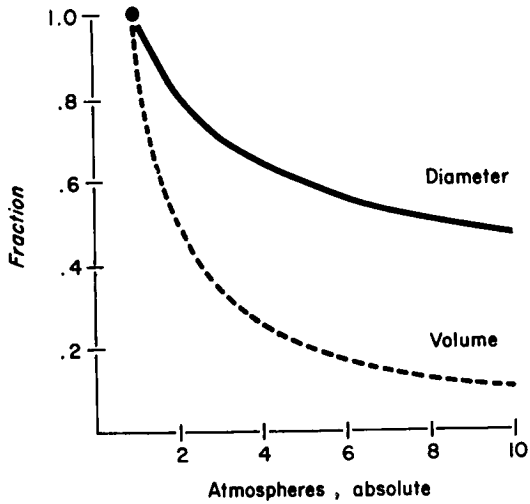

FIG. 57. Diameter and volume of a spherical bubble containing a given quantity of gas at various degrees of compression. Diameter of the bubble, which presumably is most closely related to the symptoms of decompression sickness, does not decrease as much with compression as does volume. The volume curve is drawn from the gas law, $P_1V_1 = P_2V_2$, where subscripts 1 and 2 correspond to noncompressed and compressed states. The analogous equation for the diameter curve is $P_1^{1/3}D_1 = P_2^{1/3}D_2$.

Figure 57 shows that in a case where moderate compression gives immediate relief of symptoms, the diameter change cannot have been large. Therefore we infer that the diameter for relief is near the diameter at which symptoms occur. For example, compression to 3 atm reduced a bubble to about 70% of its original diameter. If relief occurred, the diameter of the symptomatic bubble could be no more than 10/7 = 1.4 or about one and a half times as large as its post-compression value.

Fig. 58 illustrates the different roles of diffusion and compression in the resolution of a hypothetical bubble of 1 mm diameter. For this figure it is assumed that the subject has been breathing O_2 for some time, so that resolution rate is at its maximum and there is no unsteady state. The maximal rate is assumed to be 100 micra per minute, the rate for a bubble in well-stirred water (12). Two different situations are depicted—where the subject is not compressed (upper solid line) or compressed to three atmospheres (lower solid line). Under both conditions, the diameter decreases at the same rate; however, the bubble reaches zero volume in 7 minutes after compression to three atmospheres, whereas it takes 10 minutes to disappear if not compressed. The rate of gas molecules leaving the bubble increases with compression even though the rate of diameter decrease is constant. This is illustrated by the dashed curve in Figure 58 which indicates the

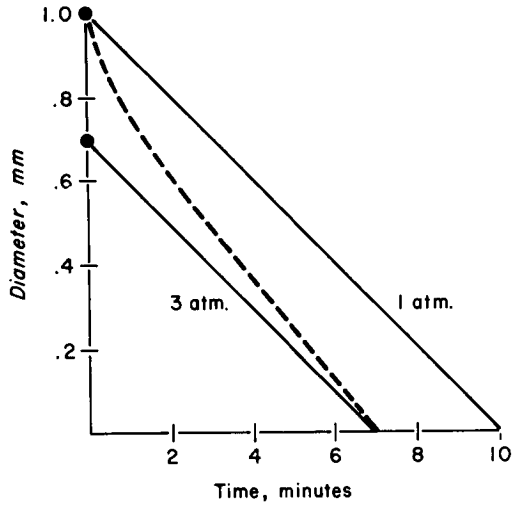

FIG. 58. Bubble resolution during O_2 breathing at ambient pressure (upper diagonal line) and under 3 atmospheres of compression (lower diagonal line). Rate is maximal and is the same in both cases. However, the bubble is smaller and disappears sooner at pressure. The dashed line shows the diameter the gas in the compressed bubble would have if it were decompressed to atmospheric pressure. The rate for the two diagonal lines is the same as for a well-stirred bubble in water. Bubbles in the body probably disappear more slowly; subcutaneous gas pockets in rats are resolved at $\frac{1}{20}$ the rate.

diameter the compressed bubble would have if decompressed. For simplicity the "surface tension squeeze" phase has been omitted from Figure 58.

Concluding Remarks

Because many factors are involved in the process of bubble resolution, many lines of discussion could be followed in considerable detail. These include possible differences in solubility and diffusion path length in various tissues, effects of O_2-breathing, relative importance of the unsteady state, and bubble growth under appropriate conditions. The theoretical framework which has been initiated here should be useful in allowing logical consideration of the effects of various factors while keeping the others in proper perspective.

A theory is only as good as the assumptions on which it is based. In particular, the theory here might be improved by use of a more sophisticated diffusion equation. The assumption of perfect stirring beyond a nonstirred shell has been applied successfully to studies of diffusion from bubbles in water (4, 12), serum (4), and blood (1). The extent to which capillary

blood in a tissue becomes partially saturated, equivalent to imperfect stirring, has been studied in subcutaneous gas pockets by Piiper, Rahn and and Canfield (7), Piiper (8), Van Liew (9), and Olszowka and Van Liew (unpublished). The findings can be summarized by saying that the diffusion equations developed above can be expected to hold for any particular gas, but that comparison of one gas to another cannot be predicted exactly from diffusion coefficients.

Acknowledgment

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20 | CHARLES L. WAITE, WALTER F. MAZZONE, MICHAEL E. GREENWOOD and REYNOLD T. LARSEN

Dysbaric Cerebral Air Embolism

Dysbaric cerebral air embolism is an acute, serious occupational hazard associated with decompression and incurred by submarine personnel undergoing escape training, individuals pursuing SCUBA diving as a vocation or hobby, and aerospace pilots exposed to explosive decompression at ambient pressures of less than one atmosphere (1–4). This condition should not be confused with decompression sickness (bends) which, though also related to decompression, has a somewhat different etiology and pathophysiology. In general, bends is less acute and tends in the average case to be of less serious import.

The connotation "dysbaric" is proposed to differentiate this form of air embolism incurred in a diminishing ambient pressure from the accidental variety occurring at one atmosphere in a hospital setting (5–10).

The relationship of morbidity and mortality to the mode of escape training which has changed through the years is given in Figure 59, and can be seen to influence both. Free ascent training is technically more difficult to master and has a resulting higher rate. The mastery of this technique by SCUBA divers is a necessity if air embolism is to be avoided.

The incidence of dysbaric cerebral air embolism in relationship to submarine escape training at New London in the past 35 years is given in Table 25. The National Safety Council estimated 60 deaths in 1965 were caused by SCUBA diving accidents, and a fair number of these were undoubtedly due to air embolism.

In the illness which is the subject of this series of experiments the individual, diver or submariner, is in a diminishing pressure situation which causes an expansion of gas in the pulmonary alveoli. If the normal exhalation route of the expanding alveolar gas is interrupted either voluntarily, as in breath-holding, or involuntarily, from trapped air associated with pulmonary tract pathology, then the over-expansion and rupture of alveoli ensues. The gas is released into the pulmonary circulation and via the pulmonary vein, left heart, aorta and carotids, enters the cerebral circulation (Fig. 60).

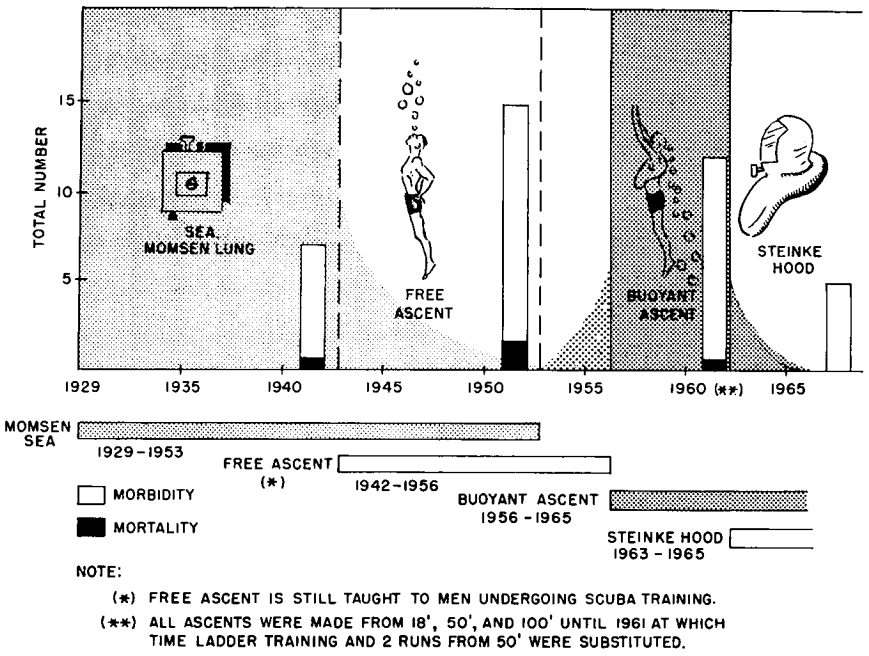

FIG. 59. Chronological chart of mode of submarine escape training, U. S. Navy

TABLE 25

Morbidity/Mortality in Relation to Total Number of Simulated Escapes and Mode of Escape. U. S. Naval Submarine Escape Training Tank, New London, Conn. 1938–1965

YEARS	MODE	TOTAL NO. ESCAPES	TOTAL NO. AIR EMBOLISM (MORBIDITY)	DEATHS MORTALITY
1930–1953	S.E.A. Momsen lung	193,000	7	1
1942–1957	Free ascent	17,583	15	2
1957–1965	Buoyant ascent	130,679	12	1
1963–1965	Steinke hood	32,679	5	0

The pulmonary events, including the vital relationships of transpulmonary and transatrial pressures leading to alveolar rupture, have been well defined (11–16).

The wide clinical spectrum of symptoms and signs associated with cerebral air embolism includes headache, vertigo, cranial nerve involvement, visual, auditory, and speech disturbances, loss of consciousness, coma, paralysis, convulsions, loss of vital signs, and death.

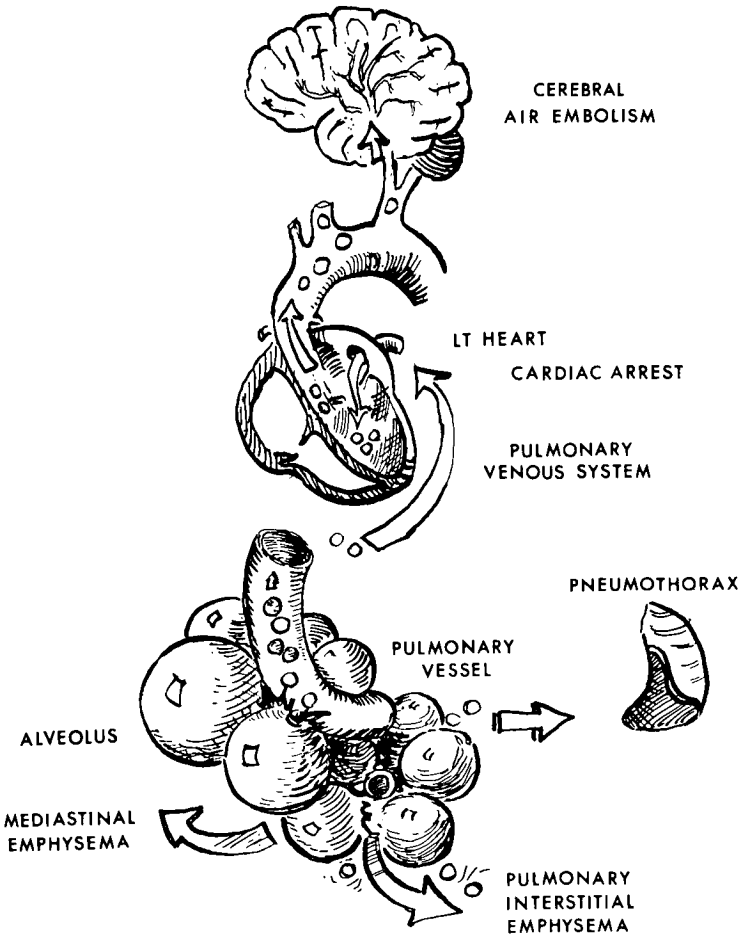

FIG. 60. Schematic diagram of potential courses of air from ruptured alveoli

Similarly, the coincident intrathoracic complications of pulmonary interstitial emphysema, mediastinal emphysema and pneumothorax have been studied and reviewed in several excellent papers (12, 13).

The cerebral events, however, have not been studied as closely, except in reports defining the clinical symptoms and signs and reviewing the experience with pressure therapy (4, 17–20).

Neither has the pressure treatment of cerebral air embolism been thoroughly evaluated or given the attention it deserves as the treatment of choice. Presently, there is little evidence, other than clinical, that speaks to the efficacy of 6 atmospheres absolute of pressure as the optimum recompression required. At the same time, there is meagre published evidence

that pressures less than 6 atmospheres absolute are totally efficacious (1, 2, 22).

Current thinking in the treatment of pressure illnesses tends towards less prolonged exposure of damaged tissues to high partial pressures of inert gas. This principle may also be applicable to the treatment of air embolism.

The occasional so-called "recurrence" of cerebral air embolism during the pressure treatment phase is a doubtful circumstance, more likely due to post-embolic cerebral damage, edema, and increased intracranial pressure.

The series of experiments to be described is directed toward a better understanding of the cerebral events of air embolism and the effects of recompression in the natural history of the injury, all with a view toward developing a more effective treatment.

Purposes of the Study

The present study was carried out for a number of related reasons, as follows:

To develop a technique to produce and observe cerebral air embolism in vivo in mammals with a high degree of consistency.

To observe grossly the effect of cerebral intravascular bubbles on the cerebral circulation and the tissues supplied by the cerebral circulation.

To observe in vivo the life history of cerebral intravascular air and its residual effect on the untreated embolized animal.

To observe in vivo the life history of cerebral intravascular air and its effect on cerebral tissue using immediate recompression to 165 feet (6 atmospheres absolute) as the mode of treatment.

To observe in vivo the cerebral cortex and cerebral blood vessels of embolized animals during the decompression phase utilizing a standard 170 foot/10 min. diving table. This was in lieu of the U. S. Navy Standard Treatment Tables III and IV. In this phase particular attention was paid to the possible reappearance or recurrence of the cerebral intravascular air.

Materials and Methods

Initial cerebral studies in vivo were done on prepared cats and small dogs, injecting air into the carotid and observing cerebral intravascular bubbles in the region of the frontal cortex. From these studies it was determined that dogs weighing 25–40 lbs. were the most satisfactory species for these experiments.

Additionally, a cranial window technique was adopted to visualize the cortex. This was done using a modification of Pudenz and Shelden's lucite calvarium technique (21). All subsequent animals used were mongrel dogs which were prepared with a unilateral cranial window 2.5 cm in diameter

FIG. 61. Cranial window (× 3.3) as seen through the dissecting microscope. Arrows indicate air filled arteries.

in the parieto-occipital area, except one dog which was prepared with bilateral cranial windows. These windows were installed 7 days prior to any experimentation to allow the animal to stabilize after the procedure. After 4 experimental runs with the cranial window, the visualization technique was changed to a simple craniotomy for all succeeding runs (Fig. 61).

Twenty-four hours prior to an experiment, the carotid artery on the same side as the window was dissected free and isolated through a cervical incision and a sterile tape looped around it. The tape was allowed to protrude through a partially closed incision and gave ready access to the carotid when embolization was desired.

Ambient air in the amount of 1–7 cc was injected into the carotid with an ordinary disposable syringe and 18 gauge needle to artificially produce the cerebral air embolism.

Recording of Results

Four modes were utilized to record the experiments. They were: direct observation and tape recording; 6 frame per second photography, color,

and black and white; color motion pictures, sound and silent; and closed circuit TV.

Types of Experimental Runs

The types of runs with the embolized animals were varied to meet the objectives of the study.

a) Initial experimental runs were concerned only with the production of a satisfactory cerebral air embolism permitting observation of intravascular bubbles and their effect on the circulatory dynamics and the cerebral tissue supplied. In this series, 5 dogs in 6 separate runs were observed. All runs were done on the surface at 14.7 psi (1 atmosphere).

b) In the second series, 3 dogs were embolized at 1 atmosphere and taken to treatment depth, then returned to surface on a standard 170 foot diving decompression table for the appropriate time on the bottom. These are hereafter referred to as "bounce dives".

c) In another series, 3 dogs were embolized at 33 feet (2 atmospheres), brought to the surface and then given bounce dive treatment to 165 feet. This was done to simulate the occurrence of cerebral air embolism in a decreasing ambient pressure environment, much as it occurs in the true situation. When dogs were embolized without treatment, the experiments were conducted in the veterinary operating suite. When the dogs were embolized and treated with pressure, the entire procedure was conducted in the large recompression chamber at the Submarine Medical Research Laboratory. This permitted room for observers, motion picture cameras, TV monitors and monitoring equipment.

Results and Observations

A total of 14 embolism experiments were conducted (Table 26). Three were unsuccessful, in that attempts to induce artificial cerebral air embolism via the carotid route could not be accomplished. This was invariably due to thrombosis of the carotid vessel incurred during the preparation.

Five dogs were embolized and not given treatment with recompression; 2 expired within 20 minutes, and 3 survived but with severe residual damage evident. The residual damage was evidenced by alterations in the state of consciousness, major paralysis, ataxia, incoordination, convulsions, muscle spasm, reflex changes, anorexia and cranial nerve damage.

Of the 6 dogs successfully embolized at 1 and 2 atmospheres, and then treated with recompression to 165 feet, 5 survived without demonstrable residual damage. One dog (#12) survived but with severe residuals in evidence of the type already described. On examination of the film record, which took several weeks to process, a rupture of a cerebral vessel coincident with the insult of the air rushing into the cerebral vasculature was noted.

TABLE 26

Summary of Observations

Date	Animal	Type of Run	Amt. of Air Inj. Carotid	Cerebral Intravascular Bubbles Observed	Treatment	Outcome & Remarks
10-23-64	Dog #1	Frontal lobe observation 1 atm.	5 cc	Yes	None	Circul. blocked—death in 18 min.
12-7-64	Dog #2	Temporal-cranial window—embolized at 1 atm.	2 cc	Yes	165 ft. bounce dive 170 ft. dive table	Cerebral intravascular bubbles disappeared 80–100′—dog survived
12-10-64	Dog #2	Temporal-cranial window—embolized at 33 ft. (2 atm.)	1 cc	Yes	None	Dog expired—12 min. Circul. effect. blocked
1-15-65	Dog #3	Occipito-parietal window 1 atm.	Repeated attempts to embolize unsuccessful	No	None	Unsuccessful Thrombosed carotid
1-21-65	Dog #3	Occipito-parietal window Embolized at 33 ft. (2 atm.)	1 cc	Yes	Surfaced—then 165 ft. bounce dive 170 ft. dive table	Very poor on surface—survived—no residuals bubbles gone at 100 ft.
1-30-65	Dog #4	Bilateral Occipito-parietal windows	Repeated attempts to inject air unsuccessful	No	None	Unsuccessful Thrombosed vessels—dog survived
2-5-65	Dog #5	Bilateral Occipito-parietal Embolized at 1 atm.	5 cc	Yes	165 ft. bounce dive 170 ft. dive table	Cerebral intravascular bubbles gone at 100 ft.
5-27-65	Dog #6	Lt. craniotomy Embolized at 1 atm.	5 cc	Yes	None	Proved bilateral widespread distribution of air from unilateral carotid injection—dog sacrificed
6-15-65	Dog #7	Lt. craniotomy Embolized at 1 atm.	5 cc	Yes	165 ft. bounce dive 170 ft. dive table	TV camera run successful—dog survived Bubbles no longer observed after 60 ft.
12-15-65	Dog #8	Lt. craniotomy Embolized at 1 atm.	Repeated attempts to embolize unsuccessful	No	None	Unsuccessful run—thrombosed vessels
12-15-65	Dog #9	Lt. craniotomy Embolized at 1 atm.	7 cc	Yes	None	Dog survived with serious residuals—sacrificed at 20 days—post-embolism. Autopsy
1-17-66	Dog #10	Lt. craniotomy Embolized at 1 atm.	7 cc	Yes	165 ft. bounce dive	Dog survived—no residuals
1-17-66	Dog #11	Skull intact	5 cc	No	None	Survived with residuals
1-18-66	Dog #12	Lt. craniotomy 2 atm.	7 cc at 33 ft.	Yes	165 ft. bounce dive	Survived but with severe residuals—dog sacrificed Film record shows severe cerebral hemorrhage coincident with bubbleinsult. No intravascular bubbles after 80 ft. Autopsy

Not only were the air bubbles expelled as a froth over the brain surface, but with restoration of the circulation by recompression, gross cerebral hemorrhage ensued. At autopsy, gross sections of this animal's brain revealed a massive deep hemorrhage in the region of the area observed and reaffirmed by the motion picture record.

Observations Concerning the Cerebral Intravascular Air

With the cerebral window exposures performed, the observations for the most part were made on the anterior cerebellar and posterior cerebral branches of the posterior communicating artery of the carotid. The arterial vessels under observation with the dissecting microscope and motion picture camera had diameters of from 30 microns to 2 mm.

Typically, the bubbles conformed to the size and the shape of the blood vessels. The majority of the air passed through the larger arteries very rapidly, but on reaching the branches of these arteries came to rest, effectively blocking arterial circulation. In some instances entire branches were filled with air, in others the air bubbles were lined up in a row with small amounts of blood separating them with thin biconcave menisci. The very small arteriolar vessels were completely filled with air and appeared as a thin, silvery network on the cortical surface. The largest arteries observed to be blocked by the bubbles produced were 2 mm in diameter. However, most of the vessels observed which were filled with air and showed evidence of circulatory obstruction were smaller than 2 mm, and were in range of 30–60 microns. This confirmed the observations of Curtillet and Curtillet (23) who, doing similar work on dogs in 1939–40, reported effective blockage in arterioles of 30–40 microns in diameter.

At the blood/air interfaces the pulsations of the heart could be seen. In some instances at a standstill, while in other small arteries there was a slow pulsating progression of the bubbles in response to the systolic pressure peaks. In the series of photographs a progression of such a bubble is seen. The pulsating nature of the progression can be seen by the small amount of blood pushed into a branch and then left behind by the recession of the pulse.

The surrounding brain tissue exposed by the cranial windows came under observation and typically showed a pallor which in the untreated cases gave way to a reactive hyperemia. Minor flare hemorrhages and petechial hemorrhages were also noted. Moderate edema was evident in some cases after an hour or more.

Of the six dogs embolized and then recompressed to 165 feet, all the bubbles in 2 dogs had vanished by 100 feet (4 atmospheres); by 80 feet in 3 dogs; and by 60 feet in 1 dog.

In every instance there was evidence of a change in bubble size and par-

tial restoration of circulation just beyond 33 feet. In none of the experiments were intravascular bubbles seen to persist after pressure equivalent to 4 atmospheres was reached.

Equally important, in no instance was there a reappearance of bubbles during and after decompression using a Standard Navy Decompression Table for 170 feet (10 min.) at a standard ascent rate of 60 feet per minute.

There was no attempt in this series to treat cerebral air embolism with pressures less than 6 atmospheres absolute, even though there is some indication that this maximum need not be applied.

A future series is planned using 4 atmospheres absolute recompression for comparison with the currently accepted 6 atmospheres and the no recompression control series.

Comments and Conclusions

In the past, the civilian medical community has not given the pressure therapy of cerebral air embolism the recognition it deserves as the treatment of choice. This was undoubtedly due to the general non-availability of such facilities in the average hospital setting. Today, however, the current interest in hyperbaric medicine has resulted in the establishment and maintenance of pressure facilities in many leading medical centers throughout the country. Personnel responsible for these facilities should develop an awareness, and indeed the technical competence, to treat decompression sickness and air embolism. With this capability the facility can be used to treat not only the occasional air embolism seen in clinical medicine, but the increasing number of civilian SCUBA diving accidents as well.

The present study, although limited in scope and design, did accomplish the following:

A technique for observing and photographing intravascular cerebral air embolism in vivo was developed and refined.

In a controlled series, the efficacy of pressure as a means to relieving the circulatory obstruction caused by air embolism was observed and reaffirmed.

Indications were obtained of the pressures necessary to relieve the air embolism. Maximum effects of recompression were observed between 33 feet (2 atmospheres absolute) and 100 feet (4 atmospheres absolute). Until further experiments are performed, however, there is insufficient evidence to say that the maximum pressure of 165 feet (6 atmospheres absolute) should be considered as unnecessary.

Indications were also obtained that prolonged recompression, as in Tables III and IV of the U. S. Navy Standard Treatment Tables, is not necessary to effectively treat cerebral air embolism. All of the successful

pressure treatment runs in this series consisted of bounce dives to 165 feet for less than 10 minutes and return to the surface at 60 feet/minute with a 2 minute stop at 10 feet (170 foot Table).

The role of post-embolic edema could not be measured or evaluated because of the unrealistic presence of the cranial window which undoubtedly modified this reaction.

In future studies in this series, it is planned to determine the LD_{100} of air for a control series of dogs in order to evaluate more effectively the efficacy of recompression to 165 feet (6 atmospheres absolute), evaluate the effect of treatment using pressures less than 6 atmospheres (absolute), evaluate the effects of hyperbaric oxygen at 60 and 30 feet added to the pressure treatment regimen, conduct histopathology studies on the cerebral tissue of untreated and treated animals, study the vascular dynamics of cerebral air embolism and alterations in intracranial pressures, and develop data on tissue enzyme patterns in cerebral air embolism with and without treatment.

Summary

The medical aspects and pathophysiology of cerebral air embolism are briefly reviewed. The term "dysbaric cerebral air embolism" is proposed to differentiate this condition incurred in a diminishing ambient pressure as opposed to the accidental variety seen in the hospital setting at the constant pressure of 1 atmosphere.

A method of artificially inducing cerebral air embolism and observing and photographing the intravascular cerebral air in living dogs is described.

Observations on the life history and behavior of cerebral arterial air at 1 atmosphere absolute (14.7 psi) and the effect of pressure therapy to 6 atmospheres absolute (88 psi) and subsequent decompression to 1 atmosphere are presented.

The use of pressure in effectively treating cerebral air embolism is reaffirmed and there is indication that a prolonged decompression following recompression to 165 feet is not necessary.

The present study confirms that 6 atmospheres absolute is effective in grossly relieving cerebral air embolism. Effective treatment with pressures less than 6 atmospheres awaits further study.

Ideas for additional studies are proposed.

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Panel on

Special Problems in the Etiology and Treatment of Decompression Sickness

A. R. BEHNKE, *Chairman*

Dr. ALVIS
Dr. BARNARD
Dr. GILLEN
Dr. GOODMAN
Dr. LUNDGREN
Dr. VAN LIEW
Dr. WAITE

DISCUSSION

CHAIRMAN BEHNKE: When Captain Yarbrough and I were conducting a series of helium-oxygen dives to 500 feet at the Experimental Diving Unit, we had a considerable number of bends cases and the response to air treatment and oxygen treatment was remarkably good. It was when Captain Van der Aue applied his test to the air dives that we got into difficulty. In other words, there was a difference between the air bends and the helium-oxygen bends. The helium-oxygen bends apparently were much easier for us to treat.

DR. BARNARD: The question has been raised regarding particular locations of bubble formation in the whole animal, and relation to position or posture. I always have some diffidence in talking about bubbles in the tissues. We have great difficulty in knowing whether there is a bubble and where it is.

I find it hard to understand when a man has been breathing oxygen for about 90 minutes between 50 and 40 feet and then develops a bend. I also find it difficult to understand the situation in a man who already has some degree of decompression sickness and is being treated and when you give him oxygen to breathe, he becomes worse. We have seen this more than once.

The only conclusion we could draw at the time was the possibility that

the situation that was giving rise to the trouble was one where tissue hypoxia was present and that adding extra oxygen, if it was a bubble, was making the bubble larger.

DR. SMITH: The equation for the growth or decay of stationary bubbles presented by Dr. Van Liew is not a good approximation. Epstein and Plesset (P. S. Epstein and M. S. Plesset. J. Chem. Physics., *18:* 1505 (1950)) have shown that, over a wide range of conditions, bubble growth or decay may be represented by the equation

$$r^2 = r_0^2 \pm (K \times t)$$

where r_0 is the radius of the bubble at zero time and K is a parameter which involves the diffusion coefficient and the degree of under-saturation or super-saturation.

Experiments we have performed on the growth rate of stationary gas bubbles in olive oil confirm the validity of the Epstein-Plesset equations.

CHAIRMAN BEHNKE: Concerning the locations of bubbles, from post mortem examination in animals we can say that bubbles are in the blood vessels. They occur in the veins and we have seen them in the arteries and throughout the whole vascular system. In the living individual, we have considered that we might use a tracer gas like radioactive krypton that would concentrate in the bubble. Then you could pick up the emissions and locate bubbles. However, it didn't turn out to be that easy.

Supersonic techniques are used but we cannot yet locate bubbles in the living individual with certainty.

CAPTAIN VAN DER AUE: Extensive damage can occur to tissue in decompression sickness. It may mimic what happens when you obstruct a vessel for a long period of time and have a central core of permanent damage with a peripheral core of transient damage. In decompression sickness the transient damage may be relieved with recompression or oxygen.

This situation may explain partly the reasons why "Table IV bends" cases show such a high occurrence rate. The cases may have occurred several hours before they ever reached a recompression chamber and you do have permanent tissue damage. No amount of pressure or oxygen will restore the already devitalized tissue but it will restore some of the peripheral core which has only been numbed by anoxia.

Therefore, it is very difficult really to evaluate the efficacy of the Table IV treatment schedule because we are dealing with permanent bends—permanent damage, I should say.

I would like to ask one question of Dr. Barnard. If we have a case of permanent damage and the bend will not disappear with recompression, how far do you take him down? I mean, do you compress to a pressure at which you get relief?

In Table IV cases we take the patient down to 165 feet and if he doesn't have relief in 30 minutes, then we keep him at 165 feet for two hours. If two hours doesn't give him relief, we consider that this is enough and begin bringing him out. A diver who develops bends coming up from a deep dive should respond very quickly to recompression but it is still possible that he might have some permanent damage. What is your opinion?

DR. BARNARD: I will try to answer. Back in 1960, Dr. Pride and myself did treat some presumed cases of air embolism in the submarine escape tank. The dive table was for 165 feet. Most of these treatments were quite successful. One man who had complete paralysis of his right arm was out of the chamber and walking about without any trouble an hour later. However, occasionally they will not be. Also there may be catastrophic happenings during decompression after treatment, perhaps with a man suddenly becoming completely blind and ending up in the hospital with gross EEG changes.

At the time we thought the 165 foot pressure treatment was best. I do not think we ever considered that one should go to a lesser pressure. In fact, our whole routine was geared to automatically going to 165 feet as quickly as possible. We followed this routine as much as possible in our diving, going to the "pressure of relief" as quickly as possible. This works and it has even worked in one particular case of a man who had a very woolly feeling in his knee after a deep dive and who, when treated by compression with air and taken to a pressure of 165 feet (this following a helium dive), developed a complete paraplegia. When this happened we had to take him further on in pressure. There was nothing else to do except go on, and we had difficulty in getting helium. We ended up with him at 300 feet on oxy-helium where, in the course of an hour, he recovered completely and he then spent the next four days coming back to atmospheric pressure.

So what I can say at the moment is that we haven't seen any cases so far which have not cleared under adequate compression.

CHAIRMAN BEHNKE: The Royal British Navy has probably forgotten more about oxygen than we now know, but it is true that we do now place emphasis on oxygen, whereas you do not use oxygen routinely in bends treatment.

DR. BARNARD: No, this is not a quite fair statement because we have friends in this country and we listen to what they have to say about oxygen treatment of bends. In the last few months, in fact, we have used the oxygen treatment with success.

CHAIRMAN BEHNKE: I think the real problem with the low pressure oxygen treatment is with the serious cases. 90 per cent of the cases of bends are minor "niggles" and can be easily handled. However, I want to ask Dr. Gillen, a neurologist who has analyzed many bends cases, what he

would do with a seriously injured, unconscious, paralyzed man who arrives for treatment. Would you use the oxygen treatment? If one starts an individual on oxygen at the surface and then applies pressure to a certain level without his breathing air, I think that makes sense. Would you wait at a pressure level, say, of 60 feet for a period of time in treating the acutely injured, very ill patient, or would you go directly to a high pressure of air?

DR. GILLEN: I am still scared in this situation, though I would prefer to use pressure and oxygen. Because I have had no experience with the low pressure oxygen treatment I would like to dodge the main issue that you bring up and try and answer one or two of the earlier questions.

One concerns the distribution of bubbles in the tissues. From a clinical point of view in analyzing some 70 cases of cerebral air embolism, the bubbles appear to be randomly distributed in both the carotid and vertebral system on the basis of symptomatology. From the point of view of recorded success in treatment, the only treatment used in the United States for cerebral air embolism which has had no incidence of failure is application of hot water bottles and a blanket, used three times successfully. All other forms of low pressure recompression schedules have failed at one time or another and all, of course, can be approached with doubt from a statistical standpoint.

Our experience in non-recompression treatment of cerebral air embolism is too small to stand statistical challenge, but it is intriguing that individuals who have developed classical cerebral embolus while making a simulated submarine escape in early training exercises from 30 to 50 feet before recompression facilities became available, were laid out on the dock, covered with a blanket and, by the time the ambulance got there, were symptom free.

We have another problem which is also intriguing to me. There are a number of individuals that we say have cerebral decompression sickness, a severe form of the bends. In the cases that I have been permitted to analyze, most of these individuals have been persons who have had "bounce" dives, most of which were dives past 150 feet, with bottom-time exposures less than ten minutes. Although many of these dives have actually been what I call no-decompression dives, within a minute or so following surfacing or during the ascent to the surface in about 15 percent of the cases, the symptoms start.

As best I have been able to find out from the people who calculate these things, there is not enough gas in the tissue to form bubbles in these cases. I wonder if these are not actually examples of cerebral air embolism from small local pulmonary lesions described in studies by Dr. Schaefer some ten years ago. The divers are affected so abruptly and they get relief so very quickly that it suggests that they actually have an arterial embolus

from a small bubble that has been abruptly introduced into the circulation. It is not a gas saturation or desaturation problem such as accounts for classical decompression sickness.

I have gone back through our 600 case records and have started to pick out these cases because they do not look like decompression sickness at all. Therefore, instead of having the original 70 cases of cerebral air embolism in this series, I may end up with 150 or 200 of them. I would like some comment on this.

CHAIRMAN BEHNKE: This is too speculative. I don't think we know anything about it yet.

DR. LAMBERTSEN: Captain Behnke, you should not let this fine panel avoid the important question concerning whether in extremely severe decompression sickness we want just to compress the patient to a very high pressure on air to decrease bubble size and cause the bubbles to gradually disappear or whether we want to compress with oxygen to oxygenate affected tissues and to speed bubble resolution. I personally favor the maximum use of oxygen in treatment of bends and air embolism, rather than the avoidance of its use. We must not let this group get away with ignoring this matter.

CHAIRMAN BEHNKE: Let me just make a preliminary statement.

Many of us in the Navy have been accustomed to seeing the miracle of recovery from bends of long duration and the future is hopeful because of the use of oxygen and pressure. It is interesting that an individual paralyzed even as long as two days can make a recovery.

It is difficult to explain these conditions unless one presupposes that there is always a trickle of blood and when the blood supply to nerve tissue is cut off, this is not complete. So even though an individual is paralyzed and you have symptoms that look very critical, there probably is a little blood flow.

Dr. Alvis has had some of the worst cases, and I would welcome his comments.

DR. ALVIS: At the Naval Base in Hawaii it seemed as though we were seeing nothing but spinal cord bends, and such cases appeared about every two weeks. It was depressing to see the end results. We treated according to all the classic methods and still had residual effects. However, I would emphasize that the residual effects at the end of treatment of decompression sickness involving the spinal cord never seems to turn out to be as bad as a comparable collection of neurological symptoms following an automobile accident.

These residual effects convinced me that there was something else involved beside the occurrence of bubbles. The more I though about it and talked to neurologists and neurosurgeons, the more I felt that a late edema

might be involved. I have no idea whether this is what happens, but we began treating spinal cord bends with the idea of preventing late edema. I was not able to follow up on this fully.

There is a related aspect of hyperbaric medicine I want to mention concerning the results of treating carbon monoxide poisoning using oxygen at increased pressure.

Sluyter of Amsterdam has pointed out that some very severely poisoned patients revive and appear to get well from carbon monoxide poisoning, then, after a short period of time they begin to deteriorate. Those that begin to deteriorate never get any better and the prospects for them are particularly bad. This delayed deterioration is explainable on the basis of a secondary edema of the central nervous system. It just seems to me there is something more than sheer coincidence in this timing and this curious development.

Certainly if I were ever in a place where I could treat a series of spinal cord bends again, I would treat them using oxygen earlier because it does appear that oxygen helps to prevent this secondary edema and I would use any other measure that neurologists and neurosurgeons think would be helpful in this regard.

Dr. Gillen: There are several approaches. If the damage is a consequence of poor oxygen transportation, whether this is because the hemoglobin mechanisms have been changed by carbon monoxide or whether the blood vessel has no flow through it, the degree of damage from the lack of oxygen in the blood vessel is related to the distance from the blood vessel and the rate of recovery is related to the replacement of oxygen in the tissue at a useful metabolic level. Even though you reconstitute blood flow and improve the recovery of this embarrassed tissue by providing it with its metabolic needs (normal blood flow with the normal nutrients and normal amounts of oxygen) the further you get from the source of the oxygen, which is the blood vessel, the harder it is to get the oxygen there. Therefore on a theoretical basis, an increase in the oxygen partial pressure would be useful.

Methods for changing edema reaction unrelated to attempts to change the local tissue problem which produced the edema would also be theoretically useful. However, they do require testing because some of them are difficult to accomplish. For instance, lowering the temperature in the spinal cord by hypothermia does reduce edema. To get the temperature of the tissues down enough requires that you lower the body temperature by the usual methods to a range of somewhere around five to ten degrees centigrade but this is extremely complicated and at the present time still is a hazardous procedure.

Dr. Roth: I am curious as to whether anyone has ever observed the

vessels in the joints or the spinal cord of animals when exposed to oxygen. Has anyone ever seen what happens to the edema? Is this really a problem or are we just hypothesizing?

CHAIRMAN BEHNKE: I am afraid we are, because when you go to the other extreme, to aviators and people with altitude decompression sickness who have had neurological symptoms for many hours, they all seem to respond remarkably well to a little additional pressure with oxygen. Of course, they have already been recompressed in coming to one atmosphere.

CHAIRMAN BEHNKE: Let us deal with Dr. Lambertsen's question and then we will close this session. You have seen severe cases treated with low pressure and oxygen. What do you do with a patient that is paralyzed? Treat him with air at high pressure or with low pressure oxygen?

DR. GOODMAN: I would increase the pressure head for administration of oxygen and avoid recompression with air which would cause further accumulation of nitrogen in the already damaged tissues with impaired perfusion. This should avoid giving the patient the bends which we would call "recurrent" and would make most effective use of the advantages of oxygen itself. I know Dr. Lambertsen agrees with me.

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Basic Requirements for Improving Diving Depth and Decompression Tolerance

Practical extension of manned undersea activity is now enjoying the temporarily fortunate position of being able to exploit the basic physiological studies made over the past several decades. Still further extension by imaginative engineering can be expected, but it will require clear definition of man's physiological and physical limitations in order to permit direct use of his peculiar assets in deep undersea operations. It must be realized that long lead time is required to accumulate the needed pertinent and accurate basic physiological information and to develop the concepts required for further important extension of man's capabilities into the deep, cold, wet undersea environment. It continues to be easier for the physiologist to design his experimental apparatus than to extract unequivocal experimental results. Similarly it is easier to design and construct undersea devices than to conceive and to validate the solution to elusive biochemical derangements produced by the high pressure environment. Advance in life sciences is heavily dependent upon the ability to integrate the results of scattered, old and new, individual studies.

Although the scope of biological stresses involved in underwater activity is as broad as the physiology of man himself, several factors are of such distinct importance that they can be grouped as primary limitations to advance further in diving. These are:

PRIMARY LIMITATIONS

Deficient Pulmonary Ventilation — Decompression Problems

Narcosis

Oxygen Toxicity

If these can be better delineated, it should also be possible to overcome a number of secondary difficulties, including:

SECONDARY LIMITATIONS

Wetness

Temperature — Communication

Vision — Propulsion

It is worth noting that each of the factors in the first group of most serious problems is concerned with the physical or chemical influences of a high pressure of the respired gas. Each of these will be now considered, emphasizing the prospects for obtaining important improvement in human tolerance.

The Limitation of Decompression

It must be recognized that the escape of inert gas which has become dissolved in body fluids during exposure to a high inspired inert gas pressure is a physical process aided and modified by physiological mechanisms such as blood flow. The physical limitations characteristic of any one gas will remain; the modifying physiological factors are adaptable to control. Hence there must be a limiting rate of escape for each individual gas. Good current estimates indicate that this limiting rate for helium in normal man may represent the rate of gas elimination from fluids which have a simple half-time for inert gas exchange of nearly four hours.

Several dynamic studies of the manner of inert gas elimination (3, 18), including the use of radiokrypton by Jones, indicate that the slowest identifiable rate of inert gas elimination is exponential and is governed by the perfusion of blood through the vessels (volume rate of blood flow per unit mass of tissue). However, this slowest tissue component defined by direct analysis of gas elimination has been found to have half-times for inert gas elimination not much greater than 30 minutes, i.e., about ten times faster than the slowest rate indicated by using bends occurrence in man as an index. Figure 62 indicates this important handicap in the quantitative

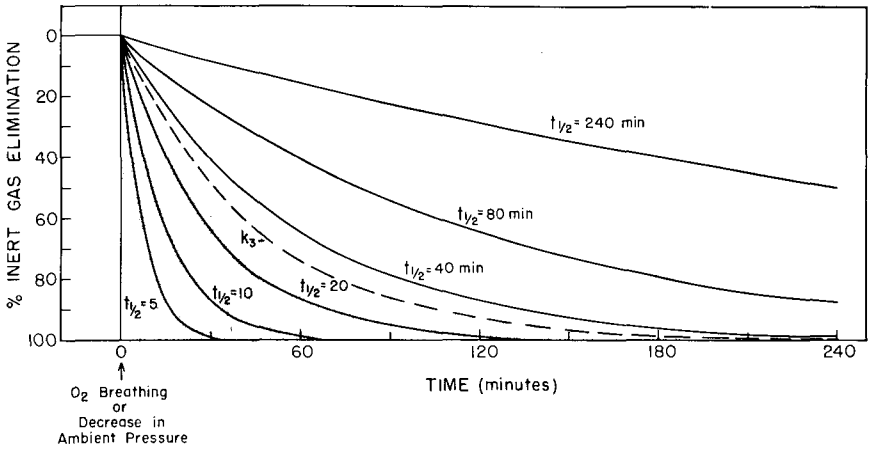

FIG. 62. The time course of inert gas elimination from the tissues

On lowering the inspired pressure of an inert gas, whether by decreasing either the ambient pressure or the percentage of inert gas inhaled, gas elimination from different body locations should occur at an infinite variety of rates. The figure shows an arbitrary series of elimination rates, ranging from a half-time of 5 minutes (which would resemble cranial cerebrospinal fluid) to the slowest rate (240 min. half-time) which have been detected by studies of bends induction in man. The shaded portion, bounded by the curve indicated k_3 (18), defines the area where direct determinations have been made. The unshaded region of the diagram is more pertinent to bends in deep or prolonged diving.

study of decompression and inert gas elimination; the shaded portion of the diagram defines areas where the gas exchange dynamics have been explored by isotope elimination methods. Beyond the limits of this approach lie the unstudied and inaccessible regions with slower rates of exchange. These are the most important to the understanding of decompression sickness.

In the recent past, much consideration has been given to the question of whether inert gas exchange with the tissues is limited by the degree of removal of gas in the perfusing blood or by diffusion of gas within the extravascular tissue fluids. It appears now that there must be a full and changing spectrum of tissue gas uptake and elimination characteristics including

1) Tissues such as lung, arterial blood, kidney, heart and brain which have such a high ratio of circulation to mass that perfusion limitation is unlikely even during extremely rapid change of ambient pressure. As an example, in mice exposed transiently to pressures equivalent to about 400 feet of sea water, it has been found possible to effect decompression at a linear rate of over 3600 feet per minute without harm (13).

2) Tissues in which a very labile circulation may at times be abundant and at other times be inadequate to remove inert gas at rates compatible

with the local diffusion. Such hypothetical tissues may vary from "diffusion limited" to "perfusion limited" and on to "diffusion limited" again. Anyone who has observed the complete cessation of blood flow in mammalian capillaries, due to microscopic circulatory adjustment, will realize that a tissue volume without blood flow can accomplish its gas exchange only by diffusion.

3) Tissues such as cartilage, or the vitreous humor and the lens of the eye, which in their normal avascular state may be diffusion limited with no possibility of modifying gas exchange through circulatory alterations.

4) Tissues damaged by normal physical activity or pathological processes to the degree that scarring and circulatory restriction leaves the tissues dependent upon long diffusion pathways.

Considering the pattern of inert gas elimination described by Jones (18), it can be deduced that the amount of body tissue which, lying beyond the slowest identifiable exponential component, could conceivably be diffusion limited must be as much as 5% of the total body mass. Since this tissue, most important in the etiology of bends, must be presumed to be diffusely scattered through the body in unknown, probably myriad and minute locations, direct study has not been feasible. Until it becomes possible to define the characteristics of the components with the slowest exchange, no quantitative judgment can be made of the success of attempts to accelerate gas removal or to prevent interference with gas elimination.

Acceleration of Inert Gas Elimination

Several significant measures with potential for speeding decompression or improving its safety have been cited in the past (21, 25, 26) and receive attention elsewhere in this volume (10, 17, 20, 35). Table 27 summarizes these measures including the use of high oxygen tensions (2), the use of mixtures of several gases (25, 34), the alternation of inert gases (17, 20, 21, 26, 35), and the combination of alternation of inert gases with fluctuation of oxygen tension (25, 26).

The Maximal Use of Oxygen

Probably the most important single measure for facilitating decompression will continue to be the use of maximum tolerable oxygen tensions a) to limit inert gas uptake during descent and at diving depth, b) to increase the outward gradient for inert gas elimination during decompression, and c) to aid in the treatment of bends when it does occur. Exploitation of the invaluable principle of maximizing diffusion gradients, well recognized by the originators of oxygen decompression following deep helium-oxygen diving (33), is still sorely handicapped by inadequate information pertaining to a) the limits of oxygen tolerance in sustained and in interrupted oxygen breathing and b) the occurrence and nature of any significant physi-

TABLE 27

Acceleration of Inert Gas Elimination

The few principles applicable to accelerating inert gas elimination are well known. They can be applied by several methods, as indicated. However, to date none of these methods has been adequately studied or more than partially exploited. In several instances even the basis or overall effect of the proposed method is not agreed upon.

SUMMARY PROPOSALS FOR ACCELERATION OF INERT GAS ELIMINATION

Principle

Increased Partial Pressure Gradient
Increased Perfusion of Tissue
Increased Activity of Dissolved Gas Molecules

METHOD	OVERALL EFFECT
Hyperthermia and Decompression	Influence of Temperature on: Perfusion Diffusion Solubility of Gases Inert Gas Gradient
Hyperoxygenation and Decompression	Influence of Oxygen on: Inert Gas Gradient Perfusion Tissue P_{CO_2}
Use of Multiple Gas Mixtures	Influence on: Diffusion Inert Gas Gradient
Alternation of Inert Gases	Influence on: Rates of Uptake and Elimination
Alternation of High and Low Oxygen Pressures	Influence on: Inert Gas Gradient Perfusion
Double Alternation of Inert Gases and High Oxygen Pressures	Influence on: Inert Gas Gradient Perfusion
Drugs and Decompression	Influence on: Perfusion

ological influences of high oxygen pressures upon the perfusion of the tissues having the slowest rates of inert gas exchange. Basic and applied studies of these factors should provide immediate and important returns.

The possibility of interference with inert gas elimination by the vasoconstrictor effects of oxygen is emphasized elsewhere in this volume (35, 37). Here it is important to recognize that, if it does in fact exist, such a vasoconstrictor influence of oxygen would be important chiefly in the same diffusely scattered regions of extremely limited blood flow which are theoretically characterized as tissues having long half-times. Thus, measure-

ment of oxygen effects on mean blood flow in well perfused organs or tissues (23) will have little direct bearing upon this question. Since the lowered arterial P_{CO_2} which normally accompanies oxygen breathing (23) has local constrictor influences upon most vascular and other smooth muscle, it would be an unfortunate error to dispense with the only safe means of increasing the diffusion gradient on the unsubstantiated assumption that hyperoxygenation itself leads to an unacceptable degree of vasoconstriction. Even if this should prove to be the case, it will be far more desirable to retain the principle of using oxygen to maximize the inert gas diffusion gradient from the cell to the capillary while simultaneously employing other, probably simple, pharmacological means to sustain blood flow in the slow tissues.

Limitations presented by the biochemical effects of oxygen will probably not be practically circumvented until many years of additional extensive work has been accomplished. However, it is possible to obtain considerable improvement in the practical use of this vital but toxic element by improved definition of human tolerance to oxygen over the widest range of pressures. An example of this definition of tolerance is shown in Figure 63, which demonstrates a synthesis of information obtained by several different investigators (24, 26, 28). The figure indicates that it is desirable to consider oxygen tolerance from the standpoint of particular limiting tissues or organs, since the quantitative relationships of tolerable depth and duration of exposure will in fact be different for various structures, depending upon the actual P_{O_2} dose at the cell and upon the susceptibility of a particular cell type to the chemical influences of oxygen. The basis for constructing the pulmonary tolerance curve is provided in some detail in another chapter of this volume (7). From such information it is evident that: a) a 30 day exposure to one-third of an atmosphere of oxygen (32) or a 14 day exposure to one-half an atmosphere of oxygen (16) produced no significant pulmonary or central nervous system effects; b) at two atmospheres of inspired oxygen pressure distinct and unacceptable pulmonary toxicity developed in eight hours but no indications of central nervous system effects were seen (7); and c) at inspired oxygen pressures from three to four atmospheres an unacceptable incidence of central nervous system toxicity occurs after much shorter oxygen exposure than is predicted for the development of serious pulmonary effects. Refinement of these predictive curves by inclusion of other tissues such as the eye, the arterial lining, the glomeruli, the endocrine glands and the gonads is now necessary.

The Extension of Oxygen Tolerance by Interrupted Exposure to High P_{O_2}

The predictive oxygen tolerance curves of Figure 63 provide a necessary starting point for developing the concept of fluctuating high and low

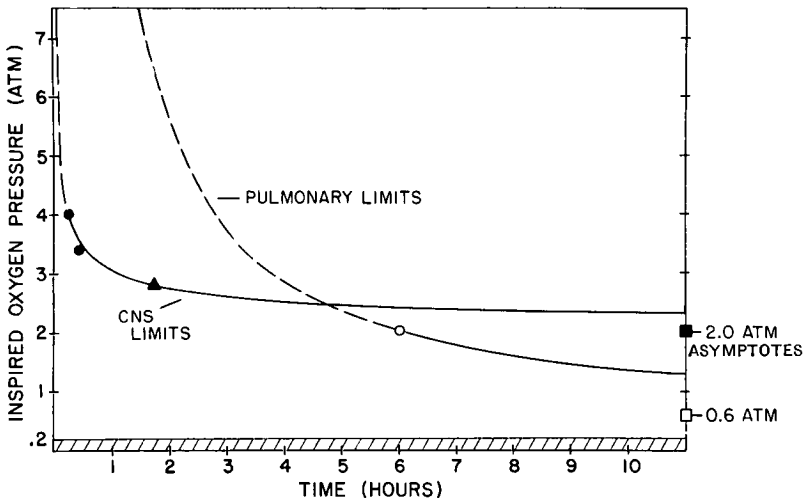

FIG. 63. Pulmonary and CNS tolerance to 100% O_2 breathing at various levels of ambient pressure in normal men at rest.

These curves are rectangular hyperbolas constructed using the available data and assuming that (a) at infinitely high inspired Po_2, the duration of pulmonary or CNS oxygen tolerance will be nearly zero (this provides one common asymptote for the CNS and pulmonary tolerance curves), and (b) at some sufficiently low inspired Po_2, there will be no detectable intolerance to oxygen even at infinite time. The Po_2 which will produce borderline pulmonary toxicity is here considered to be 0.6 atmospheres (8, 32) since 0.5 atmospheres of oxygen did not cause prominent adverse effects in 14 days (16). Central nervous system tolerance to oxygen toxicity is assumed to be borderline at 2.0 atmospheres of inspired Po_2 since exposure of subjects to O_2 for between ten and eleven hours has produced no detectable CNS effects (7).

The important findings which determine the character of the CNS tolerance curves are shown at 4.0, 3.5 (●) and 2.8 (▲) atmospheres. These represent the time of a 10 percent incidence of CNS symptoms in normal subjects studied by Yarbrough et al (38) and analyzed by the author (27). This curve is shown as a comparison with the pulmonary tolerance curve, not as an indication of safe exposure at all pressures.

The pulmonary tolerance curve, best studied at low levels of inspired Po_2, is determined from information concerning the time required to produce symptoms and a 5 percent reduction of vital capacity at 1.0 and 2.0 atmospheres (open circle) (7).

The choice of an hyperbolic relationship between oxygen pressure and duration of tolerance is based upon the demonstrations that toxicity of oxygen in small organisms and mice closely follows such a pattern.

oxygen pressures as the means of extending the usefulness of high oxygen pressures in diving, in decompression and in therapy (8, 19, 27). This approach, when systematically applied to man, should shift the curves of Figure 63 far to the right and open the way to greater use of the advantages of high Po_2 and lowered inspired inert gas pressure. The procedure of varying the oxygen tension is now an integral part of the oxygen treatment of

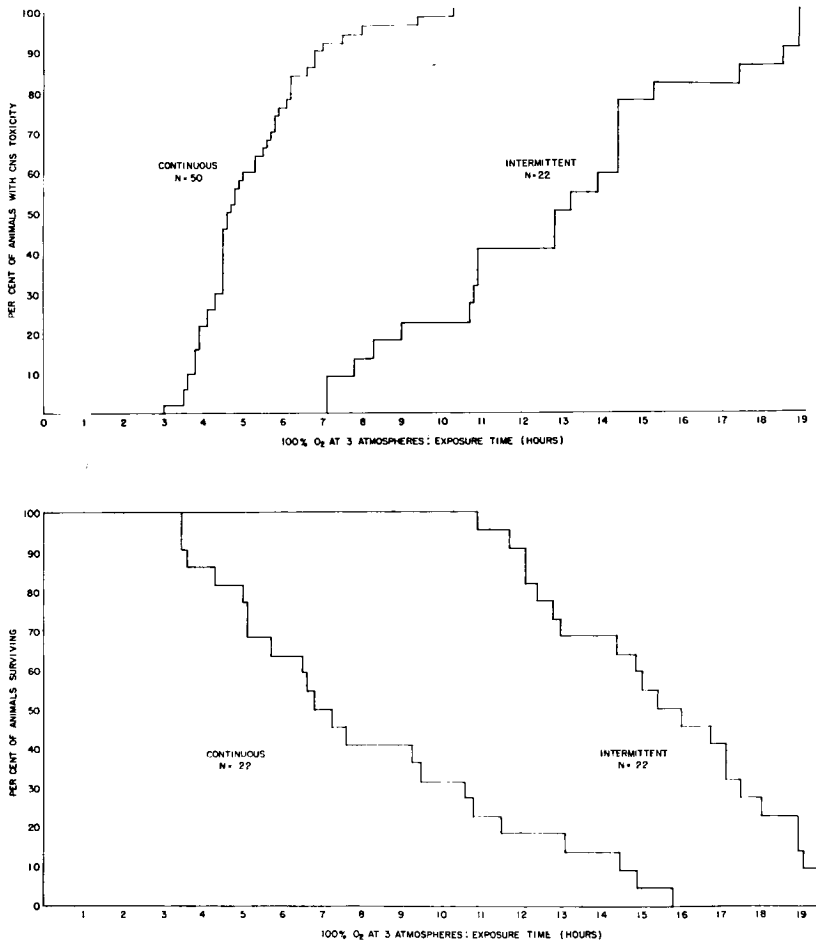

FIG. 64. Extending tolerance to high oxygen pressures by periodic lowering of inspired Po_2 .

Guinea pigs exposed continuously to 100 percent oxygen at three atmospheres absolute developed detectable CNS toxicity and died in accordance with the step curves on the left side of the figures. The alternation of 30 minutes on 100% oxygen with 10 minutes on 7% oxygen increases the total time during which pure oxygen can be breathed.

Figure 64A represents the time when each animal first showed symptoms of central nervous system toxicity. Figure 64B indicates the percentage of animals remaining alive (19, 27).

clinical bends (14) and should be exploited in bends prevention as well. Figures 64A and 64B, illustrate findings from an early study of this principle in small animals (19, 27). They show that return to normal Po_2 for ten minutes following each 30 minute exposure to three atmospheres of

oxygen pressure more than doubles the central nervous system and general tolerance to oxygen. Recent studies indicate that pulmonary tolerance is also extended (15).

Body Temperature and Inert Gas Exchange

Long experience in open sea diving has confirmed that cold water and local or general lowering of body temperature predisposes an individual to development of bends. While the interference with inert gas elimination is certainly qualitatively related to vasoconstrictor responses to cold, essentially no information is available in animals or man concerning the degree, the sites, or the other mechanisms involved in this effect of low temperature. *Lowering* of tissue temperature increases the solubility of inert gas and decreases the activity of its molecules in addition to affecting blood flow. Intentionally induced moderate degrees of deep body *hyperthermia*, with its increase in cardiac output, accelerated tissue blood flow, increased inert gas activity and gradient, decreased inert gas solubility and possible altered oxygen tolerance deserves extensive study of its potential physiological advantages and disadvantages in inert gas exchange. It is here predicted that intermittent over-warming, along with other measures, will add significantly to the safety and efficiency of decompression.

The Use of Multiple Inert Gas Mixtures as Respiratory Vehicles for Oxygen

The concept of using more than one inert gas in a single mixture to facilitate decompression has been stressed for several decades (25, 26, 34). The concept is clear but the results are not. If each gas in the gas mixture dissolved in body fluids were to behave as though it were the only gas present, considerable advantage in decompression should ensue. The hypothetical gas mixture illustrated in Figure 65 was offered at the First Symposium on Underwater Physiology to call attention to the question, which is still important and still has not had serious study. The cylinder contains nine gases, in equal proportions. Ignoring the obvious disadvantages of radon and the prominent narcotic effects of certain others, it is presumed that prolonged exposure to two atmospheres of any single one of these inert gases (with the necessary oxygen) could be followed by prompt and uneventful decompression to sea level. If the entire mixture were breathed to saturation at 18 atmospheres (close to 550 feet), each gas would exert a partial pressure of two atmospheres. Why should it not be possible to decompress immediately from a 550 foot saturation dive on such a multiple gas mixture with each gas independently leaving the tissues at its own rate and without critical oversaturation or bubble formation? Two investigations of this question, ten years ago, have led us to recognize that the answer is no. I asked Webster to analyze this problem for the First Symposium and his appraisal sensibly emphasized that the *sum* of the partial pres-

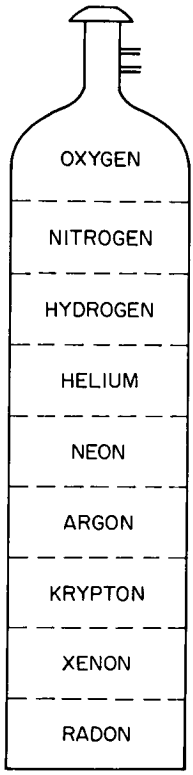

FIG. 65. The concept of breathing multiple inert gas mixtures in diving
The use at increased ambient pressure of mixtures containing many inert gases should not result in excess saturation of tissue fluids with any single inert gas if each gas in the mixture is at a maximum partial pressure of one atmosphere. Nevertheless, severe bends does occur after exposure to multiple gas mixtures, since once a cavity or a small bubble is formed, its growth depends upon the sum of the partial pressures of all gases in the tissues.

sures of gases determined the size and deformation pressure of gas bubbles in tissues (34). Concurrently an experimental evaluation of a three gas mixture (He-N_2-O_2) in animals was carried out with results as shown in Figure 66. The figure shows that while the multiple gas mixture had clear advantages over air, it produced a pattern of bends incidence not different from that found when helium-oxygen mixtures were used (31). On theoretical grounds the use of a multiple inert gas mixture should have the advantages proposed, but only until the first and most minute bubble or cavitation formed. Then the growth of the bubble would, as already stated, be a function of the sum of the partial pressures of all of the inert gases as well as the partial pressures of oxygen, carbon dioxide and water vapor. In spite of this, some

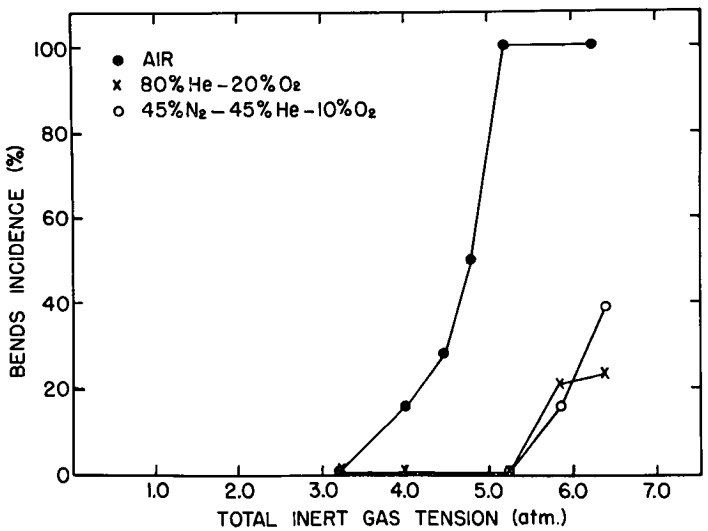

FIG. 66. Comparison of bends incidence in rats following three hour exposures to air, helium-oxygen and a nitrogen-helium-oxygen mixture at 6.4 atmospheres (31). Ascending at 25 feet per minute following near saturation exposures to pressures equivalent to 210 feet of sea water, a bends incidence curve for air was obtained for reference. A curve for helium at the same tension showed a much lower incidence of bends. When three gases (N_2-He-O_2) were employed, the bends incidence could not be distinguished from that when helium-oxygen was inspired. Exposures at higher pressures may be needed to distinguish between the two and three gas mixtures containing helium.

partial gains have been found in limited investigation of this method in man (36). Other gases such as methane, carbon tetrafluoride and sulfur hexafluoride have also been considered. Detailed study to exploit this principle is still important since it should offer advantages at shallow diving depths. The presence of nitrogen in a helium-oxygen mixture improves speech at high pressure. The alternate use of different inert gases creates a situation in the tissues which resembles that when mixtures containing more than one inert gas are breathed. Most important, even a limited improvement in decompression from the slowest tissues will shorten decompression following prolonged dives.

The Purposeful Alternation of Inert Gases

The questions related to alternation of exposure to different inert gases during diving overlap with but are different from those concerned with the use of mixtures containing several inert gases. It is possible to eliminate one inert gas from the tissues at the same time that uptake of a second gas is proceeding, and presumably without mutual interference. In the First

Symposium it was proposed that "some practical alternation of oxygen, oxygen-nitrogen, oxygen, oxygen-helium can be devised with a sequence aimed not only at extending diving duration by minimizing oxygen toxicity, but also by minimizing the need for slow decompression by permitting the elimination of inert gas in the act of extended diving operations" (27). The concept has been cited elsewhere (21, 26) and is now receiving attention in several laboratories (1, 5, 17, 21). Under certain circumstances of timing, depth and choice of gas, this principle will cause the release of one gas from a "slow tissue" at a rate more rapid than the uptake of a second gas. As additional inert gases become available, this procedure should become increasingly important.

An extension of this principle, which also deserves meticulous study for its application to bends treatment at pressures of three atmospheres and above is the purposeful alternation of nitrogen-oxygen mixtures with oxygen in the treatment of helium bends (and alternation of helium-oxygen mixtures with oxygen in the treatment of nitrogen bends (Table 28)). This principle of alternating an inert gas with oxygen will probably have its greatest application in the late phases of decompression after deep diving of short duration, after saturation diving to any depth, and as an adjunct to decompression required in excursion diving from a submerged base.

Combining the Principles of Alternation of Inert Gases with Fluctuation of Oxygen Tension

Combining several of the methods for hastening inert gas elimination has special attraction (26). Again, particularly at the late stages of a long decompression, during treatment of severe bends, or in relatively shallow diving (as to four to six atmospheres) it appears advantageous to use both the alternation of inert gases and the phasic alternation of high and low inspired oxygen pressures to minimize uptake of any particular inert gas, to increase the outward gradient for another inert gas, and to optimally extend oxygen tolerance. The pattern shown in Table 29 resembles that shown in Table 28 as a treatment of bends. There is no question but that the number of possible variations of this approach will make it difficult to arrive at an optimal procedure.

The Use of Drugs to Speed Inert Gas Elimination

One further aspect of decompression procedure concerns gains which may ultimately ensue from the use of pharmacological aids to accelerate inert gas exchange. Oxygen remains the key drug for this purpose and no other agent seems to offer promise of speeding diffusion. Drugs such as isoproterenol and aminophylline are available and should produce an increase in cardiac output and systemic vasodilation. Drugs such as nitro-

TABLE 28

Hypothetical Examples of Treatment of Helium Bends by Purposeful Alternation of Oxygen with Inert Gas-Oxygen Mixtures

Simultaneous use of high ambient pressure, high oxygen pressure and a different inert gas than that which produced the bends provides the advantages of each measure. Alternating oxygen pressures provides the benefits of high oxygen pressure while delaying onset of toxicity. Examples 2 and 3 resemble and blend with the principle of periodic oxygen interruption in the oxygen treatment of bends (Chapter 17).

EXAMPLE 1

PRESSURE (ATM)	INSPIRED GAS MIXTURE	ATM. O_2	ATM. N_2	DURATION (MIN)
1.0 to 4.0	100% O_2	1.0 to 4.0	0	10 min. or compression time
4.0	25% N_2-75% O_2	3.0	1.0	20
4.0	75% N_2-25% O_2	1.0	3.0	10
4.0	25% N_2-75% O_2	3.0	1.0	20
4.0	75% N_2-25% O_2	1.0	3.0	10
2.0	100% O_2	2.0	0	30
1.0	100% O_2	1.0	0	60

Intermittent exposure to 3.0 atm N_2 for one-third of the time is equivalent to continuous exposure to 1.0 atm N_2 and should not induce nitrogen bends while aiding the elimination of helium.

EXAMPLE 2

1.0 to 3.0	100% O_2	1.0 to 3.0	0	20 minutes including compression time
3.0	80% N_2-20% O_2	0.6	2.4	10
3.0	100% O_2	3.0	0	20
3.0	80% N_2-20% O_2	0.6	2.4	10
3.0	100% O_2	3.0	0	20
1.0	100% O_2	1.0	0	60

Intermittent exposure to 2.4 atm. N_2 for one-third of the time is equivalent to continuous exposure to the nitrogen pressure in air at sea level and should not induce nitrogen bends while aiding the elimination of helium.

EXAMPLE 3

1.0 to 2.0	100% O_2	1.0 to 2.0	0	compression time
2.0	100% O_2	2.0	0	60
2.0	80% N_2-20% O_2	0.4	1.6	15
2.0	100% O_2	2.0	0	60
1.0	100% O_2	1.0	0	60

TABLE 29

Combination of Alternation of Inert Gases with Fluctuation of Oxygen Tension for Aiding or Minimizing Decompression

This two hour dive to 100 feet with fluctuating oxygen pressure is roughly equivalent to a continuous exposure for two hours to a mixture containing about 30% helium and 30% nitrogen. Official decompression schedules for such mixtures have not yet been established. If air had been breathed for two hours at four atmospheres, a 132 minute decompression would have been required. In this schedule, if the inert gas were all nitrogen, the decompression required would be about 51 minutes; if all helium, about 45 minutes would be required. The influence of the use of both helium and nitrogen, together with terminating diving at a partial pressure of only two atmospheres of nitrogen or helium, are expected to further shorten decompression.

Activity	Depth (ft)	Inspired Gas Mixture	Oxygen (atm)	Inert Gas (atm)	Time (min)
Diving	99	85% He + 15% O_2	0.6	3.4	10
		50% N_2 + 50% O_2	2.0	2.0	10
		50% He + 50% O_2	2.0	2.0	10
		85% N_2 + 15% O_2	0.6	3.4	10
		50% He + 50% O_2	2.0	2.0	10
		50% N_2 + 50% O_2	2.0	2.0	10
		85% He + 15% O_2	0.6	3.4	10
		50% N_2 + 50% O_2	2.0	2.0	10
		50% He + 50% O_2	2.0	2.0	10
		85% N_2 + 15% O_2	0.6	3.4	10
		50% He + 50% O_2	2.0	2.0	10
		50% N_2 + 50% O_2	2.0	2.0	10
Decompression	10				?

glycerine which, while directly dilating peripheral vessels, lead to reflex vasoconstrictor activity elsewhere are unlikely to be of benefit; and still other drugs, like nicotine, probably predispose to bends by the peripheral vasoconstriction they indirectly produce.

The Limitations of Narcosis

Differences among the inert gases in their capacity to induce narcosis have been studied in several animal species (9) and are described elsewhere (6, 12) and in this volume (11). Only a few of the studies have provided the precise pharmacological dose-response information required to predict the limits of human tolerance to extremely high gas pressures. It is known that the inert atmospheric gases can be ranked in order of decreasing narcotic properties as Ar, N_2, Ne and He. The place of hydrogen is not yet established but it will probably be less narcotic than helium.

As with any drug, the increasing narcotic influences of increasing gas pressure upon each human function, such as judgment, dexterity, hearing

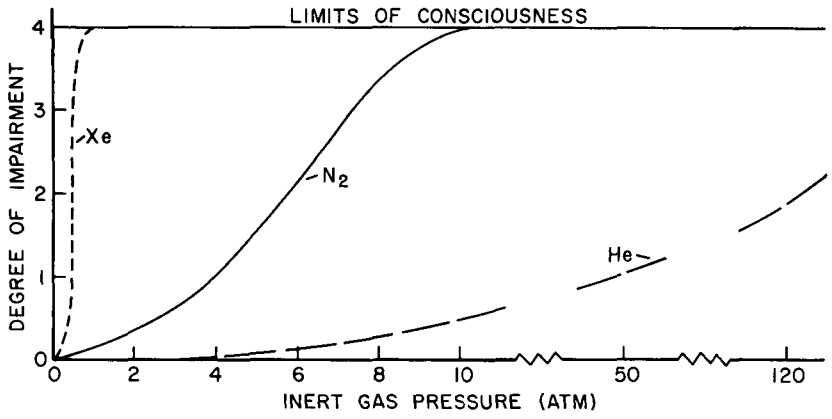

FIG. 67. Limitations imposed by narcosis

Impairment due to the narcosis produced by inert gases will vary in the form of the hypothetical "S" shaped pharmacological dose-response curves shown. The degree, but probably not the nature of the narcosis will be modified by: the characteristics of the gas (Ar, N_2, Ne, H_2, He), the absolute pressure (the dose), the effects of additive factors (CO_2, hypothermia, drugs, sleep), and the influence of antagonistic factors (drugs, exercise, purposefulness).

or even consciousness, should have the classical "S" shape of the pharmacological dose-response curve. Figure 67 illustrates diagrammatically the probable order of the gross differences to be defined for xenon, nitrogen and helium. Since none of these curves has been thoroughly established for any function in man, the figure is only an approximation. However, the curves are reasonable and indicate that serious impairment, e.g. of consciousness, occurs with less than one atmosphere of xenon and with less than 10 atmospheres of nitrogen, but helium may require more than 100 atmospheres to produce severe narcosis. This latter prediction is based upon the simple observation that at inspired helium pressures of 120 atmospheres (equivalent to about 4000 feet of sea water), mice do not lose consciousness (30). Since the dose of helium (the helium partial pressure) in the brain cortical neurons of the mouse should be exactly equal to the dose in human cortical neurons in an equilibrium state in the same environment, there is reason to believe that man might well be able to maintain useful consciousness to this extreme depth. Even if it can be learned that the human brain can function effectively when affected directly by helium pressures of 4000 feet of sea water, useful diving depth for man may still be limited by narcosis at lesser depths as additional factors aggravate the direct effects of helium or hydrogen itself. Such factors can be presumed to include carbon dioxide retention, hypothermia, sedative drugs, sleep and general central nervous system fatigue. Moderate narcosis may prove susceptible to counteraction

by central stimulants or by the arousal resulting from exercise and purposeful activity.

The Limitation of Pulmonary Ventilation

Pulmonary airway resistance increases when any gas is breathed at high pressure, and the increased resistance imposes limitations upon alveolar ventilation. Depending upon the degree and duration of exposure to extremely high pressure, these physiological limitations can be expected to include not only carbon dioxide retention and consequent exaggeration of inert gas narcosis, but also fatigue of respiratory muscles and diminished work tolerance. None of these limitations has been quantitatively defined over a range of increased gas pressures, although work is now being focused upon them. The magnitude of the problem related to airway resistance depends largely upon the density of the compressed gas breathed at any particular depth. Since nitrogen is about seven times more dense than helium, the density of nitrogen at about 200 feet of sea water is as great as that of helium at a 1000 foot depth. By contrast, the airway resistance when breathing an aqueous solution is approximately 36 times that when breathing air at sea level (22).

The physiological derangements produced by increased work of breathing and deficient pulmonary ventilation can be expected to be proportional to the degree of physical activity or other respiratory stimulation. Serious interferences with alveolar ventilation have been observed with nitrogen as the inert gas at a 600 foot depth (29), and maximal capacity to accomplish pulmonary ventilation is grossly diminished at 400 feet, even when helium-oxygen mixtures are used. The occurrence of moderately increased airway resistance does not at all exclude man from direct, purposeful underwater activity. As in the Everest mountain climbing expeditions, physiologically handicapped individuals can accomplish critically useful work if the requirement for degree of physical exertion is minimized or the pace of work is tempered by unnarcotized good judgment. Eventually, at extreme depths, ventilatory incompetence can be expected to occur even at absolute rest and, if it does, the limitation of pulmonary ventilation will prove to be the first real barrier to extending diving depth. Well before this stage is reached it is hoped that the combined skills of the engineer and the physiologist will provide for the assisted alveolar ventilation which will permit activity to the full range of depths defined by direct and unexaggerated central narcotic effects of inert gases.

Composite Influences and Interactions

It is evident that there is much hard work to be done and much basic and also immediately applicable information to be obtained. Many of the

contributors to this volume are actively engaged in this effort with an increasing energy and scope of interest. It will help all of us to remember that extension beyond present laboratory or open sea methods of diving and decompression will require many kinds of information and laborious validation of concepts and procedures. No single solution is to be expected for any limitation, and the relative value of multiple solutions will be difficult to establish.

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22 | Reynold T. Larsen and Walter F. Mazzone

Excursion Diving from Saturation Exposures at Depth

Until 1962, when man began to place submerged stations on the ocean floor at ambient pressure, nearly all diving operations had begun and ended at a pressure of 1 atmosphere absolute. Even locking out divers from submerged submarines involves starting out at the internal pressure of the submarine, approximately one atmosphere, and returning either to this pressure or to the surface of the sea itself. All standard diving tables are based on departure from, and return to, one atmosphere. A single exception is the repetitive dive table, where allowance is made for additional nitrogen in the tissues from previous dives.

Two types of diving fall outside the coverage of these tables. These are diving in bodies of water at high altitude, where atmospheric pressure is considerably below 1 atmosphere absolute, and diving from submerged stations such as the Sealab or Conshelf habitats, where the pressure greatly exceeds 1 atmosphere absolute.

In this paper, the term "saturation diving" will be applied to diving operations in which divers go under increased pressure, either in the sea or in a pressure chamber, and remain longer than 24 hours. This allows all the tissues of the body to saturate fully with the inert gas or gases being breathed. In practical terms, this requires an undersea habitat for ocean projects.

Haldane's principle of allowable ratios of tissue inert gas (1) suggests that the same no-decompression limits applying in dives from saturation at 1 atmosphere absolute to 4 atm. abs. should apply, in these special cases, to dives from saturation at ¾ atmosphere absolute to 3 atmosphere absolute and dives from saturation at 2 atmospheres absolute to 8 atmospheres absolute. If this is so, the standard tables would give inadequate protection in diving at altitude, and they would be unnecessarily restrictive in diving from submerged stations.

While it is rather widely accepted that diving at altitude increases the danger of decompression sickness, very little experimental work has been done in this area. Boycott, Damant and Haldane did give support to this hypothesis with some of their animal work (1). No sound diving tables have been prepared, because the demand for such diving has not been sufficient to justify the great effort and cost which would be involved.

In the case of deep saturation, however, the need for tables is obviously great enough to justify their preparation, and the lack thereof is a consideration of time. It is less than 4 years since Conshelf I submerged, and less than 2 years since Sealab I was put down off Bermuda. Future stations will be put down to greater depths, and attempts will be made to establish practical industrial operations from these stations. It, therefore, becomes imperative that we establish the limits which divers must observe in working below, and also above, the depth of their habitat.

The present study was undertaken as a beginning in developing tables for diving from submerged stations.

Methods

Diving tables for this study were calculated by Capt. Robert D. Workman, of the U. S. Navy Experimental Diving Unit (3). Calculations were based on the method described by Workman in 1965 (2) and derived from Haldane's principles, as previously modified by U. S. Navy experimentation. Some modifications were made in the method in that bottom times were preselected, and allowable maximum depths with no decompression for these bottom times were calculated. These depths and times are indicated in Table 30. All excursions were made after a 24 hour period of saturation at 35 feet gauge.

The entire series of dives was first performed using large dogs, then repeated using human subjects. All dives were done in dry pressure chambers at the Submarine Medical Center. Compressed air was used as the breathing gas throughout the saturation period, the excursions and de-

TABLE 30

No-decompression Excursions from Saturation in Compressed Air at 35 Feet Gauge

Total Depth (ft gauge)	Net Depth of Excursion	Bottom Time (min)
165	130	30
135	100	60
117	82	90
109	74	120
105	70	150
100	65	240

TABLE 31

Decompression to Surface after Excursion Dives

Depth and Bottom Time of Excursion	Decompression to Surface
165 ft for 30 min	Ascent to 10 ft at 5 fpm
135 ft for 60 min	2 hrs on air at 10 ft
117 ft for 90 min	1 hr on O_2 at 10 ft
109 ft for 120 min	Ascent to surface at 2 fpm
105 ft for 150 min	Ascent to 20 ft at 3 fpm 20 min on air at 20 ft Ascent to 10 ft at 2 fpm 2 hrs on air at 10 ft 1 hr on O_2 at 10 ft Ascent to surface at 2 fpm
100 ft for 240 min	Ascent to 20 ft at 3 fpm 40 min on air at 20 ft Ascent to 10 ft at 2 fpm 2 hrs on air at 10 ft 1 hr on O_2 at 10 ft Ascent to surface at 2 fpm

compression to the surface, with the exception of a period of oxygen-breathing during decompression in the human experiments as described below. The chambers were ventilated frequently with compressed air to prevent accumulation of carbon dioxide and depletion of oxygen. Rates of ascent and descent for the excursions were considered to be 60 feet/min for purposes of calculation, and these rates were actually used in the animal exposures. In the human exposures, the actual rates were 40–50 feet/min., limited by the capabilities of the chamber used. After the completion of excursion dives, subjects were held at 35 feet for 6 hours to observe for symptoms of decompression sickness. They were then decompressed to the surface, on schedules also provided by Workman (Table 31).

In the animal series, repetitive excursions were made, as many as 8 in a single saturation run. Intervals of 75 to 120 min at 35 feet separated the repetitive excursions. Decompression to the surface from 35 feet was shortened for the animals on the basis of our own calculations (vide infra). In the human series, repetitive excursions were made only once. During the first saturation exposure, two excursions were made to 165 feet for 30 min, with an interval of 4 hours at 35 feet between excursions. All other human exposures consisted of only one excursion after the initial period of saturation.

Thirteen Navy divers served as subjects for the human series, with at

TABLE 32

Description and Results of Animal Excursion Series and Human Excursion Series

A. Animal Series		B. Human Series	
Saturation exposures	7	Saturation exposures	15
Excursions		Excursions	
165/30	13	165/30	6
135/60	8	135/60	4
117/90	4	117/90	1
109/120	4	109/120	2
105/150	4	105/150	2
100/240	3	100/240	2
Total	36	Total	17
Cases of decompression sickness	0	Cases of decompression sickness	0

least two men in the chamber at all times. One pair of divers had two saturation exposures. All the others had one exposure each. Subjects were examined by diving medical officers before and after their exposures. They were kept in the immediate vicinity of the chamber for 3 hours after surfacing to be observed for symptoms of decompression sickness.

Dogs were examined shortly after each excursion by walking them in the chamber, inducing them to jump through the hatch into the outer lock, and by manipulating their extremities to find any tenderness which might be present.

Results

Table 32A and 32B lists the number of excursion dives for each depth-duration and the cases of decompression sickness for both the animal series and the human series of experiments.

One diver reported "skin bends" in the arms and ears shortly after an excursion to 165 feet for 30 min. In the strict sense, this is a manifestation of decompression sickness, but it is not treated when unaccompanied by other symptoms. It may have been precipitated by chilling of the skin during rapid ascent in the chamber. In subsequent excursions, divers dressed more warmly during ascent, and no further "skin bends" occurred. On two occasions, individual divers experienced aching pains in the lower extremities several hours after completing decompression to the surface. No skin rash was associated, nor were there any of the more serious symptoms or signs of decompression sickness. The pains did not show the progressive course typical of bends. In one case, recompression was tried without relief of the pain. It was felt that these two cases did not represent decom-

pression sickness. Possibly these aches bear some relation to the widespread, mild aches reported by several subjects during their first few days of saturation in Sealab I and Sealab II.

Discussion

The basis of decompression sickness and of decompression theory was presented by Haldane in 1908 (1) in a paper which still dominates its field. He set forth the principle of exponential saturation and desaturation of inert gas in tissues, along with the concept of theoretical tissues of differing half-times with regard to inert gas uptake and elimination. Because he worked with dives of limited depths and duration, he came to the conclusion that the slowest-saturating tissue in man had a half-time of about 75 min, and that complete saturation with inert gas occurred in an exposure of 5 hours. (This represents 4 times the half-time of the tissue, enough to produce 94% saturation. Haldane felt that this was nearly complete saturation. Present standards consider "complete saturation" to be at least 98.5% saturation, the degree produced by an exposure at least 6 times as long as the half-time of the tissue.) Subsequent work with deeper and longer dives indicates that theoretical tissues with half-times up to 240 min. must be considered in man, and that complete saturation requires an exposure of at least 24 hours, either for helium or for nitrogen (2).

Haldane postulated that the bubbles causing decompression sickness form during or after decompression, when the tissue pressure of nitrogen exceeds by too great a degree the ambient pressure. He felt that the ratio of these two pressures was the critical factor, and maintained that a tissue nitrogen pressure of twice the ambient pressure was safe in all tissues. Using this ratio, he prepared decompression tables which were widely used for many years.

Subsequent work by the U. S. Navy developed the concept of multiple allowable ratios, larger ratios for the faster tissues and smaller ratios for the slower tissues. Earlier U. S. Navy diving tables were calculated on the basis of these ratios.

It has been found empirically that the ratios which are adequate for short and shallow dives do not give adequate protection for longer, deeper dives. Present-day usage, as in the preparation of tables for this study, involves the use of maximum tissue inert gas tensions permissible for ascent to a given depth. These values, represented by the symbol M, are derived from the ratio theory as modified by experimental and field experience. They are available in tabular form both for nitrogen and for helium (2). In the slowly-saturating tissues, these values are considerably more limiting than the older ratios.

All tissue gas pressures in these calculations are expressed as feet of sea

water (1 foot = 0.445 psi), and all pressures are absolute unless otherwise indicated. Calculated tissue inert gas pressures at any given point in a dive are represented by the symbol Q.

In any dive, whether from the surface to some depth or from saturation at depth to some greater depth, all the tissues take up some additional inert gas. The amount absorbed depends upon the depth and duration of the dive and the half-time of the particular tissue. In ascending from a dive, a decompression stop must be made whenever a depth is reached where the M value for any of the theoretical tissues is equal to the actual inert gas pressure in that tissue. The tissue which will first come into equality with its M value during ascent is called the "controlling tissue", since it determines the depth of the first decompression stop. If this equality does not occur until the diver comes to or above his starting depth, no decompression stop is needed, and the dive is called a "no-decompression" dive.

In general, short dives tend to be controlled by the faster tissues and long dives by the slower tissues. In a dive requiring several decompression stops, control may shift from a faster tissue (in the earlier stops) to a slower tissue (in the later stops).

It is important to differentiate between ascent from a level of saturation to the surface and return to saturation level from an excursion to greater depth. At the saturation level, all tissues have essentially the same inert gas pressure, and the slowest tissue considered will be controlling through the entire ascent. Excursions from a saturated level are relatively brief, and faster tissues control ascent back to the level of saturation. The excursions in this study demonstrate this. These dives were calculated to bring the controlling tissue to equality with its M value on return to 35 feet. Table 33 shows inert gas tensions in the various theoretical tissues at the

TABLE 33

Nitrogen Tissue Pressures on Return to 35 Feet Gauge after Excursions
The *italicized* values are the controlling tissue tension for each dive.

Tissue Half-time	Q for Excursions Indicated						M
	165/30	135/60	117/90	109/120	105/150	100/240	
10	138	127	117	110	107	103	144
20	*119*	121	115	110	108	104	124
40	95	*105*	*105*	*105*	*105*	104	105
80	77	86	89	91	94	*99*	99
120	70	77	80	83	86	92	94
160	66	72	75	78	80	87	91
200	64	69	71	74	78	83	89
240	62	66	69	71	73	80	88

time of return to 35 ft gauge from each of the dives, and also shows the M values for nitrogen which allow ascent to 35 ft gauge. The controlling tissue tension for each dive is italicized.

It will be noted that the shortest excursion is controlled by the 20 min half-time tissue, the longest excursion by the 80 min tissue, and all the others by the 40 min tissue. In contrast, ascent from saturation at 35 ft gauge to the surface is controlled throughout by the 240 min tissue.

Comparing results of animal studies with those in man is generally difficult, and can often lead to serious error. In studies of decompression sickness, it has generally been found that laboratory animals show greater resistance to decompression sickness than does man, and that this resistance is in some degree proportional to decreasing size in the animal. Haldane attributes this phenomenon largely to the more rapid rates of respiration and circulation in small animals (1). The dog appears to have tissues with half-times up to more than 80 min. Some dogs appear to require 12 to 18 hours to reach full saturation, indicating tissue half-times up to 2 and 3 hours (4). This suggests that the dog's degree of oversaturation in these excursions should be comparable to man's in the controlling tissues. An effort was made to confirm this by diving a dog (one which made many of the experimental runs) to 130 feet for 30 minutes and surfacing directly at a rate of 60 feet/minute. This dive represented the same excursion depth and bottom time as the excursion to 165 ft for 30 min from saturation at 35 ft. Calculated tissue pressure for half-times of 10, 20, 40 and 80 min indicated dangerous excesses of nitrogen in all these tissues. About 30 min after surfacing, the dog developed clinical bends in one foreleg. Symptoms responded nicely to recompression therapy.

The lack of very slow tissues in the dog accounts for the fact that decompression from saturation at 35 ft could be accomplished much more rapidly for the dog than for man (100 min compared with 190–235 min). For both man and dog, these schedules were made quite conservative and could be shortened somewhat with little risk of decompression sickness. Since the objective of this study was evaluation of the tables for the excursions, it was considered necessary to minimize the possibility of inducing decompression sickness in surfacing, since it would be most difficult to prove this was not a result of the excursions.

On the basis of the limited amount of data obtained, a tentative no-decompression curve for dives from saturation at 35 ft gauge has been constructed. The number of exposures is insufficient to make the curve definite, but the absence of bends in any of the exposures suggests that it may err to the conservative side. Even so, this curve shows definite advantages over the no-decompression curve for diving from the surface. Considering only the net depth of the excursion (depth below the saturation

TABLE 34

Allowable Bottom Times in Minutes for Various Net Excursion Depths

Net Depth	From Surface (5)	From 35 Feet
130	10	30
100	25	60
82	38	90
74	46	120
70	50	150
65	55	240

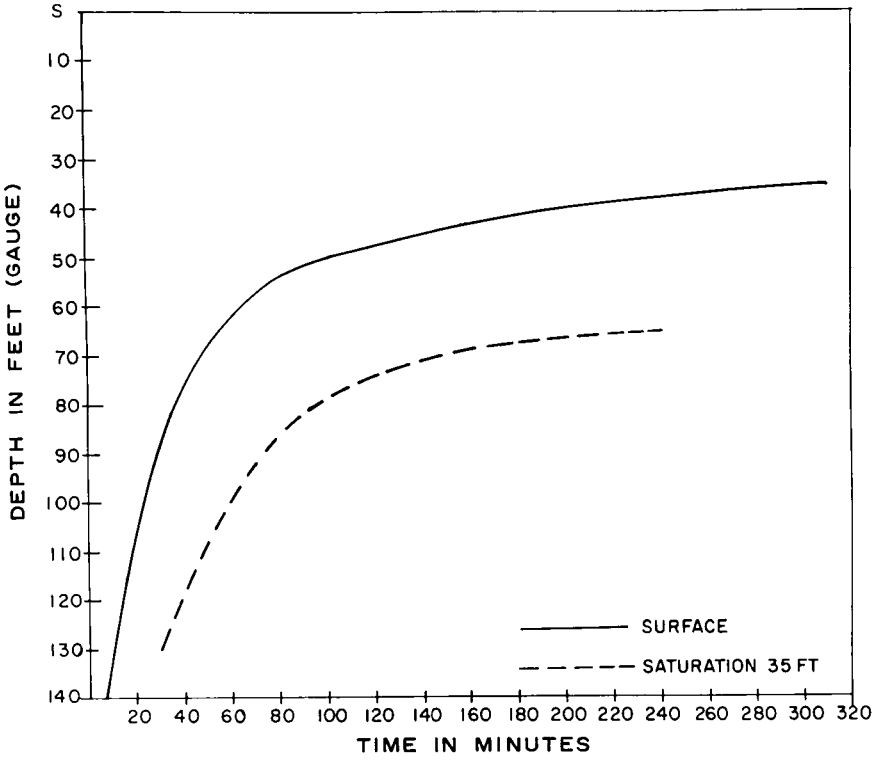

Fig. 68. Comparison of allowable bottom times for net depths (depth below the level of saturation) in dives from the surface and dives from a saturated state on compressed air at 35 feet gauge. (See Table 34).

level) it allows increases in bottom time by factors that range from slightly over two to slightly over four (Table 34, Fig. 68).

When considering the total depth reached, the increases in bottom time are even greater, ranging up to a factor of more than nine. (Table 35, Fig. 69).

TABLE 35

Allowable Bottom Times in Minutes for Various Total *Depths*

Total Depth	From Surface (5)	From 35 Feet
165	5	30
135	10	60
117	17	90
109	20	120
105	22	150
100	25	240

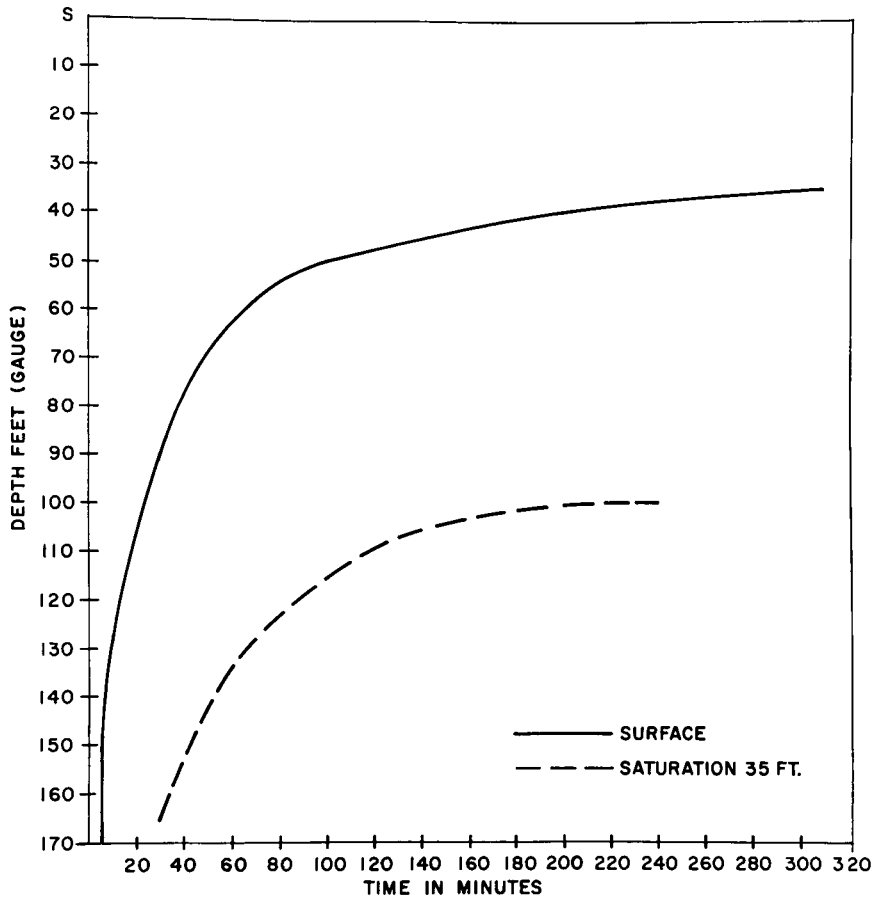

Fig. 69. Comparison of allowable bottom times for total depths reached in dives from the surface and dives from a saturated state on compressed air at 35 feet gauge. (See Table 35).

TABLE 36

Helium Tissue Pressures for an Excursion to 700 Feet Gauge from Saturation at 430 Feet Gauge

Tissue Half-time (min)	Q after 31 Minutes at 700 Feet	Q on Return to 430 Feet	M for Return to 430 Feet
10	687	660	675
20	626	*620*	623
40	563	565	575
80	516	519	571
120	497	499	569
160	487	489	543
200	481	*483*	483
240	477	478	483

It is obvious that the day of the shallow submerged station, with a compressed air atmosphere, is already past. While there might be some future application for shallow stations, the cost is high for working in depths that are accessible to surface-based divers. Conshelf II had two habitats, one at 35 feet gauge (compressed air) and one at 85 feet gauge (synthetic atmosphere). All subsequent submerged stations have been at much greater depths (193 to 432 feet), and all have had synthetic atmospheres (helium-nitrogen-oxygen or helium-oxygen). For these reasons, it is quite possible that the tables described here will never be used in actual dives. The importance of these dives in confirming the hypothesis, however, is great.

No laboratory studies have yet been completed in excursion diving from saturation at greater depths. Such studies are difficult and quite expensive, but must be undertaken if we are to learn whether the advantages described above will be further multiplied at greater depths.

An attempt can be made to predict such dives by calculation. It must be emphasized, however, that this involves extrapolation from established M values to depths where no experimental work has been done. Such figures are quite dubious at best. Accepting this major qualification, a theoretical dive might be made from saturation at 430 feet gauge (approximately the depth postulated for Sealab III) to 700 feet gauge with a bottom time of 31 minutes. Table 36 shows the tissue helium pressures and the highly speculative M values. The atmosphere, both for the station and for the excursion dive, is assumed to be 98 % helium, 2 % oxygen. Rates of descent and ascent are 60 feet/minute.

In this case, the 20 min tissue might be expected to be the controlling tissue because of the short duration of the dive. Actually, the 200 min tissue controls. Unlike M values for faster tissues, which increase more rapidly than depth increases, M values for the 200 min and 240 min tissues increase linearly with increasing depth. Rather than having a constant ratio of

$$\frac{M}{\text{abs. depth}}$$

there is a constant gradient between the two of about 20 ft (4,2). This relationship, if borne out by actual studies at these depths, will introduce a limitation on saturation-excursion diving, particularly on excursions of considerable length. Nevertheless, a net excursion of 270 feet for 31 minutes with no decompression is a handsome advantage over diving at shallower depths. Similar calculations suggest that a no-decompression excursion from 430 feet (saturation level) could be made to 600 feet gauge with a bottom time of 80 minutes (4). This dive is more practical in a continental shelf project.

A small amount of actual field experience in saturation-excursion diving has been accumulated in the course of some of the saturation projects which have been carried out. Unfortunately, very few good data are available on these dives in the publications which have come forth from the projects.

In Sealab II, divers saturated at 195 feet gauge on 75% helium, 20% nitrogen, 4% oxygen made excursion dives to 300 feet gauge. Accurate bottom times are not available, but total time of the dives ranged from 33 to 50 minutes. Breathing mixture was 85% helium-15% oxygen. In the semiclosed-circuit apparatus used, this would give a breathing bag mixture of about 13% oxygen, about 85% helium and a small amount of nitrogen eliminated from the diver's tissues.

Problems of field work include lack of precise recording of times, nonstandard and variable rates of descent and ascent, and questionable accuracy of the small depth gauges carried by the divers. While the above experiments have shown that deep excursions can be accomplished, it seems evident that laboratory studies in wet and dry chamber complexes will be far more practical for testing actual tables.

Saturated divers, while capable of large downward excursions, are sorely limited in their capacity to ascend above their saturation depth. The peculiar relationship between M and depth in the very slowly-saturating tissues is responsible for this phenomenon. It appears that a diver saturated with helium cannot ascend more than about 1 atmosphere (33 feet) above his saturation depth without risking decompression sickness (4). A somewhat greater margin might be allowable with nitrogen (2), but the narcotic properties and density of this gas make it unacceptable for deep work. The use of other inert gases, and of mixtures of inert gases, remains to be explored.

In saturation diving projects requiring work over a range of depths, the ascent limitation will probably require placing the habitat at the shallow limit of the working stratum. While this may limit the time spent on excur-

sions to the greatest depths in the working area, it will be an advantage in minimizing the pressure at which the divers achieve saturation, and therefore the decompression time required in ultimately bringing them to the surface.

If actual experience shows as great a shift in the no-decompression curve as appears likely from theory and from this early work, it should be possible to make nearly all excursions from a deep station on a no-decompression basis. This is an enormous advantage, in that the diver can return directly to the habitat in case of an emergency. If even longer excursions are necessary, it should be possible to make them with much shorter decompression periods than for comparable excursions from the surface.

Any free dive at great depths will have a considerable problem of gas supply. A diver at 700 feet will have a respiratory minute volume of several hundred standard liters/min. Any self-contained breathing apparatus used at such depths must be of a recirculating type if it is to have any practical duration. A closed circuit apparatus is the most economical in terms of gas usage. However, the need to control oxygen tension in the breathing bag within narrow limits, in order to prevent oxygen poisoning or hypoxia, presents major technological problems. Semi-closed circuit apparatus, such as the Mark VI apparatus used in Sealab I and Sealab II, is much safer but of more limited duration. In Conshelf III and, to a lesser extent, in Sealab II, hookah apparatus was used, pumping gas from the habitat atmosphere to the diver and back. This may be the most practical solution to the endurance problem. Although it shackles the diver to hoses and their hazards, it has the added advantage that a telephone cable can be incorporated into the hose.

Saturated divers making excursions at great depths probably will be able to limit their diving to excursions which carry little or no hazard of decompression sickness. Similarly, the hazard of traumatic gas embolism should be small, since the proportional expansion of gas in the chest is much less in an ascent to a deep habitat than it is in ascending a similar distance to the surface. Nevertheless, it is poor procedure to dive under conditions where no available diving tables apply. Decompression sickness might result from a very deep or very long excursion, and certainly could follow repetitive excursions. Inadvertent ascent above the saturation depth can readily produce decompression sickness, which might not be adequately treated by simply returning to the habitat. A diver unconscious from oxygen poisoning or hypoxia might easily suffer a traumatic gas embolism while being hauled back up to the habitat by his partner. Surfacing for recompression therapy at a support facility is unthinkable, since it would almost certainly produce massive, fatal decompression sickness. It therefore becomes necessary to plan the inclusion of a recompression chamber in the habitat. This further necessitates the calculation and testing of new treat-

ment tables. Present treatment tables are based on the principle of reducing bubble size. This concept might have to be abandoned for treatment in a deep saturation habitat, since increasing ambient pressure by a factor of four to six times would be utterly unfeasible with present technology. Utilization of pure oxygen to speed elimination of inert gas would have to be foregone. Minimizing, in the treatment breathing mixture, the partial pressure of that inert gas which has produced the bubbles is too important a factor in treatment to be abandoned, however. Since pure oxygen cannot possibly be used, consideration should be given to making up the breathing gas for treatment with one or more inert gases not present in the gas used for the dive. The new treatment table, then, might combine an elevation of pressure (much less in proportional terms than in present treatment tables, but hopefully sufficient to reach the "depth of relief") with shifting of inert gases to accelerate elimination of the offending gas.

For both diving tables and treatment tables, consideration must be given to the fact that submerged habitations will be put down over a considerable range of depths, probably from 200 feet or less to 600 feet or more. Since bottom topography and job considerations may preclude placing the habitat at a precise depth to accommodate the tables, it would appear that a vast number of tables might be required, based on saturation at all possible depths. It would be nearly impossible to test adequately such a profusion of tables. Hopefully, the no-decompression limits will prove sufficiently liberal that it will be sufficient to prepare tables based on saturation at a number of depths (possibly in 50-foot increments or greater) and let stations at odd depths use the table for the next shallower depth. Once the relationships are better understood, some interpolation between such tables might be possible.

Conclusions

1. The no-decompression curve for diving from the surface is shifted when excursion dives are made from saturation on air at 35 ft gauge. The shift is in the direction of greater allowable depths and bottom times, and it is of very significant magnitude.

2. The lack of specific diving tables and treatment tables for working from submerged habitats at hyperbaric pressures creates a dangerous situation for the divers involved.

3. There is an urgent need for the preparation of such tables, including enough saturation depths to provide effective coverage for divers anywhere on the continental shelf.

Acknowledgements

A special debt of gratitude is owed to Captain Robert D. Workman for his calculation of diving tables, and also for reviewing the manuscript

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Decompression Procedures for Deep, Open Sea Operations

The experiments to be described were designed both to provide further facts regarding the etiology of decompression sickness, and also to enable safe decompression procedures to be devised for deep dives in the open sea.

The first point to be established is how quickly, from the point of view of decompression sickness, does helium saturate the body tissues. Estimates have been made, but no sufficiently sound data are available. Some experiments by Duffner (1) suggest that the time to saturate the body tissues, as measured by the no-stop dive curve, is in the order of 12 hours, and hardly distinguishable from nitrogen. Looking at the solubility of helium in body tissues this result is somewhat surprising.

Assuming perfusion factors do not alter and taking as true the observations of Jones (2), then if the exponential exponent of the major slow component, assumed to be fat, is $K\alpha$ where α is the partition coefficient for the gas concerned between blood and fat tissue and K is the tissue perfusion factor, the ratio of the exponential exponents changing from nitrogen to helium will be $K\alpha_1/K\alpha_2$ i.e. α_1/α_2 where α_1 is the partition coefficient (water/tissue) for nitrogen and α_2 that for helium. Using the accepted values of $\alpha_1 = 1/5.2$ and $\alpha_2 = 1/1.7$ then $\alpha_1/\alpha_2 = 1/3$ very nearly. This means that the very slow fat component seen when breathing nitrogen will be altered when breathing helium to a tissue with a half-time 3 times smaller. Taking 60 minutes to 120 minutes as an appropriate range of values for the half-times on nitrogen one would expect the corresponding half times on helium to range between 20 minutes and 40 minutes. The effective saturation time would then be 2 hours to 4 hours.

Alternately one may suppose that in decompression sickness all the mechanisms are diffusion limited and in this case the speed of saturation would be expected to vary nearly in accordance with Graham's Law, with helium saturating the relevant tissues 2.65 times as rapidly as nitrogen. In

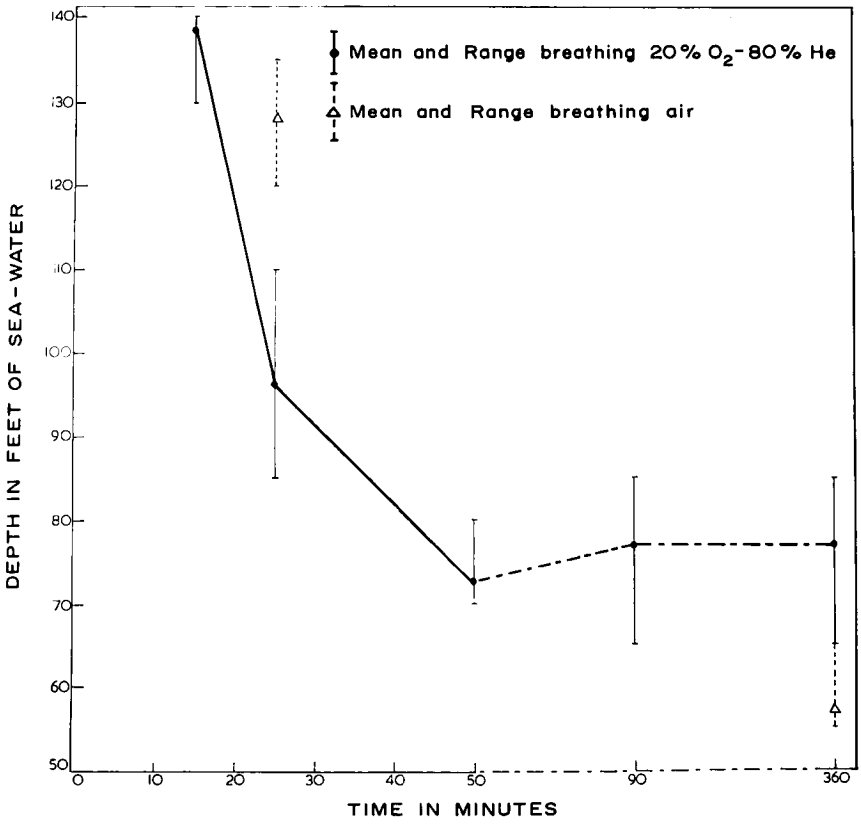

FIG. 70. Oxy-helium "No-stop" curve from data on six goats

practice, without vast numbers of experiments, this will be indistinguishable from the expectations of the perfusion limited ideas.

The first set of experiments was performed using female goats. The animal was placed in the pressure chamber and the door closed. All air inside was replaced by displacement with 80% He-20% O_2 while the animal was kept at atmospheric pressure. This took 3 or 4 minutes. Then the pressure inside was raised using 80% He-20% O_2 at a rate of 60 feet per minute to the desired level. After a certain time at this constant raised pressure the animal was decompressed at a uniform rate in 2.5 minutes back to atmospheric pressure. The door was opened and the animal brought out into air and watched for signs of decompression sickness.

The spread of results at various fixed times is displayed in Figure 70. The animals show no detectable difference in their threshold values for decompression sickness after a 50 minutes exposure. Reference to a similar curve of results on goats established using air as the breathing medium will

reveal that there is a just detectable difference between a 3 hour and a 4 hour exposure (6). Accurate comparison is difficult to make because only 6 animals were used to obtain the helium results whereas over 50 animals were used to obtain the air results. Within the limits imposed by relatively small numbers and also by the fact that searching for decompression sickness thresholds is performed using 5 feet increments, it is possible to state with confidence that goats effectively saturate with helium in not less than 40 minutes and not more than 90 minutes. Taking 65 minutes as being the average for most normal animals one would expect from both the perfusion and diffusion theories a saturation on air time of approximately 3 hours, which accords well with the practical findings.

An attempt was made to define the problem similarly using six men. The times of exposure chosen were 16 minutes, 120 minutes and 240 minutes. The procedure adopted was as follows.

Two men entered the pressure chamber and the door was closed. One man seated himself on a rowing machine, the other on a chair. They were compressed on air at 100 feet per minute. At the 35 feet level the men put on noseclips and commenced breathing 90 % He-10 % O_2 via a demand valve from a bank of high pressure cylinders on the outside of the pressure chamber. Once the desired pressure had been reached the man on the rowing machine commenced a two minute period of vigorous rowing. Upon completion of this work the men changed places, and these alternate periods of work and rest continued throughout the dive time. On decompression the men took a lung full of oxygen at either 50 feet, or just before leaving the depth, depending which was the shallower and were brought back to atmospheric pressure at a uniform rate of 50 feet per minute. The outline results are displayed in Figure 71. Certain resemblances to the goat results are immediately apparent. For short dives of 16 minutes duration there are cases of decompression sickness on helium at levels below the accepted normal practice on air.

On the other hand for the dives of 4 hours duration it seems that the helium performance is better than the air one. Using such small numbers it is impossible to state this with any certainty. The situation, particularly for the prolonged dives, is further complicated by the possibility that men can acclimatise themselves. This may be illustrated by the following observations. When the 2 hour exposures were commenced all 6 men completed a 40 ft. depth without incident. Two days later a 45 feet exposure yielded very minor fleeting pains in some of the men. This was interpreted to mean that they were near more serious troubles and therefore only 3 feet increments in pressure were now employed. The experiments continued therefore with exposures of 48 feet, 51 feet, 54 feet etc. up to 72 feet. Throughout these experiments transient post-decompression pains (niggles) were en-

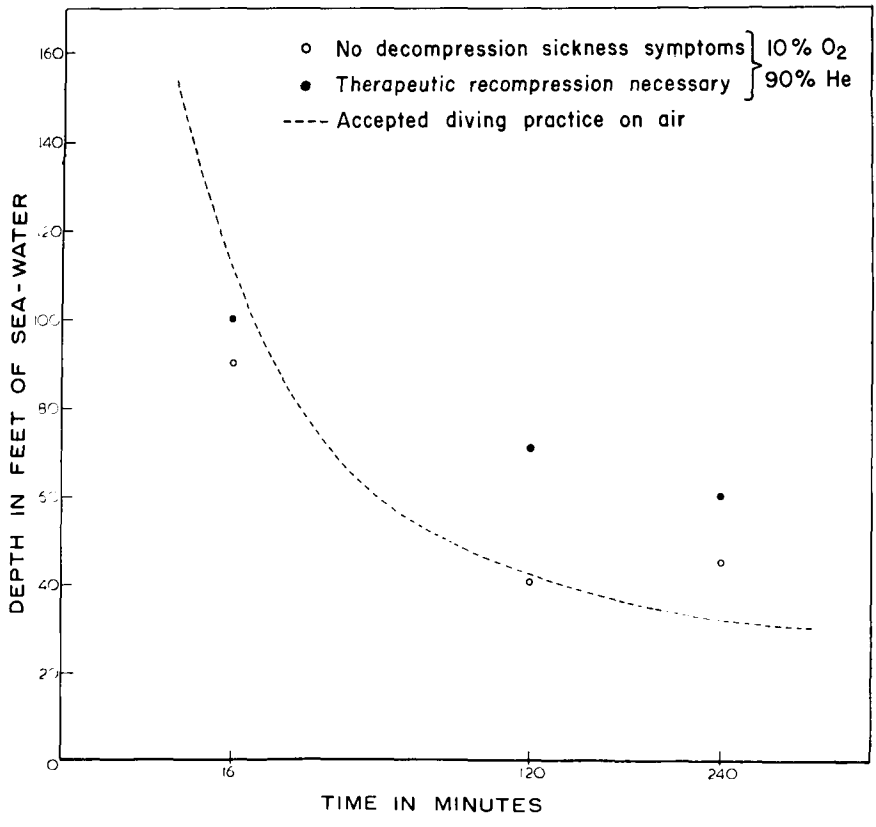

FIG. 71. Oxy-helium "No-stop" curve for men

countered at 51 feet, 57 feet, 60 feet, and 69 feet. These niggles were such a low level of trouble that it was not thought worth recompressing the man concerned. There were no itches or rashes accompanying any of these niggles. At 72 feet however, one man of a pair had a severe attack of decompression sickness almost immediately after reaching atmospheric pressure. This was considered the threshold for this group. It is of interest to note that 3 of the divers completed 2 hrs. at 75 feet without any ill effects whatsoever and that one of these three had complained of a mild transient pain after the 45 feet exposure very early in the series. Next these same men carried out 4 hour exposures. At 55 feet all men completed a trouble-free exposure, but at 60 feet two bends occurred. The position was now that 6 men had completed 2 hour dives, with minor aches and pains occurring sporadically at all pressures greater than 45 feet, but 72 feet seemed to be the upper limit for these transient post-decompression events. For 4 hour

exposures no troubles were encountered at 55 feet, but 60 feet seemed to be too much for a no-stop dive. After these 6 men had been carried through the first series of exposures, a second series not shown in Figure 71 was started with a group of 4 men. These men were given an initial exposure of 2 hours at 55 feet. One man had to be recompressed and two others had attacks of niggles. The man who had to be recompressed and one of his companions who had an attack of niggles were together tried at a later date on a dive of 4 hours at 45 feet which gave them no troubles at all.

Three facts are apparent from the results to-date.

a) The spread of pressure covering all forms of decompression sickness is very great. For the two hour exposures at least from 45 feet to 80 feet and for 16 minutes exposure at least from 85 feet to 130 feet.

b) It is possible to acclimatise to helium decompression, just as has been found amongst caisson and tunnel workers breathing compressed air (3). New starters, or men who have not dived for several weeks display lower decompression sickness thresholds. A suitable work-up period will lead to much more resistant individuals.

c) Insufficient data is available for assessing the true relative performances at 2 hours and 4 hours but it may be seen that at 4 hours the performance of a group of men on 90 % He-10 % O_2 is better than standard practice on 79 % N_2-21 % O_2 (air). Aso the preformance at 16 minutes is significantly worse on the oxy-helium than on air, even allowing for the altered oxygen percentage. These results bear a great resemblance to those obtained on the goats, and one would say by analogy that the saturation time of men would, as with goats, be much less on helium than on nitrogen, and lie between 3 hours and 6 hours.

Goats were first used to assess the following hypothesis. After a saturation exposure to pressure P_1 it is possible to ascend rapidly and safely to a pressure P_2 and that there is some simple relationship between P_1 and P_2 such that $P_1/P_2 = r$ (constant) or $P_1 - P_2 = K$ (constant). In the first instance this was tried on air, using a 6 hour exposure at P_1 followed by ascent in 2½ minutes to P_2.

The P_1/P_2 value which just gave a mild attack of the bends is obtained for each goat for a representative set of values of P_1. These threshold ratios are plotted versus the initial pressure of exposure in Figure 72. The ratio diminishes with increase of pressure and this decrease is most marked in the first 140 feet (absolute) pressure. From 140 feet to 230 feet absolute the ratio is nearly constant and these observations agree qualitatively with the power function curves expressing the relationship between pressure and ratio used in the calculation of the U. S. Navy air decompression tables (4). It is of interest to note that some of the results shown in Figure 72 were obtained by changing from greater than atmospheric pressure to sub-atmos-

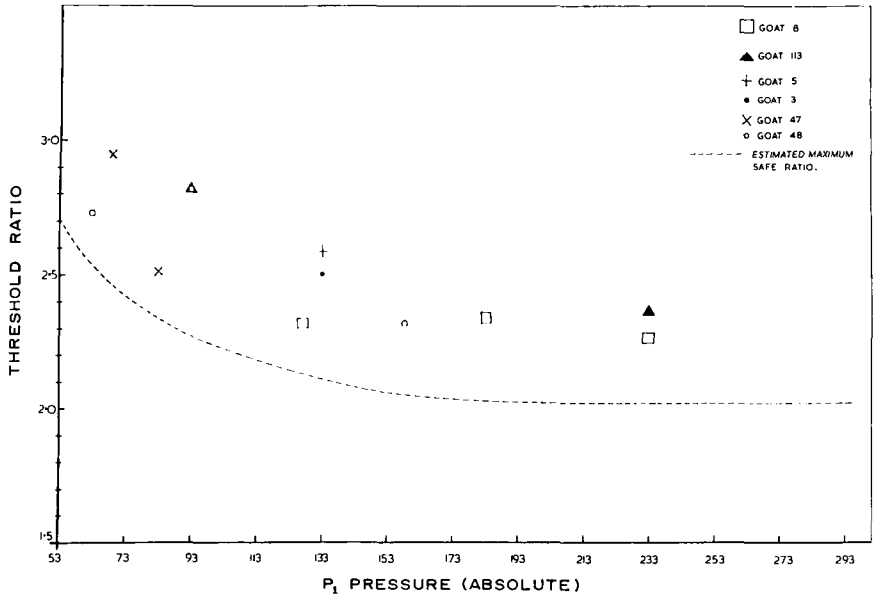

FIG. 72. Threshold ratio vs. pressure for goats breathing air

TABLE 37

Variation of Threshold Ratio following a Long Exposure to Oxy-Helium Gas

PRESSURE (GAUGE)		RATIO	
FEET SEA WATER	PSI	GOATS	MEN
45	17.8	—	2.67
66	29.4	3.0	—
350	155.9	2.09	—
600	267.2	2.00	—
800	356.3	—	1.59

pheric pressures. Similar threshold values are being obtained using helium-oxygen as the breathing medium. In Table 37 the threshold ratios for saturation or near-saturation dives on goats and men are given. On all these occasions a relatively mild attack of decompression sickness has been taken as indicating the threshold. The cut-back in the critical ratio on the goats breathing helium has the same features as on air. In the pressure range of 350 feet to 600 feet there seems to be a definite but relatively small change in the critical ratio, whereas from 350 feet to 66 feet there is a large change. With men the critical data are not well established but it has been shown that in addition to the data in Table 37 a 2 hour exposure at 500

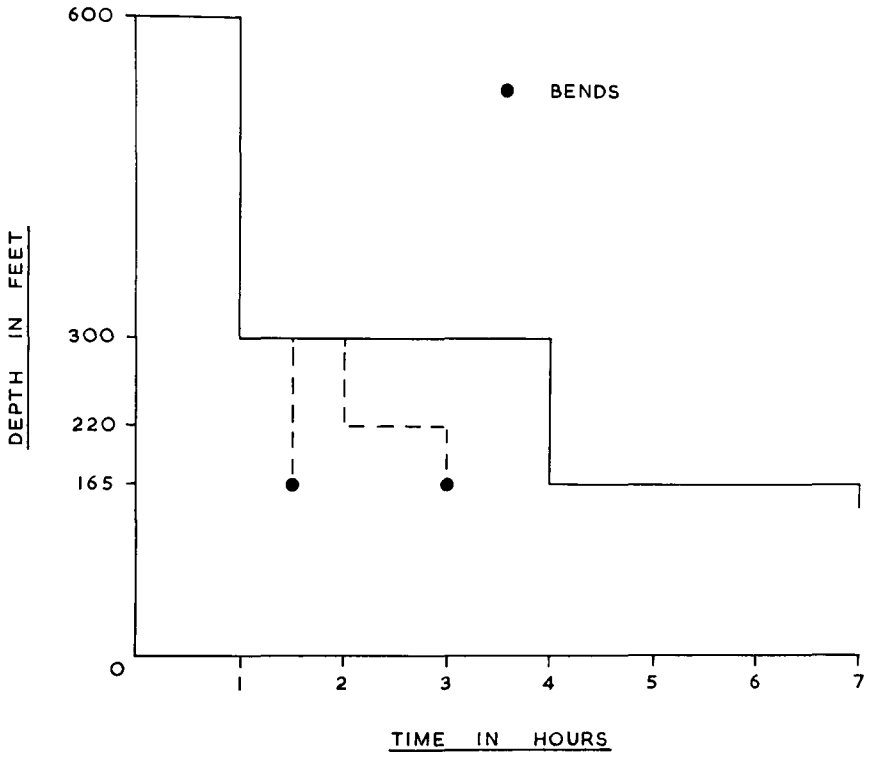

FIG. 73. Stage decompression of goats following a 50-minute dive at 600 feet breathing 10% O_2-90% He.

feet may safely be followed by a rapid ascent to 290 feet (ratio 1.65) and using 12 men, 4 hours at 300 feet may safely be followed by rapid ascent to 170 feet (1.64 ratio). The rule has now been reached that for dives at depths greater than 250 feet a 1.6 ratio or a drop in pressure of 200 feet, which ever involves the least pressure change is quite safe to establish the pressure value of the first stop following dives to depths as great as 800 feet for bottom times as long as 4 hours.

The goats were next used to establish the form of safe decompression schedules using only oxy-helium as the breathing medium. Figure 73 shows a series of attempts to reach 165 feet following a dive of 50 minutes at 600 feet by a single stage at 300 feet. A duration at 300 feet of 30 minutes was grossly inadequate to allow ascent to 165 feet, i.e. a ratio change of only 1.68 following a first ratio change of 1.9. A one hour stay at 300 feet followed by an intermediate stay of 1 hour at 220 feet was still inadequate to permit safe ascent to 165 feet. Eventually a 3 hour stay at 300 feet was found necessary to ensure trouble-free ascent to 165 feet. This served to emphasize

findings similar to those found on air (5). The rate of loss of the risk of decompression sickness is not the same as the rate of acquisition of this risk. No difference could be detected in the decompression requirements of a dive of 50 minutes duration and one of 6 hours. However when decompressing from such a dive a 50 minutes duration at a stage is certainly not equally as effective as 3 hours. This irreversibility was seen during the subsequent 3 hours stops from 165 feet to the surface. Pressure changes corresponding to a ratio of 1.3 were performed after a stage (stop) duration of 3 hours. This procedure met with complete success, but an attempt to repeat a 1.6 ratio following a 3 hours stay met with failure at the 60 feet level. Such a finding demonstrates that even after 3 hours the tissues of the animal are nowhere near returned to normal, otherwise immediate return to atmospheric pressure would have been possible, giving a ratio change of 2.82. To achieve such a ratio change would clearly require many hours in excess of the three already tested. Viewing this as a reflection of tissue half times it is possible to state that the half-times necessary to explain the tissue desaturation data in the decompression procedures are many times greater than the tissue half-times necessary to explain the saturation data.

At this juncture it may be concluded that the use of large and sudden pressure changes in the stage method of decompression creates a dangerous situation in the tissues, closely approximating an attack of decompression sickness. The possibility exists that if smaller pressure changes were made then there would be a more rapid pressure-time course back to atmospheric pressure. This hypothesis was tested a number of times on male human volunteers. Three representative sets of results are plotted in Figure 74. An exposure of 4 hours duration at 300 feet pressure, breathing 10% oxygen-90% helium, and using unacclimatised exercising subjects, was followed in many cases by rapid ascent to 170 feet with a period of 2 hours at this stage, and then rapid ascent to 120 feet with a 2 hour's pause here. These long duration stops and large pressure drops can give a successful but lengthy decompression. Several attempts were made to drop the pressure rapidly only to 220 feet and then follow in 10 feet stages a relatively smooth decompression back to atmospheric pressure. This procedure clearly did not offer any great advantages in time. In order to avoid the bends it was necessary to re-shape the pressure-time course so that the total decompression time was not significantly different from the previous technique of adopting long duration stops followed by relatively large pressure changes. There is a third possibility for achieving a shorter decompression schedule. If it is possible to ascend rapidly to a stop value which would normally be expected to give a severe attack of the bends, then there is a latent period for the appearance of decompression sickness. The situation is entirely analogous to the man at atmospheric pressure in the first phase of a surface decom-

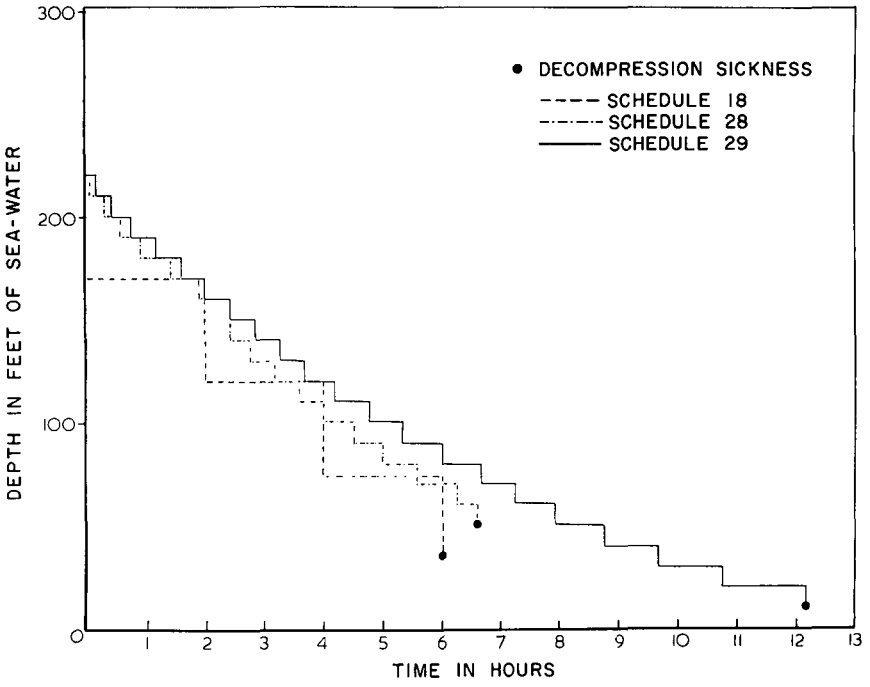

FIG. 74. Decompression from dives of 4 hours duration at 300 feet. Relative effectiveness of different pressure-time courses in preventing decompression sickness in men.

pression dive. In this latent period it is possible to change the composition of the breathing mixture and attempt to avert the impending attack. Several successful dives of this nature were attempted where the breathing medium was changed from oxy-helium to air during the latent period, with the result that very short decompression times were successfully accomplished by a team of men both in the chamber and in the sea. Unfortunately it was found that when this procedure failed to work there was a very serious form of decompression sickness, and it was decided not to pursue this technique any further.

As well as finding that the decompression pressure-time course when breathing oxy-helium was quite flexible, there were a number of puzzling observations on the role of oxygen in diving. A dive of 16 minutes to 400 feet breathing 90% He-10% O_2 gave 2 bends out of 4 attempts. When exactly the same dive, with the same decompression schedule was attempted breathing 87% He-13% O_2 then 10 trouble-free dives in the sea were performed. This confirmed the generally held view that oxygen-rich mixtures are advantageous to the diver, and agrees with previous work (6).

TABLE 38

Example of Dive Using Oxygen for Decompression from a Deep Prolonged Dive

Depth (feet)...	300	170	120	80	55	35	20	10
Time (hours)..	4	3	3	3	3	3	3	3
Breathing gas mixture.....	90% N_2-10% O_2	80% He-20% O_2			40% He-60% O_2			100% O_2

However when oxygen rich mixtures were used in the later stages of many of the lengthy decompressions necessary from deep prolonged dives they did not give any noticeable benefit. This is borne out by the following observations. The schedule to be discussed is shown in Table 38. Here the divers breathe 90% He-10% O_2 at 300 feet and 80% He-20% O_2 from 170 feet to 80 feet, 40% He-60% O_2 from 55 feet to 20 feet and oxygen for 1 hour at 10 feet. This is a reasonably successful procedure on unacclimatised men and in fact gave two transient niggles at the first attempt by a pair of divers. In one man these transient attacks were noted from 55 feet to the surface, re-occurring at every pressure stage and disappearing in a minute or two. The other diver had similar effects but only on reaching atmospheric pressure. This was considered marginally safe, but in order to test whether oxygen made any really worthwhile contribution it was decided to breathe 80% He-20% O_2 from 170 feet to 20 feet and then to change to 60% He-40% O_2 at 20 feet and 10 feet. No oxygen breathing was performed. This in theory should render the schedule alarmingly unsafe if oxygen has the role usually attributed to it. In fact 6 men attempted this dive and only one man had a transient niggle during the decompression. Far from being rendered more unsafe it was the impression that the dive was made safer. Following these dives, a number of dives of 1 hour duration at 300 feet were also tried using schedules involving oxygen breathing from 50 feet to the surface. In order to avoid bends in the last 50 feet of the schedule it became clear that it would be necessary to breathe pure oxygen for times in excess of 2 hours and such prolonged breathing of oxygen was considered undesirable. A change was made to oxy-helium mixtures without any noticeable increase in the time requirements for a safe ascent. It is now considered that breathing of oxygen during the decompression may cause vasoconstriction giving a lowered inert gas elimination rate and that this effect can offset any benefit derived from the lack of inert gas pressure in the arterial blood. Breathing oxygen or oxygen rich mixtures during the time on the bottom, or even just prior to the dive, is of course very beneficial for exactly the same reasons operating in reverse.

The main principles are now established for calculating schedules, as follows:

1) The body tissues effectively saturate in 4 hours.
2) It is possible to extend the general ideas of calculating air tables i.e. stage decompression, ratio cut-back.
3) There is an irreversibility in the uptake and elimination of the gas responsible for decompression sickness.
4) Oxygen and oxygen rich mixtures do not confer the benefit expected when breathed during the decompression.

In addition to these general principles there are several necessary controls which must be maintained on the diver, his activities and his environment. For example,

1) It is necessary to test schedules on either acclimatised men or completely unacclimatised men.
2) Hard work while on the bottom is essential to give a severe test to a schedule.
3) Work during the decompression must be reduced to the minimum.
4) Pressure measurements at sea can never follow the same pattern as in the laboratory. This is due to wave motion and sea swell as well as the fact that in any real situation the diver alters his position in the water from time to time. At depths of 600 feet for instance a variation of 15 feet may well be encountered.
5) During the dive and decompression the diver must be kept warm. In laboratory experiments the temperature ranged between 80° F and 90° F, whereas at sea in our recent trials the temperatures varied between 55° F and 60° F. The divers were very cold during the dive and for the first part of the decompression, and this was thought to be influencing the outcome of the decompression.
6) Atmosphere control must ensure accurate breathing mixtures, and carbon dioxide must not rise above a partial pressure of 1% of 1 atmosphere.
7) A schedule is not considered successful unless 10 trouble free dives are performed by 10 different divers.

Helium diving at sea has always produced more decompression sickness than in the laboratory. At present the possible contributing effects of cold and raised carbon dioxide pressures are being tested on small animals.

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24 | HANNES KELLER

Use of Multiple Inert Gas Mixtures in Deep Diving

The aim of deep diving is effective work at depths down to 1000 ft. in order to explore the Continental Shelves. Throughout this range the most important depths are from 300 to 700 ft.

Progress in research during the past few years has shown that the main physiological problem is that of decompression. From the standpoint of decompression, principally two different diving procedures have to be distinguished: a) *Living at depth* with complete saturation of the body by inert gases. This method is technically very complex, and rapid decompression is not important for the comfort and safety of the divers. b) *Classical diving* with decompression to the surface after each working period. The value of this diving method depends very much on the effectiveness of the decompression method. Short decompression adds to the comfort and the safety of the diver, and determines the level of the technical requirements and the costs. It is the aim of our own research program to minimize decompression for classical diving.

Considering the various breathing gases for use at great depth we immediately see that only helium-oxygen mixtures can be used. Hydrogen might provide another solution, but the basic problems have not yet been solved, and there is a certain probability that hydrogen will upset the body chemistry. The other gases which can be used during a dive are neon, nitrogen and argon. When we considered what the best method would be for minimizing decompression, we first thought about the possible advantages of complex mixtures such as helium-neon-argon-oxygen. We could find no indication that such combinations of inert gases would solve the problem. But there was another simple method, namely the use of different inert gases alternately during decompression (for simplicity I shall call nitrogen an inert gas, since in decompression it behaves like inert gases).

It seemed logical that gas uptake and elimination in the human body during a dive should follow to a certain degree the laws of gas diffusion and, in simplest form the laws of gas diffusion through a thin membrane. Actually this simplification is the basis of the Haldane model. In reality

the processes in the body are enormously more complicated because of the effects of perfusion of tissues with blood and three-dimensional gas diffusion and gas-exchange between the tissues and possibly other factors. Therefore, it is not possible to predict decompression without empirical experimentation.

Two basic laws of gas diffusion important in diving are those described by Graham and Henry. Henry's law states that the gas volume diffusing into a thin layer of liquid in a given time is proportional to the solubility (S) of the gas in that liquid. Graham's law states that the gas volume diffusing into the liquid is inversely proportional to the square root of the molecular weight (M) of the gas. Therefore:

$$\frac{d(\text{gas} - \text{vol})}{dt} \sim \frac{S}{\sqrt{M}}$$

For diving the amount of gas diffusing into a tissue is unimportant. It is of more interest to know how fast saturation of a tissue is reached. Obviously the saturation rate (sat) is proportional to the diffusion rate (gas volume diffusion) and inversely proportional to the solubility:

$$\frac{d(sat)}{dt} \sim \frac{d(\text{gas} - \text{vol})}{dt} \times \frac{1}{S} = \frac{S}{\sqrt{M} \times S}$$

Therefore the saturation rate is inversely proportional to the square root of the molecular weight of the gas and independent of the solubility.

$$\frac{d(sat)}{dt} \sim \frac{1}{\sqrt{M}}$$

A comparison of the inert gases shows that helium saturates 2.65 times faster than nitrogen and 3.16 times faster than argon.

For our considerations about the possible advantage of alternating gases during decompression, we made the following assumptions: When a tissue contains several gases, then the saturation degrees of the gases can be simply added to get the total degree of saturation. The critical ratio most probably is simply in an arithmetic proportion to the ratios for different gases and their saturation degree in the tissue.

$$r_{(\text{He}+\text{N}_2)} = \frac{(r_{\text{He}} \times sat_{\text{He}}) + (r_{\text{N}_2} \times sat_{\text{N}_2})}{sat_{\text{He}} + sat_{\text{N}_2}}$$

Now, when alternating different gases, it is important to consider gas absorption and elimination in the tissue separately. When we integrate the amount of gas getting into the tissue we get a straight line, since the gas diffusion into the tissue concerns pressure and constants. As the tissue approaches saturation, gas elimination also increases. The tissue is satu-

rated when elimination and absorption are equal. Since elimination is proportional to the degree of saturation at any moment, we get the well-known exponential curve (Fig. 75). But it is very important to consider that both processes occur simultaneously. When saturation is reached it does not mean that the gas flow into the tissue has ceased; it means that the gas flows in to and out of the tissue are equal. At equilibrium, "gas activity" has actually reached its maximum level. The point of these comments is that the fastest desaturation or decompression of a tissue is reached when absorption of fresh inert gas is completely stopped. This can be done by breathing pure oxygen. However, at the depths where decompression after deep diving is done this is not possible. But if we have a tissue saturated with a gas that desaturates very fast and now switch over to a gas that saturates very slowly, we have a similar ultimate effect. Bühlmann and I performed an experiment which demonstrates the effects of switching gases.

In experiments in a pressure chamber seven subjects made dives to 120 feet depth with 2 hours bottom time (Fig. 76). During the bottom time after 70 minutes, the inert breathing gas was switched from helium to argon. Immediately the helium began to desaturate rapidly. At the same time argon began to dissolve very slowly, theoretically 3.16 times slower than the helium was being eliminated. After 50 minutes bottom time with argon, the helium had been eliminated while the argon had not yet reached a critical level. The final decompression first with argon and then with pure oxygen was done in 15 minutes. The normal decompression for an air dive would be about 90 minutes; for a helium dive it would be about 60 minutes. Obviously the special trick in this particular experiment was that, of the

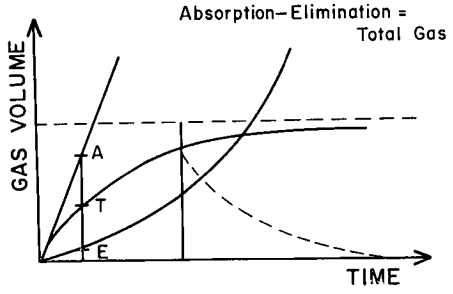
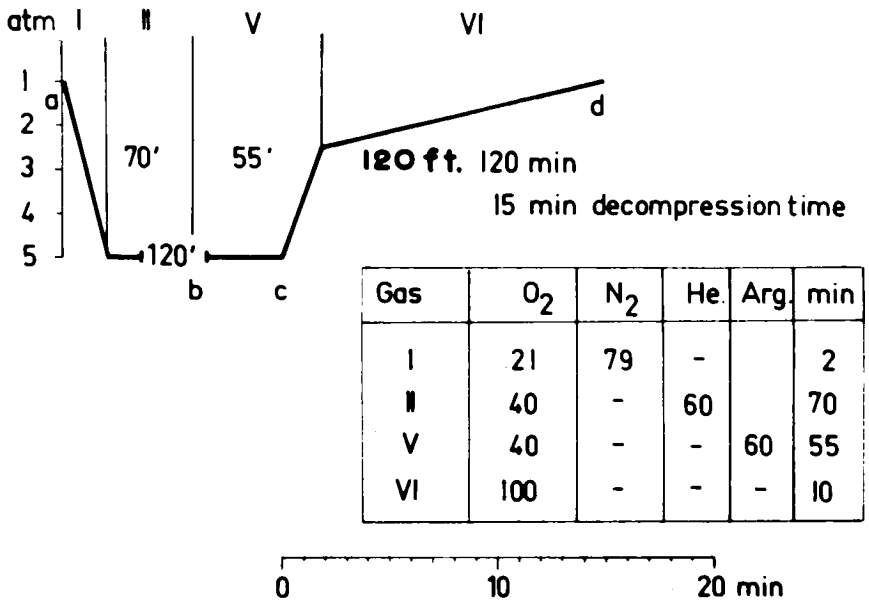


FIG. 75. The time-function of the total amount T of an inert gas which is dissolved in a tissue forms an exponential curve. It begins at zero as fresh, unsaturated tissue, and rises to a fixed level at complete saturation. The curve is the difference of the integrated amount of gas which flows *into the tissue* (at a constant rate for constant conditions) minus the integrated amount of gas which flows *out of the tissue* (the rate raising proportionally with the total amount of gas being present in the tissue at a given moment).



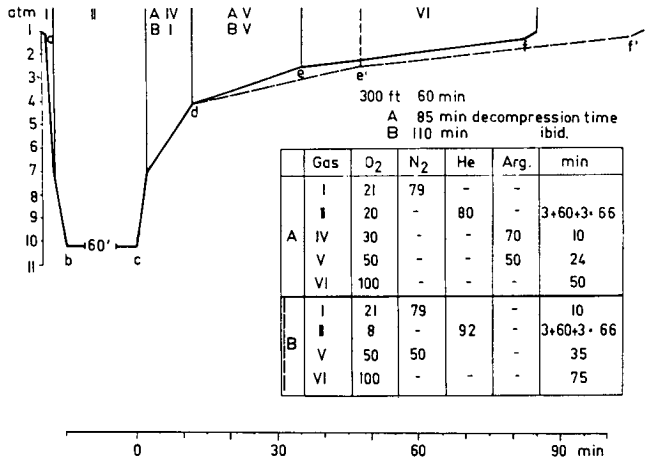
Gas	O_2	N_2	He	Arg.	min
I	21	79	-		2
II	40	-	60		70
V	40	-	-	60	55
VI	100	-	-	-	10

FIG. 76. 120 ft. dive with 120 minute bottom time (7 subjects). (Reproduced by permission, Journal of Applied Physiology.) (1)

decompression time of 65 minutes, most was spent on the bottom and according to diving procedures counts as bottom time instead of as decompression. Naturally the success of the method depends entirely on the moment of switching gases. If it is done too early, then the heavy gas may reach a level of saturation where it must be decompressed too, which then goes relatively slowly. If the switching is done too late, no great benefit results.

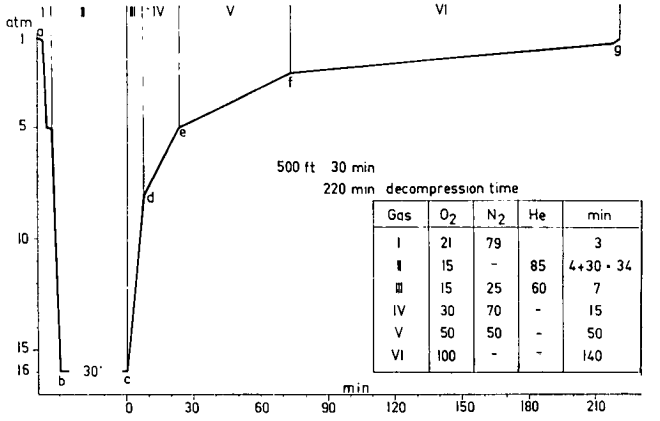
Figure 77 shows another such dive with 1 hour bottom time at a 300 ft. depth. A dive to this depth with air and air decompression according to U. S. Navy Diving Manual requires 460 minutes decompression, while a helium dive would require about 200 minutes. We did two different decompressions from 300 ft. One type involved switching to argon and 85 minutes decompression time and one switching to nitrogen and 110 minutes decompression time. The use of argon caused difficulties because of narcosis and did not show clear advantages as compared to nitrogen. Therefore, since that time we have restricted ourselves to the use of helium and nitrogen only.

A series of dives by six subjects to 500 ft. with 30 minutes bottom time is shown in Fig. 78. Here we used a technique which we had applied before in pilot experiments to 800 and 1000 ft. at the experimental diving tank of the French Navy at Toulon. It was not possible to switch from helium to nitrogen as deep as we wanted. Therefore, for the ascent from 500 ft.



	Gas	O_2	N_2	He	Arg.	min
A	I	21	79	-	-	
	II	20	-	80	-	3+60+3·66
	IV	30	-	-	70	10
	V	50	-	-	50	24
	VI	100	-	-	-	50
B	I	21	79		-	10
	II	8	-	92	-	3+60+3·66
	V	50	50		-	35
	VI	100	-	-	-	75

FIG. 77. 300 ft. dive with 60 minute bottom time (9 subjects). (Reproduced by permission, Journal of Applied Physiology.)



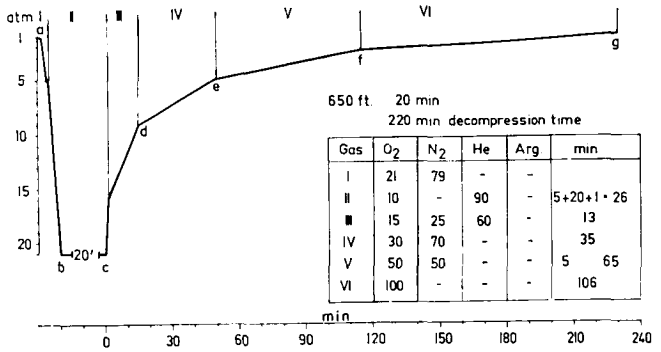
Gas	O_2	N_2	He	min
I	21	79		3
II	15	-	85	4+30·34
III	15	25	60	7
IV	30	70	-	15
V	50	50	-	50
VI	100	-	-	140

FIG. 78. 500 ft. dive with 30 minute bottom time (6 subjects). (Reproduced by permission, Journal of Applied Physiology.)

to 200 ft. we used a mixture of 60% helium-25% nitrogen-15% oxygen. That was the upper limit of nitrogen at depth. Decompression was 220 minutes.

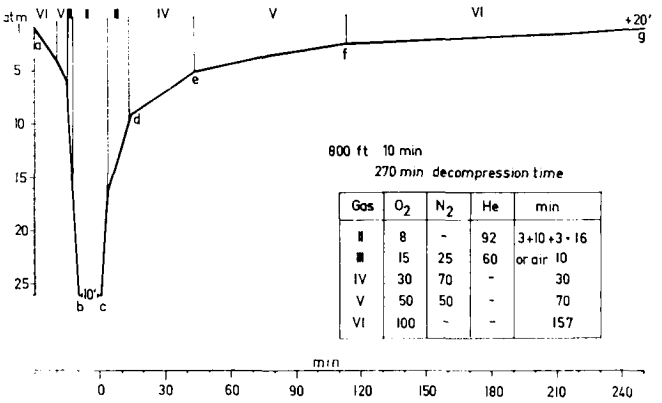
We experienced difficulties with dives to 650 ft. and 20 minutes bottom time (Fig. 79). Theoretically a decompression of about 140 minutes was expected, but we ultimately needed 270 minutes. For unknown reasons the basis for the decompression calculation used for the other dives, actually the Haldane-model combining helium and nitrogen periods with helium being 2.65 times faster than nitrogen, did not apply any more. Some im-

portant safety factors reducing the theoretical ratio had to be applied. Something was very astonishing. I was subject for the first decompression experiment with 140 minutes decompression time. I developed bends in the elbows, shoulders and knees and was treated for about 5 hours, but there was nothing alarming. The next subject tried with about 170 minutes decompression with about the same result. Another subject, with about 200 minutes decompression, suffered shock due to hypovolemia secondary to extravascular plasma loss. He was treated successfully. Again decompression was increased, to about 220 minutes, and again another subject suffered shock, even worse than the first. Finally with 270 minutes total decompression time we succeeded in decompressing satisfactorily. These experiments showed drastically that after deep dives one individual might



Gas	O_2	N_2	He	Arg	min
I	21	79	-	-	
II	10	-	90	-	5+20+1 · 26
III	15	25	60	-	13
IV	30	70	-	-	35
V	50	50	-	-	5 65
VI	100	-	-	-	106

FIG. 79. 650 ft. dive with 20 minute bottom time (5 subjects). (Reproduced by permission, Journal of Applied Physiology.)



Gas	O_2	N_2	He	min
II	8	-	92	3+10+3 · 16
III	15	25	60	or air 10
IV	30	70	-	30
V	50	50	-	70
VI	100	-	-	157

FIG. 80. 800 ft. dive with 10 minute bottom time (2 subjects). (Reproduced by permission, Journal of Applied Physiology.)

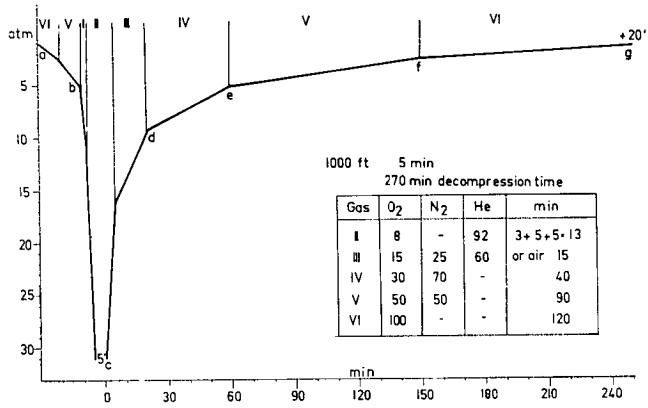


FIG. 81. 1,000 ft. dive with 5 minute bottom time (2 subjects). (Reproduced by permission, Journal of Applied Physiology.)

decompress fast with minor bends or even without any symptoms, while other subjects might suffer very dangerous effects. There is a tendency to interpret a minor degree of bends as an indication that one is close to a successful decompression. Generally this might apply, but it sometimes can lead to serious consequences.

Dives to 800 ft. with 10 minutes bottom time (Fig. 80) and to 1000 ft. with 5 minutes bottom time (Fig. 81) were successful with the same decompression time.

The dives to 300 ft. with 1 hour bottom time and to 1000 ft. with 5 minutes bottom time were performed not only in a pressure chamber but in the open sea, demonstrating that it is possible to use these decompression methods for practical purposes in the sea.

Last year in a series of experiments at 100 ft. with nitrogen and with helium and long exposures, Bühlmann demonstrated that helium really reaches saturation much faster in the body than nitrogen does (to be published). However, apart from the dives I have described, we have no final proof for the validity of the gas switching method. We do think that the experiments described indicate that the method has advantages.

Obviously the number of experiments thus far performed is relatively small, and we are aware that the decompressions described are not safe enough to be used in the water without extremely careful precautions guaranteeing the immediate diagnosis and treatment of decompression sickness.

There are many problems remaining. For example, we do not know whether tissues supersaturated with mixed gases show a different behavior with respect to bubble formation than is to be expected from the assumptions made. It is necessary to learn more about bubble formation and about

critical ratios. The problem of gas diffusion in the body is a complicated process and we are trying to work with the Haldane-model, which is convenient and also useful if one accepts that the theoretical ratio must be changed by an occult safety factor. We foresee the possible application of switching inert gases during shallow dives on the bottom, so that part of the decompression can be done at the bottom. We also hope to apply this to deep dives with bottom times up to about 1 or 2 hours at 700 feet.

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Computation Methods for Decompression from Deep Dives

As dives increase in depth and duration, the problem of computing ascent profiles that are both physiologically sound and operationally feasible becomes compounded by the fact that somewhere during ascent, the slowest tissues of the diver begin to limit the rate of his further progress to the surface.

The purpose of this presentation is to review the computational aspects of this decompression situation and to show how the computation methods used in this laboratory can be applied to the planning and analysis of deep, extended dives. Development of the mathematical statements employed to describe the inert gas transport model is given in the Appendix. The equation numbers used here correspond to those in the Appendix.

General Treatment of Linear Ascent (see Appendix, Case 5)

Even though it has already been analyzed by other workers (1–3), it is appropriate at this time to review briefly the general computation situation for gas transport during linear ascent (or descent), especially as to its implications with regard to decompression from extended, deep dives. (The terms used are defined in Table 39.)

It can be shown that during linear ascent (or descent) in which the inspired inert gas partial pressure is changed at the rate c, the driving force acting on a half-time tissue characterized by a specific time constant k is given by

$$P - \pi = \frac{c}{k} + \left(P_0 - \pi_0 - \frac{c}{k}\right) \exp(-kt). \tag{40}$$

This exponential relationship reduces to a constant value (c/k) with increasing time of ascent since

$$\lim_{t \to \infty} (P - \pi) = \frac{c}{k}. \tag{41}$$

TABLE 39

Definition of Terms Used in Developing Equations

A. Terms relating to the overall system:
- D = seawater depth, generally a function of time
- A = atmospheric pressure at sea level
- P = partial pressure of inspired inert gas
- c = rate of change of P as a function of time
- P_{O_2} = partial pressure of inspired oxygen, generally a function of time
- m = fraction of total gas pressure due to inert gas, generally a function of time
- t = time

B. Terms relating to a given half-time tissue:
- k = specific time constant = $\ln 2/t_{1/2}$
- $t_{1/2}$ = half-life
- π = partial pressure of dissolved inert gas, generally a function of time
- ΔP = excess supersaturation pressure: pressure of inert gas dissolved in tissue minus absolute hydrostatic pressure
- ΔP_s = ΔP at surface
- g = rate of change of ΔP as a function of depth
- F = driving force, $P - \pi$

C. Other terms
1. For the purposes of this presentation the pressure exerted by 1 ft. of sea water on an area of 1 sq. in. has been defined arbitrarily as 1/33 of an atm. or 0.0313 kg/cm.^{2}
2. C_1 = constant of integration

Thus we can relate the limiting values of the driving force that will become established during prolonged linear ascent (or descent) to the rate of this ascent (or descent) and to the specific time constant of any particular half-time tissue. This relationship is shown in Figure 82. Here, limiting values of the driving force in feet (Table 39) are plotted against tissue half-time in minutes for several different rates in minutes per foot of linear change of the inspired inert gas partial pressure P.

Because of this relationship it is possible to maintain a constant driving force in a particular tissue by selecting a linear rate of change of inspired inert gas partial pressure c equal to k times the initial driving force $P_0 - \pi_0$ that is to be maintained. It can be shown, in fact (Appendix, Case 4), that a constant driving force in a particular tissue can be maintained only if the change of inspired inert gas partial pressure is linear.

Imposition of a Constant Excess Supersaturation Pressure ΔP

It is frequently desirable to decompress a diver while maintaining a constant excess supersaturation pressure ΔP in his ascent-limiting half-time tissue. The following discussion will be concerned with an examination of

the time course of decompression that must be followed to achieve a condition of constant ΔP.

The time-course that must be followed by the inert gas content π of a half-time tissue for which a constant excess supersaturation pressure ΔP is to be maintained (Appendix, Case 1) is given by

$$\pi = \exp(-kt + k\int m(t)\,dt)\,[-k\Delta P \int m(t) \exp(kt - k\int m(t)\,dt)\,dt] + C_1 \exp(-kt + k\int m(t)\,dt). \quad (14)$$

Generally speaking, under actual diving conditions the form of m in this equation is determined by operational requirements. When the partial pressure of oxygen is held constant during ascent m becomes an easily definable function of depth (Appendix, Equation 14A). Interpretation of Equation 14 then becomes straightforward (Appendix, Case 2) and results in

$$\pi = \pi_0 - k(\Delta P + P_{O_2})t. \quad (19)$$

This condition is satisfied when the diver's decompression proceeds linearly according to

$$D(t) = D(0) - k(\Delta P + P_{O_2})t. \quad (21)$$

On the other hand, when the volume fraction of oxygen $(1 - m)$ is to be held constant during ascent, interpretation of Equation 14 (Appendix, Case 3) yields

$$\pi = -\frac{m}{1-m}\Delta P + \left(\pi_0 + \frac{m}{1-m}\Delta P\right)\exp(-k(1-m)t). \quad (25)$$

This condition is satisfied when the diver's decompression proceeds exponentially according to:

$$D(t) = D(0) - \left(\pi_0 + \frac{m}{1-m}\Delta P\right)[1 - \exp(-k(1-m)t]. \quad (26)$$

Parametric Analysis of the Constant ΔP Requirement

Let us now examine the ascent situation that is constrained by the requirement of a constant ΔP in the ascent-limiting theoretical half-time tissue and review how the total duration of ascent is affected by the choice of the ascent parameters m, P_{O_2} and ΔP.

Figure 83 shows the relationship between initial depth, surfacing time and the excess supersaturation pressure ΔP that is to be maintained during an ascent where oxygen is being breathed at a constant partial pressure. As we have shown, such an ascent must be linear as neither ΔP nor P_{O_2} are allowed to change with time (see Equation 21). Figure 83 illustrates

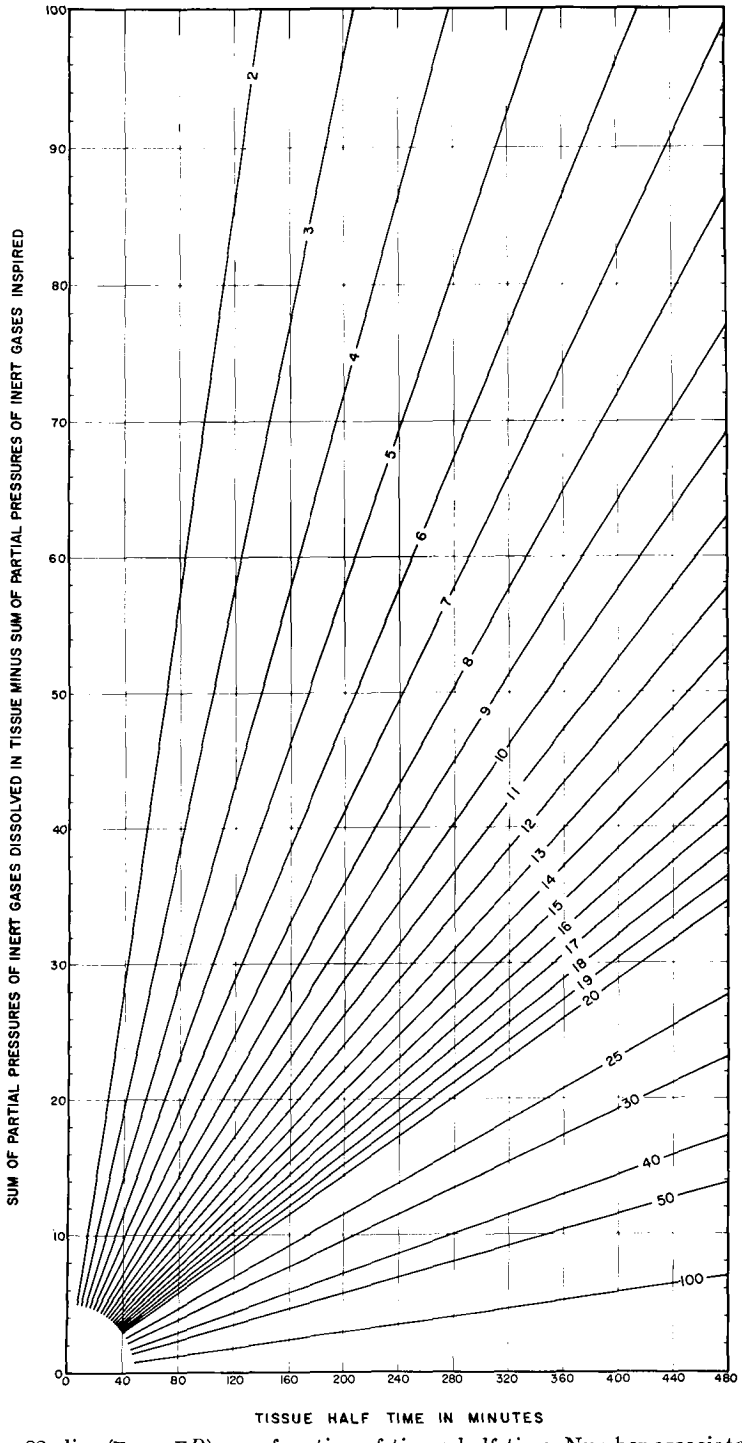

FIG. 82. $\lim_{t \to \infty} (\Sigma\pi - \Sigma P)$ as a function of tissue half-time. Number associated with each line represents rate of change c of inspired total inert gas pressure in min./ft. Ordinate represents pressure in feet of seawater per sq. in. (0.0313 kg./cm.^{2}).

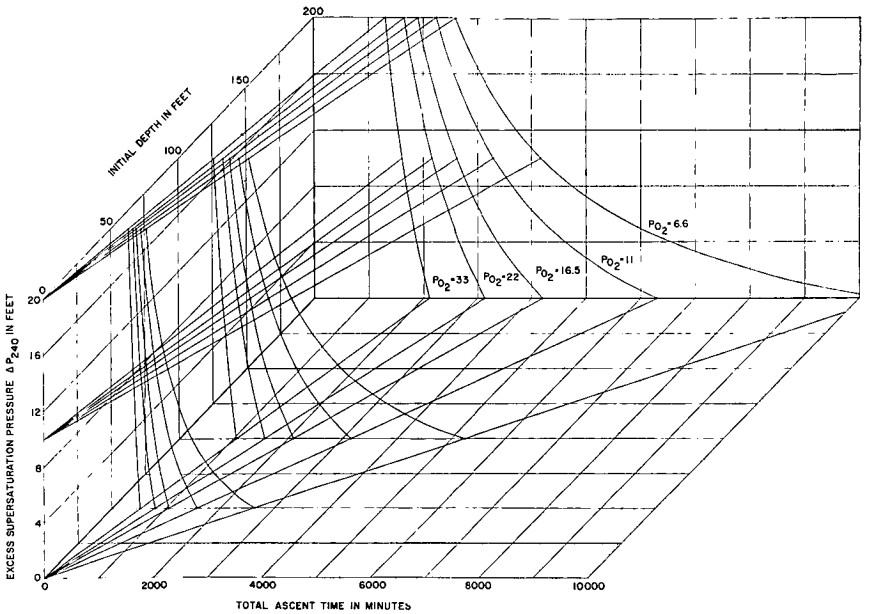

FIG. 83. Relationship between depth, excess supersaturation pressure ΔP and surfacing time for ascents limited by a 240-min. tissue. Oxygen partial pressure is being held constant at 6.6, 11, 16.5, 22 or 33 ft.

the relative impact of allowable supersaturation and inspired oxygen partial pressure on the time required to surface a diver for whom the slowest half-time tissue has become ascent-limiting. Although this display has been computed for a slowest tissue half-time of 240 min., it shows the general relationship between the parameters under discussion for any particular tissue half-time. We can see that the greatest reduction in the period of ascent that can be obtained by increasing the inspired oxygen tension will accrue when the allowable excess supersaturation pressure in the 240-min. half-time tissue (ΔP_{240}) is at a minimum. We can also see that the relative time advantage gained by breathing high oxygen tensions with a particular value of ΔP being maintained is independent of depth.

Another way of describing this situation is to say that relatively little time can be saved by increasing the allowable excess supersaturation pressure in the ascent-limiting slowest half-time tissue of a diver exposed to a constant, high oxygen tension during linear ascent. This is numerically expressed in the example given in Table 40.

A generally similar picture presents itself when the percentage, rather than the partial pressure, of oxygen is being held constant during an ascent where a specified excess supersaturation pressure ΔP is maintained

TABLE 40

Effect of P_{O_2} *and* ΔP_{240} *on Relative Duration of Linear Ascent Limited by a 240-minute Half-Time Tissue*

	ΔP_{240}, FT.		% REDUCTION OF TOTAL ASCENT PERIOD
	0	20	
P_{O_2} = 6.6 ft	100	24.8	75.2
P_{O_2} = 33 ft	20	12.5	37.8
% Reduction of total ascent period	80	50.4	87.5

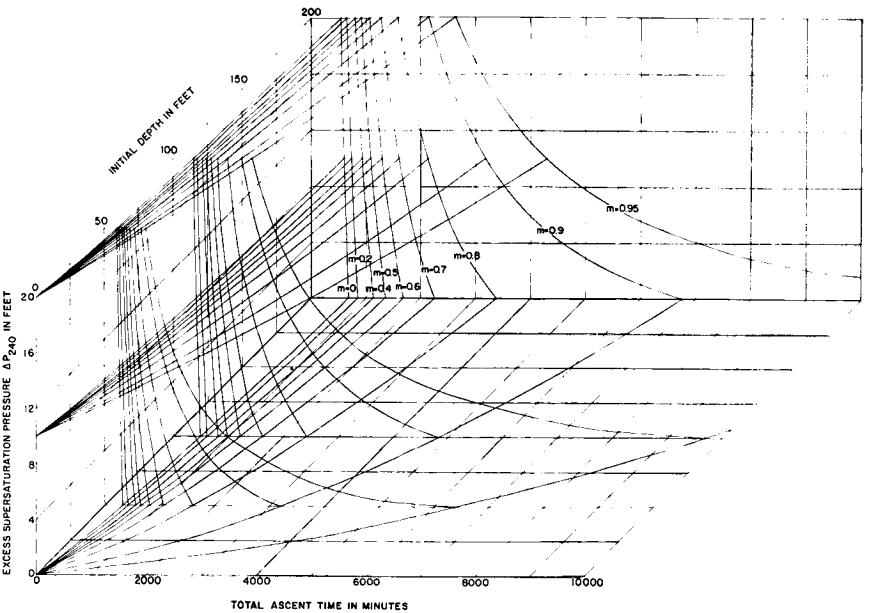

FIG. 84. Relationship between depth, excess supersaturation pressure ΔP and surfacing time for ascents limited by a 240-min. tissue. Oxygen concentration is being held constant at 5, 10, 20, 30, 40, 50, 60, 80 or 100%. (Numbers associated with each surface represent volume fractions of inspired inert gas.)

in the ascent-limiting, slowest half-time tissue. This is shown in Figure 84. Again we recognize that an increase in oxygen concentration reduces the total ascent time most drastically when the extent of supersaturation of the slowest half-time tissue is small and that relatively little time can be gained by increasing this parameter when the percentage of oxygen is maintained at a high level. (It will be noted that information describing ascent times on 5% and 10% oxygen has been included in Figure 84 to emphasize this

point. It is obvious that this portion of Figure 84 is of academic interest only.)

The chief difference between the situation presented here and that illustrated in Figure 83 is that the relative time advantage gained by breathing high oxygen percentages for any given value of ΔP does change with depth in the present case. That is to say that the greater the depth at which the slowest half-time tissue begins to limit ascent, the more effectively will the total ascent time be reduced by the introduction of a high oxygen percentage. On inspection of Figure 84 it becomes obvious that for a given initial depth this advantage will increase as the choice of ΔP is made more conservative.

Imposition of Changing Excess Supersaturation Pressure ΔP as a Function of Depth

There is considerable evidence on hand today which indicates that the extent of supersaturation that can be safely sustained by a given theoretical half-time tissue increases with increasing depth. It is therefore proper to include in our analysis the case where excess supersaturation pressure ΔP is a specified function of depth.

It can be shown (Appendix, Cases 6 and 7) that the time course that must be followed by the inert gas content π of a half-time tissue for which an excess saturation pressure

$$\Delta P = \Delta P_s + g \cdot D(t)$$

is to be maintained, is given by

$$\pi = \pi_0 - \left[\pi_0 + \frac{P_{O_2} - A + \frac{\Delta P_s - A}{1+g}}{1 - \frac{1}{1+g}} \right] \cdot \left(1 - \exp\left(-k\left(1 - \frac{1}{1+g}\right)t\right)\right) \tag{61}$$

when the partial pressure of oxygen does not change during ascent and by

$$\pi = \pi_0 - \left[\pi_0 + \frac{\frac{m}{1+g}}{1 - \frac{m}{1+g}} (\Delta P_s - Ag) \right] \cdot \left(1 - \exp\left(-k\left(1 - \frac{m}{1+g}\right)t\right)\right) \tag{54}$$

when the percentage of oxygen remains constant. These conditions are

satisfied when the diver's decompression proceeds exponentially according to

$$D(t) = D(0) - \frac{1}{1+g}\left[\pi_0 + \frac{P_{O_2} - A + \frac{\Delta P_s - A}{1+g}}{1 - \frac{1}{1+g}}\right] \cdot\left(1 - \exp\left(-k\left(1 - \frac{1}{1+g}\right)t\right)\right) \tag{62}$$

when P_{O_2} = constant, and according to

$$D(t) = D(0) - \frac{1}{1+g}\left[\pi_0 + \frac{\frac{m}{1+g}(\Delta P_s - Ag)}{1 - \frac{m}{1+g}}\right] \cdot\left(1 - \exp\left(-k\left(1 - \frac{m}{1+g}\right)t\right)\right) \tag{56}$$

when m = constant.

A graphic evaluation of theoretical ascent profiles from 100 ft. based on these mathematical relationships (Equations 62 and 56) is given in Figures 85 and 86. Plotted here are time courses of decompression with the 320-min. tissue limiting the diver's ascent. The effect of excess supersaturation pressure on surfacing (ΔP_s), depth-related rates of increase of this parameter (g), and the partial pressure or the percentage of oxygen $(1 - m)\cdot 100$ breathed during ascent are considered there.

Since the partial pressure of dissolved gas in the 320-min. tissue at a given depth must vary by nature of the selected conditions, a common denominator is needed to judge the changes in the efficiency of decompression that are brought about by the various parametric changes represented in Figures 85 and 86. This efficiency is best compared by comparing the time required to reduce by a fixed increment the gas load of the 320-min. tissue. A comparison of the times required to reduce π_{320} from 133 to 43 ft. of inert gas partial pressure (Table 41) again shows that the effectiveness of high oxygen levels in reducing the inert gas level of the ascent-limiting tissue is the more pronounced the more conservative the choice of allowable excess supersaturation pressure in the ascent-limiting tissue. For any oxygen level certain near-equivalencies between the times required to remove 90 ft. of inert gas partial pressure from that tissue may be noted between constant ΔP values and ΔP values that increase with depth at a linear rate. For example, the time periods shown in our example are almost identical for a constant ΔP of 10 ft. on the one hand, and a surfacing ΔP_s of 0 ft.

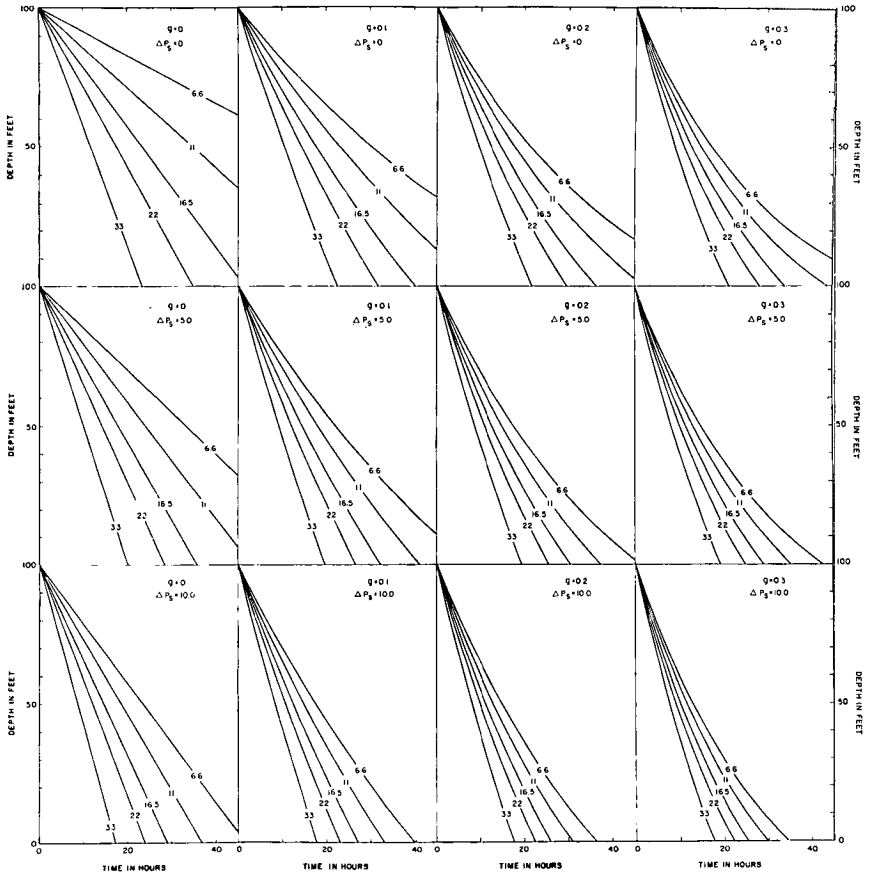

FIG. 85. Effect of excess supersaturation pressure on reaching surface (ΔP_s) and the rate of its linear projection with depth (g) on the time-course of decompression when ascent is limited by a 320-min. tissue. Oxygen partial pressure is being held constant at 6.6, 11, 16.5, 22 or 33 ft.

that increased 3 ft. for every 10 ft. of depth. For a given value of ΔP_s the relative effectiveness of high levels of oxygen in hastening tissue gas clearance decreases with increasing coefficients g of linear projections of ΔP_s with depth. Conversely, for any given value of g, the relative effectiveness of high levels of oxygen in accelerating tissue gas clearance decreases with increasing values of ΔP_s.

Under any combination of circumstances within the scope of this discussion, however, it is clear that the effectiveness of oxygen does not increase linearly with the partial pressure or concentration to which the diver is exposed. Given a conservative choice of excess supersaturation pressure,

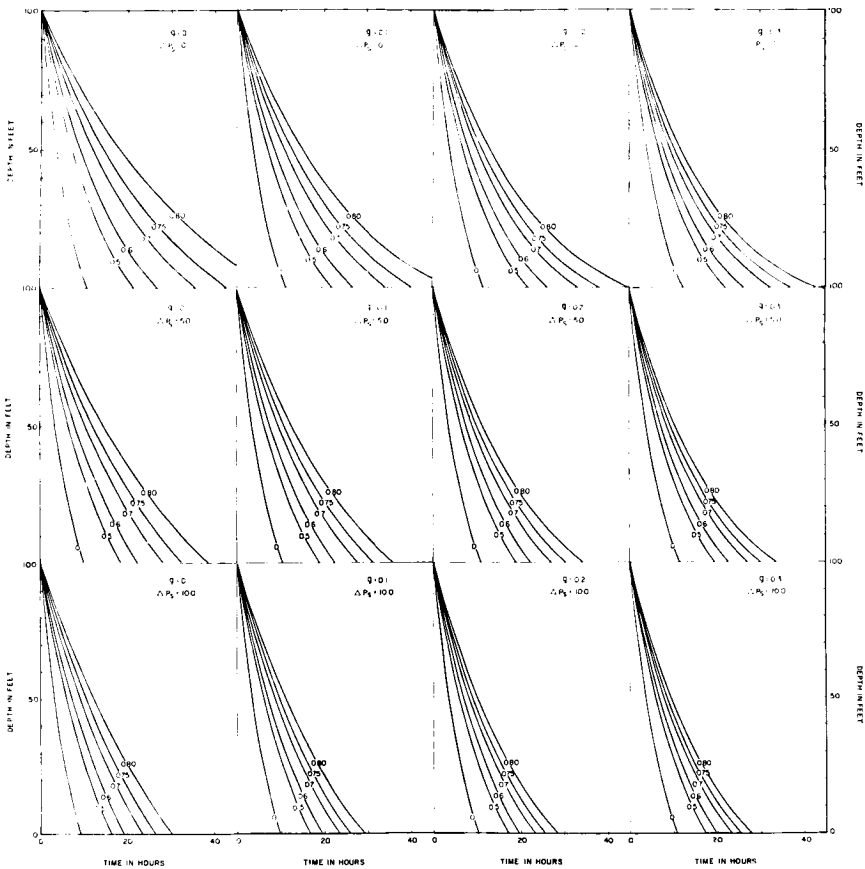

FIG. 86. Effect of excess supersaturation pressure on reaching surface (ΔP_s) and the rate of its linear projection with depth (g) on the time-course of decompression when ascent is limited by a 320-min. tissue. Oxygen concentration is being held constant at 20, 25, 30, 40, 50 and 100%. (Numbers associated with each curve represent volume fractions of inspired inert gas.)

even a few percentage point increases, say above 20% oxygen may reduce the length of a dive by as much or more time than doubling the oxygen concentration from 50 to 100%. Inspection of Figures 85 and 86 clearly documents this. Similarly, a slight rise in oxygen partial pressure above 152 mm. Hg may shorten a dive more substantially than a large increase in an already elevated partial pressure of oxygen.

Theoretical Analysis of a Saturation Dive to 650 Ft.

Mathematical analyses such as those just presented aid but do not replace the decision-making processes associated with the design of decompression

TABLE 41

Time Required to Reduce the Inert Gas Loading of a 320-minute Tissue (π_{320}) from 133 to 43 Feet

ΔP	$g = 0$				$g = 0.1$				$g = 0.2$				$g = 0.3$			
	m	t	P_{O_2}	t	m	t	P_{O_2}	t	m	t	P_{O_2}	t	m	t	P_{O_2}	t
$\Delta P_s = 0$	0	521.4	33	1259.3	0	521.4	33	1097.9	0	521.4	33	996.2	0	521.4	33	925.7
	0.5	1042.8	22	1889.0	0.5	994.2	22	1551.1	0.5	957.2	22	1360.1	0.5	928.1	22	1235.8
	0.6	1303.5	16.5	2518.7	0.6	1214.5	16.5	1956.8	0.6	1149.7	16.5	1667.8	0.6	1100.3	16.5	1488.7
	0.7	1738.0	11	3778.0	0.7	1560.6	11	2656.3	0.7	1439.7	11	2164.5	0.7	1351.8	11	1881.5
	0.75	2085.6	6.6	6296.7	0.75	1820.1	6.6	3743.3	0.75	1647.9	6.6	2867.0	0.75	1526.8	6.6	2408.1
	0.8	2607.0			0.8	2183.6			0.8	1927.4			0.8	1755.0		
$\Delta P_s = 5$	0	521.4	33	1093.6	0	521.4	33	979.8	0	521.4	33	904.9	0	521.4	33	851.5
	0.5	975.3	22	1539.2	0.5	937.4	22	1324.9	0.5	908.3	22	1194.3	0.5	885.2	22	1105.7
	0.6	1181.2	16.5	1932.9	0.6	1115.4	16.5	1608.9	0.6	1066.6	16.5	1423.5	0.6	1028.9	16.5	1301.9
	0.7	1497.9	11	2597.4	0.7	1377.0	11	2050.1	0.7	1291.8	11	1765.3	0.7	1228.5	11	1587.4
	0.75	1730.3	6.6	3582.6	0.75	1559.9	6.6	2631.3	0.75	1444.3	6.6	2192.6	0.75	1360.5	6.6	1933.7
	0.8	2048.6			0.8	1798.8			0.8	1637.6			0.8	1524.4		
$\Delta P_s = 10$	0	521.4	33	966.5	0	521.4	33	884.7	0	521.4	33	829.1	0	521.4	33	788.5
	0.5	916.6	22	1298.7	0.5	887.4	22	1156.5	0.5	864.7	22	1065.0	0.5	846.5	22	1000.9
	0.6	1081.4	16.5	1568.2	0.6	1032.6	16.5	1366.7	0.6	995.8	16.5	1242.7	0.6	967.2	16.5	1158.0
	0.7	1319.6	11	1979.0	0.7	1234.9	11	1671.2	0.7	1174.0	11	1493.3	0.7	1127.9	11	1375.9
	0.75	1483.7	6.6	2518.7	0.75	1369.3	6.6	2035.3	0.75	1289.3	6.6	1783.6	0.75	1230.1	6.6	1623.7
	0.8	1695.7			0.8	1536.9			0.8	1429.9			0.8	1352.6		

procedures from deep dives. Operational constraints related to the physical safety of diving atmospheres and to the control of their compositions under laboratory or field conditions frequently limit the choice of available decompression parameters. In addition, physiological considerations frequently override all others in the final selection of optimal conditions for ascent from deep dives.

This is illustrated by the reasoning that led to the selection of a decompression profile for a saturation dive at 650 ft. that was conducted at our Laboratory last year. A graphic analysis of this dive is shown in Figures 87A and 87B.

A bottom time of 48 hr. was chosen to assure complete saturation of all tissues with a half-time of 240 min. or less. In addition, this period of exposure gives rise to substantial gas uptake by hypothetical tissues with half-times greater than 240 min. On decompression such extremely slow and purely hypothetical tissues would be associated with large calculated excess supersaturation pressures. If mathematical analysis indicates that unreasonably large calculated ΔP values could be sustained by such tissues on decompression without the incurrence of decompression sickness, their physical existence can be denied. Thus, our choice of bottom time enabled us later on to make some judgements concerning the existence of ultra-slow theoretical half-time tissues in man.

Physiological and operational considerations led to the choice of a partial pressure of inspired oxygen of 11.5 ft. (0.35 atm.) during compression and during the first 44 hr. of exposure to maximum pressure. This level of oxygen was considered low enough to prevent significant pulmonary pathological changes or changes in other organs and yet high enough to permit significant decreases in inspired oxygen tensions during carbon dioxide rebreathing experiments that were conducted by the two divers on board without rendering them hypoxic. At this level of oxygen, inaccuracies in oxygen analyses or inadvertent excursions of the oxygen control would also impart minimal risk to the divers. In addition, this oxygen level provided insurance against possible interference with pulmonary gas exchange by the density of the inspired gas at maximum pressure.

Four hours before commencing ascent the oxygen partial pressure was increased to 14.5 ft. (0.44 atm.) to minimize further the impact of gas analysis errors during ascent.

To provide for a conservative decompression procedure consistent with operational efficiency it was assumed that the 240-min. tissue could not sustain safely more than 12 ft. of excess inert gas pressure for short periods of time or more than approximately 10 ft. over a period of days. During later stages of ascent the value of ΔP was reduced to approximately 5 ft.

In order to observe the ΔP constraint just outlined, the initial ascent was

limited to 625 ft. At that depth the following conditions prevailed for the 240-min. tissue.

$D + 33$	= 658 ft.
P_{He}	= 643.5 ft.
P_{O_2}	= 14.5 ft.
π_{240}	= 669.7 ft.
$\pi_{240} - P_{He}$	= 26.2 ft.
$\pi_{240} - (D + 33)$	= 11.7 ft.

Bearing in mind the constraints imposed by the requirement to limit the chronically sustained excess supersaturation pressure in the 240-min. tissue (ΔP_{240}) to about 10 ft. and to maintain a programmed inspired oxygen partial pressure of 14.5 ft., an ascent rate had to be selected that would ensure a final driving force of about 25 ft. (cf. Equation 23). Inspection of Figure 82 shows that an ascent rate of 14 min. per ft. met this requirement.

We recognize that faster ascent rates may have been quite safe on theoretical grounds but without applicable experience available we could not justify their use, especially since it was not the primary objective of this dive to evaluate ascent-limiting conditions of tissue supersaturation. Furthermore, conservative decompression was mandated by the imperfect state of knowledge prior to this dive of the half-time of the slowest tissue in man.

During ascent (Fig. 87B) P_{O_2} values were raised to 16.5 ft. (0.50 atm.) at 300 ft. and to 20 ft. (0.61 atm.) at 200 ft. of depth, adjusting the ΔP_{240} to a final value of 4.7 ft. From the 50-ft. level to surface the divers breathed oxygen intermittently by mask which reduced ΔP values to below zero for tissues with half-times of 240 min. or less. This procedure was instituted because operational safety precluded the maintenance of oxygen levels in excess of 25 % in the decompression chamber which made it impossible to maintain a constant P_{O_2} of 20 ft. in the chamber at depths shallower than 47 ft.

Figures 87A and 87B review the history of the excess supersaturation pressures (ΔP) and driving forces ($-\Delta P - P_{O_2}$) sustained throughout the dive by tissues with half-times of 160, 180, 200, 240, 360, 480 and 720 min.

For the purpose of this analysis the small amounts of nitrogen that were present in the system were considered to be associated with the same tissue specific time constants as helium, hence the term "sum of partial pressures of inert gases dissolved in tissue" is used in Figures 87A and 87B.

Calculated supersaturation pressures of helium sustained at a depth of 200 ft. are given in Table 42. They are roughly representative of the maximum values reached by these tissues during the dive.

General decompression experience makes it highly unlikely that theoreti-

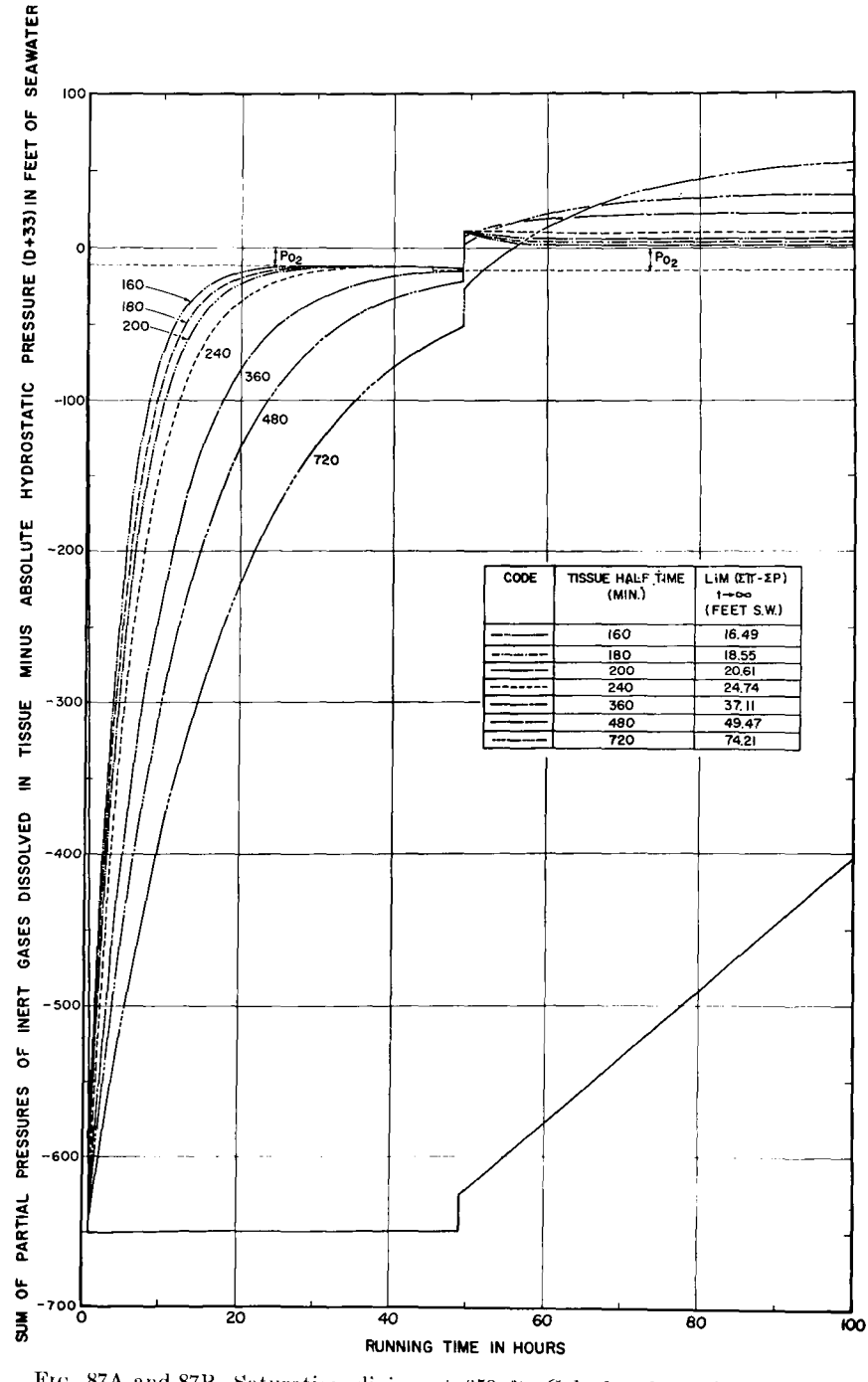

FIG. 87A and 87B. Saturation diving at 650 ft. Calculated gas inventories for seven half-time tissues.

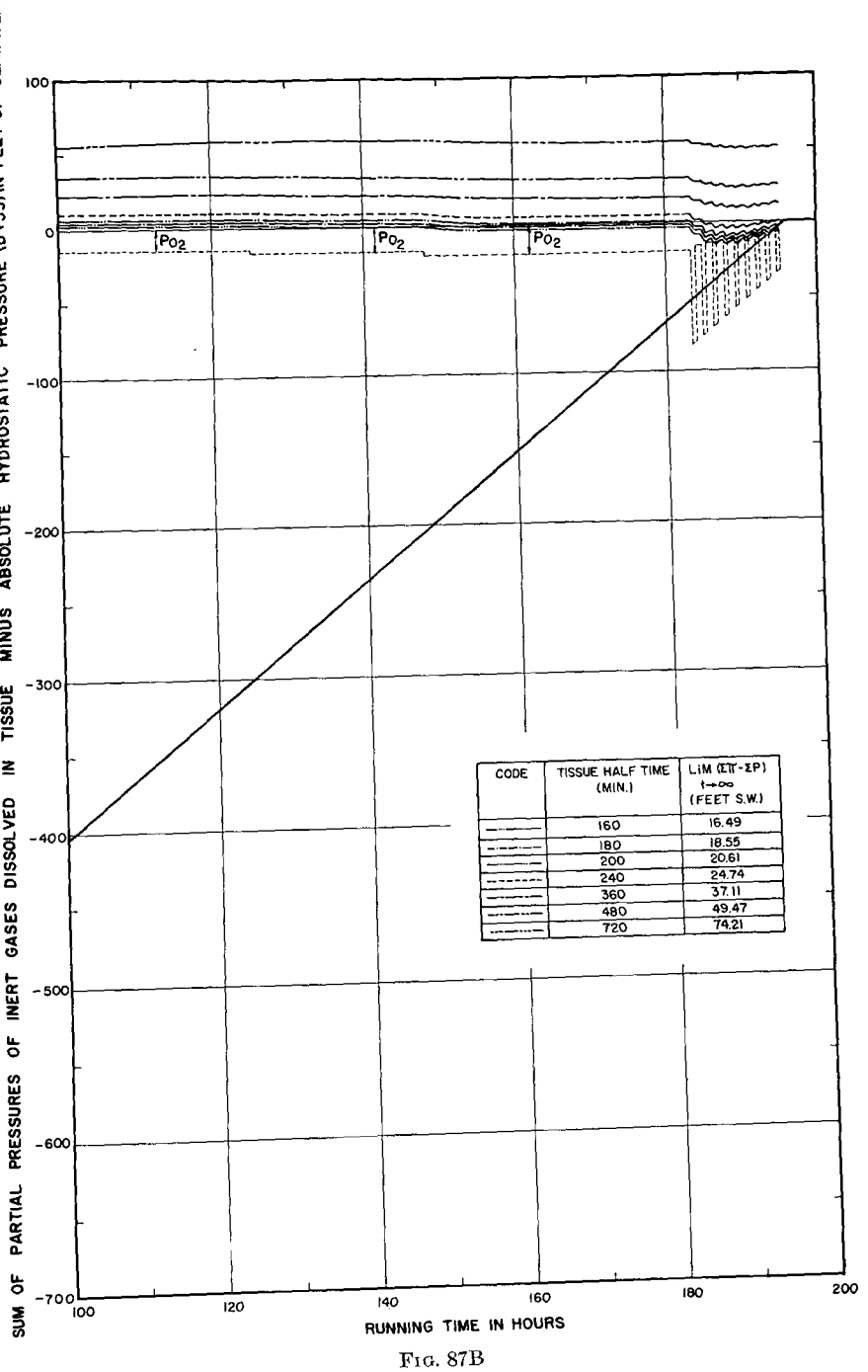
SUM OF PARTIAL PRESSURES OF INERT GASES DISSOLVED IN TISSUE MINUS ABSOLUTE HYDROSTATIC PRESSURE (D+33) IN FEET OF SEAWATER
100
0
-100
-200
-300
-400
-500
-600
-700
P_{O_2}
P_{O_2}
P_{O_2}
CODE
TISSUE HALF TIME (MIN.)
LIM (ΣΠ-ΣP) t→∞ (FEET S.W.)
160 16.49
180 18.55
200 20.61
240 24.74
360 37.11
480 49.47
720 74.21
100
120
140
160
180
200
RUNNING TIME IN HOURS

FIG. 87B

TABLE 42

Calculated Values of ΔP Sustained at 200 Feet during Decompression from a Saturation Exposure at 650 Feet

Tissue Half-Time (min.)	Calculated Helium Excess Supersaturation Pressure (ft.)
160	0
180	2.06
200	4.13
240	8.27
360	20.74
480	33.23
720	57.95

cal tissues with half-times longer than 240 min. could sustain ΔP values in excess of 20 ft. for extended periods of time. Since this saturation dive was completed without significant decompression problems, the existence of tissues with half-times longer than 360 min. in the subjects of this dive can be ruled out. Interpolated ΔP values at 200 ft. depth for the 280 and 320-min. tissue were 12.5 and 15.5 ft., respectively. These values are large enough for us to consider the existence of tissue half-times of up to 320 min. in the computation of decompression profiles from extended deep dives.

Acknowledgment

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APPENDIX TO COMPUTATION METHODS FOR DECOMPRESSION FROM DEEP DIVES

The rate at which inert gas is taken up by or released from a given half-time tissue is always proportional to the magnitude of the driving force (i.e. the difference between the ambient inert gas partial pressure and the partial pressure of the same inert gas dissolved in a given tissue) acting on this tissue. Thus

$$\frac{d\pi}{dt} = k(P - \pi) \tag{1}$$

with the boundary condition $t = 0$, $\pi = \pi_0$. The boundary condition $t = 0$

indicates the time at which a discontinuity occurs in any parameter affecting the mathematical systems discussed here. Every such discontinuity demands a redefinition of the boundary conditions for the continued valid mathematical treatment of the situation.

The total hydrostatic pressure to which the diver is exposed is balanced by the pressure of his gaseous environment. Hence,

$$D + A = P + P_{O_2}, \tag{2}$$

where

$$P = mt(D + A). \tag{3}$$

Excess supersaturation pressure ΔP is defined by

$$\Delta P = \pi - (D + A), \tag{7}$$

and the driving force F by

$$F = P - \pi = m(t)\ (D + A) - \pi, \tag{8}$$

where F is positive for gas uptake by and negative for gas release from a given tissue.

Equation (1),

$$\frac{d\pi}{dt} = k(P - \pi) \tag{1}$$

or

$$\frac{d\pi}{dt} + k\pi = kP \tag{4}$$

is a linear first order differential equation.

The general form of the solution of equation (1) is given by

$$\pi = \exp\ (-\int k dt)\ [\int P \exp\ (\int k dt)\ dt] + C_1 \exp\ (-\int k dt). \tag{9}$$

In the most general situation this expression cannot readily be integrated in terms of elementary functions and a numerical integration method is used to solve equation (1)*. However, in several special cases, wherein certain of the terms are either held constant or permitted to vary in simple linear fashion, the integration is quite straightforward, as will be shown for several cases.

Case 1: ΔP Constant

From equation (7) we have:

* The equations developed herein are in their simplest computational form for slide-rule, or desk calculator. They have also been programmed for the IBM System 360 digital computer.

$$D = \pi - \Delta P - A. \tag{11}$$

Now substituting (11) into (3) we have:

$$P = m(t)\ (\pi - \Delta P). \tag{12}$$

Now substituting equation (12) into (1) we have:

$$\frac{d\pi}{dt} + k\pi(1 - m(t)) = -km(t)\Delta P. \tag{13}$$

Integration of (13) yields:

$$\pi = \exp\ (-kt + k \int m(t)\, dt)\ [-k\Delta P \int m(t) \exp\ (kt - k \int m(t)\, dt)\, dt] + C_1 \exp\ (-kt + k \int m(t)\, dt). \tag{14}$$

When the form of m is determined the above expression may be evaluated, and the boundary conditions applied to obtain C_1.

Case 2: ΔP Constant, P_{O_2} Constant

Here the change of m as a function of time is given by

$$m = \frac{D + A - P_{O_2}}{D + A}. \tag{5}$$

From equation (2) we have the relationship

$$P = D + A - P_{O_2}. \tag{15}$$

Substituting equation (11) into (15) yields

$$P = \pi - \Delta P - P_{O_2}. \tag{16}$$

Now substituting (16) into (1) we have

$$\frac{d\pi}{dt} = k(\pi - \Delta P - P_{O_2} - \pi) = -k(\Delta P + P_{O_2}). \tag{17}$$

Integrating equation (17) yields

$$\pi = -k(\Delta P + P_{O_2})t + C_1. \tag{18}$$

Applying the boundary conditions of (1) to (18) we have:

$$\pi = \pi_0 - k(\Delta P + P_{O_2})t. \tag{19}$$

Now substituting (19) into (11) we may solve for D, thus

$$D = -k(\Delta P + P_{O_2})t + \pi_0 - \Delta P - A \tag{20}$$

but

$$D_0 = \pi_0 - \Delta P - A. \tag{10}$$

Thus (20) may be written in the form

$$D = D_0 - k(\Delta P + P_{O_2})t. \tag{21}$$

From this, the time t required to reach any point on the curve $D(t)$ is given by

$$t = \frac{D_0 - D}{k(\Delta P + P_{O_2})} \tag{22}$$

From equation (16) we see that

$$-(\Delta P + P_{O_2}) = (P - \pi) = \text{Constant} \tag{23}$$

by definition of the given condition. Equation (23) therefore is tantamount to the definition of a constant driving force F (Equation 8). Substituting (23) into (21) yields

$$D = D_0 + k(P - \pi)t. \tag{21A}$$

Thus when a constant P_{O_2} and a constant ΔP are specified for a given theoretical half-time tissue, it follows that the driving force $P - \pi$ is constant also. In either case, the ascent function must be linear. It will be shown later that during linear ascent with either P_{O_2} or m held constant, a constant driving force establishes itself with time that is characterized only by the specific time constant of a given half-time tissue and the linear rate of change of the inspired inert gas partial pressure.

Case 3: ΔP Constant, m Constant

Here the change of P_{O_2} as a function of time is given by

$$P_{O_2} = (D + A)(1 - m). \tag{6}$$

The solution for π in this case may be determined from equation (14) since the form of m is specified. Thus,

$$\pi = \frac{-m}{1 - m}\Delta P + C_1 \exp(-k(1 - m)t). \tag{24}$$

Applying equation (1) boundary conditions to (24) we have:

$$C_1 = \pi_0 + \frac{m}{1 - m}\Delta P. \tag{24A}$$

The complete solution of (24) is then

$$\pi = \frac{-m}{1 - m}\Delta P + \left(\pi_0 + \frac{m}{1 - m}\Delta P\right)\exp(-k(1 - m)t). \tag{25}$$

Substituting (25) into (11) and combining with equation (10) we obtain the following expression for D:

$$D = D_0 - \left(\pi_0 + \frac{m}{1-m}\Delta P\right)[1 - \exp(-k(1-m)t)]. \quad (26)$$

Equation (26) enables us to calculate the time t required to reach any point on the curve $D(t)$; this is given by the expression

$$t = \frac{-\mathrm{Log}\left[\dfrac{D - D_0}{\pi_0 + \dfrac{m}{1-m}\Delta P} + 1.0\right]}{k(1-m)}. \quad (27)$$

Case 4: m Constant, F Constant

Here the change of P_{O_2} as a function of time is given by

$$P_{O_2} = (D + A)(1 - m). \quad (6)$$

Substituting (28) into (1) we have:

$$\frac{d\pi}{dt} = k(P - \pi) = kF. \quad (29)$$

Integrating (29) yields

$$\pi = kFt + C_1. \quad (29A)$$

Application of the boundary conditions to the above equation yields

$$\pi = \pi_0 + kFt. \quad (30)$$

Now substituting equation (30) into (28) and solving for D we have:

$$D = \frac{1}{m}[F(kt + 1) - mA + \pi_0]. \quad (31)$$

Equation (31) may be more conveniently expressed as:

$$D = D_0 + \frac{k}{m}Ft. \quad (32)$$

If we compare equation (32) with equation (21A) we see that the time rate of change of depth is given by

$$\frac{dD}{dt} = F\frac{k}{m} = (P - \pi)\frac{k}{m} \quad (33)$$

for (32) and

$$\frac{dD}{dt} = kF = (P - \pi)k \quad (34)$$

for (21A). The conditions of the two cases are:

1. changing ΔP and P_{O_2} for equation (32)
2. constant ΔP and P_{O_2} for equation (21A)

Thus as we have already seen, maintenance of a constant driving force requires a linear rate of ascent (or descent). This linear function of time is given by either equation (32) or (21A) depending on whether or not ΔP and P_{O_2} are changing with time. Similarly, the rate of ascent (or descent) is given by either equation (33) or (34) depending upon the specified conditions.

Case 5: P a linear function of time

Given the condition that the inspired partial pressure of inert gas is a linear function of time, we have

$$P = P_0 + c \cdot t \tag{35}$$

with the boundary condition $t = 0$, $P = P_0$, and where c is a constant. Substituting into equation (1) we obtain

$$\frac{d\pi}{dt} = k(P_0 + ct - \pi) \tag{36}$$

which may be rewritten

$$\frac{d\pi}{dt} + k\pi = kP_0 + kct \tag{37}$$

and integrated to yield

$$\pi = P_0 + ct - \frac{c}{k} + C_1 \exp(-kt). \tag{38}$$

Applying the boundary conditions of equation (1) we have

$$\pi = P_0 + ct - \frac{c}{k} + \left(\pi_0 - P_0 + \frac{c}{k}\right) \exp(-kt). \tag{39}$$

Combination of equation (39) with (35) yields an expression of the time-dependence of the driving force during linear ascent or descent in which the inspired inert gas partial pressure is changed at the rate c:

$$F = P - \pi = \frac{c}{k} + \left(P_0 - \pi_0 - \frac{c}{k}\right) \exp(-kt). \tag{40}$$

It can now easily be seen that with increasing duration of ascent (or descent) the magnitude of the driving force will approach the value c/k because

$$\lim_{t \to \infty} (P - \pi) = \frac{c}{k}. \tag{41}$$

When P_{O_2} is held constant, differentiation of equation (2) yields

$$\frac{dD}{dt} = \frac{dP}{dt} = c. \tag{42}$$

Thus, for P_{O_2} = constant,

$$D = D_0 + ct. \tag{43}$$

When m is held constant, differentiation of equation (3) yields

$$\frac{dP}{dt} = m\frac{dD}{dt} = c \tag{44}$$

and

$$\frac{dD}{dt} = \frac{c}{m}. \tag{44A}$$

Thus, for m = constant,

$$D = D_0 + \frac{c}{m}t. \tag{45}$$

Case 6: ΔP a linear function of $(D + A)$, m constant

Let us consider first the case where ΔP is a general function of $(D + A)$, and m is a variable, i.e.

$$\Delta P = g(D). \tag{46}$$

Substituting (46) into (13) yields

$$\frac{d\pi}{dt} + k\pi(1 - m(t)) = -km(t)g(D). \tag{47}$$

Integrating (47) yields

$$\begin{aligned}\pi = \exp\,(-kt + k\textstyle\int m(t)\,dt)\,[-k\int m(t)g(D) \\ \exp\,(kt - k\textstyle\int m(t)\,dt)\,dt] + C_1 \exp\,(-kt + k\textstyle\int m(t)\,dt).\end{aligned} \tag{48}$$

To reduce the complexity of this situation, let us further consider

$$\begin{aligned} m &= \text{constant}, \\ \Delta P &= \Delta P_s + gD, \end{aligned} \tag{49}$$

where ΔP is the excess supersaturation pressure on reaching surface and

$$g = \text{constant}.$$

Combining equation (7) with equation (49) and solving for D we have:

$$D = \pi - \frac{\Delta P_s}{1+g} - A. \tag{50}$$

Now substituting (50) into (3) we have:

$$P = \frac{m}{1+g}(\pi - \Delta P_s - A) + mA. \tag{51}$$

Now substituting (51) into (1) we have:

$$\frac{d\pi}{dt} + k\pi\left(1 - \frac{m}{1+g}\right) = \frac{-km}{1+g}(\Delta P_s - Ag). \tag{52}$$

Integration of (52) yields

$$\pi = -\frac{\frac{m}{1+g}}{1-\frac{m}{1+g}}(\Delta P_s - Ag) + C_1 \exp\left(-k\left(1 - \frac{m}{1+g}\right)t\right). \tag{53}$$

Applying the boundary conditions of (1) to (53) we have for the complete solution:

$$\pi = \pi_0 - \left[\pi_0 + \frac{\frac{m}{1+g}}{1-\frac{m}{1+g}}(\Delta P_s - Ag)\right] \cdot\left(1 - \exp\left(-k\left(1 - \frac{m}{1+g}\right)t\right)\right). \tag{54}$$

Remembering that at $t = 0$, equation (50) yields

$$D_0 = \frac{\pi_0 - \Delta P_s - A}{1+g} \tag{55}$$

we have, on combination of equations (50), (54) and (55):

$$D = D_0 - \frac{1}{1+g}\left[\pi_0 + \frac{\frac{m}{1+g}}{1-\frac{m}{1+g}}(\Delta P_s - Ag)\right] \cdot\left(1 - \exp\left(-k\left(1 - \frac{m}{1+g}\right)t\right)\right). \tag{56}$$

When $g = 0$, equation (56) reduces to equation (26).

Equation (56) enables us to calculate the time t required to reach any point on the curve $D(t)$; this is given by the expression

$$t = \frac{-\mathrm{Log}\left[\dfrac{D - D_0}{\dfrac{1}{1+g}\left\{\pi_0 + \dfrac{\dfrac{m}{1+g}}{1 - \dfrac{m}{1+g}}(\Delta P_s - Ag)\right\}} + 1.0\right]}{k\left(1 - \dfrac{m}{1+g}\right)}. \tag{57}$$

Case 7: ΔP a linear function of $(D + A)$, P_{O_2} constant

$$\Delta P = \Delta P_s + gD \tag{49}$$

and here the change of m as a function of time is given by

$$m = \frac{D + A - P_{O_2}}{D + A}. \tag{5}$$

Combination of equation (49) with equation (15) and (16) yields

$$P = \frac{\pi - \Delta P_s - A}{1 + g} + A - P_{O_2}. \tag{58}$$

Now substituting (58) into (1) we have:

$$\frac{d\pi}{dt} = k\left[\frac{\pi - \Delta P_s - A}{1 + g} + A - P_{O_2} - \pi\right] \tag{59}$$

or

$$\frac{d\pi}{dt} + k\pi\left(1 - \frac{1}{1+g}\right) = -k\left[\frac{\Delta P_s + A}{1+g} - A + P_{O_2}\right] \tag{59A}$$

which, on integration yields

$$\pi = \frac{A - P_{O_2} - \dfrac{\Delta P_s + A}{1+g}}{1 - \dfrac{1}{1+g}} + C_1 \exp\left(-k\left(1 - \frac{1}{1+g}\right)t\right). \tag{60}$$

Applying the boundary condition to (60) we have:

$$\pi = \pi_0 - \left[\pi_0 + \frac{P_{O_2} - A + \dfrac{\Delta P_s - A}{1+g}}{1 - \dfrac{1}{1+g}}\right] \cdot\left(1 - \exp\left(-k\left(1 - \frac{1}{1+g}\right)t\right)\right). \tag{61}$$

Combination of (61) with (50) yields

$$D = D_0 - \frac{1}{1+g}\left[\pi_0 + \frac{P_{O_2} - A + \frac{\Delta P_s - A}{1+g}}{1 - \frac{1}{1+g}}\right] \cdot \left(1 - \exp\left(-k\left(1 - \frac{1}{1+g}\right)t\right)\right). \tag{62}$$

Equation (62) enables one to calculate the time t required to reach any point on the curve $D(t)$; this is given by the expression

$$t = \frac{-\operatorname{Log}\left[\dfrac{D - D_0}{\dfrac{1}{1+g}\left\{\pi_0 + \dfrac{P_{O_2} - A + \dfrac{\Delta P_s - A}{1+g}}{1 - \dfrac{1}{1+g}}\right\}} + 1.0\right]}{k\left(1 - \dfrac{1}{1+g}\right)}. \tag{63}$$

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Computer Analogues for Decompression

It is the purpose of this paper to summarize the results obtained in controlling decompression from air diving using the pneumatic analogue decompression computer developed at the Institute of Aviation Medicine, Toronto. Designed as an integral part of a diving system, the computers provide visual information to carry out a continuous ascent profile of compound exponential form. The configuration of the computer used in the earlier trials was based on analysis of current diving tables and experience (4) in terms of the Haldane (1) concept that inert gas passes independently through four parallel "tissue" compartments.

The most stringent constants obtained from this analysis were selected to permit computation as close as possible to the limiting "bends" threshold for man. These constants were half times 10, 20, 40 and 80 minutes with inert gas supersaturation ratios of 2.65, 2.15, 1.85 and 1.65 respectively. These ratios represent the quotient of the inert gas partial pressure with respect to the total ambient pressure (P_{inert}/P_A). When fixed gas mixtures are used in diving, it is appropriate and more convenient for the pneumatic computer to compute theoretical inert gas pressures using total gas pressure. Thus for compressed air diving, the supersaturation ratios are increased by the reciprocal of the inert gas mole fraction.

It was anticipated that these stringent constants would be inappropriate for long exposure times at depth, since analysis showed that the ratios decreased as exposure times are increased.

It was difficult to determine whether the ratios actually decrease or whether they appear to decrease due to the inappropriate selection of half times and "tissue" compartment configuration. It was also difficult to understand why different supersaturation ratios should be involved. Therefore an analysis was made to determine the half times required for a parallel computer configuration which would satisfy a common ratio for all compartments.

A parallel pneumatic analogue computer (designated Mk III P) was constructed with half times of 20, 40, 80 and 160 minutes with a common inert gas supersaturation ratio (P_{inert}/P_A) of 1.6 to test this analysis.

While the parallel analogue configuration of diffusion compartments has empirical justification in man, physiologically the transfer of gas between the lungs and the remote tissues can be visualized as a series or a series-parallel system of diffusion gradients.

A detailed mathematical analysis, conducted in terms of a series configuration (5), showed that a good fit to the Van der Aue "no decompression" curve (6) was obtained with a minimum of four series compartments each by itself having a 21 minute half time with a ratio (P_{inert}/P_A) of 1.6 being applied to the first compartment only to provide computer readout. Since this concept gave promise of great simplicity in design and calibration, a number of series computers designated the Mk IV S were constructed to evaluate the limits inherent in this particular system. This series arrangement effectively increases the time constant of the first compartment with time.

The decompression profile generated by this series version gave a safer ascent than that derived from the original parallel one reported previously (4) for exposures less than three hours in duration. The computer contained the information for safe decompression from exposures longer than three hours within its other compartments. The next logical step was taken in which a common ratio was applied to each of the four compartments in a series configuration. The computer readout was derived from that compartment having the highest pressure and presented a safe ascent depth on the same scale as the ambient depth. In order to increase the margin of safety further, the lowest ratio (P_{inert}/P_A) of 1.44 obtained in the earlier analysis was selected.

Such a computer (designated the Mk V S) was calibrated with four compartments each with a half time of 21 minutes and a common ratio of 1.44. Thus calibrated this configuration will have an effective half time of 174 minutes, or 8.25 times an individual compartment half time (5).

Methods

All dives were simulated in a hyperbaric chamber; many were working dives in that the prime reason for the dive concerned calibration of other equipment in which unusual dive patterns were required.

The subjects and observers formed a closely knit team which permitted observation and supervision during post dive periods. All manifestations of decompression sickness were recorded and treated, using the Goodman and Workman (7) regime in which 100% oxygen is administered and minimum recompression pressure applied.

Since the actual pressure-time history, however complex it might be, determines the safe ascent depth displayed by the computer, the only effect of following an ascent path which is deeper than indicated will be to prolong the decompression. When testing the validity of the decompression

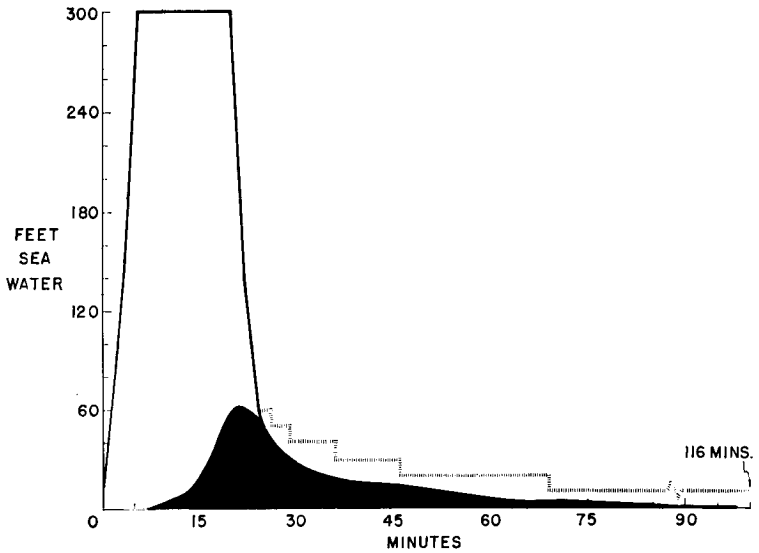

FIG. 88. Single "text book" dive (5 subjects, 11 July 1963) in which the ascent controlled by the computer (solid line) is compared with the decompression determined from the U. S. Navy diving tables (8) (broken line). In all figures the shaded area indicates the depth equivalent to the safe ascent pressure.

solution, it is essential to arrive at the surface at precisely the same time as the ascent depth indicates this to be safe. Throughout these trials, subjects were surfaced within seconds of the time indicated by the computer.

Exposures to pressure are divided into two classifications, single and repetitive. Each type of exposure may be carried out with linear or random profiles.

A linear profile is one in which the exposure to pressure is a linear function of time. These are the "text book" dives tabulated in any set of decompression tables. Figure 88 shows such a dive, the ascent from which was controlled in accordance with a computer. In all dive profiles illustrated, the depth equivalent to the safe ascent pressure is indicated by the depth of the shaded area.

A random profile is one in which the exposure to pressure is a non-linear function of time. This type of dive permits demonstrations of the computer capability beyond the linear profile restrictions inherent in decompression tables. The decompression schedules produced by the computer following random dives will be considerably shorter in time and shallower in depth than schedules from any known decompression table. The random profile is the type of dive most likely to occur in practical diving and in adventitious exposures during caisson work and in hyperbaric facilities. A

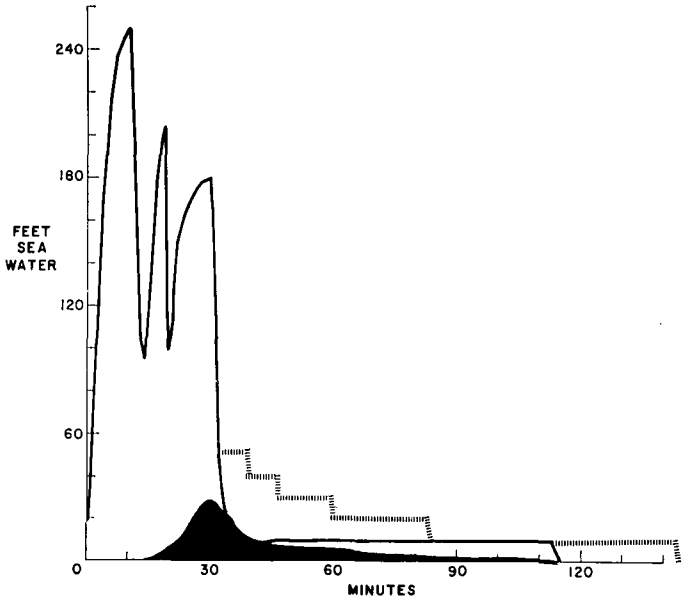

FIG. 89. Random dive (4 subjects, 16 July 1964)

deliberately exaggerated example of a random profile dive is illustrated by Figure 89.

To explore the capability of the analogue computer to deal with these alternations of pressure to the point of practical repetitive diving a series of random or multi-level dives such as is illustrated in Figure 90 was carried out. The first dive was made by seven subjects. Decompression from this dive followed an irregular path a few feet deeper than the optimum ascent depth. At the moment when the computer ascent depth indicated "sea level", one subject was "locked out" directly to the surface to act as a control. The remaining six subjects carried out a second bounce type dive until the computer indicated decompression was required; ascent was then made rapidly to 20 feet and this depth arbitrarily maintained until the computer showed that it was safe to surface at which precise time another subject was locked out. The five remaining subjects descended for a third exposure. In similar manner, a subject was surfaced precisely in accordance with the computer ascent information after the third, fourth and fifth exposures—finally, the remaining two subjects surfaced on completion of the decompression from the sixth exposure. No symptoms were noted by any of the subjects.

Another example of this type of experiment in which two dives were carried out in succession is shown in Figure 91. The first dive with seven

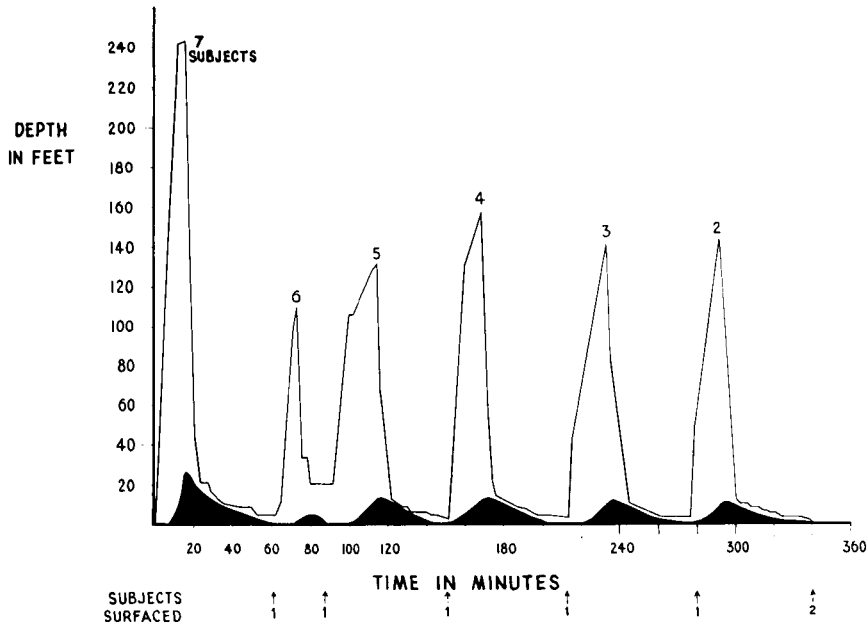

FIG. 90. Decompression computer trials. Repetitive dives (III P-1). See text for description.

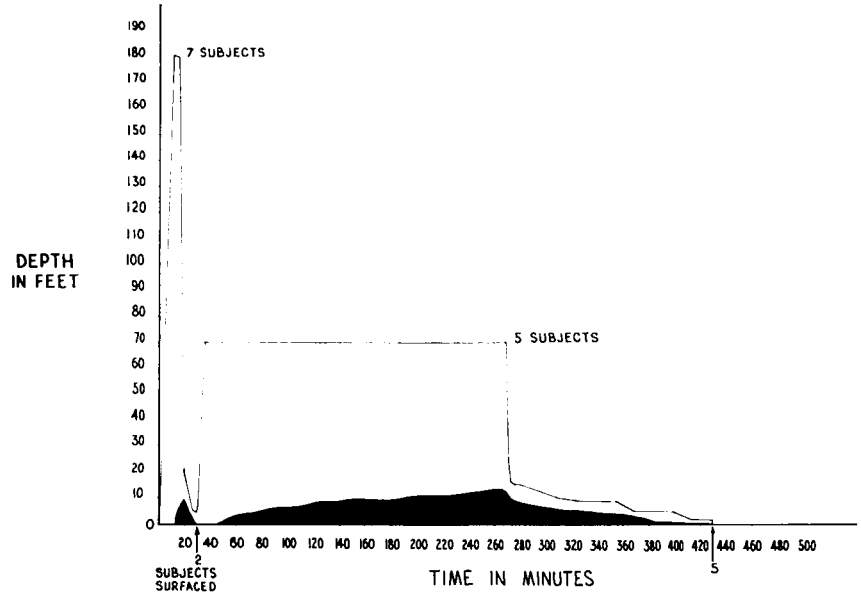

FIG. 91. Decompression computer trials. Repetitive dives (VS). See text for description.

subjects was made to a depth of 180 feet for 15 minutes. When the computer ascent depth indicated sea level, two subjects were locked out directly to the surface to act as controls. The remaining five subjects carried out the second dive to 70 feet for 4 hours, finally surfacing precisely in accordance with computer information. Each dive was symptom free.

Many experiments of this type provided a double check of the adequacy of the decompression solution. If decompressions from the later exposures are without incident, it is probable that the preceding decompressions must be of equal validity. Other repetitive dives were made with surface intervals ranging from 10 minutes to 12 hours, (Fig. 92). In this sequence of repetitive dives, seven subjects carried out the first random dive to 183 feet. After a surface interval of 19 minutes the same seven subjects carried out a second random dive to 198 feet. Following a second surface interval of 43 minutes, six of the subjects made a third random dive to 186 feet. The

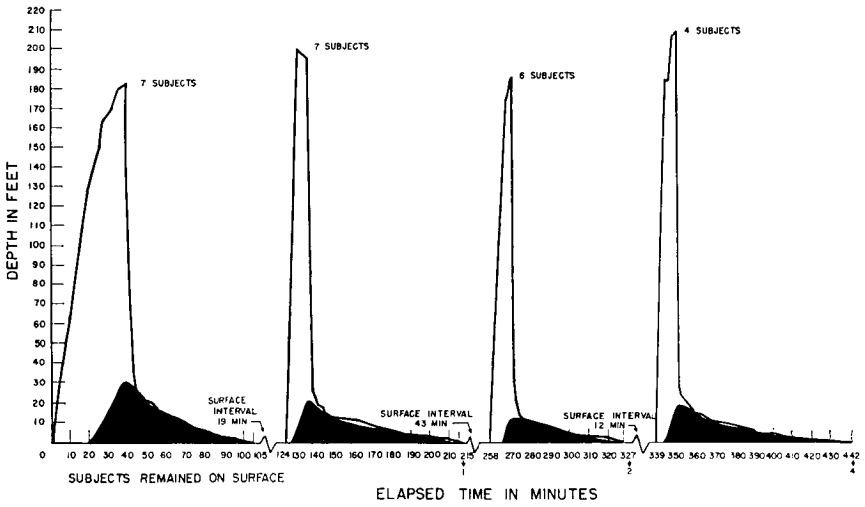

FIG. 92. Decompression computer trials. Repetitive dives. See text for description.

TABLE 43

Summary of Results with the Several Computers

TYPE OF COMPUTER	NO. OF SUBJECTS	DIVES	CLASSIFICATION OF CASES OF DECOMPRESSION SICKNESS		% INCIDENCE
			TYPE II	TYPE I	
Mark II P (4) (Parallel).....	39	523	6	20	5.0
Mark III P (Parallel).....	15	478	2	5	1.5
Mark V S (Series).....	28	852	—	4	0.5

seventh subject remained at the surface to act as a control. On completion of this dive, two subjects remained at the surface. After a third surface interval of 12 minutes, the remaining four subjects carried out a random dive to 210 feet. As in previous exposures, the ascent to surface again closely followed computer ascent information. No symptoms were noted by any of the subjects.

Results

The results of all dives, single and repetitive, are summarized in Table 43 and compared with data obtained from earlier work (4). The classification of cases of decompression sickness is that used by Golding et al. 1960 (2).

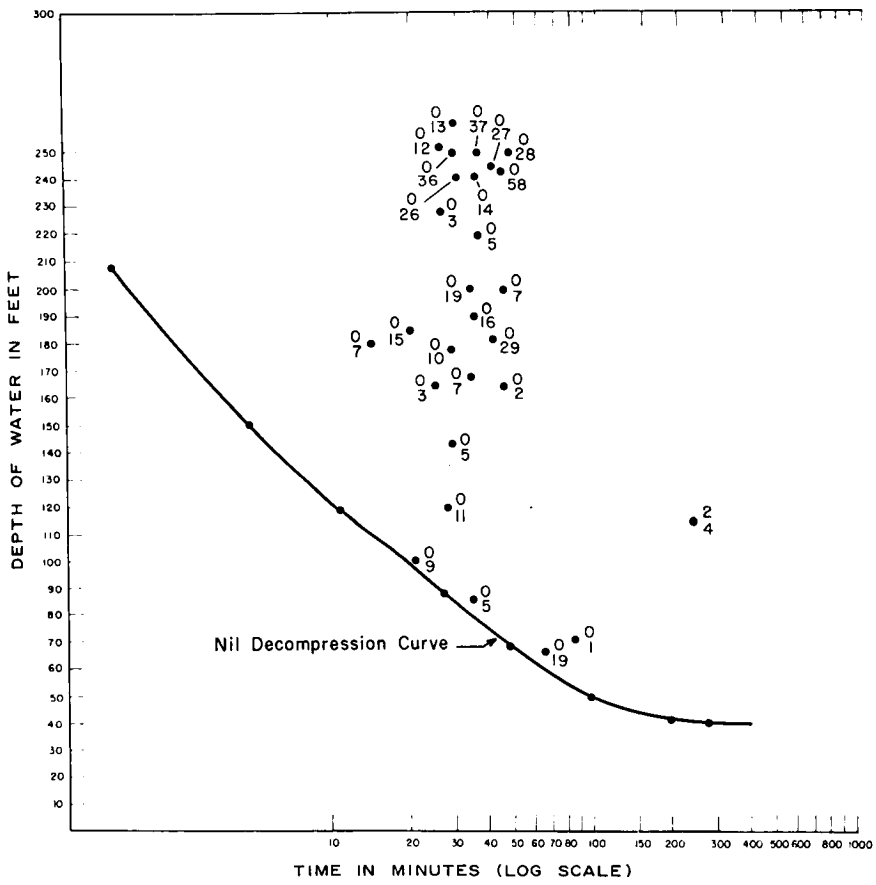

FIG. 93. Range of single dives

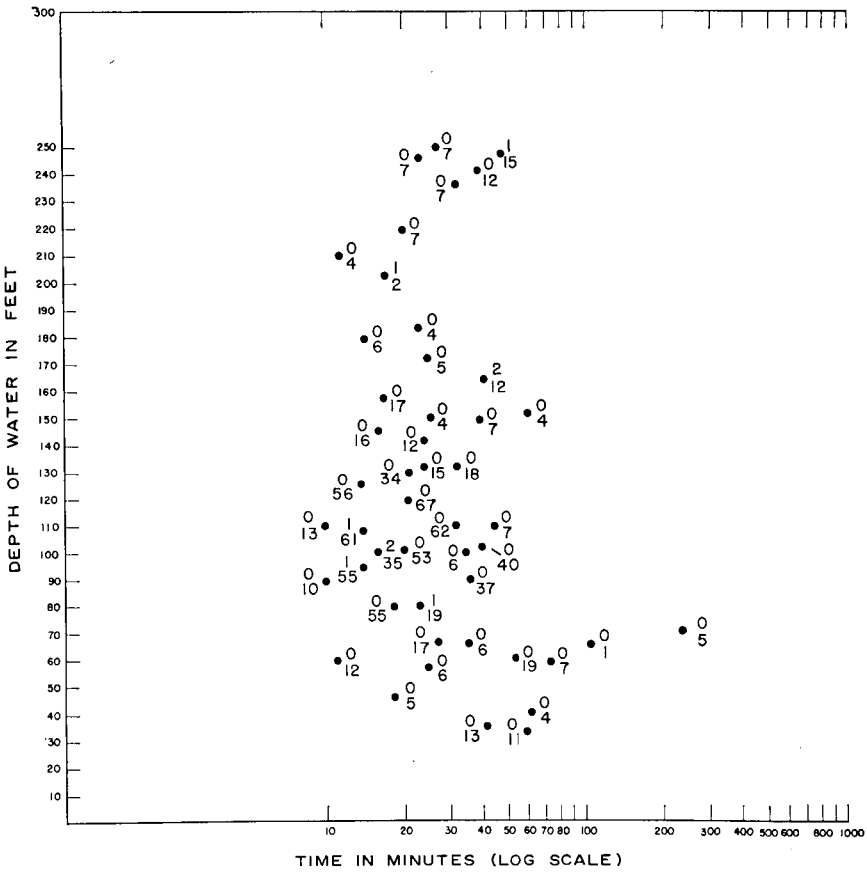

FIG. 94. Range of repetitive dives

The range of depths and bottom times of the dives using the III P and V S computers was sufficiently similar to permit them to be combined graphically. Figure 93 shows the range of single dives. Figure 94 shows the range of repetitive dives.

Discussion

The application of the tissue compartment concept to the analysis of current diving tables and experience has been based on the assumption that the transfer of gas to and from the body is symmetrical. This means that a given "tissue" compartment saturates and desaturates over a given pressure gradient with the same half time. Over the range of depth time exposures described in an earlier report (4), a comparison of the response

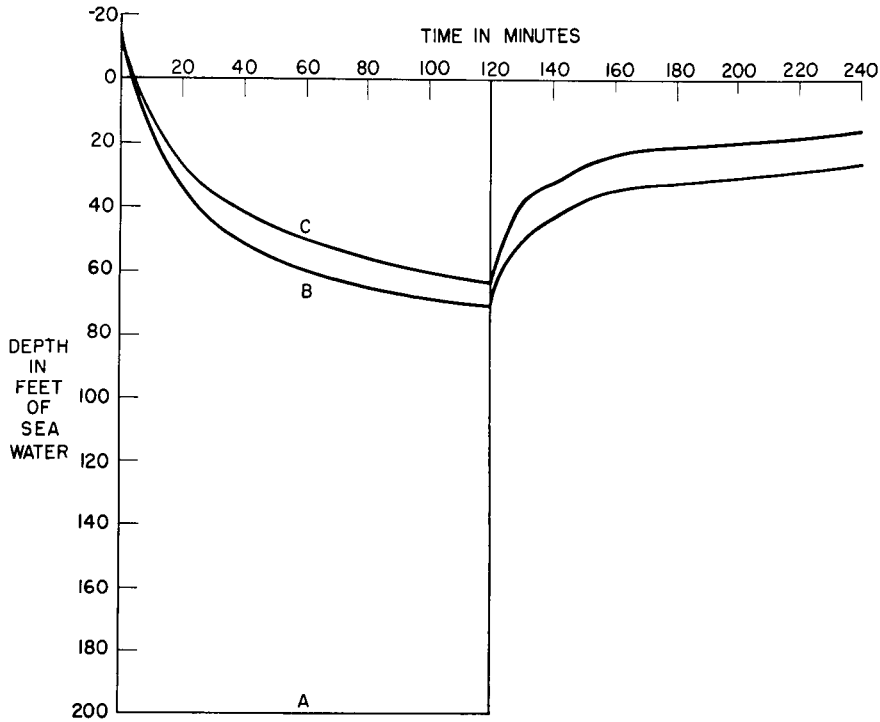

FIG. 95. Response of pneumatic and electronic analogue computers to a square wave input. Computer configuration as for a Mark V S computer: 4 compartments in series, equal desaturation half-times of 21 minutes and equal ratios for all compartments of 1.8 (P_{inert}/P_A = 1.44). Curve A: Applied pressure equivalent to 200′ (true) for 120 minutes. Curve B: Ascent depth generated by the pneumatic computer. Curve C: Ascent depth generated by the electronic computer.

of the pneumatic analogue computer with the response of a symmetrical mathematical or electronic analogue showed only minor differences. These differences were considered to be within experimental error.

In the series of dives reported here, occasional comparisons of the pneumatic computer decompression profiles were made with a symmetrical analogue. Significant differences were observed.

In devising stringent calibration test procedures for the computer, it was decided that a square wave pressure-time input profile should be used to accentuate calibration inaccuracies. The duration of the square wave input was chosen to be sufficiently long to insure that all computer compartments played a part in the response characteristics. The response of the ascent depth indicator of the pneumatic computer to such a square wave exposure, when compared with the response predicted by the symmetrical system, showed significant disagreement (Fig. 95).

A detailed examination of these differences has shown that the pneumatic computers are not symmetrical. The saturation half times are shorter than the desaturation half times between equivalent pressure differentials. This asymmetry is due to a non-linearity in the flow resistance of the orifices and their sensitivity to the pressure to which they are exposed.

Over small pressure differentials the orifices operate in the free molecular or Knudsen flow regime in which the mass flow is linearly proportional to pressure differential. Over the largest differentials used, the orifices operate in the viscous flow regime in which the mass flow is proportional to the differences of the squares of final and initial pressures. Between the two regimes, the orifices operate in a transitional mode which is not well defined theoretically. An empirical expression which describes these variations in flow characteristics has been determined. This explanation, illustrated in

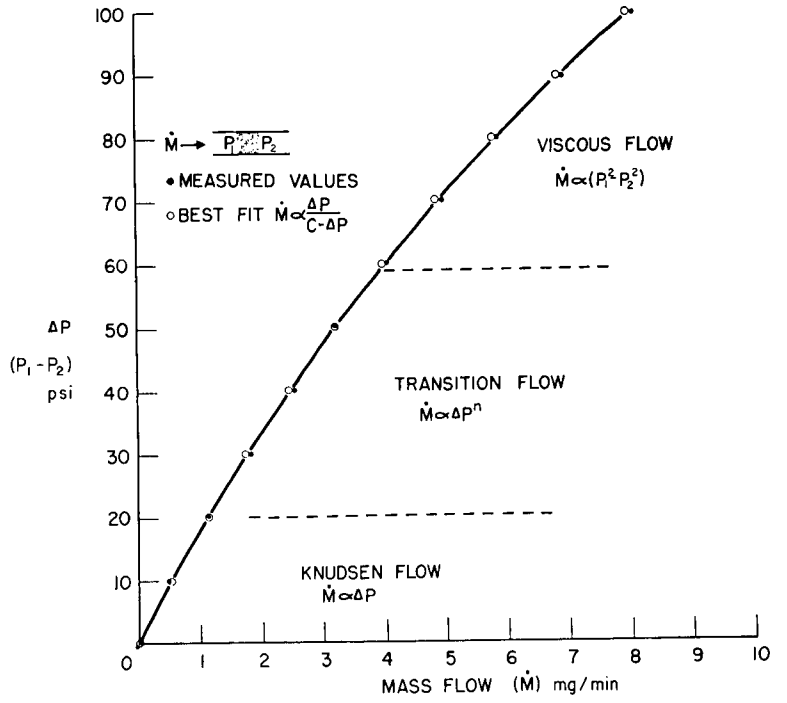

FIG. 96. Steady state flow characteristics of a pneumatic analogue computer orifice assembly. In general C is a constant dependent upon the orifice assembly and the units of measurement. The characteristics of a particular orifice assembly illustrated here has the following form:

$$\dot{M} = \frac{16.2\ \Delta P}{301\text{-}\Delta P}$$

Figure 96, is compatible with steady state flow and computer behaviour over equivalent pressure conditions.

The continuous ascent profile generated by the pneumatic analogue computer can never be faster or shallower than that generated by a symmetrical analogue model. In general it will be slower and deeper. Hempleman (3) suggested that asymmetry might be involved in his studies with experimental animals. Since the pneumatic analogue computer has provided reliable and flexible decompression information over the range tested, it might be suggested that these results are not only due to continuous computation on the actual pressure time history but also to a non-linear characteristic in the mechanism of gas transfer.

Conclusions

The pneumatic analogue computer has demonstrated some advantages in safety, decompression time and air supply economy over diving tables for decompression from single exposures.

The great advantage of the computer, however, lies in the provision of efficient decompression from random profile dives and repetitive exposures. Many of the dives described here would not have been practicable if controlled by tables, hence further comparisons are unjustified. Since an appropriate decompression profile is always available from the computer regardless of the exposure history, complicated diving operations can be carried out with considerable flexibility.

Multi-level and repetitive dives can be undertaken for example by a Medical Officer supervising the treatment of a patient in a hyperbaric facility without incurring a decompression debt longer than is strictly necessary for the precise exposure dictated by the clinical circumstances.

When considering the relative merits of the compartment configuration of a computer, the series system has some advantages over the parallel system in that longer half times can be achieved with less difficulty in orifice construction and calibration. A series configuration permits a closer fit to the Van der Aue no decompression curve when a common ratio is applied to all compartments.

It does not appear to be necessary to consider different ratios for the computer compartments, particularly in a series system, in order to generate a safe decompression profile for man when diving within the practical pressure limits for air and durations less than four hours.

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Panel on

Potential Advances in Deep Diving

C. J. LAMBERTSEN, *Chairman*

Dr. BEHNKE
Mr. HEMPLEMAN
Mr. KELLER
Dr. KIDD
Dr. LARSON
Capt. MAZZONE
Dr. SCHREINER
Wing Commander STUBBS
Dr. WORKMAN

Discussion

CHAIRMAN LAMBERTSEN: Our purposes in this and subsequent panel sessions will be to encourage full and open discussion. I hope this will be not only among the members of this excellent Panel, but that the audience will take active part as well.

Let me begin by emphasizing the great difficulty encountered in obtaining adequate and accurate information concerning the validity of potential advances in decompression procedure. How can we improve upon our methods to speed the obtaining of information?

There are great difficulties in translating information obtained in small or even large animals directly to the human. We all want to see that new decompression methods are very carefully verified in order to cover the full population. It takes a long time, very special investigators, and very special facilities to accumulate the large amount of information we need.

I would like us now to address ourselves to the differences of decompression physiology among animals, aiming at agreement regarding how investigators who do not have the equipment or the legal right to study humans at high pressure could help gain information applicable to decompression in man.

This question needs your help, since it is not an easy one to answer. I asked one of my students, Mr. Flynn, to find out how to separately appraise the time courses of several physiological compartments within the mouse. We normally don't use mice for decompression studies but, knowing that eventually statistics will be required for such work, I felt that if we did a careful decompression analysis of the mouse it might be possible to

use hundreds of these animals in the testing of theories of decompression. At this point the mouse seems, surprisingly, to have a half-time for its *slowest* tissue not much longer than two to four minutes. This may seriously limit the usefulness of this animal for some quantitative studies of decompression, but may shorten the process of study in others.

Have you any thoughts on this, Mr. Hempleman? You have made extensive use of goats for bends studies. Does the goat have slower tissue half-times than the human or is he so close to the human that you can utilize quantitative findings directly?

MR. HEMPLEMAN: Oh, no. He doesn't have the long response times to decompression sickness phenomena that man has and you cannot strictly translate findings from a goat to a man at all. You can make analogies and obtain a good general feel of the situation. I think that you would be very unwise to try and do a dive that a goat finds safe.

DR. BEHNKE: We repeatedly used the same anesthetized dogs many years ago, and were able to decompress them safely on the basis of essentially a two to one depth ratio compared with man. That is to say, we could expose the dogs to four atmospheres and decompress them without symptoms, whereas man can go to two atm. and come down to one atm.

To answer your question specifically, the species smaller than the dog have been of no help; the dog has been of help. I don't know why the Royal Navy uses the goat except that Professor Haldane in 1908 used goats and they generally do not change things over there.

CHAIRMAN LAMBERTSEN: I know that Dr. Hesser can comment on this question, since part of his presentation here is quite in disagreement with the concept of very short maximum half-times that I cited for the mouse.

DR. HESSER: Dr. Kindwall in our laboratory took into account the circulation time of the smaller animals he used for decompression studies and found that they could be surfaced safely with very high tissue nitrogen tensions, particularly in the slower tissues, without getting any ill effects at all. They did not appear to show the same syndromes or the same symptoms of the larger animals and human beings.

CHAIRMAN LAMBERTSEN: This is important. The reason for beginning discussion on this point of quantitative studies on large numbers of animals is that one of the major questions throughout our presentations concerning advancing human decompression capability related to the relative rates of entry of different gases such as helium, nitrogen, argon, and hydrogen into tissues and differences in the rates of exit from tissues as compared with rate of entry on certain occasions.

These are questions that require real information, not just superficial deduction. The panel should be willing to help define the experiments that are required to do this.

DR. WORKMAN: One of the difficulties with experimental animals, as

Dr. Kindwall had demonstrated in the spectrum of animals he used, is the significantly greater super-saturation that is permissible in these animals without any symptoms at all after decompression from air exposures.

In work which has not yet been completed and is not being reported here, Commander Reeves and Captain Beckman's group at the Naval Medical Research Institute have been using large dogs, weighing about 80 to 85 pounds, which is closer to the mass of man, for exposures on air for periods of seven hours, twelve hours and up to eighteen hours followed by direct ascent to the surface. They have very carefully calibrated the depths at which such exposures could be made without symptoms occurring and then have defined the exact depth at which symptoms did occur. They have found these repeatable. They have also found that an animal that was decompressed safely after being exposed for seven hours would not be safe following a twelve hour exposure and that this would be refined to an eighteen hour exposure. It was possible to repeat these exposures and get the same results. However, there was a wide range of depths to which these animals could be exposed and then surface directly to atmospheric pressure. Some dogs tolerated exposures as deep as about 94 feet, others only to about 54 to 58 feet.

The amazing aspect of these observations is the magnitude of the supersaturations that are permissible even in the face of what would be interpreted as relatively long exposures. If in an animal as large as the dog, such very great supersaturations are permissible, it becomes very difficult indeed to extrapolate these things to man.

There are, perhaps, some relative studies that one can do in the same animal, carefully calibrated from one gas to another. However, it remains a very interesting point in terms of decompression theory, that there can be such a magnitude of supersaturation compared to man without symptoms occurring.

DR. SCHREINER: With regard to the closing statement of Dr. Workman, I would like to say that it is indeed possible to use small animals, such as rather heavy rats. They have to be heavy to be useful in this type of experimentation. Then one can distinguish the decompression susceptibility sustained by such animals after exposure to various gases such as helium versus neon or nitrogen.

Dr. Doebbler in our laboratory is conducting these studies. There is one aspect of this form of decompression study that needs emphasis, namely that merely surfacing the animals will in all likelihood fail to reveal overt damage in a reasonable decompression schedule. Rats do not tell us about their pains so we have to go to pressures lower than sea level. The method that has been developed by Philp and Gowdey is very useful. It calls for exercise of the animals at altitude for a specified period of time after de-

compression from positive pressure. This tends to bring out latent, incomplete decompression in the animals. Then, by grading the bends that the animals in the exercise drum experience, one can get reproducible results. We have used this method successfully in the context that I have just related.

MR. KELLER: We in Switzerland are in a rather peculiar situation. We are not allowed to do experiments with animals but we can do with people whatever we like to do. Actually, in our research program we are trying to determine with people whether they develop bends or not in a diving schedule we have calculated.

Now I think it is perfectly all right to produce bends when you have long exposures. We have extremely slow saturating tissues where we expect the bends. For about half a year, practically every dive we have made has produced bends, almost every time in the knee. This seems to be the slowest tissue we could find. In the bad cases the man developed bends in the shoulders.

We had one case, however, where a man coming back from a six hour exposure to 700 feet developed bends at about 400 feet depth. Then during the treatment decompression to surface, he went into shock. We do not know why and we do not believe that it was due to decompression but it was rather dubious. There was no trouble in treating him. We got him right out in time and had him in the hospital, but this was a very peculiar case. Normally you would find it absolutely safe to try decompression on man, not to work with animals.

DR. KIDD: We have not completed our work but as a stimulus to the present discussion I will mention our use of ultrasonic energy to monitor what is going on in the individual during decompression. We have been studying this periodically for two years. First we used a single frequency, now we are using five simultaneous frequencies from 100 cycles to two megacycles and measuring the resonance absorption.

We also expect to go to a wide noise source and then frequency scanning in the pious hope that we should be detecting let us say, clouds of extremely small bubbles and monitoring the growth or decay in size and relating this to the clinical picture. All I could say right now is that, when monitoring a man during decompression, we seem to get a pretty good signature on the ultrasound which is related to his subsequent clinical course. In other words, if we get an adequate signal indication on the ultrasound the chances are extremely good of getting a clinical manifestation of decompression sickness later. The converse also is true, namely that if you get practically no signature with the ultrasound the man is clear of bubbles.

We were doing a twelve hour dive the other day and had the ultrasound on one man. There was virtually no change in the signal over about six

hours and he was disconnected. We then put it on another man who had complained of a transient itch and got quite a hefty signal. Within ten minutes he had developed full clinical bends. The other man did not.

The interesting point is that if you do follow the subject continuously you will get fluctuations in the reflected signal; it will clear up, then it might come back again. It is a very complex question as to just when you trigger off a bend. Do you trigger off a bend at one point in time and have it manifest itself some hours later?

We were hoping by this means to follow dynamically something that was happening in the individual.

CHAIRMAN LAMBERTSEN: Dr. Kidd, while you were being so hopeful, could you tell us whether you are, in fact, triggering off the bends with the ultrasonic apparatus that you are using?

DR. KIDD: A very good question. No, our energy levels are extremely small. If we are measuring resonance absorption, our energy levels are minute and the other reassuring thing is that until quite recently every subject we used the ultrasound monitor on was free of bends.

Mark you, the subject has to remain reasonably still at the time. This might be related, but it certainly hasn't increased the incidence of bends and in fact a lot of the subjects say, "May I be a subject today please, sir" because he knows he is going to be all right.

MR. HEMPLEMAN: I would like to say something about what we are beginning to think is a bit of a myth. That is, the concept of tissue half-times.

If a man is brought to the surface inadequately decompressed there is generally a latent period before the symptoms of the bends appear. It is very difficult to explain away that latent period unless you invoke the idea of the formation of "silent bubbles". Therefore, from mere observations of the delay in appearance of bends symptoms, the idea of silent bubbles, or bubbles you can't feel, must arise.

Also, there has been recently in the United Kingdom great concern about bone necrosis. There is no doubt that some men get quite massive afflictions of their bones from decompression and they do not necessarily have an attack of the bends. They do not necessarily report that they have had a pain as a result of their work in compressed air. Yet they have bone problems. Assuming that bubbles are the cause of necrosis of bone and occlusion of bone circulation then this is a second instance of the presence of bubbles not being felt by a man.

It seems that when we observe what are considered long half-times, such as the 320 minute half-times which are necessary to explain some of the results of decompression studies, we are really seeing tissue-bubble complexes. This is more than borne out by many of our deep dives. In some

of these the decompression is very prolonged and we have been ascending in little incremental jumps of ten feet at a time. A small jump of ten feet will cause a mild, transient something to happen to the man which will die away and he will be all right until we do the next little incremental jump nearer to the surface when he will get another little pain which will also die rapidly away. There is no doubt in the mind of anybody watching that there is something lying in wait for you, expanding on the principle of Boyle's Law to give you a little nip of it on the way to the surface. In these circumstances, I cannot see how you can expect the gas to come out as it went in.

DR. BEHNKE: We have heard that when you decompress an individual, as from 600 feet, and drop the pressure to 300 feet, bubbles undoubtedly form. What we see then is not a decompression but a treatment table.

The two to one ratio concept has pretty much gone by the board. I think the delta *P* ratio has also gone by the board. We have also heard a lot about supersaturation. However, there is no physical principle that should lead us to believe that the blood can carry a gas away from the tissues in the state of supersaturation.

We come then to what I call the isobaric oxygen window principle of decompression in which you decompress in such a way that at no time does the inert gas pressure in the tissues or in venous blood together with CO_2 and water vapor exceed ambient pressure.

In the model saturation dive that was made to 650 feet at Tonawanda, the oxygen window principle was exactly what was used for the most part. At no time was there a state of supersaturation; I have calculated on the basis of the per cent oxygen which was used during a large part of the dive that the oxygen pressure in the capillaries dropped.

The pressure head for gas diffusion of helium from the body is about 140 millimeters of mercury and the elimination of gas at that pressure head and on the basis of a 54 minute half-time tissue, takes 14 minutes per foot.

In the U. S. Navy saturation dives to 200 feet (SeaLab) the rate of decompression was ten minutes per foot. That was a borderline situation. It was a little too rapid and I believe some subjects got bends.

We can consider that men can be used safely if it is true that the falling oxygen pressure in the capillaries is the window through which the inert gas diffuses into the blood and is carried away without bubble formation. I am speaking now of a state of elimination of gas seen only in the saturation dives which we started many years ago but only got to 90 feet.

If this is true then during decompression if you raise the partial pressure of oxygen, as by 100 millimeters, to a safe level in the lung, you should be able to cut down by many hours the time for elimination of inert gas.

Therefore, I would approach it this way: for a saturation dive to a rea-

sonable depth such as 100 feet or 200 feet, I would decompress with a given oxygen pressure on the basis that at no time would the inert gas pressure be permitted to be in excess of ambient pressure.

CAPTAIN MAZZONE: We have talked about using animals in decompression research. I think that when we make the change from the animal to the man we are extrapolating. The first time that anybody takes animal results and applies them to man he had better not leave the laboratory until the last man is out and has been observed for twelve or twenty-four hours.

In our particular case we must have the approval of the Secretary of the Navy before we can do animal experiments. We then have to pick an animal that is appealing to the people who sit in the line of review. If our reviewers, who have to approve our research before we can apply it to humans, like dogs, then we'd be foolish to use a mouse. We have also tried goats.

DR. WORKMAN: I want to get back to the question of supersaturation.

Many observations are as difficult for others to interpret as they are for us. However, Dr. Larsen described a series of excursion dives from an equilibration depth of 35 feet, a return to that depth and a stay there for a six hour period to observe whether anything really did occur during that time. I think there is little question but that these people have had a significantly greater amount of nitrogen in their tissues upon return to 35 feet, where they remained safely for six hours, than one would expect could be sustained, at least far greater than an equilibration level at 35 feet.

This kind of observation must be explained. Unfortunately we can't get in to the tissue sites and know what concentrations of gas are there, but certainly for some period of time in accordance with any hypothesis of gas uptake and elimination there must have been elevated concentrations of gas in tissues.

As was noted, every one of these dives was done without event, so it is one of the things that must be interpreted.

CHAIRMAN LAMBERTSEN: We didn't want to get into a hassel over the relative advantages of animal versus human work. I think we can now put the topic to rest. It is obvious that when in an investigation a fruit fly is the best animal to use for a particular purpose that's what should be used.

Can we now go on to extend the topic Dr. Workman dealt with? I think the concept of excursion diving and the limitations and implications of it are of extreme importance to this group.

MR. GIUDICE: Dr. Workman just brought something to my mind. Is it possible that part of the problem is that you would like to have instrumentation that would get into the tissue sites so that you could see what was going on there?

DR. WORKMAN: The problem involves being able to get some idea of what the gas concentrations in the tissue are without disturbing the system while you are doing the analysis.

There have been some studies of this type done, sacrificing the small animals and analysing tissues for nitrogen. However, it is quite difficult to get any good anatomical relationships of tissue tensions such as concentrations in muscle, in joint capsule or in various fluids.

CHAIRMAN LAMBERTSEN: Actually, it is probably not an anatomical problem in the true sense, since the sites of interference with inert gas elimination are probably diffuse and may vary from one exposure to the next.

DR. MACKAY: The comment about not believing in half-times raises an old story.

As has been pointed out, these equations for gas uptake are all equations describing the diffusion of gas through a very thin membrane. Actually, we are dealing with diffusion of gas from arteries into a slab of tissue. When you actually have diffusion through a finite expanse you do not have an exponential process so there is no such thing as a true half-time.

It appears that perhaps one can fit the observed curves of a diving table with a fewer number of constants by considering a cylindrical diffusion model rather than the compartment model in which it is assumed that everybody is made up of a bunch of infinitely thin little boxes.

CHAIRMAN LAMBERTSEN: I think that is a very pertinent comment. It relates to a question I want to ask the panel. Are there 1,000 sites of limited gas elimination or only one or two where circulation is suddenly grossly interfered with by the effects of activity, cold, sympathetic reactions, or vasomotor influences? The usual concept of limitation of gas elimination by inadequate perfusion of the tissue with blood should give way to the concept of a limitation of diffusion as circulation actually stops in certain capillaries.

Dr. Behnke, will you comment on this?

DR. BEHNKE: We can say perhaps this would be the case in bone. If one breathes helium for perhaps twenty minutes, that is far short of saturation. Then it requires several hours decompression to get the helium out. Apparently, diffusion has taken place in the body, so that it takes just about as long to get the gas out after a short exposure as it does out of a long exposure. While this looks all well and good and one could say, "Why not decompress on one tissue half-time?" we can't do that. We are not sure which tissues give rise to pain, with the exception perhaps of bone.

In an Air Force experiment a doctor put his hand in a vacuum chamber and decompressed the air around it. This produced a swelling about two and a half times normal without producing any pain. Pain apparently is not caused by gas in tissues if the gas can expand, but in bone you have

a situation that is perfusion limited and what gets in bone has to get out by means of the blood and if the bubbles are too large they don't get out.

I would say that we can consider bone as a limiting organ so far as the body is concerned. If our skeletal structure were cartilaginous we would be all right.

DR. SCHAEFER: One has to try to find a way to explain the unusual variations in decompression tolerance. There have been brought out recently wide individual variations in certain factors and one of these involves different cycles in blood flow at 30 minutes and 3 minutes. Recently we found something very interesting which plays a role in terms of regulation. We have found every two minutes a proportionate increase in red cells going into the capillaries which amounts to a kind of an increased flow and a stop. This then would be the same as an oxygen valve or choke. I've found out that individual differences are particularly expressed in terms of cycles, and I think this is a point of approach to find out the basis for individual differences.

DR. GARRETT: I have a comment very similar to Dr. Mackay's, namely that the half-time concept is severely limited.

If a compartment is saturated, the elimination would be zero order if this were an intermediary compartment between other compartments because then the rate determining step, still proportionate to the amounts that are in that compartment, would be invariant with time for a definitive level.

Regarding another comment that was made, I am convinced that the gas goes in as it goes out, below equilibrium saturation levels. On the other hand, as our British colleague has stated, we have bubble formation and this would be a different phenomena.

WING COMMANDER STUBBS: I would like to add to the point that was raised by both Dr. Garrett and Dr. Mackay. In our work on the pneumatic analog we have been using very thin virus filtration material as our orifice; this means we are dealing with orifice mean size something like 0.05 microns. We do observe an exponential law of behavior, in a very peculiar way, as we were trying to bring out in our paper on the computers today.

If one were to take a single compartment system which would be just a membrane and a small compartment and expose it suddenly to a pressure of 200 feet, you would find that you would get an exponential behavior. As an example, the half-time for a given system would be 13 minutes. If on the other hand you now lower the pressure suddenly to ambient, you will find that the system will again obey an exponential law. However, the half-time will now be of the order of 21 minutes.

If you go one step further and you apply a vacuum to one side with the initial condition inside the chamber being ambient pressure, you find the half-time now has shifted to 27 minutes.

So what we have observed is not only that exponential law applies with thin membranes between compartments but that the half-time shifts as a function of the final absolute pressure.

This is most interesting in that we were trying to get a fit with some of our air dives and with some of the preoxygenation/denitrogenation experiments being carried out at Brooks Air Force Base with the Manned Orbiting Laboratory project in mind. We found that the pneumatic computer showed a very slow desaturation indeed, even on 100 per cent oxygen.

So there is definitely an exponential law of behavior in this model but it does vary its half-time depending on the final pressure.

MR. GREENWOOD: Dr. Kidd, what is the size of the computer you are talking about, and does the diver in its ultimate form take this computer under water or is it going to be on the surface?

DR. KIDD: The usual sort of computer we are talking about today is about six inches long and about three inches in diameter. We have tested it in the sea. It is hooked up to the breathing apparatus and becomes part of the equipment.

Of course the same sort of thing can be used to monitor a chamber and then it doesn't have to be small or pressurized. We have various types of these; they sense the pressure either from the breathing apparatus or from the chamber, and present the information as visual information or as a command signal.

CHAIRMAN LAMBERTSEN: Can either Commander Stubbs or Dr. Kidd tell us if the computer technique might provide some help in answering the question relative to whether the perfusion versus diffusion concepts are correct for the slowest tissues? Can we reverse the technique of devising computers to fit man, and make use of the computer to help us learn about him? What have you concluded by now?

DR. KIDD: I think the conclusions are incomplete. This was really the point of using the ultrasound: having got a computer which seemed to give a pretty good answer, we used this as a tool for knowing where our subject was in time. We then devised a series of dives going by computer and then disobeying the computer by given numbers of feet of pressure, going two to four to six feet shallow from the computer and then using the ultrasound to monitor what was going on in the tissues.

I don't think this answer has shed any light on the question you answered but this was our attack. We have a lot of work to do but I think it shows promise. I think it is well worth more people than ourselves pursuing it.

CHAIRMAN LAMBERTSEN: I would now like to ask Dr. Larsen a question relative to whether he feels that the use of computer techniques, especially the portable computer analog, would aid in any way the very important effort of working out the excursion dive procedures for unusual excursion dives from one depth to another.

DR. LARSEN: All the excursions that we have done thus far have been on air. In terms of the deep saturation method that we hope to work with this is unrealistic. We have plans to go into deeper excursions and the promise that the computer seems to show with regard to repetitive dives and even in dives over an irregular bottom, indicates that it would, if successful, be extremely helpful in minimizing decompression for variable depth working dives.

CHAIRMAN LAMBERTSEN: I was going to ask whether the portable analog computer technique would eventually put mathematicians out of business too.

DR. SCHREINER: I would like to refer to what Dr. Larsen just said. The question that immediately comes to my mind on whether or not the Canadian computer is directly applicable to excursion dives from the saturation level goes back to a point that Dr. Kidd raised. That is that the apparent half-time of gas exchange of the model he described is a function of the particular depth or total pressure. If this is true, then it would have to be determined whether there is a parallel for this shift in man at this depth and below. If there is, then I would say that this computer indeed would be a very useful tool.

However, mathematicians will never be put out of business because they are needed to aid the physiologists in taking the "guess" out of some of the parameters that they wish to study.

DR. ROTH: Commander Stubbs, does the pressure sensitivity hold for the electrical analog as well as the pneumatic?

WING COMMANDER STUBBS: No, it does not. We built the electrical analog which was just an RC system in various configurations in the early days, since we weren't sure which configuration we wanted to look at. We had it versatile in that we could switch a minimum of four compartments into either parallel configuration or series configuration and then put all the diving information we could get our hands on through it to see which gave the most interesting results.

That computer is completely linear and therefore symmetrical and it is only by the use of the electronic one to compare some of our diving profiles that we have begun to detect non-linearity in the pneumatic one. We didn't think it would be there in view of the very small flow rates.

We thought we would stay in the Knudsen and premolecular flow where the commonly used diffusion equation, which is a linear one with respect to delta P, would apply. Now, if the pneumatic analog with its membranes of very tiny porous size when matched with time constants of the order on which we have all observed in man does get into a non-linear region, then perhaps man also does get into a non-linear region where viscous flow is starting to play a role. This might well explain some of the observations

of other investigators, such as presented here. We have not any verification of this yet.

MR. KELLER: I think that what a computer can do is not much more than what any mathematical equation can do. A computer is just a means to use an equation in a practical way.

My personal belief is that all mathematical models which are easy to handle and reasonable to handle are much too simple to follow the decompression process and we have found some very alarming evidence for that. When dealing with our 650 foot dives, we found that there is some barrier between dives with ten minutes bottom time and twenty minutes bottom time, a barrier we could not explain. What I mean is this; if one does a dive, for instance, with twelve minutes bottom time, one gets maybe a decompression of 120 minutes. If one increases the bottom time by one minute, decompression is increased by maybe twenty minutes or so. Then suddenly, if one increases the bottom time by one more minute, one requires a double decompression time. Suddenly there is a complete break in the situation, rather than a steady increase in decompression time.

We could follow this barrier through a certain range of trials. We got it somewhere between 400 feet and exposures of about 40 minutes down to 1,000 feet with one minute at the 1,000 feet depth. One minute is on the safe side of the barrier. With five minutes one is on the bad side.

CHAIRMAN LAMBERTSEN: I think it is very important that this panel should not, however unintentionally, leave the impression that all diving is mathematics, all is electronics or all pneumatics when in fact we are using these methods in order to try to understand the reactions of a very variable human or animal subject. The intrinsic physiological alterability of man is tremendous. It therefore seems to me to be of considerable importance that we not accept the human as he is and let him be a passively variable object in the course of the searches for the truth of decompression, but that we realize that this human is a changing object who can to some degree be altered at will. He is not one mass of tissue with constant mathematical compartments that can be always described in the same manner. He is, in fact, a changing object as stresses are imposed upon him. One of the additional questions that we have to deal with, then, is whether we can, by using man as an experimental subject, help ourselves learn faster what we want to find out; to force man into a more uniform physiological state we must pay attention first to the circumstances under which we do experimentation on humans and second to preventing some of the physiological responses which alter blood flow.

How can we purify this human in order to make him a more usable experimental subject?

DR. SCHREINER: I want to respond to Mr. Keller because we computed

the dives that he recently published in the Journal of Applied Physiology and found that they all have one thing in common. They all end up in a situation in which, at about the 30 foot level or so, the slowest tissue seems to be the limiting one. That is, he arrives at the same end values eventually, regardless of how deep he was because his time-depth combinations all result in this particular barrier, as he calls it. It is not surprising to me at all that if he increases his bottom times at any of these depths that this barrier just described would occur sooner at a greater depth.

This brings up the point that, although what we have said today is theory, at least it is a theory that responds to the observations that we make in our own laboratory and also helps us explain observations made by others. So while I am in full agreement that man is not a rigid mathematical, well defined model, there are certain things one can extract from man dives. I would urge the greater availability of such data to qualified investigators, because only in the comparison of this data as we were able to do with the ones that Mr. Keller published, can we determine just how exact mathematical models are when applied. This requires the co-operation of all groups that can make a contribution.

WING COMMANDER STUBBS: I agree that no one should believe that man is a perfect mathematical model. However, our belief is that one must start somewhere even if you do not make a computation model, although the model may seem simple, when you are dealing with four or more compartments. When you make the low resistance elements non-linear this is by no means a simple computation by any standard method of computation. We are really saying that we must start first of all with the simplest model, based on Haldane, see how close we can come, and then modify it. This does at least give a means of assessing whether or not the model is of any use.

CHAIRMAN LAMBERTSEN: I hope none of you really believes I am against experimentation.

DR. ROTH: There are two aspects of the problem that seem to show anomalous behavior: one is the changing supersaturation ratios, and the other is the quantum changes that you get in terms of sensitivity at depth.

I think one aspect of the whole problem that has been overlooked in the mathematical models is the old problem that Piccard brought out in the thirties: there are critical bubble sizes and there are also critical numbers of nuclei per volume of tissue required to get a bubble beyond the critical size. I have never seen this concept plugged into the models to see if this is indeed what the supersaturation ratio anomalies really represent.

Has anyone thought about this as an addition to the exponential computer models?

CHAIRMAN LAMBERTSEN: I will ask Dr. Behnke to try that, because he has talked about it in the past.

DR. BEHNKE: That is a very pertinent comment. Mr. Hempleman has pointed out these critical ratios. Everything points to something critical happening and it is probably quite true that you can decompress in two ways. You can decompress according to the isobaric principle I mentioned earlier and you can decompress with a certain number of bubbles present. I think this is quite true, and the two would be entirely different.

Most of our decompression, in fact, has been on the bubble principle. You can't bring a man out in ten seconds from the depth of 100 feet which we have done many times and not expect to have bubbles, but these men remain symptomless and therefore you have a silent bubble situation. You do have the two different situations and certainly it would be a big help to us if we could get a computer to tell us the difference between gas elimination when gas is present in bubble form, and when gas is present in solution.

DR. WORKMAN: I'd like to add a point about some of the variability of man as the subject during the dive itself. I am a little chagrined that Haldane mentioned this factor in 1927 in his book, "Respiration", and it has been overlooked in our reading, that upon exposure to increased oxygen tension one had to consider that there would be some diminishing of the perfusion rates of blood to the tissues. He estimated at that time that it would take about 15 % longer during oxygen breathing to provide an equivalent perfusion with blood and so eliminate the amount of gas that would be removed during air breathing.

Some studies on men breathing oxygen at one atmosphere and two atmospheres and some on animals have quite definitely demonstrated that there is a perfusion decrease not only of renal artery flow but in the extremities as well. If one decreases the blood flow to the mass of tissue by any significant amount then there has to be a compensatory period of time provided for, to make up this blood flow so that the opportunity is provided for gas exchange to take place.

If this is only a 25 per cent reduction of perfusion rate the equivalent time, then, for the same volume of blood flow goes up to about 133 per cent. If this is so for very slowly perfused tissues it is quite a significant increase in time. Some of the studies have indicated that cessation of oxygen breathing and going back to air at shallow depths has not resulted in return to normal perfusion within quite significant periods of time, perhaps hours.

Another aspect of decompression and variability is the time required for a significant amount of bubbles to form in long sustained decompression.

This time dependence concerns what must be an increasing probability for the necessary number of molecules of gas to occur in one volume of tissue for a bubble to form.

This may well relate somewhat as a time dependence function as well, to the gas molecular density that Piccard had mentioned in his article.

MR. HEMPLEMAN: It seemed to us, as a result of our experiences, that there were three sorts of diving decompression that we could do. One was the sort Dr. Behnke is advocating, where you employ very small pressure drops and keep just ahead of a state of tissue over-saturation. This involves you in very long decompressions.

Another is to take big, Haldane-like steps to first stops and you have a bubble which the subsequent decompression keeps silent. This, incidentally, is different from an out and out therapy; Dr. Behnke said it is therapeutic from then on but it is not.

The third way is to carry out what we have called a "beat the bubble" technique. That is a common technique of diving known as surface decompression where you bring a man to such a point that, in a very short space of time he would get a catastrophic attack of decompression sickness but you push him back and squash the bubble down and carry out the decompression. If at that crucial latent period you can insert some form of other breathing medium such as air, then you can beat the actual bubble growth curve so that you can decompress yourself rather rapidly.

Now this has an awfully all-or-none look about it and if you don't succeed you virtually have something rather serious go wrong with you, but when you succeed it is very good. It is just not "on" as a practical routine, although we have had quite successful dives on it.

CHAIRMAN LAMBERTSEN: We would like to have a decompression chamber available there.

MR. HEMPLEMAN: Oh, yes.

CHAIRMAN LAMBERTSEN: This is the exact point at which to close this discussion.

27 | PETER B. BENNETT

Performance Impairment in Deep Diving Due to Nitrogen, Helium, Neon and Oxygen

Among the major factors likely to cause performance impairment at depths in excess of 300 feet are inert gas narcosis (17) and oxygen toxicity (16). An associated factor is carbon dioxide retention as a result of hypoventilation and the increased oxygen partial pressure (11, 13–15, 30, 38).

In any deep dive all of these factors are present to varying degrees and the resulting impairment is usually a function of all three. This paper will consider the extent of this mutual involvement and the effect of these factors on the efficiency of the diver at depths down to 800 feet.

Compressed Air Intoxication

The problem of compressed air intoxication has already been considered in some detail in my recenty published monograph (17). It is however clear that the cause of the narcosis is the increased tension of nitrogen, associated causes being the density and oxygen partial pressure of the respired mixture. These may cause an increased carbon dioxide tension which synergistically potentiates the narcosis (11–14, 17, 25, 26).

During deep diving to depths in excess of 300 feet, Adolfson and Muren (2, 3) have studied compressed air intoxication on 30 subjects at 400 feet. In an arithmetic test the number of sums correct was reduced by 61.6 %

with 25% more errors. Subjectively the narcosis was severe, being more similar to that found with hallucinogenic drugs such as LSD 25, rather than with alcohol.

Barnard, Hempleman and Trotter (8) and Albano (4) have compared the narcotic effect of air at 300 feet with mixtures of 95% N_2-5% O_2 or 96% N_2-4% O_2 respectively. In the former experiments, whereas air breathed at 300 feet caused an impairment of 44.4% in arithmetical efficiency, the mixture induced a 60.7% decrement. In the experiments by Albano (4), the mean impairment with air at 300 feet was 40.6% compared with 50.6% in men breathing 96% N_2-4% O_2. Decreasing the oxygen partial pressure and thereby increasing the nitrogen therefore potentiates the narcosis. Conversely, increasing the oxygen partial pressure at a constant nitrogen pressure may also potentiate the narcosis due to the associated increase in carbon dioxide tension and its synergistic action (13, 14, 17, 25, 26).

It should be remembered that the levels of narcosis described were derived from pressure chamber experiments with men usually at rest. The narcosis is likely to be greater in men wearing breathing equipment, swimming and working underwater due to the presence of exogenous or endogenous carbon dioxide. Frequent exposure will however result in some acclimatisation. It is also possible to dive for brief periods to 500 feet or perhaps even deeper with little or no narcosis, provided compression is extremely rapid (18).

Rate of Compression

It is generally believed that rapid compression enhances narcosis due to carbon dioxide retention as a result of compressional inflow of gases into the lungs (1, 5, 9, 22). However, if insufficient time is permitted for the nitrogen tension in the brain to reach the critical molar concentration necessary to induce narcosis, the carbon dioxide factor is less important.

Men have been compressed to 400 and 500 feet in 20 seconds and their performance examined until decompression at 5–6 ft./sec. 40 seconds later (18). As the time at depth was only 40 seconds, two choice reaction time was used to test for narcosis. No tests could however be made during the 20 second compression, as the men were far too busy ensuring that their eardrums remained intact. At 400 feet the expected value of reaction time due to learning factors in 10 subjects was not significantly different from control values, but at 500 feet there was a significant 14–15% decrement in reaction time accompanied by euphoria (Table 44).

This level of impairment compares with a decrease of some 20% in two choice reaction time reported by Kiessling and Maag (29) in 10 subjects breathing air at 100 feet and a 10% decrease in 14 subjects at 150 feet of

TABLE 44

Effect of Very Rapid Compression with Air to 400 Ft. and 500 Ft. on Two-choice Reaction Time (1/100th sec) (18)

	400 Ft.	500 Ft.
Atmospheric pressure	40.1 ± 6.8	30.7 ± 4.4
Expected result (learning)	37.8 ± 5.8	29.9 ± 3.7*
Actual result at diving depth	37.2 ± 4.8	34.2 ± 4.0*
Difference expected-actual	+0.06 ± 2.3	+4.4 ± 2.2
Return to atmospheric pressure	36.1 ± 5.8	30.0 ± 3.8

* $p = 0.02$.

TABLE 45

Oil Solubilities and Other Physical Constants of the Inert Gases (27, 28, 31)

Gas	Molecular Weight	Sol. in Olive Oil	Temp (° C)	Oil-Water Sol. Ratio
He	4	0.015	37	1.7
Ne	20	0.019	37.6	2.07
N_2	28	0.067	37	5.2
Ar	40	0.14	37	5.3
Kr	83.7	0.43	37	9.6
Xe	131.3	1.7	37	20.0

air reported by Shilling and Willgrube (37). The narcosis at 500 feet was therefore minimal but there can be no doubt that a slow compression rate such as 100 ft./min. would have resulted in the men being incapacitated on reaching depth.

The Narcotic Potency of Neon

For more prolonged diving to great depths however other less potent inert gases must be used instead of nitrogen. The narcotic potency of inert gases has been related with varying success to most of their physical characteristics such as partition coefficient and molecular weight (10), adsorption coefficients (22), thermodynamic activity (20, 24) and clathrate formation (34, 35). The best relationship is found with oil solubility (10, 27, 28, 31) (Table 45).

On this basis neon is 3.5 times less potent than nitrogen and helium 4.5 times less potent. The latter has therefore been the choice for deep diving but neon could be a useful alternative. Marshall (33) seems to have been the first worker to have studied the narcotic potency of neon. She found the pressure required to produce reversible inhibition of reflex activity in the tibial nerve of frogs was 10 atmospheres of argon, 17 at-

TABLE 46

Comparative Effect on Performance of Exposing 10 Men to a Partial Pressure of 4.6 Atm. Abs. (152 Feet) of Nitrogen or Neon (17)

	Nitrogen (air 190 ft.abs.)	Neon (65.6% Ne-16.4% He-18% O_2 233 ft.abs.)
Sums correct	−12*	−3.3†
Sums attempted	−12*	−1.7‡
No. of ball bearings	−15.6*	+2.7**

* $P < 0.001$.
** $P < 0.05$.
† $P < 0.01$.
‡ Not significant.

mospheres of nitrogen, 54 atmospheres of neon and no effect even with 82 atmospheres of helium.

We have exposed ten men to 200 feet breathing a mixture of crude neon (80% neon and 20% helium) and oxygen giving an absolute neon partial pressure of 152 feet. This was compared with a similar partial pressure of nitrogen by exposing men to compressed air at 190 feet absolute.

The tests for narcosis were simple two figure by one figure multiplication, the score being the number of sums attempted and correct in two minutes and a test of manual dexterity and neuromuscular coordination, in which, in 40 seconds, as many ball bearings as possible were picked up one at a time with a pair of smooth ended tweezers and dropped into a tube whose diameter was just sufficient to permit entry of a ball bearing.

The results indicated that neon caused little or no narcosis at this partial pressure (Table 46).

Similar experiments in 2 subjects at 300 feet with a neon partial pressure equivalent to 212 feet add emphasis to its low narcotic potency. The mean number of sums correct improved from 8 on the surface to 11.5 at 300 feet and the sums attempted improved from 10 to 12. The number of ball bearings in the tube also improved from 11.5 to 13 with no subjective sensation of narcosis. Many more experiments are required with this gas as it does seem to be of low narcotic potency. However at present British neon is twice the cost of helium and some reduction will be required if neon is to be used more extensively.

At present we are therefore left with oxygen-helium as the mixture of choice for deep diving. Using this mixture what is the potential hazard of such a mixture as regards oxygen toxicity?

The Effects of Inert Gases on Oxygen Toxicity

In 1961 Linaweaver (32) carried out experiments at depths down to 130 feet which suggested that breathing oxygen-helium rather than air, the depth-time oxygen limits could be exceeded. Lanphier (30) showed that this was because air at 100 feet causes hypoventilation which, with factors such as the increased oxygen partial pressure and the increased respiratory work due to the breathing apparatus, produces a serious carbon dioxide retention.

At shallow depths most of these problems can be overcome by breathing helium-oxygen and using more efficient breathing equipment. Lanphier however predicted that with the advent of very deep diving these problems would occur even breathing helium-oxygen. Wood (38) added emphasis to this prediction by reporting a marked reduction of maximum breathing capacity in men breathing helium-oxygen at 15 atm. abs.

The time to oxygen convulsions was therefore compared in Wistar rats exposed either to 5.3 atm. abs. oxygen or a 90% He-10% O_2 mixture at 53.3 atm. abs. In the presence of helium there was a dramatic reduction in the time to convulsions (Table 47).

It seems probable that the reduction is due to hypoventilation as a result of the increased density of the mixture causing carbon dioxide retention which synergistically potentiates the toxicity. Support is given by studies of the comparative influence of argon, nitrogen and helium on oxygen toxicity in rats at a pressure of 18.6 atm. abs. It was observed that the

TABLE 47

Effect of 48 Atm. Abs. Helium on the Time to Convulsions in Rats Exposed to 5.3 Atm. Abs. Oxygen

Gas Mixture	5.3 Atm. Abs. Oxygen	48 Atm. Abs. Helium 5.3 Atm. Abs. Oxygen
Time in minutes from start of compression to a convulsion	22	6
	17	6
	18	7
	15	6
	23	7.5
	22	6.5
	21	5.5
	25	6
	16	7
	24	5.5
Mean time	20.3 ± 3.52	6.3 ± 0.67

TABLE 48

Effect of 13.3 Atm. Abs. Helium, Nitrogen or Argon on the Time to Convulsions in Rats Exposed to 5.3 Atm. Abs. Oxygen (16)

Gas Mixture	5.3 Atm. Abs. O_2	5.3 Atm. Abs. O_2 13.3 Atm. Abs. He	5.3 Atm. Abs. O_2 13.3 Atm. Abs. N_2	5.3 Atm. Abs. O_2 13.3 Atm. Abs. A
Time in minutes from start of compression to a convulsion	26	25	20	16
	25	24	17	19
	20	20	24	18
	19	20	20	18
	21	23	18	16
	27	27	20	15
	24	22	20	16
	25	19	24	17
	27	25	21	20
Mean time	23.8 ± 3.03*†	22.8 ± 2.74	20.4 ± 2.36*	17.2 ± 1.64†

* $P < 0.001$.
† $P < 0.001$.

TABLE 49

Changes in Cortical Oxygen and Carbon Dioxide Tension in Chloralosed Cats at 8.67 Atm. Abs. Helium, Nitrogen or Argon and 2.34 Atm. Abs. Oxygen (13)

	aO_2* (mm Hg)	P_{CO_2} (mm Hg)
8.67 atm. abs. He-2.34 atm. abs. O_2.....	+297.9 ± 69.6	+5.1 ± 2.18
8.67 atm. abs. N_2-2.34 atm. abs. O_2.....	+121 ± 52.7	+12.1 ± 3.55
8.67 atm. abs. A_2-2.34 atm. abs. O_2.....	+91 ± 62.4	+20.5 ± 5.29

* aO_2 denotes cortical available oxygen.

greater the density of the mixture the shorter the time to convulsions (Table 48).

Further support is given by measurements of cortical carbon dioxide and oxygen in chloralosed cats (13, 16). The greatest increase in carbon dioxide tension, in cats exposed to 11 atm. abs. of either argon-oxygen, nitrogen-oxygen or helium-oxygen, is found with the argon mixture and the least with the helium mixture. Conversely, the greatest increase in cortical oxygen is found with the helium mixture and the least with the argon (Table 49).

In addition to this problem of potentiation of oxygen toxicity by helium and other inert gases is the question whether, even with a gas of low narcotic potency such as helium, men will be able to perform efficiently at very great depths.

Performance Impairment due to Helium-Oxygen

Based on fat solubility, narcosis equivalent to air at 100 feet should be present with helium-oxygen at some 450 feet and that equivalent to air at 300 feet would be expected at about 1,350 feet. When factors such as carbon dioxide retention due to the density, viscosity and increased oxygen partial pressure are also included, the limits as regards performance efficiency are likely to be only about 1,000 feet.

During the deep diving experiments carried out recently at the Royal Naval Physiological Laboratory we have measured the performance efficiency of divers in between periods of hard work on a rowing machine at depths between 300 and 800 feet for periods up to 4 hours. Earlier studies have already shown that there is no significant narcosis in men breathing helium at depths down to 200 feet (6, 19).

In the present studies the tests used included the arithmetic and ball bearing tests described previously and a maze tracking test, devised by Albano, which is a sensitive tracking task involving drawing with a pencil a line between two other lines $\frac{1}{12}$" apart; the score being the number of times the pencil touches the sides and the distance travelled during $1\frac{1}{2}$ minutes. The maze and ball bearing tests were chosen to quantify hand, limb or even whole body tremor reported by some of the divers during previous deep helium-oxygen dives. The tests were carried out on the surface and so far as possible at regular intervals during the 1 or 4 hour exposure at depth and again on return to the surface.

In 4 men at 300 feet breathing 90 % He-10 % O_2 tremor was present as shown by a decrement in both the ball bearing and maze tests. The arithmetic test was little affected. The deterioration in performance was at its worst during the initial 30 minutes of exposure and gradually improved over the 1 hour at depth (Fig. 97).

A very similar result was found in 4 men breathing 90 % He-10 % O_2 at 400 feet. Again the deterioration was at its worst initially and was followed by a gradual improvement. There was considerable individual variation in sensitivity and tremor was the prime cause of the performance impairment, arithmetic being little affected (Fig. 98).

At 500 feet, 2 subjects were tested over 1 hour breathing 95 % He-10 % O_2 and 2 on a mixture of 92.5 % He-7.5 % O_2. With the mixture of 7.5 % O_2 tremor was again marked, with little or no impairment of the arithmetic test. This suggests that the tremor is not a function of helium narcosis but is due to other factors (Fig. 99).

With only 5 % oxygen at 500 feet however the ball bearing test showed an improvement rather than decrement and the maze test was less affected. This result infers that the cause of the tremor is probably associated with the increased oxygen partial pressure (Fig. 100).

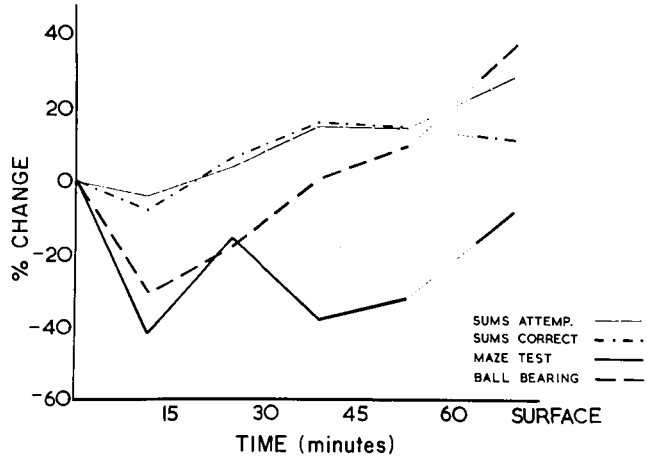

FIG. 97. Mean percentage change in performance in 4 subjects breathing 10% oxygen-90% helium at 300 feet for 1 hour.

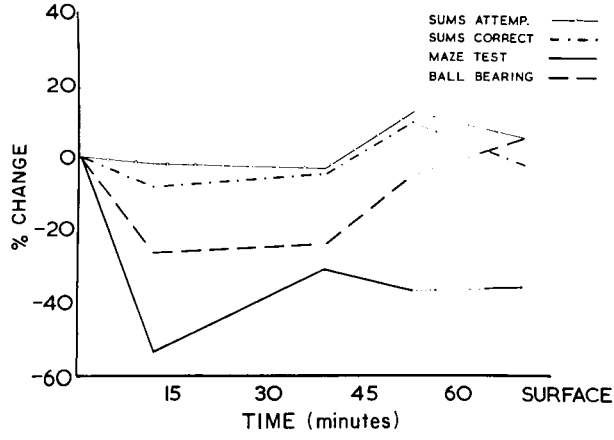

FIG. 98. Mean percentage change in performance in 6 subjects breathing 10% oxygen-90% helium at 400 feet for 1 hour.

At 600 feet, 6 subjects breathing 95% He-5% O_2 were tested over 4 hours with arithmetic, the ball bearing test and five choice reaction time (15). At this depth, in addition to the tremor, there was evidence of an impairment in mental performance as shown by a significant decrease in the number of arithmetic sums correct. However after 1 hour performance was little difference to that on the surface before compression (Fig. 101).

The performance impairment was sometimes accompanied by dizziness and nausea and very occasionally by vomiting during the latter part of the

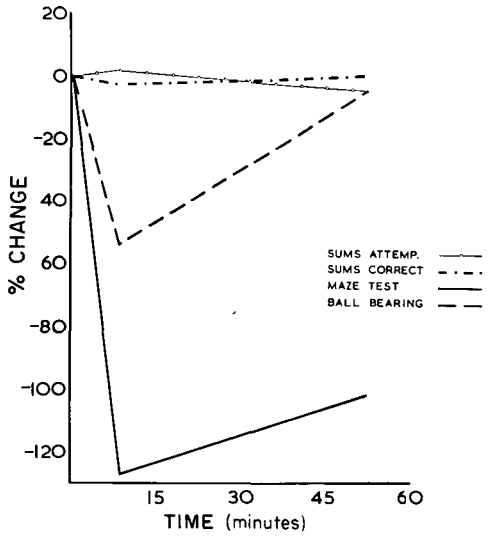

FIG. 99. Mean percentage change in performance in 2 subjects breathing 7.5% oxygen-92.5% helium at 500 feet for 1 hour.

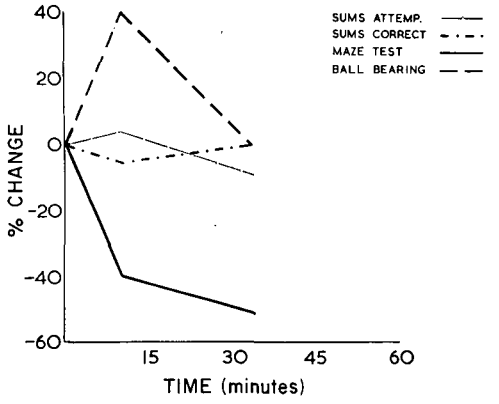

FIG. 100. Mean percentage change in performance in 2 subjects breathing 5% oxygen-95% helium at 500 feet for 1 hour.

exposure or at the initial stops during decompression. There was considerable inter-individual sensitivity. Two subjects who showed little quantitative impairment did report dizziness but were apparently able to exert enough self control to prevent any performance decrement. Whereas another showed a 60% decrement in the ball bearing test and another a 50% decrement in the number of sums correct.

Comparison of the mean deterioration during the initial time at depth

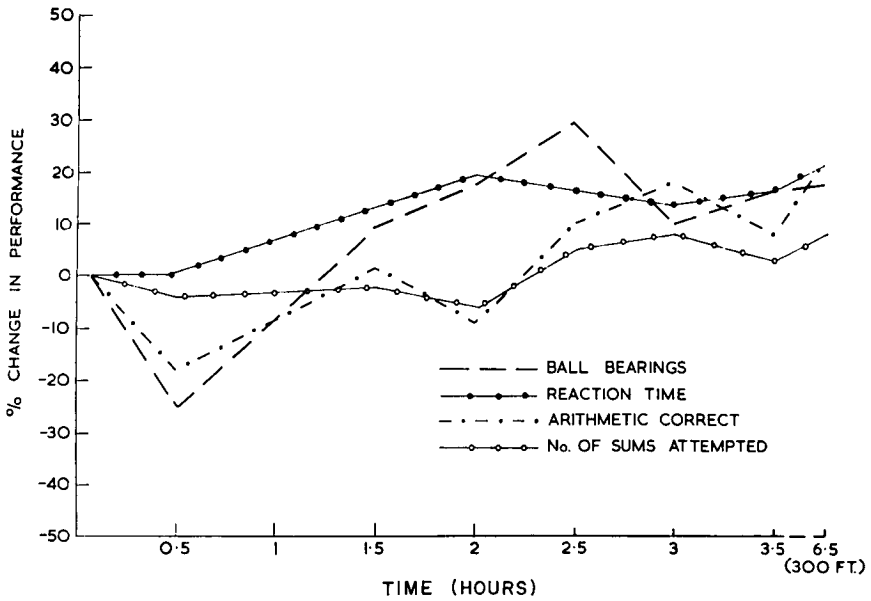

FIG. 101. Mean percentage change in performance in 6 subjects breathing 5% oxygen-95% helium at 600 feet for 4 hours (15).

TABLE 50

Comparative Performance of 6 Subjects at 600 Feet and 4 Subjects at 800 Feet Breathing 5% Helium-95% Oxygen during the First 20 Minutes at Pressure (15)

	600 FT.	800 FT.
Sums correct	−18%	−42%
Sums attempted	−4%	−6%
No. of ball bearings	−25%	−53%

in 6 men at 600 feet and 4 at 800 feet indicates that at 800 feet the performance decrement is 100% worse than at 600 feet. Both tremor and narcosis are severe. In fact both the quantitative measurements and subjective sensations are similar to those found in men breathing air at 300 feet (Table 50).

It is therefore evident that men exposed a further 200 feet to 1,000 feet on a 95% He-5% O_2 mixture can expect to be very severely affected indeed.

The Cause of Oxygen-Helium Tremble and Its Prevention

Although the deterioration in arithmetical performance at 600 feet and 800 feet may be due to helium narcosis neither the tremor, nausea and occasional vomiting nor the improvement after time at depth are similar

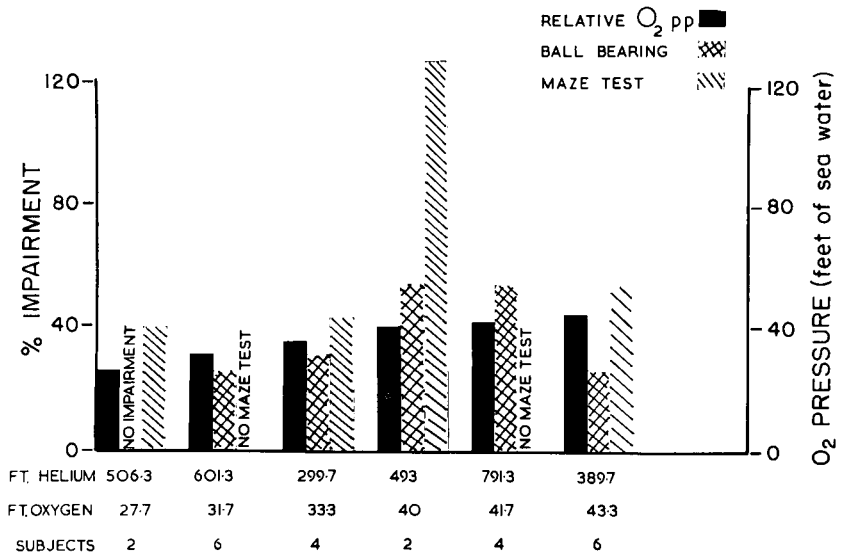

FIG. 102. Histogram of the mean impairment in the ball bearing and maze performance tests related to the oxygen partial pressure at depth.

to inert gas narcosis. The rate of compression does not seem to be the direct cause, for at 800 feet the mean compression time was 8 minutes 48 seconds, at 600 feet, 14 minutes 33 seconds and at 500 feet, 8 minutes 48 seconds.

The most likely cause would seem to be a hypercapnia due to too high an oxygen partial pressure accompanied by hypoventilation as a result of density and viscosity factors (21, 30, 38). That a significant 54.4 % decrease in maximum breathing capacity occurs when breathing 95 % He-5 % O_2 at 500 feet was reported by Wood (38) at the last Symposium. Experiments by Lanphier (30), as discussed earlier in this paper and also by Seusing et al (36), point to the significance of an increased oxygen partial pressure and density in causing retention of carbon dioxide.

Although the results at 400 feet are anomalous, a histogram of the percentage impairment in the ball bearing and maze tests relative to the oxygen partial pressure suggests oxygen may indeed be one of the agents responsible (Fig. 102).

Barlow, McIntosh and Donald (7, 23) while investigating "shallow water blackout" in men using closed circuit oxygen sets at 20 feet reported exactly similar signs and symptoms as we have found in deep oxygen/helium diving. Are we now experiencing the initial stages of "deep water blackout"?

Rebreathing 50 litres of oxygen without absorbing carbon dioxide produces carbon dioxide intoxication with no signs of distress. Barlow and

co-workers noted a considerable variation of sensitivity in different subjects which was related to their rate of ventilation. Among the signs and symptoms which occurred were dizziness, tingling of the limbs and visual disturbances. Haziness, euphoria or sleepiness were common in sensitive subjects, without any change in the ventilation rate. Flushing of the face, dilatation of the pupils and sweating were present and muscular trembling was reported in some men, mainly in the arm, shoulder and neck muscles. Although hardly detectable in some subjects, in others they were coarse and violent and spread to all parts of the body. As the carbon dioxide intoxication became severe, the men worked at a feverishly increased rate, ignoring instructions, until they reached a stuporous condition and consciousness was lost. During recovery, consciousness was regained in less than a minute but many experienced an "off effect", with frontal headache, nausea or vomiting and a general fatigue and malaise.

These signs and symptoms of carbon dioxide intoxication in the presence of high oxygen tensions have been purposely described in detail as they are remarkedly similar to those found in our deep diving experiments, especially where 30–40 feet absolute oxygen was present. It is the use of helium in combination with a high oxygen partial pressure which appears to permit hypercapnia to occur. As indicated by the cortical P_{CO_2} and P_{O_2} measurements in cats described earlier, helium/oxygen will encourage increased carbon dioxide tensions in conjunction with high oxygen tensions so that a compensatory increased ventilation does not occur.

The solution may be to markedly reduce the oxygen partial pressure to probably as low as ½ atm. abs. (15 feet) at depths in excess of 400 feet. This will also help to reduce any synergistic potentiation of helium narcosis. Unfortunately, as a result decompression may be more prolonged. If, as a result of this measure, the density and viscosity is such that hypercapnia still results, a warning should then be given by an increased rate of ventilation. Further solutions may be to add a percentage of a higher density gas such as neon to the breathing mixture or to use some form of assisted ventilation.

Clearly many variables can affect performance efficiency in such very deep diving. It is however most important that every future opportunity should be taken to quantify them, for here may be a far more formidable barrier to the future of very deep diving than decompression sickness.

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28 | JOHANNES A. KYLSTRA

Advantages and Limitations of Liquid Breathing

Experimental evidence indicating that lungs can function as gills was presented for the first time four years ago (1). The potential practical importance of this phenomenon was clear. Decompression sickness and "inert" gas narcosis are due, directly or indirectly, to the compressibility of gases. The properties of water hardly change at all with pressure, and it would be a truly inert respiratory gas diluent at any depth in the ocean. Moreover, no excessive amounts of inert gas would dissolve in the blood and tissues of a diver with water-filled lungs so that he would be free to come to the surface at any time and as rapidly as he desired without fear of bubble formation. It is the purpose of this paper to briefly summarize currently available information in this field, and to discuss limitations of gas exchange in water-filled lungs.

Experimental Evidence

Adult mice (2), rats (3), and dogs (4) have been reported to live for prolonged periods of time submerged in salt solutions equilibrated with oxygen at high pressures. Under these conditions the submerged mammals continued making respiratory movements, were apparently capable of extracting adequate amounts of dissolved oxygen from the aqueous environment and were not killed by hydrostatic pressures of up to 160 atmospheres (2), which is equivalent to a depth in the ocean of one mile. The composition of the aqueous environment was found to drastically affect experimental results under otherwise identical conditions. Mice submerged in a hyperbarically oxygenated balanced salt solution at 25° C lived up to 40 minutes, in sea water 12 minutes, and in tap water only 6 minutes (5). Mice submerged in a hyperbarically oxygenated balanced salt solution to which tris(hydroxymethyl)aminomethane had been added lived markedly longer than in the unbuffered solution (2). Gas analyses of the arterial blood of liquid-breathing hypothermic dogs submerged in a hyperbarically oxygenated salt solution revealed adequate oxygenation but retention of carbon dioxide. Greatly increased intrathoracic pressure

fluctuations clearly reflected the extra work required to move liquid instead of gas through the trachea and bronchi (4). Such experiments provided indirect evidence of respiratory function of saline-filled lungs, but gas exchange through the skin and mucous membranes could not be excluded (6).

Pulmonary gas exchange during liquid breathing was measured in normothermic dogs who were mechanically ventilated with a hyperbarically oxygenated modified Ringer solution maintained at 37° C (7). Liquid ventilation resembled pump ventilation with air except that volume displacements of the respiratory medium occurred by gravity instead of a piston (Fig. 103). The amount of oxygen taken up from the liquid in the lungs and the amount of CO_2 eliminated from the body through the liquid-filled lungs was computed from the difference between dissolved gas content of inhaled and exhaled liquid (7). The oxygen consumption ranged from 31 to 93 ml/min. The respiratory exchange ratio varied from 0.3 to 0.7 at arterial carbon dioxide tensions from 43 to 80 mm Hg. At inspired oxygen

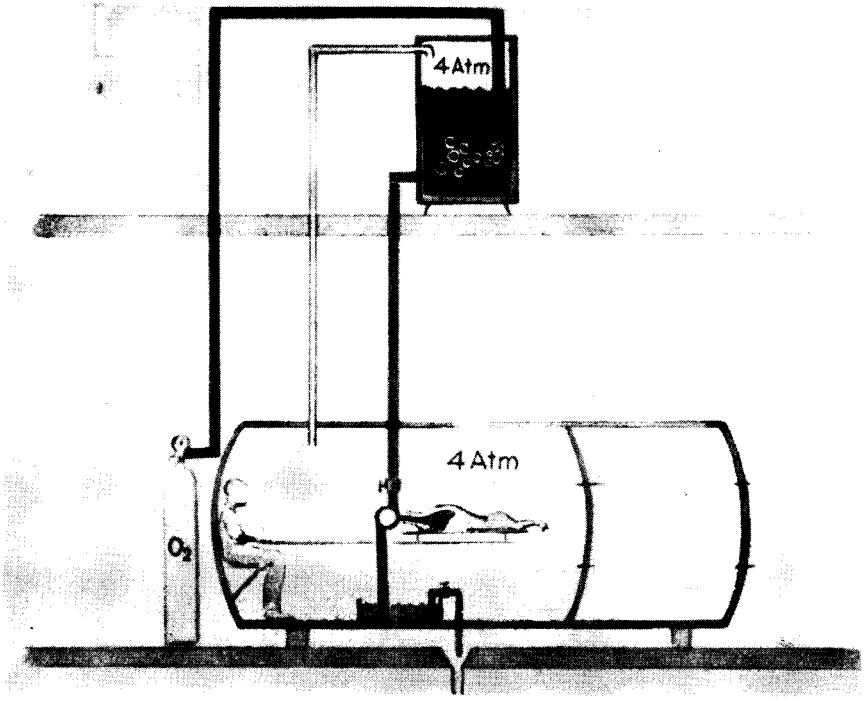


FIG. 103. Experimental set-up for liquid ventilation. Circle indicates valve system which alternately opens and closes inflow and outflow lines.

tensions ranging from 3,310 to 3,640 mm Hg the arterial oxygen tensions ranged from 32 to 1,790 mm Hg at expired minute volumes ranging from 1 to 3.5 liters and respiratory frequencies ranging from 6 to 12/min. Mixed expired oxygen tensions ranged from 2,240 to 3,080 mm Hg and mixed expired carbon dioxide tensions from 6 to 18 mm Hg. Computed overall respiratory dead space ventilation for O_2 ranged from 63 to 72 and for CO_2 from 69 to 86 per cent of the total minute ventilation. In "alveolar" samples taken at increasing distances from the lung along the outflow tube, the oxygen tensions were progressively higher and the carbon dioxide tensions progressively lower. At the end of the experiments, liquid was drained from the lungs by gravity. The dogs' lungs were then at once inflated forcefully and this was repeated from time to time during the subsequent period of stage decompression of the chamber (8).

No particular emphasis was placed on resuscitation. Even so, 7 out of 16 dogs survived the procedure. One dog appeared well for one week but died 11 days after the experiment. Three dogs are now healthy and pleasant family pets. One of them was pregnant, but this was not realized at the time. She delivered 9 healthy pups 44 days after the experiment. The gestation period of dogs ranges from 53 to 71 days (9). Three dogs were sacrificed 22, 90 and 116 days after the experiment. They appeared to be in good health and showed no signs of respiratory embarrassment. Histologic examination of the lungs of one dog 22 days after liquid ventilation revealed a remarkable degree of focal scarring. Dense eosinophilic membranes with chronic inflammatory cells and fibroblasts were seen in alveolar and bronchiolar luminae. Only minor pathological changes were found in the lungs of the other two dogs (7).

Theoretical Considerations

Net transfer of gases in the lung can occur by bulk flow (including possible turbulence) and diffusion. Bulk flow normally accounts for no more than a small fraction of the net transfer of gases from ambient air to the interface between alveolar air and blood (10). Recent studies on intrapulmonary mixing of dissolved gases in liquid-filled excised dogs' lungs indicate that dissolved gases, likewise, are distributed over the total volume of liquid in the lungs largely as a result of diffusion rather than by mechanical mixing (11). There are good reasons to believe that the same is true for net transfer of gases in the gills of fish. Thus it would appear that, in general, gas exchange between the internal and external environments of aerobic organisms occurs primarily by diffusion along concentration gradients which are maintained by ventilation and perfusion of the organs of respiration.

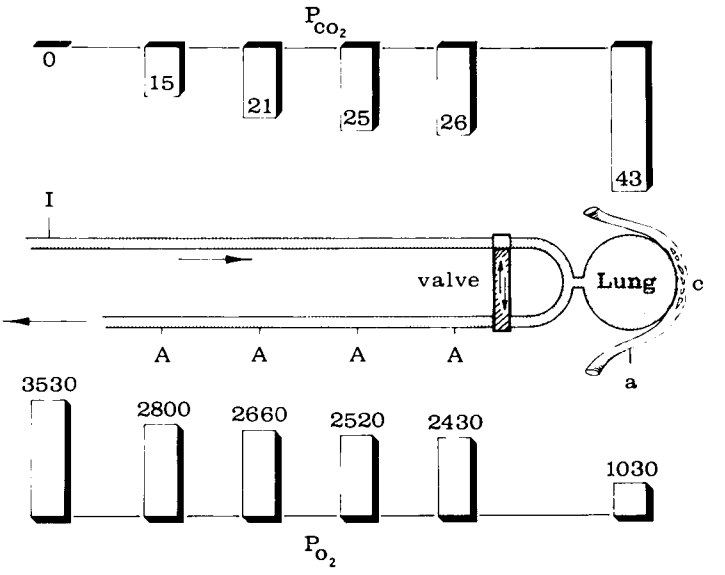


FIG. 104. Schema of the overall gas exchange system and measured gas tensions (mm Hg) in samples taken during liquid breathing experiment in a dog. L = lungs; I = inspired liquid; A = alveolar liquid; a = arterial blood; c = alveolar capillary.

In water-ventilated dogs, the partial pressures of oxygen in liquid exhaled into a long sampling tube were progressively higher and the carbon dioxide tensions were progressively lower at increasing distances from the lung (Fig. 104). It was postulated that the gas exchange units of the lung were filling and emptying concentrically so that liquid expelled first from the lungs had been located at a greater distance from the alveolar wall than subsequently exhaled liquid. Thus it appeared that the overall pulmonary gas exchange in the liquid-filled lungs was diffusion limited, and that remarkably large gas tension gradients persisted within the exchange units as a result of the slow rate of oxygen and carbon dioxide diffusion in water. The pulmonary gas exchange in water-breathing dogs was similar to the computed gas exchange in a lung model consisting of spherical exchange units in which gas transfer occurs by diffusion.

The Lung Model

The lungs are visualized as being composed of a great number of identical spherical exchange units with a radius a (Fig. 105). The spheres are assumed to have an initially uniform oxygen concentration and oxygen is removed by the blood from the surface at a constant rate. The spheres initially do not contain carbon dioxide and the carbon dioxide concentration at the

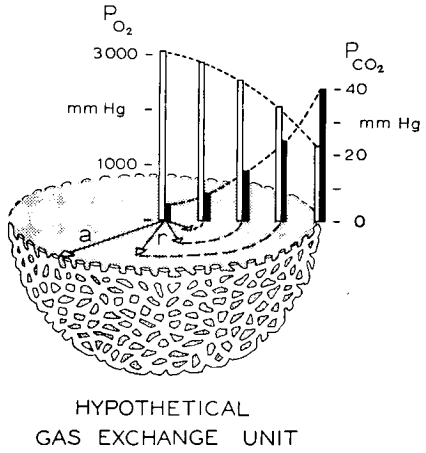


FIG. 105. Oxygen and carbon dioxide tension gradients in a hypothetical gas exchange unit of the lung. a = radius of the sphere; r = distance from the center.

surface is assumed to remain constant. The gas tensions at the surface of the spheres are assumed to be equal to the gas tensions in the arterial blood. The partial pressures of oxygen and carbon dioxide existing within each exchange unit at the end of a respiratory cycle at a distance r from the center and t seconds after the beginning of the cycle can be computed from appropriate solutions to the diffusion equation given by Crank (12) after some simple modifications which are presented elsewhere (13). The partial pressure of carbon dioxide within the exchange unit is a function of distance from the center for different values of Dt/a^2 in which D represents the diffusion coefficient of carbon dioxide and t is the time of diffusion. The partial pressure ot oxygen at a given distance from the center of an exchange unit depends upon the initial oxygen tension in the sphere which is equal to the oxygen partial pressure in the ambient environment, upon the oxygen flux at the surface, the radius of the sphere, the diffusion coefficient of oxygen, and the time of diffusion. The carbon dioxide tension gradient within an exchange unit decreases with time and no appreciable CO_2 tension gradient persists at the end of a respiratory cycle if the value of Dt/a^2 exceeds 0.5. As far as oxygen is concerned, however, a partial pressure gradient within the exchange units exists as long as there is flux at the surface. The slope of this oxygen tension gradient is directly proportional to the amount of oxygen removed by the blood from the surface per unit area and the radius of the sphere, but inversely proportional to the diffusion coefficient of oxygen.

The diffusion coefficients of oxygen and carbon dioxide in air are approximately 5000 times greater than in water (Table 51). Normally, alveolar

TABLE 51

Certain Physical Properties of the Environment

Property	Units	Air	Water	Air/Water
D_{O_2}	cm^2/sec	0.178	0.0000322	5528
D_{CO_2}	cm^2/sec	0.139	0.0000255	5455
α_{O_2}	$cm^3/cm^3/mm\ Hg$	0.001316	0.0000299	44
α_{CO_2}	$cm^3/cm^3/mm\ Hg$	0.001316	0.000724	1.8
η	gm/sec/cm	0.0001904	0.006947	1/37
d	gm/cm^3	0.001117	0.99336	1/900
s	η/d	0.19	0.007	27

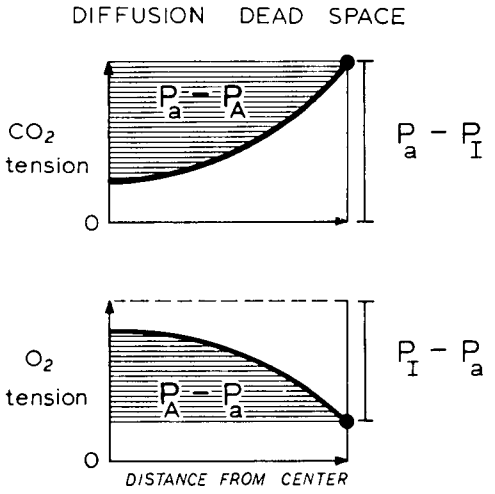
D = diffusion coefficient
α = solubility coefficient
η = viscosity
d = density
s = kinematic viscosity
D_{O_2} and D_{CO_2} in air at 0° C; all other values at 37° C.

air tends to have a homogeneous composition with a carbon dioxide tension similar to the partial pressure in arterial blood, because the Dt/a^2 values are well in excess of 0.5. In water-breathing dogs, however, carbon dioxide diffusion within the exchange units was so slow that large diffusion gradients persisted throughout the respiratory cycle. Likewise, the oxygen tension throughout each individual exchange unit normally tends to be virtually uniform and approximately equal to the partial pressure of oxygen in arterial blood. When dogs were made to breathe water in which oxygen diffuses so much more slowly than in air, remarkably large oxygen tension gradients appeared to be present within the exchange units.

It would seem reasonable to assume that a model, which adequately describes gas exchange in the lungs of liquid ventilated dogs, would be equally useful in describing the net transfer of gases within the lungs of mammals in general. It should be kept in mind, however, that the mean diffusion distance in the lungs may be different in an air-breathing animal than in the same animal while breathing water.

Diffusion Dead Space

Persistence of diffusion gradients within individual exchange units implies differences in mean gas tensions between the contents of the exchange units and arterial blood. Such differences can be expressed in terms of respiratory dead space defined as the actual or virtual volume of inhaled air or water which, after leaving the respiratory organ, has failed to reach gas tension equilibrium with arterial blood. Total respiratory dead space can consist of the anatomical dead space where no gas exchange occurs,



$$V_{D_{diff_{O_2}}} = \frac{P_{A_{O_2}} - P_{a_{O_2}}}{P_{I_{O_2}} - P_{a_{O_2}}} \times V_A$$

$$V_{D_{diff_{CO_2}}} = \frac{P_{a_{CO_2}} - P_{A_{CO_2}}}{P_{a_{CO_2}} - P_{I_{CO_2}}} \times V_A$$

FIG. 106. Diffusion dead space

a distribution dead space which results from unequal ventilation and perfusion of different gas exchange units and, finally, a diffusion dead space which results from persisting gas tension gradients within individual exchange units. Figure 106 illustrates the diffusion dead space concept. From a mechanical point of view, dead space implies inefficiency since energy is wasted in propelling larger volumes of water or air through the respiratory organs than would be required in terms of actual inhaled oxygen content and optimal exhaled carbon dioxide content.

Diffusion dead space imposes a serious restriction on gas exchange in water-breathing lungs. In a high-pressure environment it is not difficult to provide a submerged mammal with enough oxygen since the partial oxygen pressure in the liquid can be raised at will to meet almost any metabolic demands under almost any circumstances. The amount of car-

bon dioxide exhaled with each breath, however, depends primarily on the partial pressure of carbon dioxide in the blood flowing through the alveolar capillaries and the solubility of carbon dioxide in the liquid present in the air spaces of the lung. The carbon dioxide partial pressure in blood represents the balance between the rate of production in the tissues and the rate of elimination through the lungs. Neither of these factors is affected by an increased oxygen pressure in the environment. An isotonic salt solution equilibrated with carbon dioxide at a pressure of 40 mm Hg, such as normally exists in arterial blood, contains approximately 30 ml of dissolved CO_2 per liter at 37° C (Table 51). One liter of exhaled air normally contains approximately 50 ml of carbon dioxide. One might expect, therefore, that approximately twice as much water as air would have to be exhaled each minute to dispose of equal amounts of CO_2. This implies that a water-breathing mammal would have to expend at least 60 times more energy in filling and emptying his lungs than an air-breathing mammal, since in the absence of turbulence, it requires approximately 36 times more work to propel equal volumes of water instead of air through trachea and bronchi (Table 51). If flow were turbulent, even more work of breathing would be required. The presence of a diffusion dead space for carbon dioxide necessitates even larger minute volumes of liquid ventilation than required for adequate alveolar ventilation in the absence of diffusion limitation. It is very likely, however, that trachea and bronchi would collapse during expiration at minute volumes of ventilation theoretically required for adequate carbon dioxide elimination.

Diffusion dead space for oxygen and carbon dioxide as a function of diffusion time and diffusion distance in the lung can be represented graphically in a diffusion time-distance diagram (Fig. 107). The mean diffusion distance in water-breathing dogs was approximately 0.4 mm (7). The mean diffusion distance in the normal human lung has been estimated to be 1 mm (14). If we assume that the diffusion distance is the same during air breathing and water breathing, then it is possible to compare the ventilatory efficiency of air-breathing and water-breathing lungs. In Figure 107, respiratory frequencies ranging from 5 to 60 per minute have been plotted at the approximate mean diffusion distances for dog, and man. One can now see why diffusion dead space normally is not appreciable and why diffusion dead spaces may be very large when water is breathed instead of air.

In mechanically ventilated water-breathing dogs, carbon dioxide elimination was invariably deficient. One must anticipate that in man the elimination of carbon dioxide would present even more of a problem. Untoward effects of carbon dioxide retention can be minimized for limited periods of time by intravenous administration of tris(hydroxymethyl)aminomethane

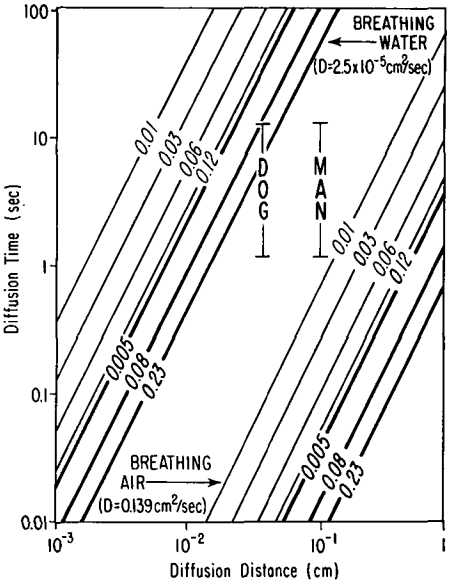


FIG. 107. Diffusion time-distance diagram. Thin lines represent diffusion dead space for oxygen; heavy lines represent diffusion dead space for CO_2. Numbers indicate fractions of alveolar ventilation.

(15). It is possible that such an approach might overcome the inherent gas exchange limitations and facilitate liquid breathing in future human underwater activities.

Summary and Conclusions

The use of water instead of nitrogen as a respiratory gas diluent would protect divers from decompression sickness and inert gas narcosis. Dogs have breathed a pressure-oxygenated salt solution and survived. Gas exchange in liquid-filled lungs is diffusion-limited and at least 60 times more work is required to propel equal volumes of water instead of air through the trachea and bronchi. These factors seriously restrict carbon dioxide elimination in water-breathing mammals. In human underwater activities, liquid breathing will be possible only if the untoward effects of carbon dioxide retention can be minimized effectively.

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29 | JOHN V. SALZANO, WILLIS H. BELL, WILLIAM B. WEGLICKI and HERBERT A. SALTZMAN

Metabolic, Respiratory and Hemodynamic Responses to Exercise at Increased Oxygen Pressure

Introduction

Measured oxygen consumption lags behind metabolic requirements of the body during the initial phase of submaximal exercise while breathing air at sea level. The resultant deficit may reflect inadequate delivery of oxygen to actively contracting muscles. Therefore, exercise should be a useful model for testing the efficacy of increased atmospheric pressure in augmenting transport of oxygen to muscle. During exposure to high oxygen tensions signs of toxicity occur more rapidly if strenuous labor is performed (1, 2). Therefore, exercise in a hyperbaric environment also provides a sensitive model for evaluating the early changes in physiological processes that may herald the development of obvious toxicity. For these reasons certain hemodynamic, metabolic and respiratory responses of healthy young subjects were measured continuously at one and 2.02 atmospheres of air and oxygen pressure before, during and after exercising submaximally. The results of these studies provide the basis for this report.

Method

Healthy unconditioned men submitted to the following experimental sequence during which physiological measurements were obtained: Eight to 10 minutes while at rest, light exercise (warm up) at a workload of 306 kg M/min. on a bicycle ergostat for five minutes, recovery from the warmup for 7 to 12 minutes, submaximal exercise at a workload of 765 kg M/min. for eight minutes and a final recovery period of 12 minutes.

In 12 studies the subjects performed the experimental sequence at both one and 2.02 atm. abs., after 15 minutes of preoxygenation, while breathing oxygen from a closed circuit respirometer of special design. In another series

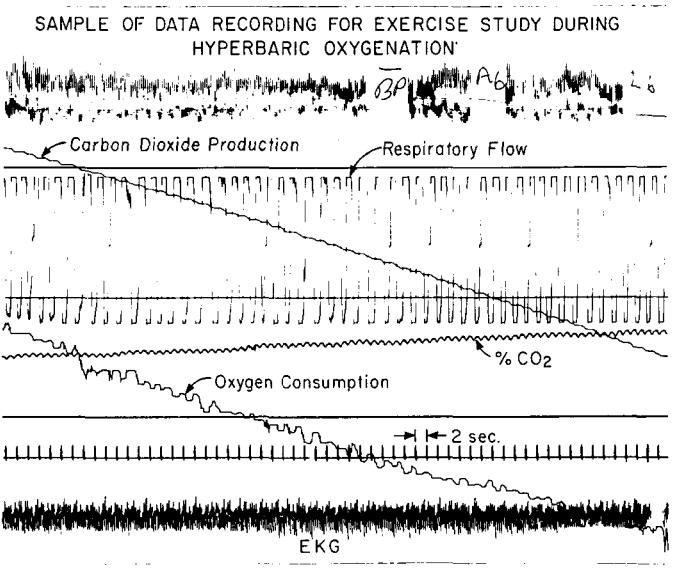

FIG. 108. This record was obtained during exercise. The subject rebreathes pure oxygen from a closed respiratory circuit in which volume is monitored with a modified Krogh spirometer. Carbon dioxide is absorbed by a suitable scrubber; therefore, the decrease in the volume of oxygen contained in the circuit reflects, in a continuous manner, oxygen consumption. Mixed expired air carbon dioxide concentration, as monitored by an infra red sensor, is instantaneously multiplied by expiratory flow, derived from the spirometer, in an analog computer; the integrated product represents carbon dioxide elimination.

8 subjects exercised at 2.02 atm. abs. of oxygen pressure only, while respiring from an open circuit respiratory assembly; in each of these studies submaximal exercise was maintained for up to 12 minutes. In 5 studies at one atm. abs. the subject performed the experimental sequence while breathing air from an open circuit respiratory assembly and oxygen from the closed system. Figure 108 shows typical recordings from an exercising subject. Blood was drawn from an indwelling arterial needle at 12 specific times during each sequence for analysis of gas tensions, pH and lactic and pyruvic acid concentration. From these continuous and intermittent observations certain indices of physiologic performance were observed, computed and tabulated.

Results

The results indicate primarily hemodynamic, metabolic and respiratory performance before, during and after submaximal exercise. Unless designated otherwise, the reported observations were accomplished while

TABLE 52

Effects of Oxygen Breathing at Pressure on Response to Exercise

	1 Atm. Abs. O_2		2.02 Atm. Abs. O_2	
	Rest	Exercise	Rest	Exercise
Heart rate (beats/min)	80 ± 10*	143 ± 17	75 ± 9	131 ± 17
Blood pressure (mm Hg)				
systolic	132 ± 16	182 ± 20	131 ± 13	185 ± 18
diastolic	85 ± 15	94 ± 13	85 ± 9	96 ± 12
Pulmonary ventilation (L/min)	15 ± 6	35 ± 9	16 ± 12	33.5 ± 7
Respiratory rate (breaths/min)		21 ± 3.5		17 ± 2.5
V_{O_2} (ml/min)	389 ± 150	1875 ± 300	510 ± 300	2147 ± 400
V_{CO_2} (ml/min)	392 ± 150	1409 ± 280	442 ± 300	1684 ± 400
Respiratory exchange ratio		0.79		0.82

* ±standard deviation.

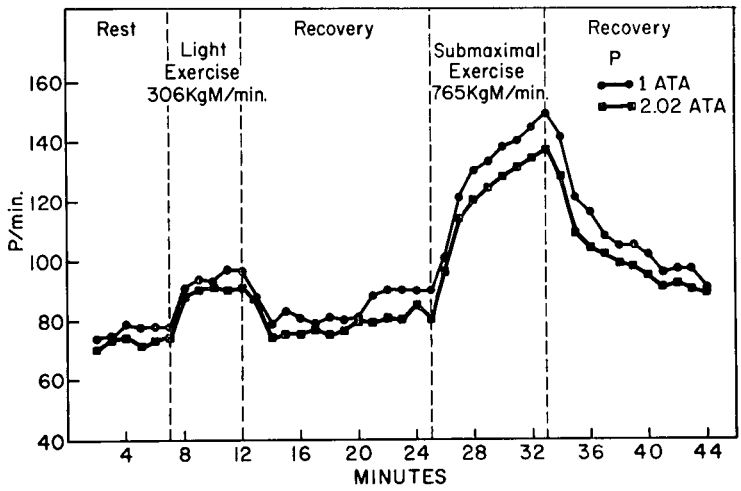

Fig. 109. Pulse rate (P) changes during hyperbaric oxygenation with exercise

breathing pure oxygen from a closed circuit system. The results are summarized in Table 52 and illustrated in Figures 109, 110, 111, 112.

Mean values for oxygen tension of arterial blood were 98 mm Hg at one atm. abs. air, 500 mm Hg at one atm. abs. oxygen and 1100 mm Hg at 2.02 atm. abs. oxygen pressure.

Mean computed excess lactate, as derived from enzymatic determinations of lactic and pyruvic acid in arterial blood, rose during exercise at

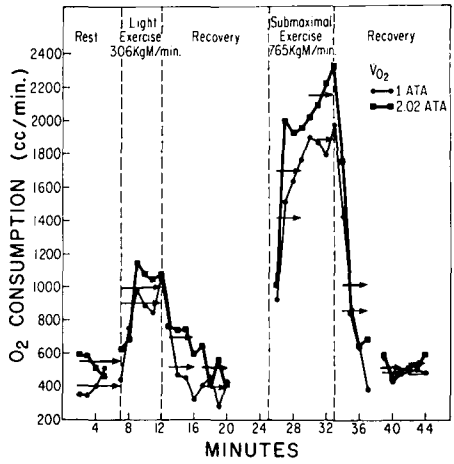

FIG. 110. Oxygen consumption ($\dot{V}O_2$) changes during hyperbaric oxygenation with exercise.

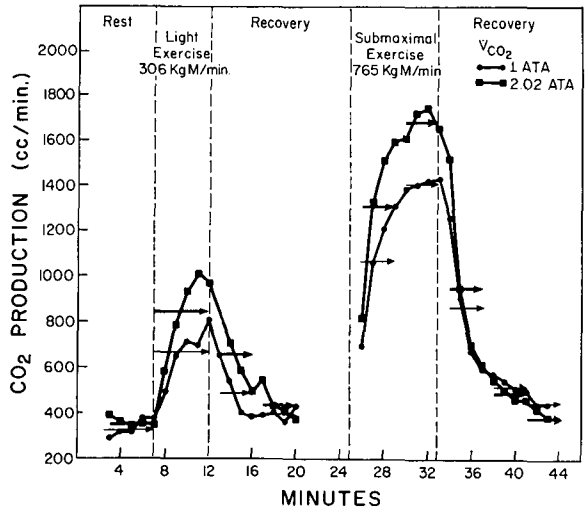

FIG. 111. Carbon dioxide production ($\dot{V}CO_2$) changes during hyperbaric oxygenation with exercise.

one atm. abs. oxygen pressure and remained stable during the last four minutes of performing strenuous labor; a similar response occurred at 2.02 atm. abs. oxygen pressure (Fig. 112).

During exercise, the carbon dioxide tension of arterial blood correlated most directly with the oxygen tension of the inspired gas, increasing from a mean value of 29.1 mm Hg at one atm. abs. air to 43.5 mm Hg at 2.02 atm. abs. oxygen pressure as summarized in Table 53. During the last

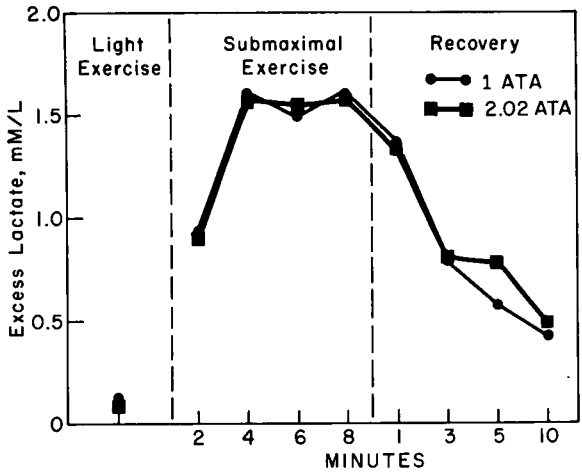

FIG. 112. Excess lactate levels at 1 and 2.02 atm. abs. on oxygen

TABLE 53

Arterial Carbon Dioxide Tensions ($Paco_2$) at Rest, Exercise and Recovery under Various Environmental Conditions

ENVIRONMENT	PRE-EXERCISE	EXERCISE				RECOVERY			
		2ND MIN.	4TH MIN.	6TH MIN.	8TH MIN.	1ST	3RD	5TH	10TH
Air: 1 atm. abs. open circuit 5 subjects	33.0 ±4.9*	36.3 ±7.2	34.2 ±7.2	32.6 ±3.6	29.1 ±9.1	31.2 ±4.2	30.5 ±4.0	28.6 ±2.9	28.1 ±2.6
O_2 : 1 atm. abs. closed circuit 5 subjects	32.4 ±5.0	36.8 ±3.3	37.4 ±2.0	31.1 ±3.2	31.4 ±4.9	31.9 ±5.5	30.2 ±4.4	30.6 ±2.8	30.4 ±5.8
O_2 : 1 atm. abs. closed circuit 12 subjects	31.6 ±8.4	38.7 ±6.8	38.8 ±6.9	40.3 ±7.0	39.2 ±11.5	36.0 ±5.8	31.4 ±5.9	31.2 ±5.2	30.6 ±6.5
O_2 : 2 atm. abs. closed circuit 12 subjects	32.4 ±8.3	39.3 ±8.4	37.6 ±7.6	37.0 ±7.9	37.1 ±7.9	33.9 ±6.1	28.8 ±5.0	27.1 ±4.3	30.1 ±7.5
O_2 : 2 atm. abs. open circuit 8 subjects	32.9 ±2.4	41.7 ±7.5	42.8 ±3.8	43.8 ±4.5	43.5 ±5.4	40.3 ±4.5	35.7 ±3.7	34.3 ±3.6	33.9 ±3.0

* = ± standard deviation.

minutes of exercise at 2.02 atm. abs. oxygen pressure the carbon dioxide tension in arterial blood rose in some instances beyond 60 mm Hg.

At 225 points in time during the study simultaneous measurements of carbon dioxide tension were accomplished for arterial blood and mixed

expired air. In 86 instances, the tension of carbon dioxide in mixed expired air exceeded that in simultaneous samples of arterial blood, a reversal of the anticipated relationship; 75 percent of these reversals occurred at 2.02 atm. abs. oxygen pressure and in all but a few cases appeared either during the late phase of exercise or during the early minutes of recovery. The reversals observed at one atm. abs. recurred frequently in a given subject at the same point in the experimental sequence at 2.02 atm. abs. In one subject reversal occurred at the same points in the experimental sequence when the experiment was repeated after an interval of one month.

Discussion

During hyperbaric oxygenation normal men responded to exercise with slower heart rates and unchanged blood pressures when these hemodynamic indices were compared to responses at one atm. abs. Previous observations of normal resting subjects also revealed a slower heart rate and unchanged blood pressure during hyperbaric oxygenation; in these studies cardiac output was determined and proved to be significantly less during hyperoxygenation (3). From these measurements an increase in peripheral vascular resistance and a rate dependent decrease in cardiac output could be computed. Furthermore, other experiments in animals and man have demonstrated regional vasoconstriction during exposure to very high oxygen pressures (4, 5). A similar increase in peripheral vascular resistance and decrease of cardiac output can be inferred for exercising hyperoxygenated man, although direct measurements of systemic blood flow are lacking in these studies.

The occurrence of bradycardia during hyperbaric oxygenation is well established, although the pathways leading to this response are incompletely understood. Bradycardia associated with hyperoxygenation has been abolished or prevented by administration of the vagolytic agent atropine, indicating the efferent pathway through which this response is mediated (6). The stimulus and afferent pathway is of even greater interest. Available experimental evidence indicates that regional blood flow will decrease as the oxygen tension rises in blood perfusing the area (7), a comparable response for systemic blood flow is also possible.

The observed increase in systolic, diastolic, and pulse pressure during exercise occurs independently of concomitant changes in oxygen tension. Similar pressor responses have been observed previously in other studies of normal exercising subjects, although the diastolic pressure response has varied, rising slightly, remaining unchanged or falling in different populations (8, 9).

Respiratory rate decreased and tidal volume increased at 2.02 atm. abs., although there was no significant change in pulmonary ventilation. These

changes in the ventilatory pattern indicate a partial shift in respiratory work expenditure from a nonelastic to an elastic category. Since elastic work is unaffected by increased atmospheric pressure, this altered ventilatory pattern should reduce the work of respiration to less than would be the case otherwise at 2.02 atm. abs.; nevertheless, the overall net effect is a substantial rise in the oxygen cost of breathing.

In this study the workload and experimental sequence were devised to provide stable levels of oxygen consumption in unconditioned subjects during submaximal exercise; this expectation was fulfilled at one atm. abs. At 2.02 atm. abs. of oxygen pressure, however, the subjects consumed significantly larger amounts of oxygen during exercise. This increase in oxygen consumption may be due to a) the greater oxygen cost of breathing denser gases and of moving the limbs in a dense environment; b) accumulation of oxygen in tissue depots; c) a decreased efficiency of energy production by aerobic metabolism; or d) a relative decrease in anaerobic metabolism.

The available evidence supports most strongly hypothesis a) that more work must be expended to breathe in a hyperbaric environment (10–12). Furthermore the simultaneous measurements of carbon dioxide elimination in this study were similar both qualitatively and quantitatively to the changes seen for oxygen consumption, supporting the impression that not only was oxygen uptake greater during the hyperbaric exposure, but that more oxygen was consumed in aerobic metabolic pathways.

Hypothesis b) that the body continues to accumulate oxygen in depots seems unlikely since the storage capacity is demonstrably limited and because all subjects were preoxygenated for at least 30 minutes prior to performing submaximal exercise (13). Should regional perfusion change significantly, however, with blood flow increasing markedly to areas that were relatively ischemic, then storage of oxygen in these more accessible tissues would continue for a longer period. This possibility is difficult to prove or disprove.

Another possible explanation for the increased oxygen consumption at 2.02 atm. abs. is hypothesis c) that more oxygen is required to yield an equivalent amount of energy because of a decrease in formation of high energy phosphate compounds as has been reported at five atm. abs. of oxygen pressure (14). One proposed mechanism for reduced production of high energy compounds such as adenosine triphosphate would be impaired efficiency of electron transport mechanisms (15). Although these biochemical effects are usually seen only at oxygen pressures greater than those used in this study, comparable metabolic derangements might be induced by the increased metabolic requirements of exercise and therefore appear at a lower inspired P_{O_2}.

Another explanation for the increase in oxygen consumption during

exercise, that in hyperoxygenated exercising man there is a relative decrease of anaerobic metabolism, is a hypothesis supported by the observation that computed excess lactate concentration in arterial blood did not increase, as would be anticipated, but instead remained unchanged at the higher level of work performed at 2.02 atm. abs. of oxygen pressure; this finding suggests that either an increased consumption or a relatively decreased production of excess lactate has occurred during hyperbaric oxygenation. In either case the result would be a larger dependence upon aerobic metabolic pathways.

The respiratory exchange ratio falls during exercise to a constant value approaching 0.8 at both one and 2.02 atm. abs. This observation is consistent with a stable metabolic state and with metabolism of both fatty and nonfatty substrates.

In this study arterial carbon dioxide tensions rose during exercise when the subject was exposed to high oxygen pressures; this relationship was most evident in experiments using an open circuit respiratory assembly. In some instances the arterial carbon dioxide tensions increased remarkably at the end of the exercise period. Previous studies have shown an increased alveolar carbon dioxide tension during exercise when exposed to high oxygen tensions (16, 17, 18). This rise in P_{CO_2} during exercise may reflect a decreased ventilatory sensitivity to carbon dioxide in a hyperoxic setting (19, 20).

Hypercapnea has been observed previously during exposure to increased barometric pressures, both in divers and in exercising subjects (11, 21). In previous studies the contribution of the increased work of breathing to hypercapnea has been difficult to evaluate, although the alveolar P_{CO_2} will rise as a function of increased resistance to laminar air flow if an external resistance is placed in the respiratory pathway (22). In this study the measured resistance of both respiratory assemblies was low and the resistance of the external systems was probably unimportant. A contribution to increased carbon dioxide tensions by a higher internal airway resistance seems at least possible; this factor may act synergistically with very high oxygen tensions in arterial blood during a hyperbaric exposure to produce marked hypercapnea.

The normal gradient between arterial and mixed expired carbon dioxide concentrations decreased during exercise at 2.02 atm. abs. of oxygen pressure and in some instances transient reversal occurred. This unusual observation, that the carbon dioxide concentration in mixed expired air exceeded that of arterial blood can most easily be explained by phasic changes in carbon dioxide tension of arterial blood not revealed by intermittent sampling. As a result, the measured arterial P_{CO_2} may have fallen below the mean tension in alveolar gas in a manner similar to that inferred for end

tidal samples during exercise by Matell (23). The only other feasible explanation for a higher tension of carbon dioxide in expired air than in arterial blood is active secretion of carbon dioxide into expired air; physiological examples of this phenomenon have never been documented, and this possibility seems remote.

The early occurrence of oxygen toxicity is well documented in individuals exposed to high oxygen tensions who are laboring strenuously (1, 2). Under controlled conditions in the laboratory the early onset of oxygen toxicity has been observed as well in hypercapneac animals (2, 24). The occurrence of hypercapnea in subjects during exercise at elevated oxygen pressures should render them more vulnerable to developing obvious toxicity than would be true for eucapneac individuals; higher carbon dioxide tensions may be a major factor, therefore, in the early occurrence of oxygen toxicity in physically active personnel exposed to hyperoxia. An additional factor in the early development of oxygen toxicity suggested by this study may be decreased efficiency of energy production while maintaining an increased oxygen consumption.

Acknowledgment

This report was supported in part by USPHS Research Grants HE 07896, HE 5662, HE 5663, HE 07563, and a grant from the Life Insurance Medical Research Fund.

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30 | R. W. HAMILTON, JR.

Physiological Responses at Rest and in Exercise During Saturation at 20 Atmospheres of $He-O_2$

This presentation will describe a chamber saturation dive in which two normal subjects were exposed for 48 hours to a pressure equivalent to 650 feet of sea water, or roughly 200 meters, followed by a multiday decompression breathing helium and oxygen. Part of the justification for the experiment was to assess the operational and medical problems of this type of dive; observations on these topics have been reported elsewhere (6, 11). The major physiological purposes were to establish man's ability to do useful work at these depths, to study the responses to exercise in the high-pressure helium-oxygen environment and to determine the effect that living in this environment has on the respiratory response to CO_2.

Methods

The routine of exercise experiments began several days before the dive, continued through the "bottom time" and resumed again after decompression was complete. The usual procedure was for each subject to do one experiment in the morning and another in the afternoon.

An experiment consisted of a series of measurements taken under control or "resting" conditions, followed by a twenty-minute period of exercise, toward the end of which the measurements were repeated. The measurements included respiratory minute volume, end-tidal P_{CO_2}, cardiac rate response, oxygen consumption and carbon dioxide production (3, 4).

The experiment was conducted in a deck decompression chamber, the one described elsewhere (9) and in this volume (Chapter 9) as a component of the first combined deck decompression chamber-submersible chamber

operation. It is just over 5 feet in diameter with a volume of 138 cubic feet, and was refitted for laboratory use.

The chamber atmosphere during the high pressure phase was 94.5% helium and 4% nitrogen, plus 1.5% oxygen; this was equivalent to breathing 35% oxygen at sea level. With this gas mixture, the density was roughly 3.7 times that of sea level air.

During the pre-dive period procedures were devised and practiced that required a minimum of voice communication from the divers to the observers, since severe speech limitations are imposed by helium at 20 atmospheres.

During each experimental run the subject reclined on the bunk, inspiring chamber gas through a low-resistance valve system and mouthpiece, and expiring through a large stopcock. Exercise was performed by using the same device as that used in the Gemini earth-orbiting spacecraft. The subject stretched a rubber bungee cord by extending his feet, the level of exercise being determined by the frequency of stretching. Each pull to full length required 21 foot pounds or 2.9 kilogram-meters of work.

During the experimental periods the second diver served as technician. By manipulating the stopcock he collected samples of expired gas in 30-liter weather balloons over timed intervals. He then forced the contents of each bag through a dry test gas meter located inside the chamber, and recorded the volume.

The layout of the experiment is shown in Figure 113, which shows the configuration for experiments conducted with the chamber pressurized. Gas analyses were all performed outside the chamber on gas samples reduced to atmospheric pressure. End-expiratory gas for carbon dioxide measurement was sampled continuously from the mouthpiece, reduced to atmospheric pressure, and drawn into an infrared carbon dioxide analyser. A breath-by-breath recording was made from which inspired and end-expired CO_2 tensions were calculated. The same CO_2 sampling line was transferred briefly to each bag of expired gas for a measure of mean expired P_{CO_2}.

Oxygen was sampled from the chamber or the expired gas bag through a nylon sampling line by which samples were passed through a drying tube to a paramagnetic oxygen analyser. An excess flow was used to reduce transit time in the sampling lines. The volume of gas removed from each sample was added to the gas meter reading.

For oxygen analysis in the experiments performed at sea level, a small pump was inserted in the sampling line to force the sample through the analyser at the same rate as when the chamber was under pressure. For sea-level CO_2 analysis, the pickup unit was connected directly to the line leading to the mouthpiece, and standards were introduced through the same lines as the experimental samples.

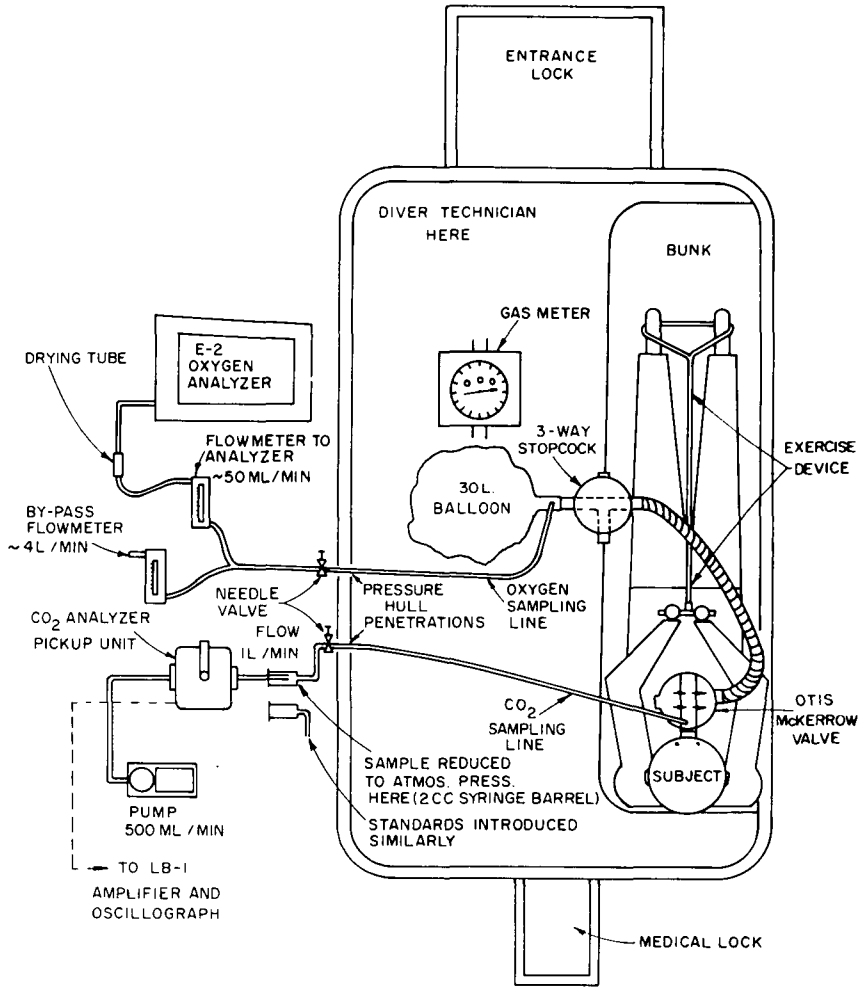

FIG. 113. Arrangement of equipment for exercise experiment. The diagram shows setup for operation with chamber pressurized. The gas sampling lines are shown in the configuration used in experiments with the chamber under pressure. For sea level experiments a pump was added in the oxygen sampling line downstream of the needle valve, and the CO_2 sampling line was connected directly between the pickup unit and the needle valve.

Cardiac rate was monitored continuously throughout each run by means of electrodes attached to the subjects in the morning and left in place all day.

An experiment began by having the subject accommodate to the mouthpiece for at least three minutes and this was followed by two 2-minute sampling periods. He then began to exercise, and after fifteen minutes of

exercise, two more 2-minute collections were made. A single level of exercise was used for each experiment; the maximum rate used during the dive was 174 kilogram-meters per minute, or just over 28 watts. This level resulted in about one liter per minute of oxygen consumption. It would have been desirable to have used additional, higher work levels.

Results and Discussion

In order to assess the physiological significance of experiments such as these, it is necessary to focus on several specific aspects of performance. As a working hypothesis it was assumed that the predominant feature of the high pressure environment would be the increased density of the breathing medium. Other factors that may be important, however, and that must be considered in interpreting our results are: helium as a pharmacological or narcotic agent, the effects of confinement and inactivity, the unusual thermal properties of helium, the high humidity in the chamber, and the slightly increased oxygen tension.

With the thought in mind that effects of gas density on respiration would be the limiting factor, several conditions were considered that might have been affected by the increased work of breathing. Comparisons were made at sea level and at 650 feet of the following parameters: oxygen consumption during exercise, ventilatory response to exercise, change in alveolar carbon dioxide pressure during exercise and the cardiac rate response to exercise.

Since the manner of imposing the amount of work done was somewhat crude, measured oxygen consumption was compared with the intended level of energy output (Fig. 114). It appears that Subject 2 (Christensen) showed about the same oxygen consumption for a given level of exercise at sea level and at depth. Subject 1 (Noble), on the other hand, seems to have consumed more oxygen at depth for a given work load than he did at sea level.

It should be noted in Figure 114 that there was no appreciable change in oxygen consumption at rest while the subjects were in the helium atmosphere, as compared to the sea level values.

Figure 115 shows these same data plotted as differences from control values, which was accomplished by transposing all resting values to the origin. To permit a comparison of the average slopes of the two groups of lines, sea level and 650 feet, the average slope of each group was determined by fitting a least squares regression line to the points. One 0,0 value was entered into the calculation along with each of the points shown. Using the *t*-test (5, p. 177), the least squares regression lines representing the averages of the two groups were compared and found not statistically different. So although a given level of exercise appears to require slightly

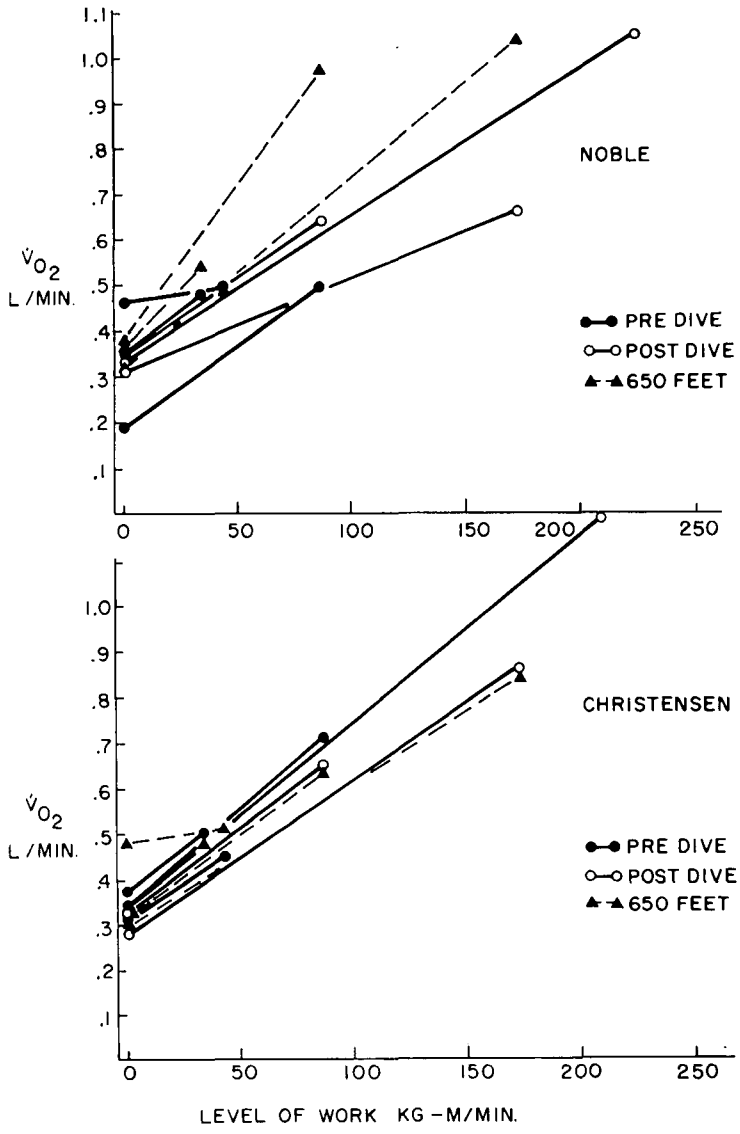

FIG. 114. Oxygen cost of exercise. Oxygen consumption is shown as a function of exercise level.

more oxygen when performed at 20 atmospheres, the difference is not important at the relatively low levels of exercise used in these experiments.

The effect of the dense atmosphere on the ventilatory response to exercise was considered. Figure 116 shows the increase in respiratory minute

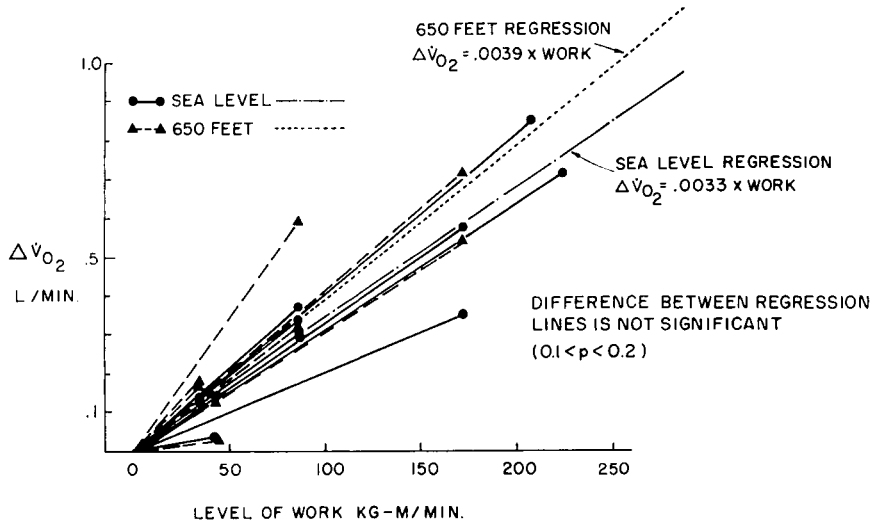

FIG. 115. Oxygen cost of exercise. Composite graph showing increase in oxygen consumption as a function of exercise; data from both subjects. Regression lines were calculated to represent the average slope of each group of points (sea level and 650 feet) using the method of least squares. One "0, 0" point was entered in the calculation for each point shown.

volume as a function of increased oxygen consumption for the same experiments as above. The level of exercise is expressed as oxygen consumption since the oxygen consumption more nearly expresses the actual amount of work performed by the subject than does the number of times he pulled the Gemini exerciser. According to the average values, represented by the least squares regression lines, the ventilatory response to exercise is reduced at depth by 38% and this reduction is statistically significant. This reduction in ventilation during exercise results in a slight accumulation of CO_2. Figure 117 shows resting alveolar P_{CO_2} values on the left end of each line and values measured after 15 minutes of exercise on the right. (The end-tidal P_{CO_2} values were corrected with an empirically determined factor that corrects for the washout of dead space as a function of tidal volume. It is therefore justified to refer to these P_{CO_2} values as closely approximating "alveolar" (7)). Considerable variation was found, even in the points determined at rest. A significant point is that the resting CO_2 values at 650 feet were not very different from those determined at sea level. The post-dive measurements are indicative of mild hyperventilation; more will be said about the post-dive conditions below.

For comparison all the lines were pooled together and plotted as differences (Figure 118). The dotted lines show that there was a consistent

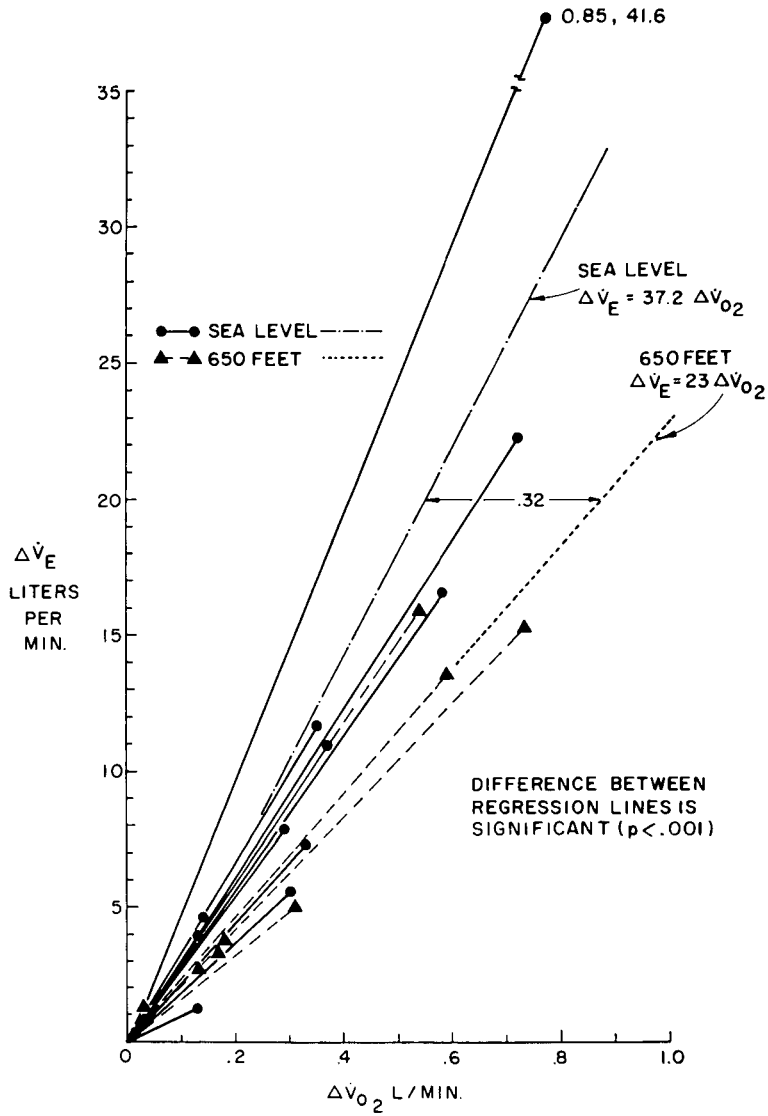

FIG. 116. Increase in ventilation with exercise; data from both subjects. In this and subsequent graphs the level of exercise is represented by oxygen consumption. Regression lines calculated as in Figure 115. The 0.32 value represents the extra oxygen consumed at depth when ventilating at 20 liters/min., but represents more than just the extra work of breathing.

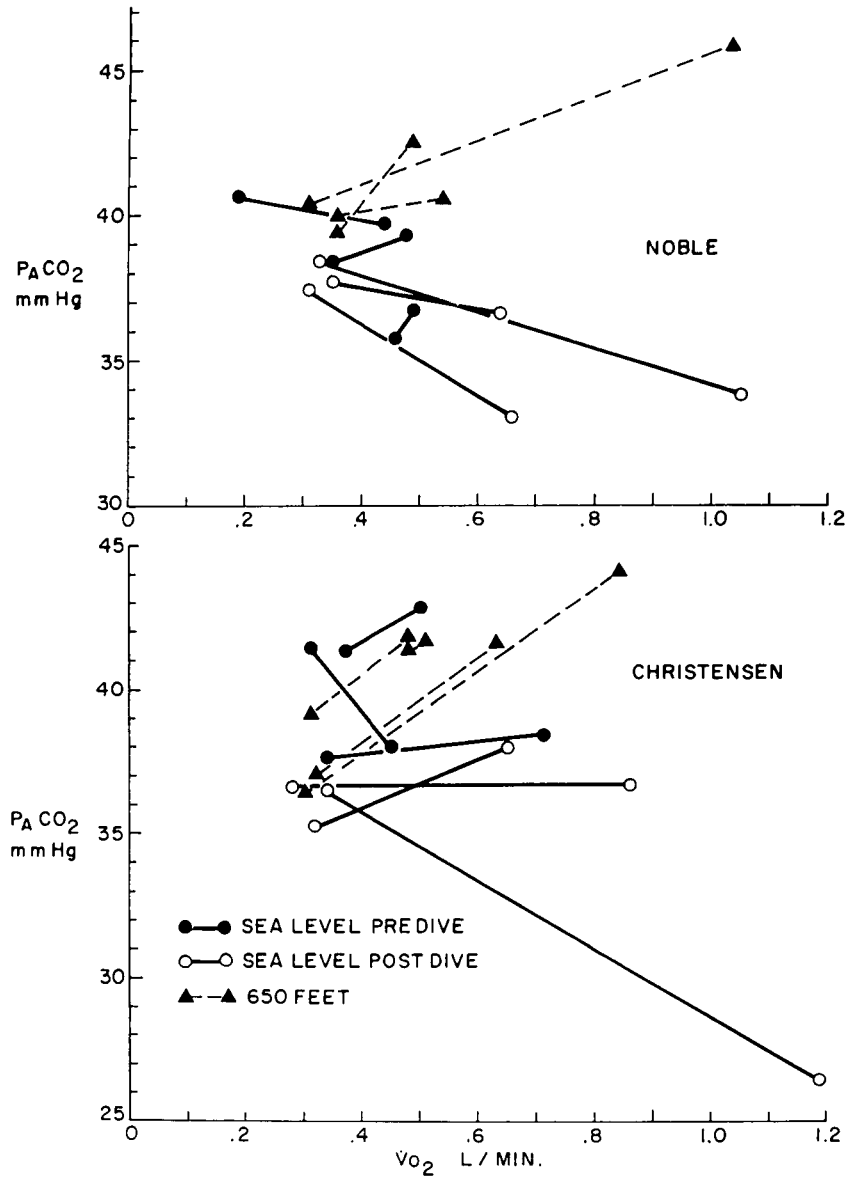

FIG. 117. Effect of exercise on alveolar CO_2. Each line represents a single experiment, with the point on the left end determined at rest and the one on the right after 15 minutes of exercise.

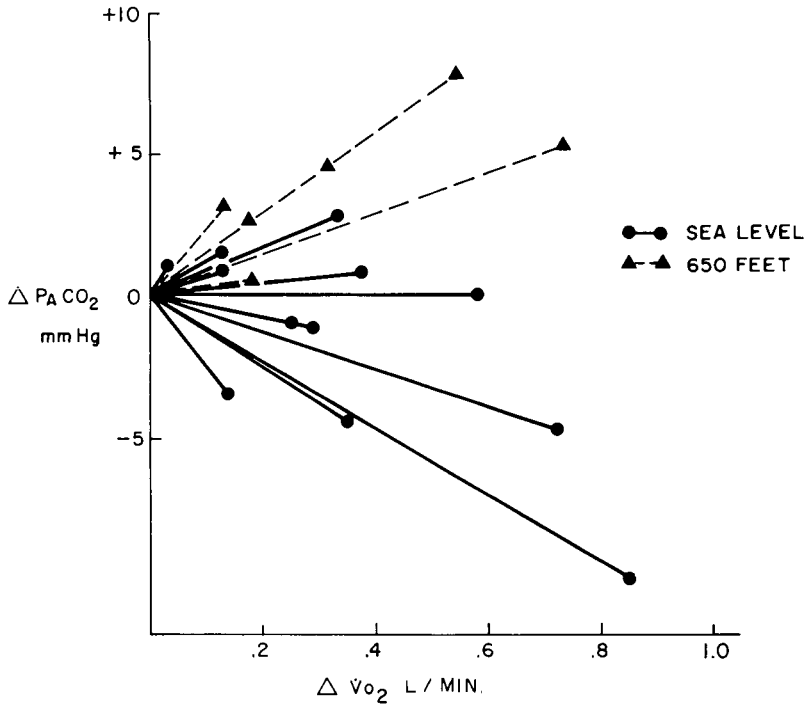

FIG. 118. CO_2 buildup as a result of exercise. Same values (both subjects) as shown in Figure 117, redrawn so as to represent changes from a single starting point. The slight buildup of CO_2 during exercise at 650 feet is evident in all experiments.

tendency for alveolar P_{CO_2} to increase with exercise at 650 feet, while the sea level experiments show the expected slight decrease or no change. This slight rise in P_{CO_2} agrees with some of Lanphier's earlier data, in the cases where gas density and exercise level are comparable (8).

Resting and exercising heart rates are shown in Figure 119. Two things stand out in this figure. One is a tendency for resting heart rates to fall into distinct categories according to the experimental conditions. The other is the occurrence of strikingly parallel responses under all three conditions. The parallel response suggests that there is no special cardiopulmonary stress as a result of moderate exercise at 650 feet.

The resting heart rate values show two features which deserve comment. First, the post-dive rates are unusually high. The days following the long decompression, when the post-dive experiments were carried out, were typical, hot, humid, oppressive August days. The stress of heat and humidity undoubtedly affected the subjects. This, plus the possible effect of six days of physical deconditioning, probably explains the elevated heart rates

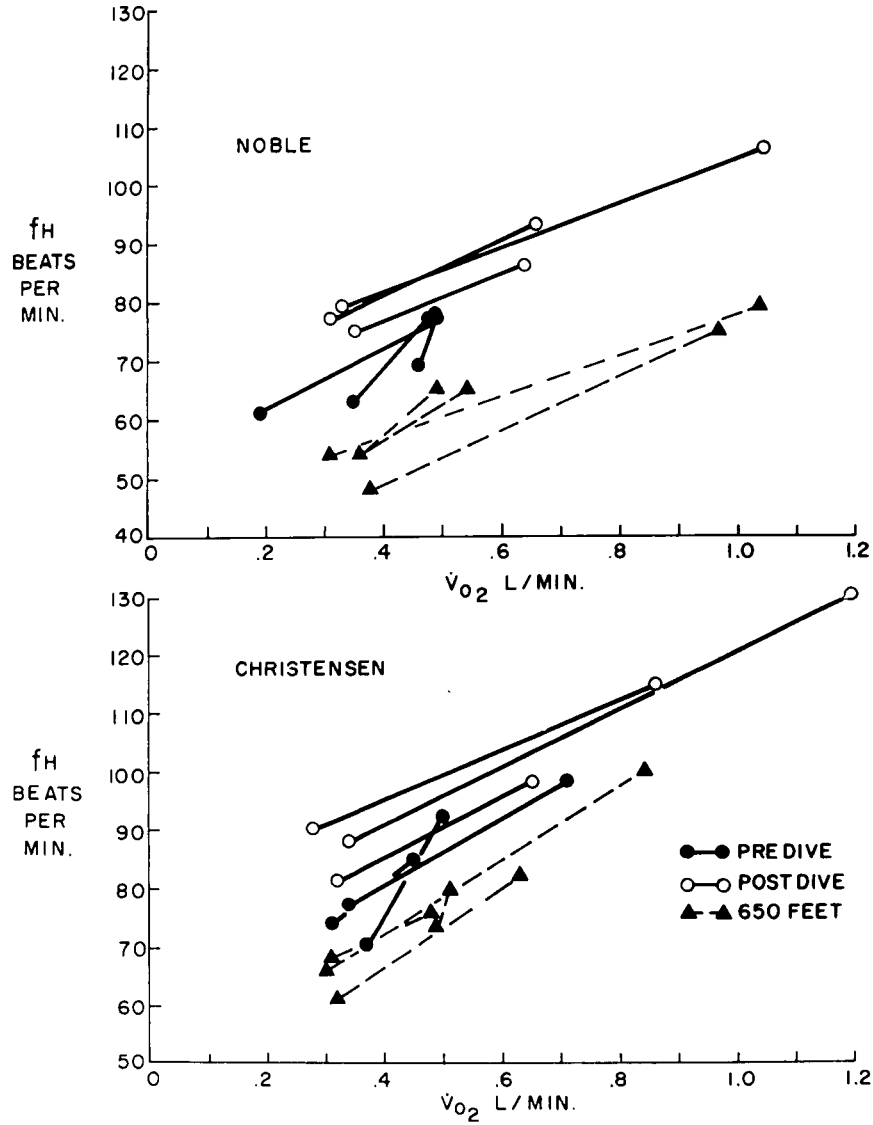

FIG. 119. Cardiac rate response to exercise. Points on the left end of each line are determined at rest, those on the right after 15 minutes of exercise.

in the post-dive period, and probably accounts also for the slight hyperventilation seen at the same time.

The bradycardia seen at depth is not easily explained. This finding is consistent among all heart rates taken with the subjects resting, including

rates determined from the clinical ECG's that were performed each day. Relative inactivity is a possible cause, but bed-rest experiments do not usually reveal much change in only two days (12). Bond has mentioned the possibility of a general metabolic "slow down" during prolonged submergence, but did not propose a mechanism or indicate the nature or magnitude of any actual metabolic change (1). It is not possible to judge whether the bradycardia is a direct pharmacological effect of the high helium pressure.

By inserting a large weather balloon in the breathing system as shown in Figure 120 and adjusting the system for rebreathing, it was possible to produce a controlled buildup of the subject's own CO_2. This provided the

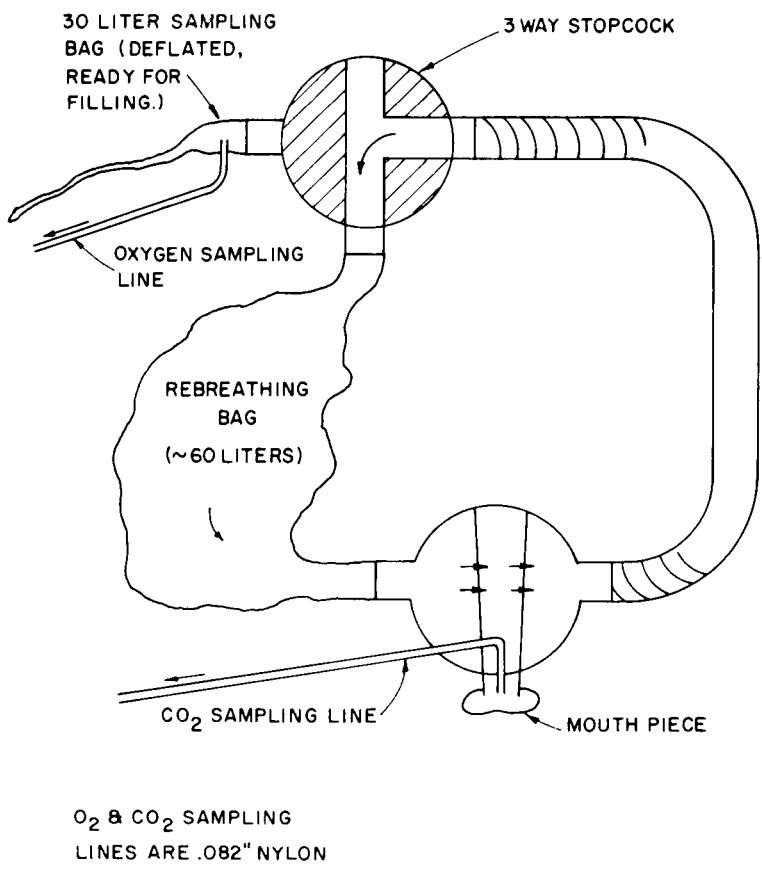

FIG. 120. Arrangement of apparatus for CO_2 response experiments. The breathing system was modified to include a rebreathing bag, to which oxygen was added to minimize hypoxic stimulus.

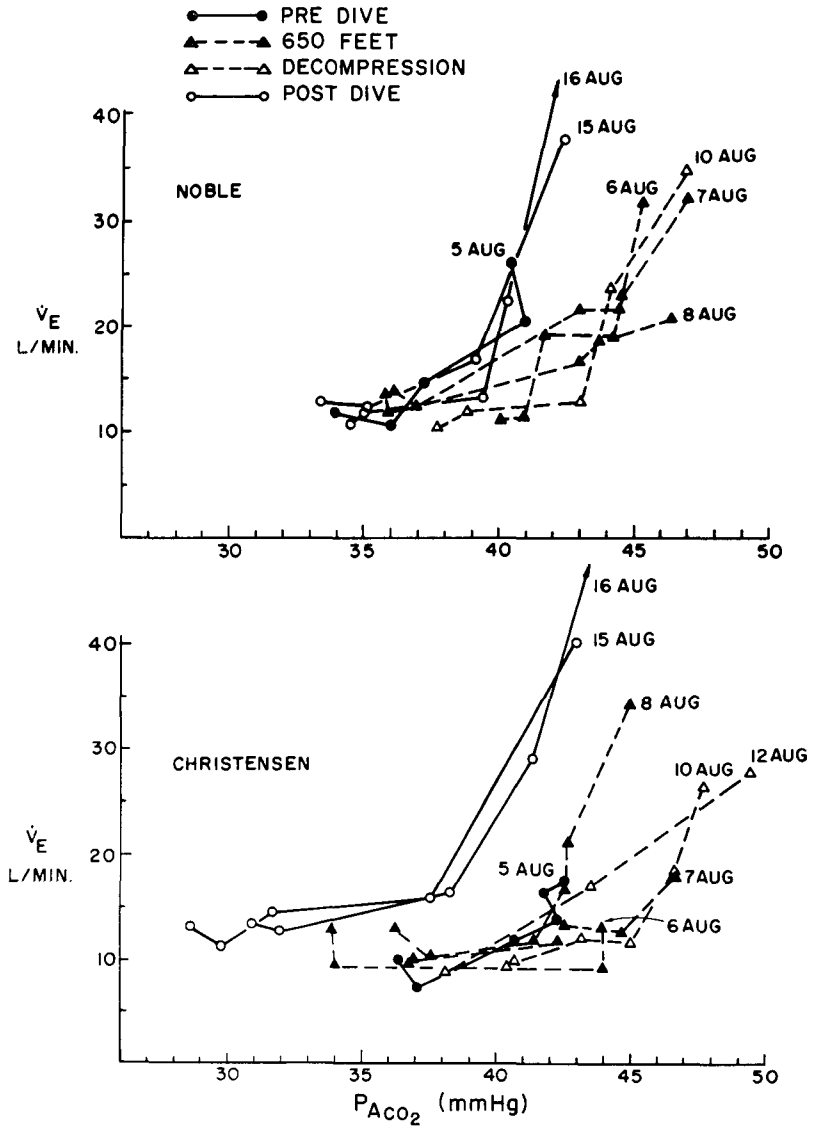

FIG. 121. CO_2 response curves, showing increase in respiratory minute volume as a function of alveolar CO_2 .

basis for constructing CO_2-ventilatory response curves for use in a search for modification of respiratory reactivity to carbon dioxide. Sufficient oxygen was available in the chamber atmosphere to minimize the hypoxic stimulus in the experiments performed at pressure, and in the sea level experi-

ments extra oxygen was added to the rebreathing bag. After control runs the subject breathed from the rebreather until a definite increase was seen in end-tidal CO_2, at which time the stopcock was switched to the sampling bag for a timed volume measurement. During such a collection period the subject breathed a constant level of CO_2, since no new CO_2 was entering the rebreather at the time. This rebreathing procedure was repeated several times at increasing levels of end-tidal CO_2.

The results of these experiments are shown in Figure 121. The predominant finding here is a distinct shift to the right of the steep part of the response curves done at depth. Whether this is accompanied by a change in slope is not certain. Experiments by others, with added external resistance, have shown a change in slope along with a shift of the response curves similar to that observed here (2, 10). No definite time-related trends can be seen in these curves that might indicate accommodation to the environment. The rather low "resting" values of P_{CO_2} we feel were due to psychic stimulation, possibly combined with inadequate rest period before the beginning of measurements.

Summary

In two subjects exposed to the pressure equivalent of 650 feet, moderate exercise cause no increase in oxygen consumption and a slight rise in end-expiratory CO_2. The ventilatory response to exercise was much reduced, but the heart rate responded in a normal way. CO_2 response curves were shifted to the right, but showed little change in slope.

These experiments show that man can spend long periods of time at the depths of the continental shelves and can perform moderate physical work there. It is not known what the physiological limitations of deeper saturation diving will be.

Acknowledgment

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31 | E. H. LANPHIER

Interactions of Factors Limiting Performance at High Pressures

Many factors can doubtless limit or impair physiological performance at extreme ambient pressures. We can by no means be sure that we are even vaguely aware of all such factors, and failure to consider one or two important ones could confound our best efforts at prediction and extrapolation. Few if any of the familiar limiting factors operate entirely alone. Most of them are influenced unfavorably when others are also operative, and in some cases we suspect what amounts to a vicious circle of interactions.

My main concern here is with such cross-influences and interactions, but putting them into perspective requires at least an attempt to predict the limitations that the major factors would impose if present alone. Our present lack of knowledge is such that these predictions may be very far afield of the truth. So little quantitative information is available concerning most of the interactions that they can be discussed only in general terms. Both deficiencies serve to point out and define the kinds of information that we need.

Some known factors have deliberately been omitted from consideration. I have assumed, for example, that divers will somehow be kept comfortably warm and that breathing apparatus must somehow provide the equivalent of free access to CO_2-free gas. The effects of submergence are assumed to be the same at all depths, and the rate of compression is not considered. Purely psychological elements have been neglected. Effects of hydrostatic pressure have been disregarded in the uncertain hope that they will not be evident in the range of depths that man can penetrate as a useful gas-breathing mammal.

Useful activity at depth requires both mental competence and some ability to do physical work. But if a choice must be made, physical capacity clearly means little when the brain is disabled. Inert-gas narcosis thus seems a logical starting point for the discussion.

INERT-GAS NARCOSIS

At the top of Figure 122, I have indicated a rough classification of the narcotic effects encountered when breathing air under optimal conditions at increasing depths. It is reasonable to suppose that narcotic impairment by any other gas would show a similar gradation with increasing pressure and that the corresponding levels could be predicted if we knew the narcotic potency of the gas compared to that of nitrogen. Unfortunately, we do not have very firm information of this sort for helium. Carpenter (1) has reported studies suggesting that helium is about one ninth as narcotic as nitrogen. If this is correct, we would expect helium to have corresponding effects at the depths indicated by the lower diagonal line of Figure 122. (I have considered a 99 percent helium-one percent oxygen mixture and simply determined at what depth the partial pressure of helium would be nine times that of nitrogen in the upper line.) Whether literally accurate or not, this projection calls our attention to the probability that we will find a very large span of depth between noticeable and incapacitating levels of

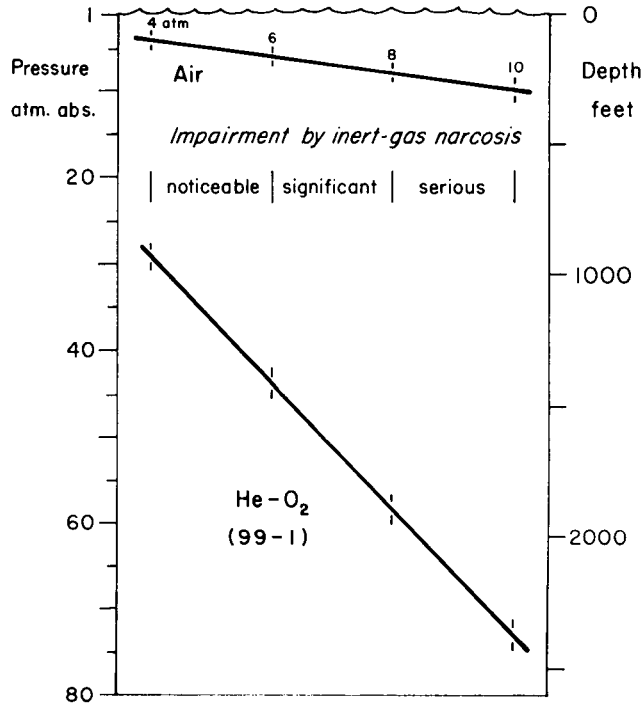

FIG. 122. Degrees of impairment by inert gas narcosis. The impairment experienced in diving with air is projected into greater depths for a 99% He-1% O_2 mixture on the basis of the assumption that helium is one ninth as narcotic as nitrogen.

helium narcosis. Whether a man can actually function effectively within this range will depend largely upon the presence or absence of factors that would potentiate the narcosis.

RESPIRATORY FACTORS

Ventilation

As the density of any gas increases with increasing depth, we can expect progressive elevation of the work of breathing. This, in turn, will cause reduction of a diver's capacity for physical exertion. In itself, this can become an important limiting factor of performance at depth. A diver must have a certain capacity for muscular effort in order to be useful and safe no matter how many mechanical aids we plan to provide. However, we would be less concerned about this factor if we could always be sure that the sensation of dyspnea would keep a diver from exceeding his respiratory capacity in exertion and that his ventilation, within this capacity, would always be proportional to his CO_2 production. If such were the case, abnormal elevation of the arterial P_{CO_2} would be a rare occurrence. Unfortunately, no such assurance can be given.

I have presented data (2) indicating subnormal alveolar ventilation and pronounced elevation of alveolar P_{CO_2} in divers working at rather modest depth with breathing apparatus that they considered quite acceptable and with no complaints of respiratory distress. Elevations of P_{CO_2} were remarkable in some divers even during moderate work at the surface using an optimal breathing circuit. Determinations of arterial P_{CO_2} during work on the same subjects in Lambertsen's laboratory substantiated the conclusions we had reached from end-tidal measurements in these men (3, 4). Similar findings were reported at about the same time by Goff and Bartlett (5). More recently, Jarrett (6) has found large elevations of alveolar P_{CO_2} during work while breathing air at pressures up to 4 atm. A similar trend was noted during mild exertion at 650 ft in the Ocean Systems saturation dive, as reported here by Hamilton. Beyond the apparent tendency of some divers to retain CO_2 during exertion under any conditions, the main factor favoring such retention seems to be an increase in the work of breathing. Elevation of the inspiratory P_{O_2} also contributes, and Lambertsen and his associates have shown a definite alteration of the respiratory response to CO_2 at high oxygen pressures (7).

Elevation of P_{CO_2} is capable of causing loss or impairment of consciousness at extreme levels, and it is recognized as a factor accelerating the onset of oxygen poisoning (8). Here, however, we are more concerned with its ability to potentiate narcosis. In 1939, Behnke and Willmon (9) noted such an apparent effect in divers breathing air during salvage of *U.S.S. Squalus*. Case and Haldane (10) confirmed the phenomenon experimentally

in 1941. It now appears most unlikely that CO_2 retention is basically responsible for narcosis (11), but no one who has gone from competence to coma as a result of exercising for about three minutes (2) is likely to underestimate the importance of the potentiating effect of CO_2 when some degree of narcosis is already present.

At any rate, we have ample reason for concern about the restriction of respiratory capacity that may develop when helium is breathed at greater depths. Several indices of the work of breathing have been investigated at various depths and with different breathing media, but the largest body of data concerns maximum breathing capacity (MBC), also known as maximum voluntary ventilation (MVV). This measure provides a means of evaluating relative degrees of ventilatory restriction and of comparing different conditions on that basis. Density of the breathing medium is the main factor affecting MVV at depth, and it is reasonable to suppose that values with helium at greater depths could be predicted simply on the basis of relative density and known values for air at various depths. First, it is of interest to consider the relative density of various He-O_2 mixtures. Figure 123 shows that although pure helium is less than one-seventh as dense as air, the relative density increases markedly with addition of oxygen or nitrogen. For example, an 80% He-20% O_2 mixture is almost exactly one-third as dense as air.

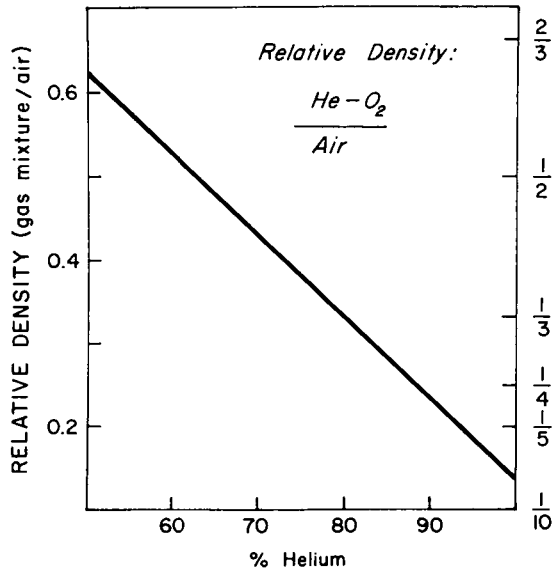

FIG. 123. Density of various He-O_2 mixtures relative to that of air at the same ambient pressure. The density of such mixtures is greatly influenced by the proportion of the heavier gas.

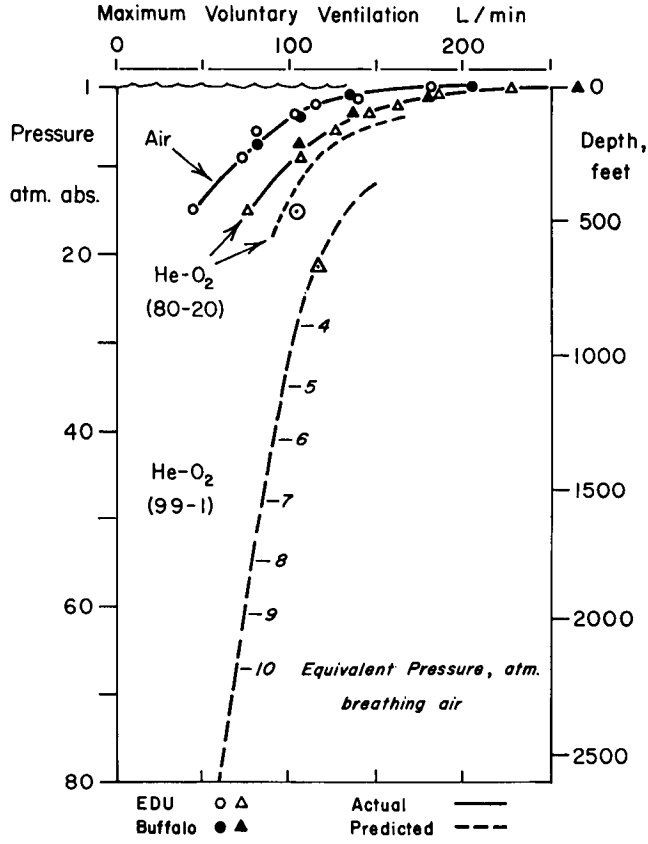

FIG. 124. Measured and predicted values of maximum voluntary ventilation. Curves for "actual" values are derived from the work of Wood (12) at the U. S. Navy Experimental Diving Unit and of Maio and Farhi (13) at the State University of New York at Buffalo. Predictions are based on relative density. The single circular point represents Wood's value for 95% He-5% O_2 at 15 atm. The triangular point represents the mean of six determinations in two subjects at 650 ft (Ocean Systems saturation dive, 1965).

The upper curve in Figure 124 represents MVV at various depths when breathing air. It is based primarily on the findings of a U. S. Navy Experimental Diving Unit (EDU) study reported by Wood (12). At Buffalo, Maio and Farhi (13) made similar measurements to a pressure of 7.5 atm, and the agreement is remarkably good. The upper dashed curve represents predicted values for a gas one-third as dense, assuming that a given MVV would be possible with the lighter gas at a pressure three times as great as with air. The intervening curve indicates values actually obtained, at EDU and in Buffalo, with an 80% He-20% O_2 mixture. The prediction

based on relative density is thus checked and found to be unduly optimistic. It approaches the value reported by Wood for 95 percent helium at 15 atm (indicated by the large circular point). There are several possible reasons for the discrepancy, but I have found no better basis for such predictions.

The curve labeled He-O_2 (99-1) in Figure 124 represents another projection based on relative density, and we might expect that it, too, is overoptimistic. However, the triangular point indicates the mean of MVV values obtained at 650 ft during the dive reported by Hamilton in this symposium. It suggests that the predicted curve may be reasonably accurate. If so, we could say for example that a man breathing 99 percent helium at about 60 atm should have about the same respiratory status as when breathing air at about 9 atm. Pressures equivalent in such terms have been indicated on the predicted curve.

The "equivalent depths" based on MVV are within one atmosphere of those seen in Figure 122 for equivalent narcosis. If both predictions are reasonably accurate, then we might also expect to find about the same interactions between narcosis and respiratory factors with helium at depth that we find at the equivalent depths breathing air. Proof for such a simple relationship would be welcome since most of our knowledge about these factors might then be projected into the unfamiliar situation. Unfortunately, we would soon find that we have remarkably little detailed information ready for such application. It would be encouraging, however, to believe that information gained with air or other heavy gases at readily accessible depths would be applicable to the problems of diving with lighter gases at great depths.

Proceeding solely with existing impressions, we might predict that narcosis itself will be the primary limiting factor and that its potentiation by CO_2 will become a problem chiefly when more-than-minimal exertion is attempted. At the depth where narcosis sets the practical limit, the capacity for sustained exertion will probably be very small. However, it is likely that this factor will prove less important in itself than in the fact that any attempt to do harder work will promptly accentuate narcosis. Among many other questions, it would be of great interest to know whether these relationships would be modified materially by a breathing apparatus that assisted, rather than hindered, a diver's ventilation.

Increased work of breathing may not be the only respiratory effect capable of causing CO_2 retention or otherwise interacting with other limiting factors. We have been interested, for example, in possible alteration of the distribution of inspired gas with increasing density. Studies to date (14) suggest a measurable change between one and 6 or 7 atm with air, but it is too early to evaluate the possible significance of such changes or even

to be sure what they represent. For example, it is likely that they reflect an increase in stratified inhomogeneity of gases in the smaller airways rather than a change in regional distribution (15).

Gas Diffusion

A closely-related question concerns the possibility that an increase in density causes significant impairment of diffusion of CO_2 or oxygen within the gas exchange units of the lung. Bean (16) and others have suggested that such impairment would cause retention of CO_2 at depth, but little serious attention has been devoted to the question. The matter was reopened in Buffalo by Kylstra's studies in liquid breathing (17), where "diffusion dead space" is clearly a major problem in gas exchange. The probable importance of this factor under various other circumstances was then considered (18). Figure 125 represents application of such calculations to the question of CO_2 diffusion in the pulmonary gas phase when breathing either air or helium-oxygen at depth.

The extent of mixing, by diffusion, of freshly inspired gas with gas already in the exchange units of the lung should be proportional to the diffusion coefficient and the diffusion time and inversely proportional to the square of the distance across which diffusion must take place. Kylstra and his associates pointed out that diffusion mixing should be essentially complete when

$$\frac{Dt}{a^2} = 0.5 \qquad (1)$$

where D = the diffusion coefficient in cm²/sec, t = diffusion time in sec, and a = the diffusion distance in cm. (Values less than 0.5 would indicate less complete mixing and an increasingly large diffusion dead space for CO_2.) The diffusion time is taken to be the duration of a single respiratory cycle and is thus equal to 60 divided by the respiratory frequency (f) in breaths per minute, as indicated on the abscissa of Figure 125. I assumed that the diffusion coefficient under increased pressure would be equal to $D_{(1\ \text{atm})}/P$, where P = pressure in atm abs. By thus entering P and rearranging equation (1) to solve for P, it was possible to calculate the pressures at which the value of 0.5 would be maintained with different values of a and t. The diagonal lines of Figure 125 indicate these pressures for air and helium respectively. The average diffusion distance in the human lung is not definitely known. Staub (19) has presented values that suggest a distance of about 1 mm, but Cumming and his associates (15) believe that 2 mm is a better estimate. This was employed in the calculations of Figure 125. A diffusion coefficient of 0.139 cm²/sec was used for CO_2 in air at 1 atm. There is uncertainty concerning the corresponding binary diffusion

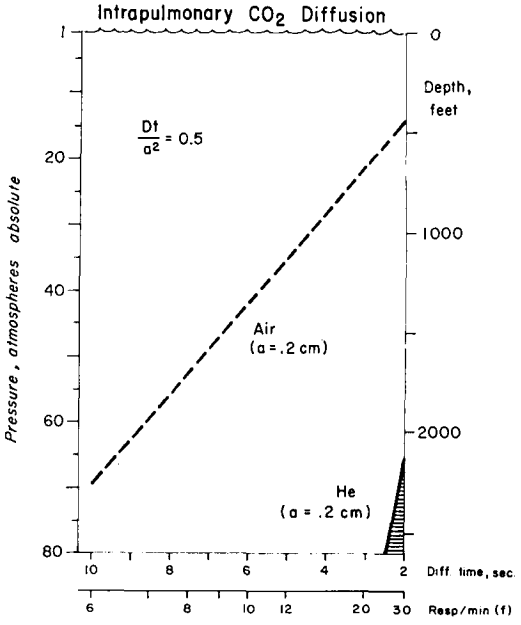

FIG. 125. Intrapulmonary diffusion of CO_2 vs. depth. The diagonal line (air) and shaded area (helium) indicate pressures beyond which the value of Dt/a^2 would fall below 0.5 (see text) at various respiratory frequencies and resulting diffusion times.

coefficient for CO_2 in helium. A value of 0.67 was employed, this being the lowest that could be derived by interpolation from data presented by Jenkins and Cook (20).

Figure 125 invites the conclusion that increased gas density will not significantly impair the diffusion of CO_2 at any depth where air is likely to be the breathing medium. In the case of helium, the critical value is reached only with high respiratory frequencies at pressures which other considerations suggest may be close to the limit for practical diving.

Intrapulmonary diffusion of oxygen can be considered in similar terms, as in Figure 126. According to Kylstra, *et al.* (18), the diffusion dead space for oxygen is approximated by the equation

$$V_{D_{\text{diff } O_2}} = \frac{1}{1 + 15\dfrac{Dt}{a^2}} \cdot V_A \qquad (2)$$

where V_A = alveolar volume and the other values are as already defined. The diffusion coefficient at increased pressure was again assumed to equal $D_{(1\text{ atm})}/P$. The limit arbitrarily chosen was an oxygen diffusion dead space of 2 percent of the alveolar volume, hence

$$P = \frac{15\ Dt}{a^2\left[\frac{1}{0.02} - 1\right]} \tag{3}$$

The diffusion coefficients at 1 atm were assumed to be 0.178 and 0.88 for O_2 in air and helium respectively. Values of P were computed for different diffusion times and for diffusion distances of both 1 and 2 mm. The resulting lines in Figure 126 indicate the importance of the value chosen for the latter. At 1 mm, the conclusion indicated is that there should be no significant diffusion problem for oxygen with either air or helium. But if the diffusion distance is 2 mm, a diffusion dead space of 2 percent of the alveolar volume may exist in the midst of practical diving depths with either gas. Compensation for such a dead space can be achieved by elevating the inspiratory oxygen pressure, as happens automatically when air is breathed at increasing depths. At any given depth, however, exertion will increase the size

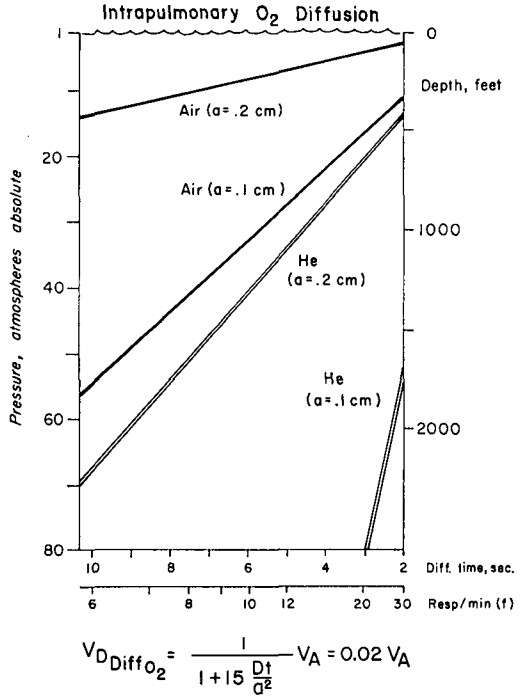

FIG. 126. Intrapulmonary diffusion of O_2 vs. depth. Solid lines (air) and double lines (helium) indicate pressures beyond which the diffusion dead space for oxygen (see text) would exceed 2 per cent of the alveolar volume at various respiratory frequencies and resulting diffusion times. Diffusion distances of 1 and 2 mm are represented, indicating the large influence of this factor (a).

of the diffusion dead space by increasing the respiratory frequency and at the same time will increase the significance of that dead space by increasing the oxygen consumption. It is conceivable that under some conditions, maintenance of a normal inspiratory P_{O_2} could result in hypoxia during exertion and that preventing this might require a higher oxygen pressure than is otherwise desirable.

FACTORS RELATED TO OXYGEN

Many potential problems will be avoided if the oxygen pressure can be kept close to the normal surface value during exposure to high ambient pressures. Oxygen poisoning itself is foremost among these, but the number of other interacting factors is impressive. The respiratory response to CO_2 is reduced by high oxygen pressures, and CO_2 retention is enhanced particularly during exertion (2, 7). CO_2 retention, in turn, can accelerate the onset of oxygen convulsions. Incapacitating degrees of carbon dioxide intoxication itself are more likely to develop with hyperoxia (21). High oxygen pressure also appears to potentiate inert-gas narcosis, probably through enhancement of CO_2 retention either at the ventilatory level or, as Hesser (22) suggests, by interference with elimination of CO_2 from the tissues. The "oxygen syncope" described by Miles (23) is an added potential hazard. Few of these factors have been studied in the combined presence of high oxygen pressure and very high gas density or pronounced narcosis, but it seems certain that the undesirable effects and interactions would be compounded. We can only hope that neither diffusion dead space nor any other unfamiliar problem will require elevation of oxygen pressure at great depth.

CONCLUSIONS

Acknowledging the great uncertainty of such predictions, it seems likely that inert-gas narcosis and increased work of breathing will be the main factors limiting man's penetration of great depths with gaseous breathing media. The relative importance of these factors and the nature of their interactions may well be very similar to those found with heavier gases at lesser depths. If so, existing knowledge and studies conducted at relatively low pressures may be applicable to the problems of great depth. Intrapulmonary gas distribution and diffusion appear likely to be much less important than the work of breathing in determining respiratory limitations; but possible problems related to the diffusion dead space for oxygen deserve further attention. Any factor that requires significant elevation of oxygen pressures at depth will probably invite added complications.

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Panel on

Limitations of Physiological Performance at Extreme Ambient Pressures

C. M. HESSER, *Chairman*

Dr. BENNETT
Dr. GOODMAN
Dr. HAMILTON
Dr. KYLSTRA
Dr. LANPHIER
Dr. SALTZMAN
Dr. SALZANO
Dr. SCHAEFER
Dr. WOOD

Discussion

CHAIRMAN HESSER: We will now open discussion.

DR. PEGG: It is worth mentioning that the Minnesota Mining Company has made some fluoro-carbon liquids which are quite nice for mammals to breathe (Clark, L. C. and Gollan, F., Science 152: 1755, 1966). They dissolve large quantities of oxygen and carbon dioxide; they are not anesthetic and apparently are not toxic. You can put a mouse in a beaker of this substance at room temperature and pressure, provided it is equilibrated with oxygen, and he will last several hours. They all seem to survive.

DR. BACH: Assuming that we do go on to fluid breathing, has anyone thought about the problem of vision in this connection?

DR. KYLSTRA: In an entirely aqueous environment refraction would be a problem. I believe the French have made some sort of contact lenses which would compensate for this altered refraction. Does Dr. Lambertsen, perhaps, know more details about that?

DR. LAMBERTSEN: Contact lens development for underwater swimming was begun a decade ago under the Panel on Underwater Swimmers. How-

ever, in relation to fluid breathing by man, I can only ask whether it really makes any difference, if one is unconscious from carbon dioxide retention, whether his index of corneal refraction is correct.

DR. LANPHIER: A man of vision should not be so dubious about a great advance like liquid breathing. Dr. Hesser, could you let us hear from Dr. Brauer, because I think there is a two-fold discrepancy in the estimates that Dr. Bennett and I used for limits of tolerance to helium and I think there is more recent data than either of us could work with.

DR. BRAUER: We have maintained monkeys at high pressures while making electroencephalographic measurements. We can say that down to about 2,000 feet for times of about half an hour the monkeys are cheerful, can respond to sound, move spontaneously and have a normal electroencephalogram.

If you go very much beyond that time you begin to see changes and we are not quite sure at this point whether these changes refer to Dr. Lambertsen's suggested ultimate limit by respiratory difficulties. There is some evidence that we are seeing effects of increased respiratory resistance, but we may be at the threshold of narcosis.

Dr. Bennett told us that his subjects begin to have trouble with muscle coordination at about 800 feet. I would like to show you an electroencephalogram indicating what happens in our monkeys regularly under certain circumstances of high pressure. Vehement grand mal seizures occur, followed by a typical postictal period which extends for several minutes. This continues for about half an hour with the usual intervals between convulsion and silence. We see these coming on regularly at 1500 feet, or slightly under 50 atmospheres.

The seizures come on under conditions of helium breathing and hydrogen breathing, with the oxygen pressure at or below one atmosphere.

We have some problem with CO_2 control in exposures, especially at the very high pressures. In all of our helium compressed monkeys we have had convulsions, but if we slow down the rate of compression, as we did in one monkey, then these are stalled off at least until very much higher pressures, for example 85 atmospheres, than those at which they occur with slightly higher compression rates.

On compression in hydrogen we have seen convulsions only in two cases and in both cases the monkeys were suddenly compressed about 150 feet or so in a few seconds and they convulsed. The convulsions subsided very quickly.

I have a suspicion that what we are seeing in the helium animals is similar to things that Dr. Bennett is seeing in humans. We feel that this is not an obligatory consequence of compression. We can in fact stall off those convulsions by slower compression and lower oxygen partial pres-

sures and so I suspect this is not an inherent phenomenon of high helium pressure. We still do not understand it but it is certainly something to pay attention to. Two minute, five minute or ten minute intervals will elapse before the convulsion comes on and it then continues.

This is a hazard and it is rather obvious that in human subjects we are beginning to see something like it at shallower depths.

DR. SMITH: Do these convulsions improve with time, as Dr. Bennett's subjects seem to?

DR. BRAUER: Yes, we suspect they do subside somewhat. Obviously, we cannot repeat grand mal seizures of this type for very long and still have a subject. What happens in fact is that the convulsive activity becomes short and the period of EEG silence becomes long and it finally becomes frightfully long and you go get a fresh monkey.

DR. BENNETT: If you have such a low oxygen partial pressure, could you get cortical or cerebral oxygen tension measurements in conjunction with those convulsions to make sure you have enough oxygen in the brain at these depths?

DR. BRAUER: I agree, we need both oxygen and CO_2 measurements, of course, to make these meaningful. We are working on electrodes to do this right now. I think both the oxygen and CO_2 concentrations that the animals are actually breathing are slightly lower than the figures I showed you, which are effluent gas from the chamber.

DR. LUNDGREN: Dr. Bennett, in the studies of human performance under high air pressures have you seen a training effect from experiment to experiment in the same individual? In experiments conducted by our navy this was definitely the case, at least with the experimental observers who were with the subjects in the chambers. They were subject to the same kind of objective testing or measurements as the subjects, and it is quite surprising to see the observer giving the subject orders, handing paper to him, and so on. We have the impression that they perform better and better with training, but if they are faced with something unexpected you may encounter a breakdown.

I wonder whether you see this because the exercise-cycle type of measurements that you do, while objective, is a bit different from field conditions.

DR. BENNETT: There is little doubt that there is acclimatization to narcosis. Certainly with the oxygen-helium tremor effect there is some acclimatization but not enough to really help very much. A fresh subject coming into the pressure chamber for the first time is quite severely affected. The tremor you saw on the film was not particularly mild, but we have had much more severe cases than that. We have noted many muscles twitching, with the subject very uncomfortable, moving about very much, dizzy and sick.

CHAIRMAN HESSER: We now should discuss the observations made during exercise at very high pressure.

DR. SCHAEFER: Dr. Hamilton made a remark that the cardiac rate decreased during the 650 foot saturation dive and he referred to the possible effect of helium in producing this. Although he had an increase of tidal volume and a shift of the CO_2 response curves to the right, I think these changes are simply due to pressure effects because with the adaptation to high pressure you develop different respiratory patterns of very high tidal volume and reduced rate. Usually we find that divers who have adjusted to high pressure have very large tidal volumes, reduced cardiac rate and a shift in the response to CO_2. I think this corresponds with your finding under high pressure and believe you do not have to refer this to a helium effect which would be difficult to define.

DR. BENNETT: I would also like to ask Dr. Hamilton whether he is satisfied that the measurement which he used for end-tidal CO_2 is in fact a valid method. We have had difficulty obtaining repeatable, significant results.

DR. HAMILTON: The reduction of CO_2 to ambient pressure produces several problems. One is that you have to measure carbon dioxide at such a low percentage. This provides one advantage in that the analyzer is now linear, but the sensitivity is limited.

Reducing the gas sample to atmospheric pressure leads also to a reduced response time. Then, when the respiratory rate was above about eight per minute there was a tendency for peak carbon dioxide pressures to be lowered by passage through the sampling tube. This had to be quantitatively identified. In many cases respiratory rate was not higher than 8 per minute. Although the divers breathed 15 or 18 times per minute at rest with no mouth piece, when they put on the mouth piece they tended to breathe at 5 per minute so the rates were usually slow enough for our sampling system, in spite of its rather long response time.

DR. LANPHIER: Before Dr. Hamilton gets too apologetic, we ought to recognize that it is a considerable technical achievement to have made the kind of measurements that were reported this afternoon, not only by him, but by others at such high pressures.

DR. HAMILTON: There is another aspect of the validity of end-tidal samples as indexes of alveolar gas tensions. Dr. Lambertsen has obtained data by simultaneous measurement of arterial P_{CO_2}, end-tidal P_{CO_2} and tidal volume which permits correction for the error in end-tidal P_{CO_2} which is related to the effect of a small tidal volume. In no case was this dead space washout correction more than one or two millimeters. We used this in cases where the tidal volume was quite low.

DR. GOODMAN: We have obtained end-tidal samples in an automatic,

intermittent, breath-by-breath manner. These successive end-tidal samples were not vented to the atmosphere, but they were collected one after another anerobically as a weight of fluid was displaced in a vessel which exactly balanced the pressure throughout the whole system.

Then at the end of the time period this sample of alveolar gas was shunted out of the chamber and analyzed in the laboratory with the Scholander apparatus. In this manner I think our data of 330 feet has some credence with a full scale calibration of one or two percent. I do not see how you can get it much steeper than that.

DR. BRAUER: Dr. Fenn's presentation reminded us of hydrostatic pressure effects. It is quite obvious that in dives down to four or five hundred feet we are not yet encountering these, but at the depths about which Dr. Lambertsen has been talking and at the levels toward which most of us are looking now, we are beginning to approach a region where some of these effects, at least in their subtler features, are to be looked for. At 100 atmospheres for instance, Scholander and his group have shown marked changes in oxygen solubility and displacement of the hemoglobin dissociation curves. These effects raise considerable confusion with conventional respiratory measurements.

MR. WELLS: I am in Scholander's laboratory doing work on the dissociation curve of hemoglobin and the determination of changes in the pH of blood at 100 atmospheres. The dissociation curve seems to be shifted about 16 percent to the right at half saturation at 100 atmospheres of hydrostatic pressure. We know that there is also a change in the pH of about 0.3 pH units due only to hydrostatic pressure. It is difficult right now to say exactly what is causing the shift of the dissociation curve of hemoglobin to the right, but it is well within the range of that which would be produced by a shift in the pH only. However, the exact cause can not be determined right now. A shift of 0.3 pH units, I believe, would be in the range which would bring about clinical symptoms of acidosis.

DR. BENNETT: I consider that the extrapolation to these very great depths, which seems to be based on Carpenter's figures for effects of inert gases on electrical convulsive shock threshold, are extreme in some ways. Certainly looking at the men that we have had at pressures of 800 feet I do not believe we are going to push them very much further in depth, not certainly during the first hour, anyway. Provided there is in fact a sufficient improvement over the first hour to the second hour you can probably go on. Otherwise we will not be able to.

DR. LANPHIER: What would happen if you should try it with lower oxygen levels?

DR. BENNETT: We have done this once and thought we were going to

show some very special advantage. However, the subject was the worst we had ever seen him.

I would like to raise another point in connection with rate of descent. Dr. Goodman's case seemed to be very much narcotized, with a descent of 128 feet per minute. I want to stress that we have done many compressions at a rate of four and five hundred feet in twenty seconds without any appreciable narcosis. It may be that there is a barrier that you go through; at a particular rate of compression you may be made very narcotic, but you can beat it if you go really fast.

DR. GOODMAN: In the British submarine escape trials there were similar rapid compressions and no narcosis. The curve of the rate of compression was in fact reminiscent of a pressure-volume curve and not a straight line. What type of compression were you using in the study you refer to?

DR. BENNETT: It was as fast as we could get it. We just opened everything and that was the way it went off.

DR. LAMBERTSEN: In understanding rapid compression it is necessary to consider alveolar carbon dioxide pressure and alveolar ventilation as well as the rising inert gas tension. There should be a way of determining how carbon dioxide tension changes in the alveoli during compression. The rate at which it changes will depend upon the relationship between rate of entry of carbon dioxide coming in from the mixed venous blood, the rate of compression, the rate of ventilation of the alveoli and also the dilution of the alveolar gas by new gas which is coming in.

These different factors operate concurrently. On breathholding with a closed glottis and no ventilation, there should initially be a rise in alveolar carbon dioxide tension on descent, regardless of rate. Breathholding with an open glottis should add new gas to the alveoli without other ventilation and alveolar P_{CO_2} should tend to be constant regardless of rate.

If you increase the rate of descent and also ventilate the lungs, then it might be possible to actually go through what you call a barrier and have this new rate of descent actually cause a lowering of P_{CO_2}, so it seems to me we have two distinct problems in increasing the rate of our descent. One of these, with breathholding, should result in a rise of P_{CO_2} and the narcotic effects of carbon dioxide itself. The second could very well lead to hypocapnia.

DR. BENNETT: In any case, I think if you go fast enough you still will not get enough nitrogen to the brain in time to produce narcosis. It may be a straight CO_2 narcosis problem then, but certainly not a nitrogen narcosis problem.

MR. KELLER: Actually I have been four times under a pressure equivalent to 1,000 feet and in one dive the descent was at a rate of 700 feet to

1,000 feet per minute. During that dive I had violent sensations of narcosis. During the other three dives which were at the slower rate of about 70 to 100 feet per minute narcosis was moderate.

It is my personal impression that narcosis at depths of 1,000 feet with 95 percent helium is about equal to air at 200 feet.

DR. KYLSTRA: Mr. Keller has dived to 1,000 feet breathing gas. Would he like to try it breathing water? I am sure he would not get any narcosis then.

DR. SALTZMAN: We have been asked why we chose initially to compare one and two atmospheres of oxygen in the exercise study Dr. Salzano and I have reported. This was because the principle used required a closed-circuit oxygen system in order to monitor continuously both oxygen consumption and CO_2 elimination.

We therefore elected the disadvantage of comparing oxygen against oxygen at a single sitting to do a pilot study using the same respiratory system rather than compare oxygen against air at the same sitting using two different respiratory assemblies.

This choice led to uncertainties in the results and we are in the process of comparing subjects using oxygen at 2 atm. and an open circuit, with subjects breathing air at one atmosphere in an open-circuit situation.

These studies are continuing and raising some questions, answering others.

DR. LUNDGREN: I would like to hear comment on the remote possibility that intestinal gases such as methane and others contribute to the narcotic effect at high pressure. By this I mean the reabsorption of intestinal gas into the blood, not such gases from the chamber itself.

MR. EDEL: Dr. Bennett has commented that rapid compression gave an advantage in reaching depth before the nitrogen concentrations in the brain reached narcotic levels. However, when you are breathing helium in oxygen at depths below 200 feet for long periods and then switch to nitrogen in oxygen there seems to be a very rapid development of narcotic effect.

DR. WOOD: I can not give any figures or exact data. However, during the 15 atmosphere study we made, the average time before narcosis became incapacitating from the time of switch from helium to air, varied from about two minutes to above five minutes. At five minutes we interrupted the run and started ascent. Only one subject that I am aware of remained functional at five minutes and even he had a good deal of narcosis.

My own experience has been at least one complete lapse of consciousness breathing air at that level and several other subjects became totally unable to carry out planned activities.

DR. BENNETT: When we were doing electroencephalographic studies

several years ago we also did the exchange of helium-oxygen mixtures and air and found a reverse in the EEG patterns in about four minutes. This is the same order of time that Dr. Wood mentioned.

DR. GOODMAN: On an abrupt change from air to argon-oxygen at a depth of 231 feet with continuous reaction time testing it takes about three to three and a half minutes for reaction time to plateau.

DR. HAMILTON: We have made some crude psychological tests during neon-oxygen breathing at a 650 foot depth. We found slightly better performance while they were breathing neon than while breathing helium, possibly because they were more motivated.

CHAIRMAN HESSER: We have time for a few more questions. I would like to ask Dr. Bean whether he has any comments on the CO_2 retention during descent?

DR. BEAN: During World War II experiments related to explosive decompression were carried out on dogs in which a catheter was placed way down into the bronchi. On rapid compression the P_{CO_2} went up. There were also blood pH measurements carried out at the same time. These were parallel to the changes in P_{CO_2}. In explosive decompression the effect was opposite, actually "sucking out" the oxygen from the alveoli and from the venous blood.

This deoxygenated blood is the first surge of blood that gets to the heart and then to the brain after explosive decompression. The relationship of this to CO_2 in rapid decompression is an interesting feature.

DR. LEITH: The question of what happens to the alveolar P_{CO_2} during rapid changes in ambient pressure is an important one. During the 1920's and 1930's a respirator known as a barospirator was used to put lungs at rest in the treatment of tuberculosis. In this respirator a subject could lie completely immobile, making no respiratory movements, his chest size not changing, as he was ventilated adequately by pressure fluctuations within the device from plus 50 cm to minus 50 cm of water at normal respiratory rates. These were adequate for maintaining a normal arterial P_{CO_2}, so to the extent that this is applicable, I would suppose that Dr. Lambertsen's thought that the P_{CO_2} might actually be falling during rapid compression because of addition of gas to the alveoli would be likely.

CHAIRMAN HESSER: Dr. Lundgren, you have been exposed to this Thunberg chamber. Have you any comments?

DR. LUNDGREN: You are quite right. We can easily produce hyperventilatory effects in the barospirator.

DR. BENNETT: Our continuous cortical P_{CO_2} measurement in the cat with the P_{CO_2} electrode showed that during the rapid compression phase we always had a fall of P_{CO_2}, accompanied by a rise in P_{O_2}. After the fall in P_{CO_2} during the compression phase it comes back up.

DR. BARNARD: There is another comment worth making on this question of what is happening to the alveolar P_{CO_2} during compression. Dr. Bennett mentioned that in our studies we did not observe narcosis within the short time available when we were doing fast compressions at anything from three to five hundred feet per minute. I wonder if part of the apparent confusion of interpretation is not due to the fact that we are failing to consider a simple and practical matter. That is, that very many men during a rapid compression spend time breathholding while doing a Valsalva maneuver to force air into their middle ears. If you breathhold for twenty seconds this presumably has less effect than breathholding for a much longer period.

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Possible Role of Hydrostatic Pressure in Diving

I begin this discussion of the effects of hydrostatic pressures by a quick survey of the ranges of pressure with which biologists are concerned, as illustrated in Figure 127. The chart is upside down in a sense because the vacuum of space is at the bottom where the pressure is marked as zero. The logarithmic scale of pressure begins at sea level with 1 atmosphere, and the lowest point in the ocean is at 1000 atmospheres which is marked as the limit for life. Perhaps this is a limit only because living forms have never had access to any niche where the pressure is still greater, for we have learned a great respect for the ability of living things to survive under the most hostile conditions, perhaps even out in space. Bridgeman (3) attained pressures of 10^5 atmosphere in the laboratory, and the pressure in the center of the earth is over a million atmospheres. In the center of our own sun it is 10^{11} atm., and in the center of the largest stars, the white dwarfs, it is estimated to be 10^{15} atm. (17). Physiology is interested in pressures which are vanishingly small on such a large scale as this, and the partial pressures of O_2 and CO_2 at least begin to be effective at pressures below 1 atmosphere.

At pressures above 1000 atmospheres proteins are coagulated, enzymes are inactivated, red blood cells disintegrate, blood coagulates and viruses are destroyed. It is remarkable enough that any organisms can live at the deepest points in the ocean. The study of these organisms began with the work of Regnard in 1884 (30). This Frenchman studied the organisms dredged up from 200–300 atm. (1.5–2 miles) in the Challenger Expedition, and recorded 78 different species living at such depths. This work has been continued by many others, notably in more recent times, by Zobell at the Scripps Institution. He studied the organisms brought up by the Danish

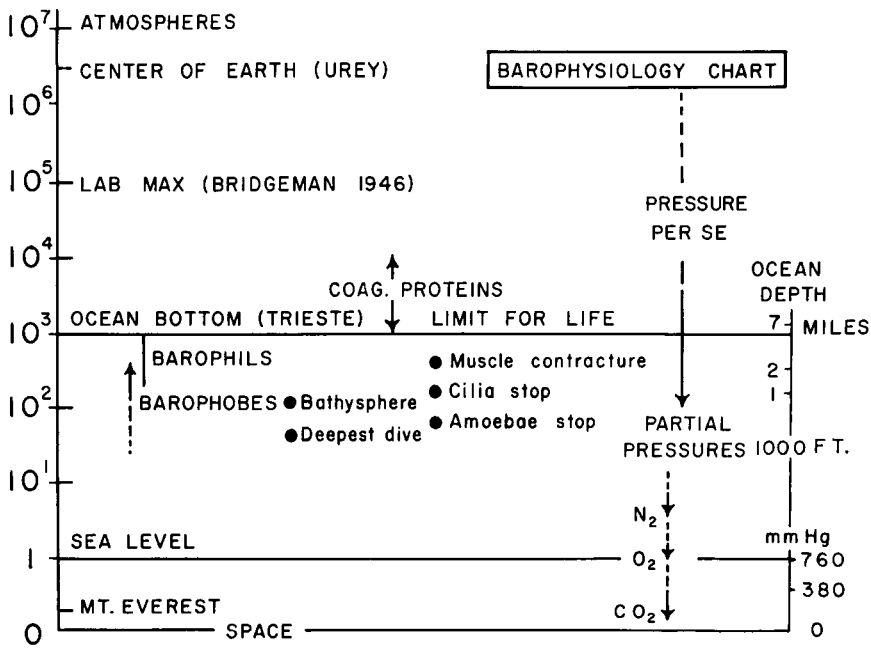

FIG. 127

Galathea Expedition, and found that some organisms, which he called the barophils, would live only at great depths and would not grow at sea level. Conversely, the barophobes were killed by pressures of 1000 atmospheres.

The effects of high pressures on frog muscles have been particularly well studied by many investigators. Regnard (30) tested the effects of high pressures on frogs submersed in water, and found that the muscles became rigid at 400 atmospheres or 12,000 feet, far beyond diving depth. Surface fish become stiff and rigid at 2.9–3.0 km. Certes (9), in France, in 1884, also found paralysis or "la vie latente" in various organisms at pressures of 100–200 atmospheres. Leonard Hill, (20) in England, repeated some of Regnard's experiments on frogs, in 1912, with similar results from the effects of pressure *per se*. In 1914 (10) Ebbecke, in Bonn, recorded continuous contractures of muscles (without action potentials) at 300–400 atmospheres. These contractures continued as long as the pressure was maintained, and occurred equally well in muscles rendered non-irritable by fatigue, narcosis or exposure to isotonic sugar solutions. He also reported a long series of other experiments on the effects of rather high pressures.

In cardiac muscle of turtles, Cattell and Edwards (8) in 1930, showed that an increase of pressure of 1000 psi (68 atm.) increased the tensions

produced in each beat of the heart by 42%, but at low temperatures of 5° C, this enhancement by pressure disappeared. Similar increases of twitch tension were found in frog muscle, and Dugald Brown (4) in 1936, reported that this was true only if the pressure was applied during the first 0.04 sec. of the contraction phase. This very striking enhancement of the twitch tension correlates well with the decrease in volume of muscle which occurs in contraction first reported by Ernst (16) and confirmed by Meyerhof and Möhle (28) and others.

The effect of hydrostatic pressure on the nervous system was investigated by Ebbecke (13) who observed that a decerebrate frog suspended in water showed twitching of the toes at pressures of 100–150 atmospheres so long as the spinal cord was intact. More recently, Spyropoulos (32, 33) has studied the effects of pressure on the giant axone of the squid and on toad nerves. Most of the effects he observed, such as prolongation of the action potential, occurred only at pressures of some 300 atmospheres or more, but the threshold membrane current was observed to decrease even at pressures of about 7 atmospheres. This should be of particular interest from the point of view of underwater physiology.

Another interesting effect of pressure was pointed out by Marsland and Brown (26), who noted that pressure enhances the gelation of gelatin but inhibits gel formation by myosin and methyl cellulose. This is due to the fact that gelatin shrinks when it sets but myosin expands. Because of the solating effect of pressure, cell division becomes impossible at pressures above about 300 atmospheres (29). In general, cells appear to behave like myosin and they lose their gel structure under pressure and become sols. For this reason pressure stops amoeboid movement, as shown by Marsland and Brown in 1936. At the same time, the relative viscosity of the protoplasm was diminished when tested by centrifugation under pressure. Marsland also studied the movements of chromatophores on the scales of the fish *Fundulus*, and found that these bodies became sols under pressure, and thus permitting the pigment granules to migrate, perhaps because of a contraction of smooth muscles. Anyhow, in the expanded state of the chromatophore, the pigment granules could be moved by centrifugation, while in the unexpanded state they resisted centrifugation, and seemed to be fixed in a firm gel.

In 1942, Johnson, Brown and Marsland (21) observed that biological luminescence can be inhibited to 56% of the control by chloroform (.05 M), but at high pressures of 4000 psi, this inhibition fails to occur. They showed very elegantly that narcotics tend to inactivate the enzyme luciferase involved in the luminescence reaction, and this inactivation is prevented by pressure, because the inactive form of the enzyme occupies a larger volume than does the active form. Thus, pressure may cause a reversal of narcosis.

To apply this to divers it may be that pressure *per se* may tend to antagonize to a small extent the narcosis due to high pressures of inert gases. A similar, very striking, antagonism between pressure and narcotics has been reported by Spyropoulos (32), who found that the narcotizing effect on nerve of 3–7 % ethanol would be almost completely opposed by high pressures.

The interrelations between pressure and temperature was shown very nicely by a study of luminescence by Johnson et al (23). Between 0 and 25° C temperature accelerates the reaction of luciferase with luciferin, and increases the luminescence. The activation of this enzyme involves an increase of volume, and over this temperature range a pressure of 476 atmospheres inhibits the reaction. At temperatures above 25° C, however, the enzyme is denatured, and this reaction also involves an increase in volume as the enzyme unfolds. At high temperatures therefore, pressure inhibits the denaturation, and therefore increases the luminescence. Inhibition by pressure is, therefore, reversed in part by an elevation of the temperature.

As a further example of the interrelations of temperature and pressure, I will now describe some experiments which I have been doing recently with *Streptococcus faecalis*, in collaboration with Dr. Robert E. Marquis, of the Department of Microbiology, and Mrs. Mary Philpott (unpublished). The primary purpose of these experiments was to observe the effects of inert gases and of equivalent hydrostatic pressures on the growth of an anaerobic organism. The cultures were contained in small vials enclosed in lucite chambers which could be pressurized to a maximum of 41 atmospheres. Growth of the bacteria was followed by measuring the opacity of the culture with a beam of light and a photoelectric cell. Figures were obtained for the time required to reach the middle of the log phase of growth, and for the percentage difference in growth at that time. Argon at 41 atm. and 24° C caused a 20 % decrement in growth (measured at 50 % of the control maximum) and xenon did the same, but at a much lower pressure of about 5 atmospheres. Incidentally, xenon seemed more effective in the presence of 1 atmosphere of oxygen than in an oxygen-free atmosphere. Nitrogen, in a few experiments, acted much like argon, but helium had a smaller effect of about 5–10 %.

The effects of pressure *per se* were tested by filling the culture vial with the culture medium and closing it with a rubber stopper. Without a gas phase and under 41 atmospheres of pressure, growth was inhibited to the same degree as by helium at pressure. As expected, the effect of pressure was definitely less at temperatures above 30° C than at 24° C or below. From these experiments it is concluded that helium showed no narcotic effect at this pressure, but pressure alone at the relatively low value of 41 atmospheres had a measurable effect on the growth rate.

Simultaneously with the pressure studies, measurements were made of the volume changes of the culture growing at 1 atmosphere of pressure. For this purpose the culture was introduced with sterile precautions into a 25 ml. volumeter—open to the outside only through a capillary tube 0.5 mm. in diameter. The amount of lactic acid formed was also measured, approximately, at the end of the experiment, by titrating the culture from a pH of about 4.5 back to its original pH of 6.8. The amount of alkali needed for this neutralization was taken as a measure of the amount of lactic acid formed, since it is known that *Streptococcus* relies chiefly on glycolysis for its metabolic needs. During the growth of this organism we observed that the volume of the whole culture steadily increased throughout the growth phase. The average increase in volume in 15 experiments was 0.63 cu. mm. per ml. of culture, or 20.3 ml. per mole of lactic acid formed. This agrees well with the figure of 24 cc per mole of lactic acid obtained by Meyerhof and Möhle (28) in solutions where glycolysis was taking place. The increase in volume in these experiments was easily measurable, and amounted to some 4–6 cm on the capillary tube. It was definitely not due to the accumulation of any gas in the medium. Calculations (by Dr. Marquis) of the volume change expected from formation of peptide bonds or synthesis of DNA, showed that these would be relatively small and negligible. Addition of lactic acid to the culture medium (in one experiment) showed no significant change in volume. These results indicate, therefore, that the inhibiting effect of pressure was chiefly due to the volume increase resulting from glycolysis during growth.

A further confirmation of this figure for the volume change is obtained from our measurements of the decrease in growth rate caused by the pressure at the experimental temperature of 24° C. Johnson, Eyring and Polissar (22, p. 305) give the following equation as applicable to the velocity constants k_1 and k_2 of any process under pressures p_1 and p_2 where the volume change per mol is ΔV:

$$k_{p_2} = k_{p_1} \exp\left[-\frac{(p_2 - p_1)\,\Delta V}{RT}\right]$$

Using this equation we have calculated that the ΔV in our experiment should have been 18 cc per mole, which is very close to our experimental value of 20 cc per mole. Considering all the factors involved in these figures, such a good agreement may well be fortuitous, but the results are certainly of the right order of magnitude.

In the human body there must be plenty of reactions which depend in part on energy from glycolysis. We could expect that such reactions, and any other reactions involving an increase of volume, should be inhibited to an appropriate degree by pressure. It can be calculated that at 1000 ft. depth or 30.5 atmospheres, and at body temperature, glycolysis would be

inhibited 3% and phosphocreatine, or ATP breakdown, both of which result in a decrease in volume, would be accelerated about 2–3%. Similar changes in velocity could be expected from other reactions with comparable changes. It is not impossible that even these small changes in rate could have a significant enough effect on the precise timing of trains of nerve impulses, refractory periods or other processes, to produce some noticeable effect on human performance tests, and the cumulative effects over many hours might be even more significant.

From these considerations I would conclude that there is a borderline chance of finding some symptoms due to hydrostatic pressure of 30 atm. or 1000 ft. What then are the chances of finding symptoms due to helium?

Carpenter (5) found, in mice, that the ED_{50} for inhibition of electroshock convulsions by helium occurred at a pressure 10 times that needed for nitrogen. Schreiner (31) found 50% inhibition of growth of *Neurospora* at a helium pressure 23 times that needed for nitrogen. Marshall (25) found no inhibition of frog reflexes at a helium pressure 5 times that needed for inhibition by nitrogen, although an effect could have been expected from the lipoid solubility which is only 4.5 times as great for nitrogen as for helium. At 30 atmospheres of helium, therefore, it might be concluded that the effect might be the same as that found at 1.3 to 3 atmospheres of nitrogen where the symptoms of nitrogen narcosis are again borderline.

In saturation dives to 600 ft. both Bennett (personal communication) and Schreiner have observed some symptoms, some of which, at least, can be attributed to the elevated alveolar CO_2 tension. Some others may have been due either to helium or to the pressure *per se*, and it is impossible to choose at present between these two possibilities. Schreiner's subjects both mentioned some minor joint pains and some tremor while on the bottom, before decompression began. There was also some evidence in one subject of cutaneous irritation. Bennett reported some tremor, sweating, dizziness and redness in the face, all of which was ascribed to CO_2. Some deterioration of mental performance was thought to be due to helium narcosis. To resolve this problem of the possible practical role of hydrostatic pressure in diving, it seems necessary to use fish or mammals inhaling water instead of gas. More quantitative comparisons of helium and nitrogen effects may also contribute to the accurate prediction of helium narcosis. The problem is still further complicated by certain similarities between pressure effects and narcotic effects which Ebbecke (12) pointed out many years ago. The cause cannot be determined very well from the nature of the effects observed.

At the risk of being unscientific, it might be pointed out that there is a popular belief that arthritic patients can sense the fall of pressure preceding a storm. Even less scientific is the notion found in the early German litera-

ture on high altitudes, that joints are held in place, partly at least, by the atmospheric pressure so that the joint pressure would be deficient at altitude. Be that as it may, there is no a priori reason why man should not be endowed with some subtle sensitivity to pressure even when the pressure is evenly distributed without any deformation of the tissues, such as that which stimulates the baroreceptors in the carotid sinus, for example.

Certainly in lower organisms there are such baroreceptors the exact mechanism of which still defies our understanding. Thus Hardy and Bainbridge (18) reported that decapod larvae will swim upwards when the pressure is raised 0.5–2.0 atmospheres. Later, Enright (14) produced convincing evidence that the Amphipod crustacean, or beach fleas, *Synchelidium*, and other related forms, will swim upwards in sea water, when the pressure is raised as little as 25 cm. of water. With a gas phase present, as in the swim bladders of fish, this is easily understood, but no gas could be found anywhere in these crustaceans and their compressibility was measured as less than that of sea water (15). When they were evacuated no gas bubbles appeared, and they were not floated to the surface by the increased buoyancy from expanding gas. It is also reported that biting insects, like arthritic patients, can detect the fall of pressure preceding a storm, and flies are said to escape the quick slap of a hand, not by visual but by pressure clues (34). The sensitive spot was believed to be Johnstone's organ in the second joint of the antennae, but this was merely a conjecture without experimental evidence. Similar reports of pressure sensitivity in many species have come from Haufe (19), in mosquitoes, and from Knight-Jones and Qasim (24) and Baylor and Smith (1), in plankton organisms. Mother Nature still has her secrets and should not be underrated.

I must leave this subject in a most unsatisfactory state, but that is the way the problem stands at present. We are not yet in a position to rule out hydrostatic pressure as a possible factor of some minor importance in the deepest dives. I have also provided a very inadequate review of the vast literature on the effects of pressure. For a more complete review I can refer you to Cattell (6) for the earlier literature, and the book by Johnson, Eyring and Polissar (22) for the more recent literature, including their especially valuable contributions to the physicochemical aspects of the subject. There is also an interesting article by Marsland (27) in the Scientific American. Hydrostatic pressure may or may not be a potential hazard to deep diving, but it is certainly a useful tool for biologists in improving their understanding of vital processes.

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Influences of High Pressures of Inert Gases upon Cell Activity

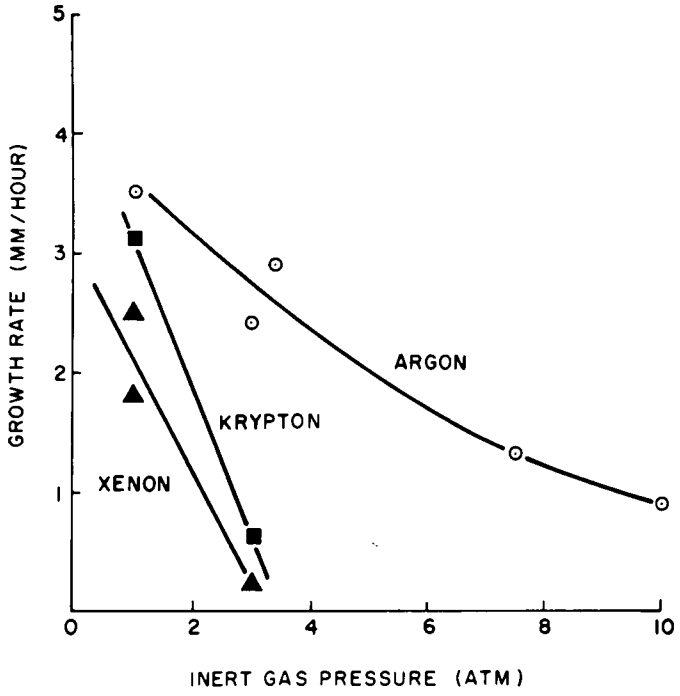
Certain gas molecules can be introduced into biological systems without becoming metabolically altered. These "inert" gases include the noble gases (helium, neon, argon, krypton, xenon), many hydrocarbons and halogenated hydrocarbons, nitrous oxide, sulfurhexafluoride, and for most organisms, nitrogen and hydrogen. It has been well recognized, however, that most of these gases, especially at elevated partial pressures produce narcosis in higher animals and decreased response to stimuli in isolated nerve tissue (17). Recent work by Gottlieb and Weatherly (7) demonstrated also that krypton, xenon, and nitrous oxide caused an inhibitory effect on ability of gastrocnemius muscle to produce tension.

While it has appeared likely that such physiological effects need have a cellular, subcellular, or molecular basis, only within recent years has evidence demonstrated clearly defined biological effects of inert gases in relatively simple systems.

This paper describes the experimental observations of inert gas effects that have been made on cellular and molecular systems and relates these to current understanding of cell structure and function. Several working hypotheses have emerged which may now be pursued toward a unified interpretation of the molecular basis of inert gas behavior in living systems.

Cellular Level Effects

Using a filamentous fungus, *Neurospora crassa*, Schreiner *et al.* (20) observed a dependence of linear growth rate on the nature of the diluent inert gas in environments containing 0.95 atm. "inert gas" and 0.05 atm. oxygen. These observations were extended to include partial pressures of nitrogen and the noble gases up to 120 atm. (2). Data are shown in Figure 128a and 128b. For the noble gases, partial pressures required for 50% inhibition of growth were: Xe (0.8 atm.), Kr (1.6 atm.), Ar (3.8 atm.), Ne (35 atm.), and He (~300 atm.).



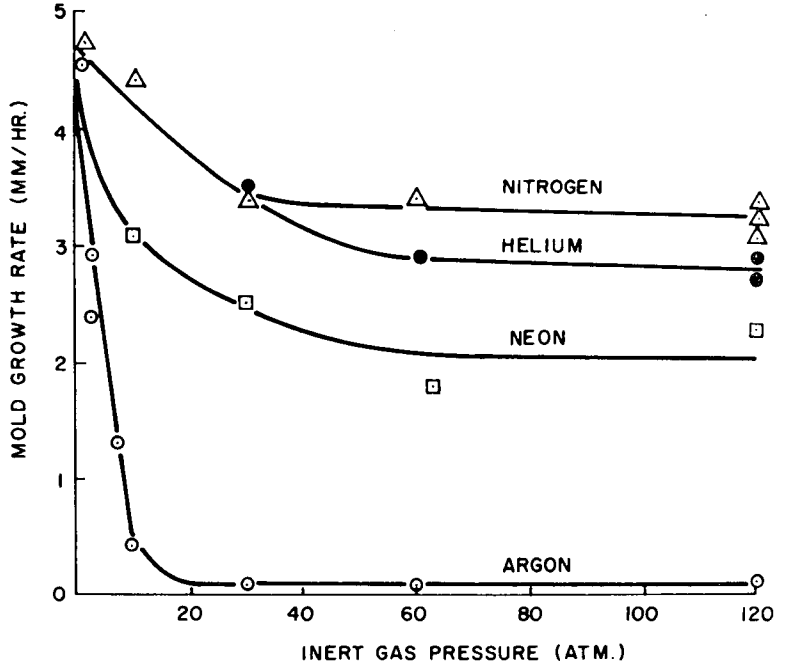


FIG. 128a and 128b. Effects of increased partial pressures of inert gases on growth of *Neurospora crassa*, (from J. Bact. *91:* 622, 1966).

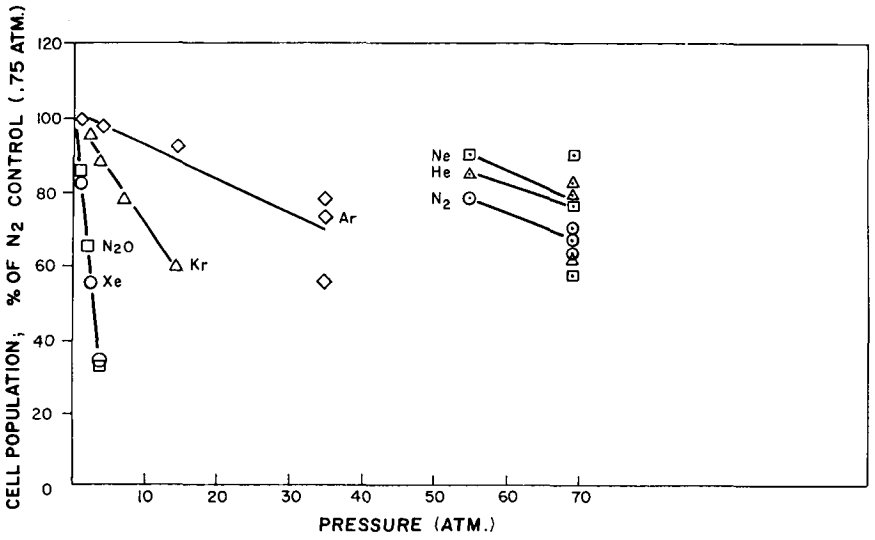


FIG. 129. Effects of increased partial pressures of inert gases on growth of HeLa cells.

The logarithms of these pressures are linearly related to the logarithms of polarizabilities and the ionization potentials of the gases, both parameters that govern weak interaction forces (i.e. electrostatic, dispersion and induction forces).

These studies have been extended to include a study of growth of monolayer cultures of HeLa cells under various partial pressures of inert gases (1). Data in terms of percentage of growth of controls at 1 atm. in a N_2 system (containing 0.2 atm. O_2 and 0.05 atm. CO_2) are shown in Figure 129. Until recently experimental facilities did not allow study of cell cultures at pressures above 70 atm. where one may reasonably expect N_2, Ne, and He to be more clearly distinguished in their relative effectiveness. Argon, krypton and xenon were markedly inhibitory in increasing order of effectiveness. Nitrous oxide was as inhibitory as xenon; this has also been found with *Neurospora*. With HeLa, growth with various gases at various pressures correlated well with lipid solubility but not water solubility.

Inhibition by xenon of both HeLa and *Neurospora* appears to be completely reversible unless (in the case of HeLa) the inhibited condition is allowed to prevail for extended periods of time.

Subcellular Effects

Looking beyond phenomena associated with the whole cell we have measured under phase contrast microscopy the rate of movement of subcellular inclusions in growing hyphae of *Neurospora* (21). This gives a meas-

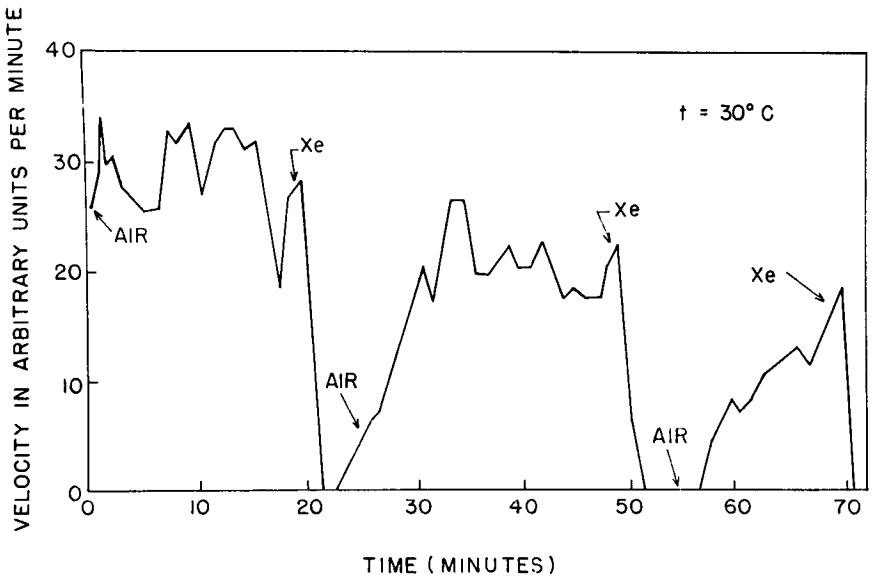


FIG. 130. Inhibition of protoplasmic streaming in *Neurospora crassa* by xenon, 80% xenon-20% oxygen.

ure which is assumed related to protoplasmic or tidal streaming. At 1 atm. (0.8 atm. inert gas-0.2 atm. oxygen) streaming is rapidly and reversibly inhibited by xenon, krypton and nitrous oxide but not by helium or nitrogen (the latter serving as a control). Some representative results obtained with xenon are shown in Figure 130. Kavanau (8, 10) has interpreted protoplasmic streaming as an intracellular membrane dependent process of mass exchange.

Isolated mitochondria should afford an extremely interesting subcellular system for studying the effects of inert gases. Levy and Featherstone (12) reported the absence of inert gas effects on oxidative phosphorylation in mitochondria. Examination of the rates of swelling of rat liver mitochondria, anaerobically and aerobically, in xenon and helium atmospheres at 1 atm. pressure has shown no differences between the gases.

Kavanau (9, 10) has formulated a very interesting model of intramembrane dynamics which allows interpretation of a variety of cellular and subcellular phenomena including impulse transmission, streaming, active and facilitated transport, locomotion, and amoeboid movement. This model required dynamic reversible changes to take place in the micellular ultrastructure of cytoplasmic and intracellular membranes. One can readily envisage the inhibition of these dynamic intramembrane transformations by inert gas molecules.

Molecular Level Effects

Many of the inert gases form solid hydrates whose structures and properties have now been well studied (15, 26, 27). In addition clathrates are formed by various phenols and quinones with inert gases. Biological conditions of temperature and pressure are in all cases reasonably far and in most cases extremely far from those under which hydrates and clathrates are stable. This does not preclude the existence of some hydrate or clathrate-type structuring in solutions under physiological conditions. Frank and Evans (6) first proposed on thermodynamic grounds the increased ordering of water molecules by nonpolar solutes and Pauling (14) and Miller (11) have evoked hydrate "microcrystals" or hydrate-like ordering by inert gases and other narcotics to explain a molecular basis for anesthesia.

In collaboration with Dr. George Safford we have investigated the structure of liquid water and ice in the presence of xenon using neutron inelastic scattering spectroscopy (18). Intermolecular interactions involving hindered translations and rotations of water molecules (900 $cm.^{-1}$ to 8 $cm.^{-1}$) are observed. Spectra of xenon-water show, in addition to frequencies found for pure water, the presence of new structure involving hydrogen-bonded water molecules at temperatures and pressures at which xenon hydrate is not expected to be stable but at which biological effects occur. Indeed the structure persists to very low and high temperatures. These findings mean that inert gas-water structuring must be taken into account under biological conditions but do not support directly the hydrate theory of Pauling and Miller.

Mortimer and Bauer (13) demonstrated an affinity of various heme proteins for gaseous nitrogen, hydrogen and argon and interpreted the interaction as due to electrostatic (ion-induced dipole) and dispersion forces. Featherstone *et al.* (5) found solubility evidence for the association of xenon with specific proteins, especially hemoglobin. Previously Featherstone had shown a correlation between relative pressures of inert gases for narcosis and molecular polarizabilities. It was assumed therefore that xenon-protein interactions could be ascribed to dispersion forces.

Schoenborn, et al. (22) have observed increased hydration in solution of hemoglobin in the presence of xenon. Xenon association with hemoglobin was thereby strongly indicated. More recent studies by x-ray diffraction of electron density have located the xenon at specific defined sites in both myoglobin and hemoglobin (23, 24).

We have been able to demonstrate that some defined enzyme systems respond to increased partial pressures of nitrogen, noble gases, and nitrous oxide. Thus tyrosinase, which catalyses the addition of molecular oxygen to phenols such as tyrosine, is inhibited by all inert gases examined (Table 54) (19). The order of effectiveness of the different gases is not as clearly recog-

TABLE 54

Activity of Tyrosinase in the Presence of Increased Pressures of Inert Gases

Gas	No. of Observations	Partial Pressure (atm.)	Enzyme Activity*
Air	12	1	39 ± 3
Helium	5	31	33 ± 4
Neon	7	31	27 ± 4
Argon	5	31	27 ± 4
Nitrogen	5	31	23 ± 4
Air	22	1	54 ± 6
Helium	3	31	46 ± 0
Krypton	6	20	45 ± 4
Xenon	6	2	40 ± 2

* Enzyme activity units ΔO.D. $\times$ min^{-1} $\times$ 1000 for optical path of 3.3 cm.

nized as with cell growth, but N_2O and Xe appear much more active than Ne, Ar, and N_2 which in turn are more active than He. Similar inhibitory effects have been found with lipoxidase, which catalyses the reaction between unsaturated fatty acids and molecular oxygen. With acetylcholinesterase, a hydrolytic enzyme, however, only N_2O inhibited significantly at pressures up to 30 atm. Other enzymes and pressures to 130 atm. are currently under study, in our laboratory.

Clements and Wilson (3) measured the effects of various inert gases on interfacial tension of protein, lipid, and lipoprotein films spread on water. Film pressure increases caused by some eleven gases differing in narcotic activity by over 500-fold were used to calculate partial pressures required for equivalent tension changes. These pressures were linearly related to partial pressures for equivalent narcotic effects in mice. It would appear that inert gases act to expand the film, to replace interfacial water, or to reduce the energy of the interface by interaction between gas and water in the film. Processes determined by membrane bound enzymes (i.e. respiration) or membrane structure (i.e. membrane permeability, excitability, etc.) could thus be altered.

In the case of the inert noble gases correlation between biological effectiveness and ionization potentials suggests another mechanism of intermolecular interaction, that of charge-transfer (Table 55). This type of interaction has been well studied in the case of biological molecules other than inert gases (16, 25) and appears likely to have far reaching biological significance. Inert gases of low ionization potential should act as charge-transfer donors in undergoing complex formation with acceptor molecules of high electron affinity or quantum mechanically low lying empty molecular orbitals. Considerations of this acceptor property (16) at once suggests various quinones

TABLE 55

Polarizabilities and Ionization Potentials for the Noble Gases (4)

Noble Gas	α,A^3	I.P., e.v.
Helium	0.204	24.59
Neon	0.392	21.56
Argon	1.63	15.76
Krypton	2.46	13.99
Xenon	4.01	12.13

(i.e. indole-5,6-quinone, a unit of melanin), biliverdin, certain polyenes (i.e. cartenoid precursors) and oxidized form of nicotin-amide adenine dinucleotide and riboflavin phosphate among others. Since change-transfer complexes afford sharp electronic spectra we have initiated a visible-ultraviolet spectroscopy study of model compound (acceptor)-noble gas (donor) systems.

In summary we must conclude that observable biological effects of metabolically inert gases extend through all levels of organization from molecular systems to intact higher organisms. Definite intermolecular interaction occur under biological conditions of temperature and pressure, between inert gases and water and certain biopolymers. These interactions may so inhibit the dynamic transformations which appear to occur within membranes as to manifest themselves as the observed inhibitions of physiological functions which would be dependent upon membrane dynamics. In addition, other possible types of intermolecular interactions (i.e. charge-transfer) may play a role in more specific biochemical situations.

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Decompression Sickness in Experimental Animals

Controlled studies of decompression sickness in experimental animals frequently have been hampered by a lack of techniques which produce a syndrome containing all of the gradations of severity which occur in human subjects. Consequently, much work has been done utilizing explosive decompression as the challenge, and death as the endpoint. Obviously, this experimental situation does not parallel precisely the conditions which are experienced by divers, aviators and caisson workers. In 1962, Berry and Smith (1) reported that two aviators became incapacitated with bends while they were flying a T33 trainer. The cabin altitude of the aircraft was about 8,000 feet, but these men had been SCUBA diving shortly before take-off and their body tissues must have been supersaturated with inert gas. This report led to the development of a technique which produces a high incidence of decompression sickness in rats and which also permits the observer to grade the rats according to the severity of their attack.

The technique has been described amply in the literature (2–5). Briefly, it is as follows: rats are exposed for two hours to a pressure of 5.4 atmospheres absolute in a well-ventilated chamber containing baralyme as a carbon dioxide absorbent. The pressure is then halved in three stages with a five-minute stop at each stage (Table 56). The total decompression time is about 17 minutes. Rats which are decompressed in this manner do not display any signs of decompression sickness at atmospheric pressure, even though their tissues are saturated with nitrogen (3). The rats next are placed in a ventilated and temperature-controlled altitude chamber and rapidly decompressed to a simulated altitude of 10,000 feet, where they are kept for 30 minutes. During this exposure to altitude the rats are exercising constantly in a motor-driven treadmill which forces them to walk at the slow rate of about 10 feet per minute. With this moderate enforced exercise any disturbance of gait, whether caused by muscle and joint pain or the formation of bubbles in the nerves and spinal cord, immediately becomes evident. Several degrees of severity of the bends have been recorded, ranging from minor transient ataxia, through stiffness

TABLE 56

Stage-Decompression

65 psig*	for 120 minutes
65 to 32 psig	in 30 seconds
32 psig	for 5 minutes
32 to 16 psig	in 30 seconds
16 psig	for 5 minutes
16 to 8 psig	in 10 seconds
8 psig	for 5 minutes
8 psig to sea level	in 5 seconds

* psig = pounds per square inch, gauge.

TABLE 57

Score System for Indicating Severity of Signs and Symptoms of Decompression Sickness

Score	Description
0	No visible signs
1	Indefinite and transient disturbances of gait
2	Stiffness of hind legs
3	Dragging of hind limbs
4	Complete paresis of hind quarters, rat could use only the front limbs
5	Complete paresis
6	Death

of the hind limbs and posterior paresis, to complete paresis and death (Table 57). This technique not only makes possible the detection of some of the more subtle manifestations of decompression sickness but also permits the administration of drugs at a time when the animals are "at risk" but before the signs of the bends develop.

Body Composition and Susceptibility to Decompression Sickness

Paul Bert was undoubtedly the first investigator to note that thin animals survive rapid decompression much better than fat ones. Subsequent experimental observations by Boycott and Damant (6), Behnke (7) and many others have emphasized the importance of body fat as a reservoir of stored nitrogen for the formation of bubbles.

The initial experiments also showed that older and fatter rats were more susceptible to the bends. In Table 58 the incidence and severity of the bends in a group of 65 rats with a mean weight of 299.0 gm. are compared to those of a much heavier group of 34 rats having a mean weight of 451.9 gm. In the light group, 52% showed signs of decompression sickness and 20% died. In the heavy group, 86% had symptoms and 50% died. These differences were highly significant ($p < 0.01$). In this and some other tables percentages are used for ease of comparison, but statistical analyses

TABLE 58

The Incidence and Severity of Bends in Heavy (Old) Rats and Lighter (Younger) Rats

Group	Number	Mean Weight (gm.)	% Incidence and Severity of Bends				χ^2
			None	Mild	Marked	Death	
Controls	67	348.9	100				
Light	65	299.0	48	22	10	20	$p < 0.01$
Heavy	34	451.9	14	18	18	50	

TABLE 59

Relation between Body Fat and Susceptibility to the Bends

Group	Number	Mean Starting Weight (gm.)	Mean Final Weight (gm. ± SEM)	Fat as % Total Weight	% Incidence and Severity of Bends				χ^2
					None	Mild	Marked	Death	
A	7	295.5	171.3 ± 4.30	1.92	100				$p < 0.02$
B	11	291.4	286.6 ± 6.30	5.18	36	64			$p < 0.046$
C	8	290.5	331.4 ± 9.45	8.42		63	37		
D	11	291.8	364.5 ± 9.40	10.76	9	45	37	9	
E	11	292.7	379.6 ± 6.10	15.11		64	27	9	

in all cases were done using the actual numbers. Control rats, not previously compressed, displayed none of the signs which were observed in the stage-decompressed groups.

A similar experiment was designed to separate the factor of body fat from the factors of age and sex. Fifty-five male white rats, all born on the same day, were divided into five groups of 11 and each group was fed a special diet, containing one to five calories per gram of food, for a period of six weeks. At the end of this time the rats were subjected to the standard experimental conditions of compression followed by stage-decompression and exercise at altitude. After this, two rats from each group were killed by a blow on the skull and the carcasses were vacuum-dried, minced, and analyzed for fat content by acetone-ether extraction. The results are shown in Table 59. There was a good correlation between the fat content of the

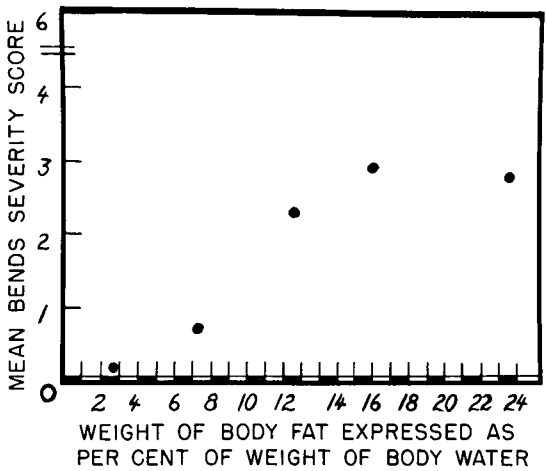

FIG. 131. Relation of fat:water ratio to bends. The fat, expressed as a percentage of body-water, of six groups of rats of the same age but different weights is plotted against the average bends-score of each group.

groups and the incidence and severity of the bends. The rats in group A, which had only 1.9% fat, were emaciated and in poor condition, but not one got decompression sickness. In group B (5.18% fat) none were seriously affected. The only deaths occurred in groups D and E which had the most body fat (10.76% and 15.11% respectively).

Pace and Rathbun (8) recommended that body fat should be related to total body water because the latter is independent of fat and is a more constant value. Consequently, the mean fat content of each group was expressed as a percentage of the mean total body water content for the group and plotted against the group's mean bends-score (Fig. 131). There appeared to be a critical fat-water ratio beyond which susceptibility rose markedly.

Because total body water is related to the volume of blood and interstitial fluid and because these are involved in the transport of nitrogen to the lungs for elimination, the larger the fat reservoir in relation to total body water the greater the risk of bubble formation and bends. It would thus seem reasonable to postulate that dehydration might also increase susceptibility by increasing the fat-water ratio.

To test this hypothesis, 24 male white rats were weighed accurately, injected intraperitoneally with the diuretic mercurhydrin (7.0 mg./kg.) and deprived of water for 24 hours. Feces and urine were collected from each rat, weighed and the weight subtracted from the weight loss of the rat to yield an approximation of the water loss during the 24-hour period. The rats were then compressed, stage-decompressed and exercised at altitude.

The bends-score of the dehydrated group was compared to that of a similar group of control rats. The results are shown in Table 60. Seventy-one per cent of the dehydrated rats were severely affected (Stages 3–6) and 37 % died (Stage 6). In the control group, 55 % were severely affected and 25 % died. These differences were not statistically significant but when the mean weight loss (40.5 gm. ± 2.77 SEM) of the *dehydrated rats which died* was compared to that of *those which survived* (29.0 gm. ± 4.16 SEM), it was significantly greater ($p = 0.02$). Taken together, these results indicate a trend toward an increase in susceptibility in the dehydrated rats.

A more thorough study of the effects of dehydration was then undertaken. Eighteen male white rats with a mean weight of 575.8 gm. were deprived of water for 96 hours and then tested for their bends-susceptibility. The results were compared to those obtained from two groups of control rats, one having a mean weight not significantly different from the *original* weight of the water-deprived group, the other having a mean weight not significantly different from the *final* weight of the water-deprived group. After being scored for the bends, six rats from each group were destroyed (if not already dead from decompression sickness) and analyzed for fat and water content. The results are shown in Table 61. There was no significant difference in the incidence or mortality rate between any of the groups. All the rats were old and heavy and therefore very susceptible. The dehydrated rats which died at altitude, however, did so in significantly less time (3.2 minutes ± 1.23) than either those of the heavy control group (7.3 minutes ± 1.30, $p = 0.03$) or the light control group (10.3 minutes ± 2.31, $p < 0.02$).

The body compositions of the three groups are compared in Figure 132. When compared to the heavy controls (HC) which paralleled the original composition of the water-deprived rats, the dehydrated group lost a considerable amount of body water and also some fat and protein (L.D.M.). These latter losses can be explained by the fact that deprivation of water was accompanied by complete anorexia during the 96-hour period. A casual comparison of the dehydrated group (D) and the light controls (LC) reveals little difference in their body composition. In order to demonstrate such a difference it was necessary to relate each body compartment to the others. No differences in fat content between any of the groups could be demonstrated regardless of whether fat was expressed as a percentage of body weight, a fraction of body-water (the upper decimals in the bar graph) or a fraction of the lean dry mass. When body-water was expressed as a ratio of the L.D.M. (the lower numbers in the bar graph), however, the dehydrated group had significantly less water than either the heavy controls ($p < 0.01$) or the light controls ($p < 0.001$).

The body composition of the rats which died at altitude was compared

TABLE 60

Fluid Loss and Incidence and Severity of Bends of Rats Injected with Mercurhydrin (7 mg/kg) and Deprived of Water for 24 Hrs.

Group	*N*	Mean Normal Weight (gm. ± SEM)	Mean Weight Loss (gm. ± SEM)	Mean Weight of Feces Excreted (gm. ± SEM)	Mean Fluid Loss	Bends-Score (No. Rats in Each Stage)						
						0	1	2	3	4	5	6
Dehydrated	24	430.8 ± 16.20	37.1 ± 2.50	4.12 ± 0.247	33.0	—	4	3	7	—	1	9
Control	20	422.3 ± 15.17	—			1	1	7	2	3	1	5

TABLE 61

The Effects of Dehydration on the Incidence and Severity of Decompression Sickness in Rats

Group	*N*	Mean Weight (gm. ± SEM)	*p*	% Incidence and Severity of Bends			*p*	Min to Death ± SEM	*p*
				None (0, 1)	Mild (2, 3)	Marked (4, 5, 6)			
Heavy controls	18	588.4 ± 13.45	n.s.*		6	94	n.s.	7.3 ± 1.30	0.03
		Before 575.8 ± 17.08							
Dehydrated	18	After 487.0 ± 8.63	<0.001		22	78		3.2 ± 1.23	
			n.s.				n.s.		<0.02
Light controls	12	474.9 ± 7.19		17	8	75		10.3 ± 2.31	

* Not significant.

with that of those rats which survived. Figure 133 shows that the rats which died had significantly ($p < 0.001$) more fat and somewhat less water than those which lived.

The survival times of the rats which died at altitude (and which were analyzed for fat and water content) were correlated with body composition expressed in a number of different ways. The results are shown in Table 62.

There was no significant correlation between survival time and body fat expressed as a percentage either of *body weight* or of L.D.M. In any combination in which body water was the predominant correlate for body composition, however, a good (and highly significant) correlation *was* obtained. When fat was expressed as a percentage of *body water*, r was -0.64 ($p = 0.025$); with body water alone r was $+0.74$ ($p < 0.01$). In

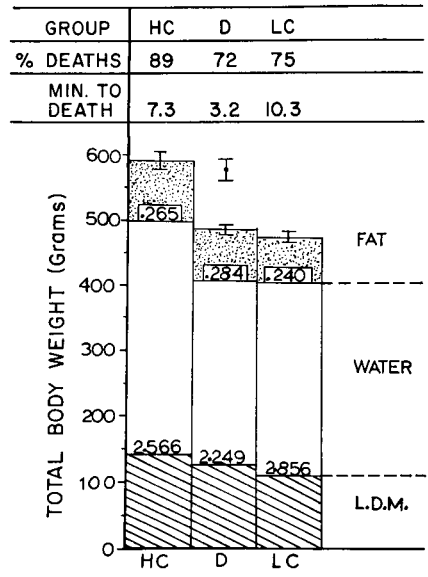

FIG. 132. The body composition of a group of dehydrated rats (D) is compared to that of a group of controls (HC) having a mean weight not significantly different from the *original* weight of the dehydrated group and another control group (LC) having a mean weight not significantly different from the *final* weight of the test group (D) after dehydration. The mortality rates from the bends, and the mean survival times of each group are shown at the top of the graph.

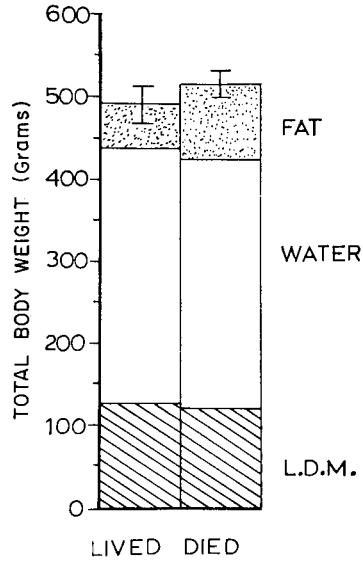

FIG. 133. The body composition of dehydrated rats which died of the bends is compared to that of the dehydrated rats which survived.

TABLE 62

Correlation between the Survival Time of Rats which Died at Altitude and Their Body Composition Expressed in Different Ways

	r	SE_r	p
1. Body fat as % lean dry mass	−0.36	±0.295	0.3
2. Body fat as % body weight	−0.55	±0.265	>0.05
3. Body fat as % body water	−0.64	±0.243	0.025
4. Body water as % body weight	+0.74	±0.214	<0.01
5. % excess fat = $100 - \frac{\%\text{ body water}}{0.732}$	−0.76	±0.205	<0.005

the last set of figures survival time was correlated with body composition using a formula devised by Pitts (9) based upon the observations of Pace and Rathbun that laboratory animals have an average water content which is 73.2 % of the lean body mass (total weight minus fat). This formula (% "excess fat" = 100 − % body water/.732) relates each individual to a standard obtained from a very large sample and magnifies any deviation of the fat from normal body composition. When this formula was used, it yielded the highest ($r = -0.76$) and most significant ($p < 0.005$) correlation between survival time and body composition.

These results not only confirm once again that body fat is by far the most important feature of body composition in determining an individual's susceptibility to the bends, but they also indicate that dehydration can increase susceptibility. On the basis of these observations, it would seem that the measurement of whole-body specific gravity is the best practical guide to body composition, at least in the normal individual, because it is dependent upon all of the body compartments. In the dehydrated subject, however, it may be misleading. In comparing the dehydrated rats (D) with the light controls (LC) in Figure 132, it will be seen that the dehydrated rats had slightly more fat and slightly more lean dry mass. These two increases would yield a specific gravity very close to that of the light controls, even though their body compositions can be shown by analysis to be quite different.

The Pharmacological Treatment of Experimentally-Induced Bends

There have been many reports of pharmacological agents relieving or preventing decompression sickness under experimental conditions. Narcotics (10), autonomic depressants (11), surfactant agents (12) and anticoagulants (13), have been shown to be beneficial in the experimental situation, but clinical experience has not usually supported these observations. Recently, however, Barthélémy (14) reported the successful treatment with heparin of bends in divers.

The protective effect of heparin was studied under our standard experimental conditions. Because heparin has two important actions, i.e. anticoagulant effect and lipemia-clearing activity, two other agents were studied also; bishydroxycoumarin, an anticoagulant without lipemia-clearing activity, and partially-depolymerized hyaluronic acid (PDHA), a substance which has been reported to be a lipemia-clearing agent but which is not an anticoagulant (4, 15–17).

Heparin (1–3 mg./kg.) or PDHA (50 mg./kg.) was injected intraperitoneally into older, heavy male rats (450 gm.) and the results were compared (Table 63) to those obtained with similar, saline-injected rats, some of which were included in each experimental group. There was no significant improvement in the incidence or severity of the bends. This was true both when the agents were injected before the two-hour compression and when they were injected after stage-decompression but before the ascent to altitude.

In another experiment younger, lighter (350 gm.) rats were used and the injections were made after stage-decompression (before the ascent to altitude). The results are shown in Table 64. Again each group contained some rats which received a drug and some which were injected with saline. Four groups of rats were given heparin intraperitoneally in doses of 0.5, 1.0, 1.5 or 3.0 mg./kg. In all of the groups which were injected with heparin fewer rats got the bends (the differences were statistically significant in three of the four groups) and fewer rats were severely affected (the differences being statistically significant in two of the four) than in the saline-injected control groups.

Three groups of rats of similar weights received PDHA in doses of 2, 10 or 50 mg./kg. (Table 64). When the results were compared to the control group there were no significant differences in either the incidence or severity in the group which was given PDHA at 2 mg./kg. In higher doses (10 or 50 mg./kg.) however, PDHA markedly reduced both incidence and severity and the differences were highly significant. Although heparin was effective at a lower dose level than PDHA, increasing the dose of heparin did not lead to a further reduction of incidence or severity, whereas higher doses of PDHA yielded a greater and more significant reduction of both.

The di-sodium salt of bishydroxycoumarin (5.0 mg./kg.) was injected intraperitoneally into rats weighing about 400 gm. immediately after stage-decompression. This dose, which produced a moderate but significant prolongation of the prothrombin time within 15 min. of the injection, did not alter significantly either the incidence or the severity of the bends when the results were compared to a similar group of saline-injected rats (Table 65A). Nor did 20.0 mg./kg. of bishydroxycoumarin, given 13 hours before the experiment, change the incidence or severity even though the pro-

TABLE 63

Heparin and PDHA Given to Heavy Rats before Compression or after Stage-Decompression

Injection	*N*	Mean Weight (gm. ± SEM)	% Incidence and Severity of Bends			χ^2 Compared with Controls
			None (0, 1)	Mild (2, 3)	Severe (4, 5, 6)	
Normal saline (Controls)	50	435.3 ± 22.75	20	28	52	
Heparin 1–3 mg/kg						
Administered before compression	20	453.4 ± 9.30	10	30	60	n.s.
Administered after decompression	18	426.6 ± 9.00	22	11	67	n.s.
PDHA 50 mg/kg						
Administered before compression	26	473.8 ± 12.08	31	27	42	n.s.
Administered after decompression	18	439.3 ± 12.79	28	17	55	n.s.

TABLE 64

Heparin and PDHA Given to 350 gm. Rats after Stage Decompression

Injection	*N*	Mean Weight (gm. ± SEM)	% Incidence and Severity of Bends			χ^2 Compared to Controls	
			None (0, 1)	Mild (2, 3)	Marked (4, 5, 6)	Incidence (0, 1)	Severity (4, 5, 6)
						p	*p*
Normal saline (Control)	72	348.8 ± 2.66	38	24	38		
Heparin (mg/kg)							
0.5	20	367.9 ± 5.45	60	35	5	n.s.	<0.02
1.0	25	350.7 ± 3.49	64	24	12	<0.05	<0.05
1.5	29	342.5 ± 5.00	62	7	31	0.03	n.s.
3.0	25	340.6 ± 5.30	60	16	24	0.05	n.s.
PDHA (mg/kg)							
2.0	22	348.6 ± 2.52	37	27	36	n.s.	n.s.
10.0	30	356.2 ± 3.81	80	13	7	<0.01	<0.01
50.0	34	358.3 ± 3.37	82	15	3	<0.001	<0.001

thrombin time was 5 times the normal level at the time of stage-decompression.

Our results indicate that these protective effects of heparin and PDHA are much less closely related to anticoagulant activity than to some other property because first, PDHA did not produce significant anticoagulation

TABLE 65

Bishydroxycoumarin Given to Moderately Heavy Rats (±400 gm) before and after Stage-Decompression

Table 65A

Injection	*N*	Gp. Mean Weight (gm. ± SEM)	Incidence and Severity of Bends							χ^2 with Saline-Injected Controls
			0	1	2	3	4	5	6	
Normal saline	18	400.6 ± 5.49	—	3	8	4	—	—	3	
5.0 mg/kg after compression	18	402.0 ± 5.40	—	2	11	4	—	—	1	n.s.
20.0 mg/kg 13 hr. before compression	18	384.4 ± 6.96	—	2	9	7	—	—	—	n.s.

Table 65B

Injection	*N*	Prothrombin Time (sec.)	*p*	
Controls	10	16.75 ± 0.578		
15 min. after bishydroxycoumarin (I.P. 5.0 mg/kg)	12	26.34 ± 2.934	<0.01	<0.001
13 hr. after bishydroxycoumarin (I.P. 20.0 mg/kg)	11	82.20 ± 7.058		

TABLE 66

Whole-Blood Clotting Times in Anesthetized Rats

Injection (I.P.)	Time after Injection (min)	*N*	Clotting Time (sec ± SEM)	Degree of Prolongation	*t*-Test with Saline-Injected Controls
Saline 1.0 ml	15	27	98.5 ± 6.20		
Heparin 0.5 mg/kg	15	15	149.7 ± 12.27	1.5 × normal	$p < 0.001$
Heparin 0.5 mg/kg	45	15	88.3 ± 5.40	—	n.s.
Heparin 1.0 mg/kg	30	16	140.3 ± 12.75	1.4 × normal	$p < 0.01$
Heparin 3.0 mg/kg	30–45	21	271.6 ± 48.35	2.7 × normal	$p = 0.001$
PDHA 10.0 mg/kg	15–30	18	103.0 ± 11.35	—	n.s.

(Table 66) at a dose which markedly lowered the incidence and severity of the bends, and second, bishydroxycoumarin did not give protection against the bends when it was given at a dose which greatly prolonged the prothrombin time.

It is possible that the protective property of these substances may be

related to the lipemia-clearing activity which they both possess. The formation of a lipoprotein layer on a gas bubble was discussed by Harvey et al. (18) who felt that the resulting increase in surface tension would inhibit bubble growth. Malette (12), on the other hand, postulated that the formation of such a film would produce a more rigid structure, less able to conform to the configuration of the vascular bed and thus more liable to cause a stoppage of the circulation. Other workers (19) have expressed the view that fat embolism might be important in the etiology of decompression sickness and Stutman (20), on the basis of experiments with lipemic dogs, speculated that individuals with a tendency to be hyperlipemic might be potential victims of decompression sickness, especially after a high fat meal.

The further possibility that the protective properties of heparin and PDHA may be related to sludging of the blood as described by Behnke (21) cannot be dismissed.

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35 | E. B. SMITH

Decompression Experiments with Various Inert Gases

An important factor which can be varied in decompression experiments, the nature of the inert gas diluent, has received less than its proper share of attention. By experimenting with a wide variety of gases it is possible, in principle, to obtain important information concerning the mechanism of decompression sickness.

Fully fluorinated gaseous compounds are of particular interest since their properties are anomalous, due to their comparatively weak intermolecular forces. Their solubilities in water are among the lowest recorded, but in non-polar solvents, though they exhibit large positive deviations from ideality, their solubilities are more normal. This unusual behaviour is illustrated in Table 67. In proceeding from one gas to another, changes in the water solubility are normally reflected by a comparable change in fat solubility but this is not the case for fluorine compounds. These anomalous properties have been utilised in an attempt to define the site of action of general anesthetics. It was found that the anesthetic pressures of fluorine compounds were consistent with the predictions of the lipid solubility theory but inconsistent with those of the hydrate theory (1, 2), whereas the data for other gases did not provide a satisfactory means of discriminating between the two theories. Similar considerations can be applied to the problem of decompression sickness.

The Experiments

The decompression experiments which have been performed on mice involved firstly the direct observation of intra-vascular bubbles in exposures which allowed visualization of arterial and venous networks, down to vessels of about 0.05 mm in diameter. The exposures which have proved convenient are a reflected flap of thoracic and abdominal skin, the mesentry, and the femoral arteries and veins. Secondly, detailed post-mortem examinations of the animals were performed to ascertain the final distribution of bubbles. Thirdly, a study is in progress to investigate quantitatively, as a function of exposure times, the maximum pressures of various

gases from which mice may be rapidly decompressed without hazard. This last aspect of the investigations may shed light on the nature of the phases in which the gases that produce decompression sickness dissolve. Experiments with SF_6 suggest that the tendency of gases to cause decompression sickness is more closely related to their total body solubility or to fat solubility than to their solubility in the aqueous phases of the body (Table 68). Study of the rate of uptake of fluorine compounds will provide a severe test of existing theories of gas uptake. Perfusion limited models predict that, because of their low water solubility and relatively large fat solubility, their uptake will be very slow. Thus for SF_6 the half-saturation time for man is estimated to be 20 hours on the Kety-Mapleson (3) model.

The Arterial Paradox (4)

We have made motion pictures of the manner of appearance of bubbles in the blood vessels, as in a skin flap of a mouse. In a typical case the

TABLE 67

Properties of Inert Gases

Gas	Solubility Ostwald Coefficient 37° C		Diffusion Coefficients $\times 10^5$ (cm^2/sec) in Carbon Tetrachloride 25° C
	Water	Olive Oil	
He	0.0095	0.017	20
Ne	0.0109	0.022	6.3
H_2	0.0190	0.057	9.8
CF_4	0.0043	0.072	2.0
N_2	0.0141	0.076	3.5
Ar	0.0293	0.150	3.6
SF_6	0.0045	0.260	1.71
Kr	0.0492	0.49	—
N_2O	0.47	1.6	—

TABLE 68

Comparison of Rank Order of Inert Gases

	Low				High
Decompression sickness ($1/P_\infty$ for mice)	He	N_2	Ar	SF_6	N_2O
Water solubility	SF_6	He	N_2	Ar	N_2O
Fat solubility	He	N_2	Ar	SF_6	N_2O
Total body solubility	He	N_2	Ar	SF_6	N_2O

P_∞ is the maximum pressure from which a rapid decompression to atmospheric pressure is possible without hazard after long exposure.

animal, anesthetized with pentobarbitone, was exposed to a pressure of 10 atm. (gauge) of a 90% N_2-10% O_2 mixture for 30 minutes and then rapidly decompressed. The first bubbles were observed some 4 minutes after decompression moving distally in the main artery, followed by a column of gas which progressed into the smaller arterial branches. About half a minute after the appearance of gas in the arteries bubbles appeared in a small venous branch, moving centrally. Some two minutes later the larger venous channels and some smaller veins were filled with air. The arterial tree was by this time completely gas filled.

Similar results were obtained when the mesenteric vessels and femoral vessels were observed. The sequence of events appears to be relatively independent of the rate of decompression and of the oxygen partial pressure. Decompression in oxy-argon and oxy-helium mixtures gives rise to the same effects. The large quantity of gas in the arteries is paradoxical since the rapidly desaturating arterial blood would be expected to be the area least liable to bubble formation except at the moment of decompression.

Three general explanations can be considered: 1) Gas may be forced into the arteries from the lungs, a possibility which can be ruled improbable on three counts. First, the lungs on removal from a dead animal showed no sign of damage and could be inflated without subsequent collapse. Second, very rapid decompressions (less than 4 seconds) produced no ill-effects in mice exposed to 10 atm. for only 1½ minutes. Thirdly, the pulmonary vein and left auricle were almost invariably free of bubbles in striking contrast to the right auricle. The observations that arterial bubbles in the skin sometimes occurred in the absence of mesenteric bubbles rules out gas forced into vessels from the abdominal cavities as the cause of the arterial bubbles.

2) The assumption that the pulmonary capillaries rapidly exchange gas with the atmosphere may not be valid after prolonged exposure to high pressures or after rapid decompression. The absence of anoxia, even when animals survive for many minutes before bubbles appear, makes this explanation difficult to accept.

3) Wagner (5), who observed that arterial bubbles appeared before venous bubbles in the pial vessels of cats, suggested that the first bubbles arose in an unlocated venous area and passed through the lungs into the arterial system. The massive quantity of gas which flows into the arteries and the absence of bubbles in the pulmonary vein are difficult to understand on the basis of this model.

If, however, this last explanation is correct, the body must comprise areas in which the primary (venous) bubbles occur and other areas in which secondary (arterial) bubbles are first observed. In these areas the venous

bubbles behave as if they arose from leaks of arterial gas through arteriovenous anastomoses.

Experiments with Fluorine Compounds

When animals are decompressed after exposure to He, Ar and N_2, the severity of the symptoms is broadly related to the extent of bubble formation observed in post-mortem examination. However, for the fluorine compounds we have studied, CF_4 and SF_6, this does not appear to be true. Mice decompressed after exposure to high pressures of these gases may show symptoms characteristic of decompression sickness but in many cases no bubbles are visible within the animals in post-mortem dissection. (Table 69). Recompression experiments have shown that the symptoms can be alleviated even when it is believed that no visible bubbles are present. This suggests that bubbles, too small to be observed by our techniques, are present in the central nervous system.

It is possible, though the symptoms produced by decompression sickness are not easily differentiated in mice, that two distinct causes of death can occur. First, death due to circulatory collapse due to massive bubble formation in the blood vessels, perhaps analogous to chokes in man, and second, death due to micro-bubbles in the central nervous system. As symptoms arising from both these effects may be present for all gases other than fluorine compounds it is not easy to define uniquely the cause of death. It is hoped that fluorine compounds will allow the investigation of the effects of decompression in the central nervous system without the attendant circulatory disturbances which occur simultaneously in mice when other gases are used.

It is generally observed that the onset of symptoms is most rapid when helium is used and slowest for experiments with SF_6. The growth of bubbles in liquids supersaturated with these gases is being investigated and may shed some light on this point.

TABLE 69

Occurrence of Visible Bubbles in Mice after Rapid Decompression to Atmospheric Pressure

Gas	Initial Pressure Range (atm)	Number of Experiments	Number of Fatal Experiments	Number of Fatal Experiments without Visible Bubbles
He	11–15	25	13	0
N_2	9–11	44	19	0
Ar	5–6	18	5	0
SF_6	3–4	36	22	16
N_2O	1¾–2¼	12	3	0

Conclusions

The use of a variety of gases has proved of some interest when applied to the problem of decompression sickness in mice. In particular the anomalous properties of fluorine compounds are providing a novel means of investigating: (1) the mechanism of uptake of gases into the tissues; (2) the relation between solubilities in various media and decompression sickness; (3) the different roles of intravascular and extravascular bubbles in causing decompression sickness; and (4) factors which influence the rate of onset of the symptoms of decompression sickness.

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36 | R. M. ROSENBAUM and M. WITTNER

Oxygen Toxicity at the Cellular Level: Studies with Cells in Tissue Culture

For several years we have been studying effects of oxygen at atmospheric and hyperatmospheric concentrations on a variety of cell systems. Wherever possible an attempt has been made to utilize results from cellular studies to extend understanding of what occurs in the intact mammal exposed to high concentrations of O_2. By this way we hoped to gain information concerning the pathogenesis of oxygen toxicity in the mammal. The lungs of mammals exposed to oxygen have been of particular interest in this respect. Various investigators (1, 2, 3, 4, 5) have described a variety of pathology but the evidence is now fairly convincing that remarkably little pulmonary damage and minimal pathology can be detected within the mammalian lung attributable to direct exposure to either single atmospheric concentrations of pure oxygen or even to hyperbaric concentrations of the gas (6). This does not mean that changes in lung are not present. Rather special techniques can show these but more significantly, many changes seen in specialized tissue such as lung are also apparent in simple cell systems. While the initial concern was with biochemical data derived from homogenates of whole lungs from oxygen exposed mammals (7, 8), this alone did not suffice to describe possible subtle morphologic effects not detectable by routine methods. Accordingly, study was begun on mammalian cells derived from appropriate tissues and exposed to conditions similar to those employed on intact experimental animals. Following an initial pilot study, the experiments were extended into areas wherein tissue culture techniques would be utilized. While the overall problem has proven to be quite complex, experience to date has shown that a number of questions can be dealt with and it is the purpose of this paper to state some of

these. In addition, the problems involved in their study and some preliminary data will be described.

Use of Tissue Culture Methods

Several technical problems immediately appear when applying hyperatmospheric pressures to cells in tissue culture. Development of a suitable vessel that will simultaneously permit observation of contained material, maintain sterility and withstand the required pressures was the first step to be surmounted. Much of the problem has been solved by using existing tissue culture glassware and placing this completely within the pressure vessel. Although distinctly different than an earlier design (9), two model vessels currently in use in this laboratory have proven quite versatile (Fig. 134). Use of a manifold system in combination with gas chromatography permits programmed analysis of the gaseous microenvironment of each culture tube utilizing samples of 3 μl and simultaneous analysing for N_2, O_2 and CO_2.

Other problems are not so simply dealt with. The first of these is the all too obvious fact that cells die with increased concentration of O_2 and they die quite rapidly at hyperatmospheric levels. A number of investigations (10, 11, 12, 13) all recorded marked inhibition of growth as well as metabolism in cell lines well established in culture and quite stabilized as regards their nutritional requirements on minimal essential media. All

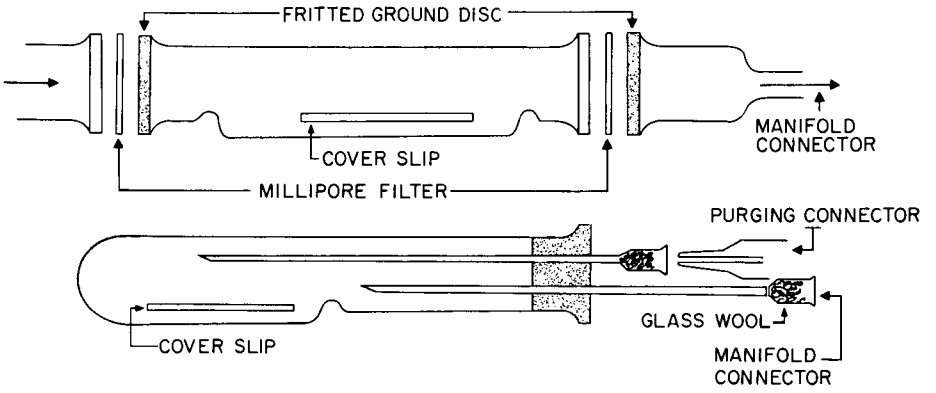

FIG. 134. Two basic designs for tissue culture flasks modified for use under pressure. Both are employed in a larger pressure vessel thus eliminating strain and providing glass partitions thin enough for microscopic observation. The lower vessel can be constructed with readily available equipment but requires an initial purge with gas. "Manifold connectors" are employed for gas chromatographic analyses of the vessel contents while under pressure.

experiments to date, appear to have employed cells exposed to no higher than 95% O_2 at a single atmosphere pressure. With the cell lines used and under the nutritional conditions employed thus far, cells such as HeLa, HLM, L5178Y and Y5 strains all showed signs of O_2 toxicity as manifested by reduction in O_2 consumption even below those levels seen with complete absence of oxygen. This fact itself suggests that even at these levels of oxygen the cells underwent an inhibition of intermediary aerobic metabolism and were incapable of undergoing anaerobic respiration such as would be the case under conditions of anoxia. In this laboratory, essentially identical results have been obtained using L cell variants (mouse fibroblasts) (Fig. 135). These data, however, pertain to 95% O_2 atmospheres at 760 mm Hg. At pressures over this level, no cultures we ever examined have survived for more than 12 hours unless specific procedures are followed.

Generalized Effects on Cultures Exposed to 1–3 atm. abs. O_2

It is important to emphasize that to-date none of the nutritional support medium used for L cell culture in these studies appears to be affected by oxygen at pressures up to 4 atm. abs. for periods as long as one week. Thus, the application of O_2 under pressure does not appear to alter the nutritional medium itself. However, since as yet extended serial transfer of cells under hyperatmospheric O_2 concentrations is not possible, media

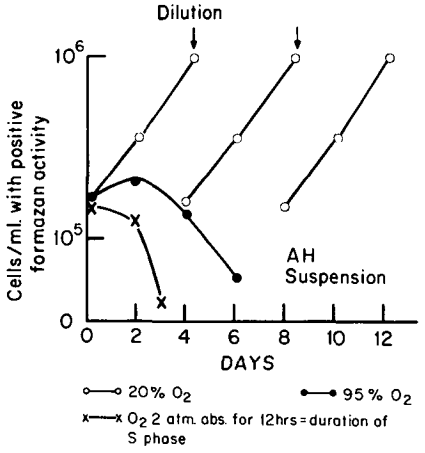

FIG. 135. Cellular proliferation and decline with normal atmospheric concentrations of O_2, 95% O_2 and hyperbaric O_2 (2 atm. abs. for 12 hours). Ordinate values indicate cultured cells showing a positive deposition of formazan produced by transfer of hydrogen via succinic dehydrogenase activity to a tetrazole thereby producing a colored, insoluble reaction product. This represents a marker for cell viability as a function of aerobic respiratory capability. Subculturing of cells grown in 20 per cent O_2 took place at points marked dilution.

employing low concentrations of natural biologics such as fetal calf extract or horse serum or even completely defined media such as NCTC-109 have been used.

Under 2.5–3.0 atm. abs. O_2, cells respond as shown in Figure 136 which, in comparison with cells exposed to lower oxygen concentrations, seems to represent an acceleration of events leading to nearly complete breakdown of the culture by 12 hours. These cells exhibit a rapid loss in adhesiveness and monolayers soon become dispersed. Individual cellular clusters may appear stabilized in that they do not exhibit classical cytolysis, they remain morphologically intact provided the culture tube is not returned to lower O_2 concentrations or normal air. Such morphologic arrests induced by oxygen have been described for free living protozoa (14). When exposed to succinate as an additional substrate, these cells are incapable of transferring hydrogen to a ditetrazole and there is thus no formation of a colored formazan reaction product indicative of dehydrogenase activity (Fig. 135). Thus, they are not capable of undergoing normal aerobic respiration. In this respect, it is also of interest that cells so treated with 2–3 atm. abs. O_2 show no leakage of intracellular hydrolase activity into the medium whereas control cultures, killed by thermal shock, do show significantly higher levels of leaked hydrolase activity within a short time. This appears to confirm the contention of the stabilizing effects of oxygen on the lysosome membrane (14) also observed as a result of the recent electron microscopic studies of Schaffner and Felig (15).

Experiments performed recently in our laboratory have yielded preliminary data suggesting that a relationship may exist between the overall cell cycle and the degrees of resistance and susceptibility to O_2 shown by certain cell strains during different stages of their respective life cycles.

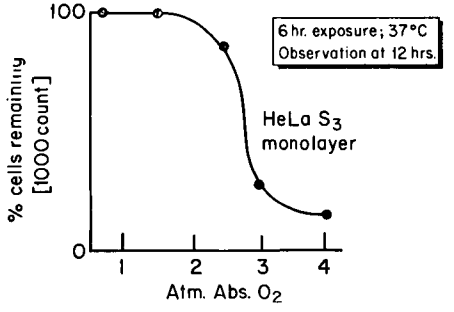

FIG. 136. Loss of cells from monolayer during a 6 hour exposure to various pressures of pure O_2 as indicated on the abscissa. The graph does not show cytotoxic effects of oxygen which become increased at the higher pressures. Loss of adhesion to the glass surface and apparent damage to intercellular binding properties provide the overall effect.

Synchronous cultures (16) of either L or HeLa strain cells grown in monolayer seem especially sensitive to O_2 during the *S* or synthetic phase of their cycle. In other words, the period of deoxyribonucleic acid synthesis, so necessary for further cell reproduction, is extraordinary labile to oxygen. This is quite interesting especially in view of the observation of Conger (17) showing the breakage of chromosomes and the destruction of chromatin in symbiotic protozoa of the wood feeding roach *Cryptocercus* by oxygen (18). The actual mitotic process is similarly a very sensitive period as far as O_2 toxicity is concerned. We have shown direct inhibition of mitoses by oxygen during the metaphase of division in marine eggs (9) and the mammalian cell appears similarly affected. In the mammalian cell cultures studied to-date, the G_2 or post-synthetic phase of the cell cycle appears least sensitive to O_2 but this is frequently so close in time relationship to mitoses that it is difficult to separate the two. Also, the G_1 or presynthetic stage shows some degree of resistance to O_2 toxicity but further experiments will need to be completed before these precise relationships can be established.

The effects of oxygen on some aspects of protein secretion can be studied in a tissue culture system. To study this, "organoids" reconstituted from suspended cultures derived from bovine thyroid are being employed. Under TSH stimulation, these cells aggregate and reconstitute into follicle-like structures which secrete a protein which appears to be thyroidoglobulin. The ability of cells to again engage in macromolecular synthesis in the culture thus provides a model system for studying effects of O_2 on protein synthesis. A basic understanding of the O_2 inhibition of this synthesis may become useful in ascertaining the synthetic capacity of pulmonary alveolar epithelium once it becomes possible to study cells derived from lung epithelium and capable of *in vitro* surfactant production.

Preliminary Experience with Lung Cultures

We have been attempting to culture fetal or newborn calf pulmonary epithelium in monolayer. To-date, these cultures have presented several problems chief among which is the fact that, once in culture, the appearance of altered epithelial cells is virtually impossible to distinguish from macrophages. We should ideally want a reaggregated cell system which presents an organization such as can be obtained with primitive cells such as embryonic chick lung (19). Unfortunately, this cannot be so readily accomplished with mammalian cell types and success has been attained only in maintaining suspended epithelium for periods up to 36 days following exposures of up to 3 atm. abs. O_2 for short periods up to 12 hours.

Explants of lung appear to be a useful compromise for the time being. With these, histologic relationships appear clearly and cytochemical

reactions seem identical to that seen in normal intact lung (20). Experience in this area is still quite new but *in vivo* experiments and initial explant culture observations (7) show significant differences in the resistance of fetal and newborn tissue to oxygen at increased pressures as compared to little or no resistance on the part of more adult tissues. Preliminary experiments suggest that ability to elaborate surfactant may be a major factor in this age difference. Although the primary constituent of surfactant is a phospholipid moiety, a protein or series of proteins may be involved (21). The chief goal in these studies will be to ascertain whether lung explants can produce surfactant material.

Significance of Tissue Culture Studies in Developing an Overall Concept of O_2 Toxicity at the Cellular Level

In a field where many of the practical problems are obvious and the need for their rapid solution is all too apparent, the intensive study of cells in culture may seem leisurely, if not downright casual. We have, perhaps with some whimsy, begun to look upon our cells as divers in a microenvironment with a need for adapting to this environment to no less a degree than would be required of man in his exploration of factors involved in life support beneath the sea or in other situations calling for a closed environment. Figure 137 presents one concept of some interactions of oxygen toxicity in the mammalian lung that appear to govern development of pulmonary pathology. A focal point of this proposed etiologic sequence is the effect on cell metabolism. While specifically dealing with the lung, an area of immediate interest, similar relationships might be diagrammed for other organ systems in oxygen exposed mammals.

The questions that can be asked using this lung diagram as a basis, for example, are many and complicated. Understanding the effects of oxygen on protein synthesis could provide a step towards analyzing alveolar surfactant synthesis and so provide a metabolic event immediately responsible for the histopathologic picture seen in O_2 poisoned lungs. The significance of cell membranes and their role in cellular O_2 toxicity are extremely important (22). Does oxygen provide a direct effect on cellular external limiting membranes causing leakage of protein from vascular endothelium or does it act on intercellular cement causing exudation between adjacent cell boundaries? Will chronic exposure to hyperatmospheric concentrations of oxygen limit the body defense mechanisms normally provided by phagocytic processes in macrophages and specialized epithelial cells? Observations with bound hydrolase activity and the inactivation of these enzymes by oxygen suggest this possibility. Further progress in this area seems likely through carefully designed tissue culture experiments.

While we have had no experience with nerve in culture, we should point

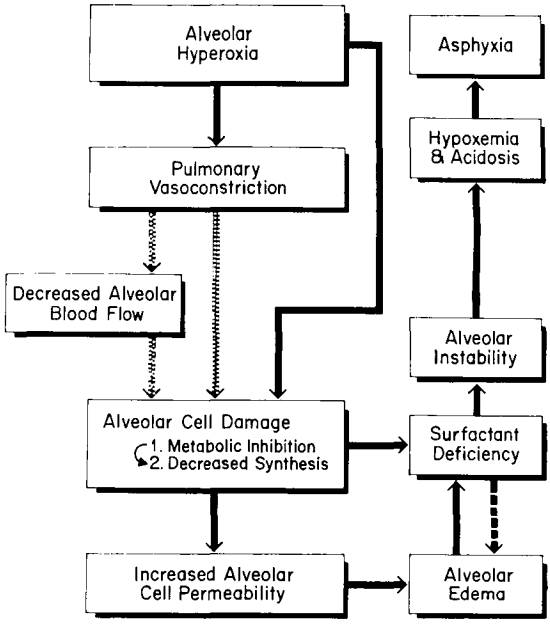

FIG. 137. Scheme of possible interactions leading to pulmonary pathology with exposure to high oxygen concentrations. The focal point of effects on cell metabolism and synthesis are indicated. (From: Wittner and Rosenbaum, Proc. Third Internatl. Conf. Hyperbaric Med., In press, 1966).

out the possible value of tissue culture methods in exploring direct effects of O_2 on these cells especially as concerns influences on the myelin sheath. Finally, other organs which clearly appear to be a target for oxygen should not be neglected. It is not inconceivable that chronic intermittent oxygen saturation of tissues would effect immediate vital functions as well as cellular activities of significance on long term consideration. Thus, while Schaffner and Felig's recent study (15) on the effects of increased O_2 concentrations on hepatic structure generally showed reversible effects, cells of the mammalian reproductive system appear to show irreversible changes. Since these involve failure of division of Sertoli cells of the testis or alteration of the ovum so as to bring about follicular cysts, effects at the cellular level are significantly at play.

Aside from understanding the deleterious effects of O_2 toxicity in mammals, it is possible to consider other applications resulting from a further knowledge of the direct effects of O_2 on cells. The apparent inhibitory effect on the utilization of intracellular hydrolases and the resultant limitation of cellular autolysis make it not unreasonable to consider concentrations of oxygen, acting either synergistically with x-irradiation or alone,

as a means of food preservation once initial bacterial activity has been controlled. Should such ever prove practical, then the storage of gaseous components vital for life support could serve a dual purpose.

Acknowledgment

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Pulmonary Oxygen Tolerance and the Rate of Development of Pulmonary Oxygen Toxicity in Man at Two Atmospheres Inspired Oxygen Tension

The breathing of oxygen at increased partial pressure has well established usefulness in diving, decompression and therapy (8, 15, 17, 26, 27, 29, 30, 31). Maximum benefit from use of oxygen in diving or decompression requires oxygen breathing at the highest practical pressure for the greatest period of time compatible with freedom from significant adverse effects. However, the usefulness of oxygen is limited by its acute and chronic toxicity (1, 5, 11, 12, 23) which, at sufficiently great pressure and duration of exposure, should affect any living cell. Because the lung is exposed to higher oxygen tensions than is any other vital organ, pulmonary oxygen tolerance may well ultimately prove to be the limiting factor in the use of high oxygen pressures for prolonged periods of diving and decompression. Therefore, to aid in the effective employment of oxygen and to avoid serious toxic effects, it is necessary to define the rates of development of pulmonary oxygen toxicity over a range of potentially useful oxygen pressures.

This presentation concerns a phase in the development of pulmonary tolerance curves in normal men. The immediate goal involves the definition of pulmonary oxygen tolerance at 2.0 atmospheres (3) and the comparison of the findings with several previous studies (2, 4, 9, 10, 18, 19, 20, 21, 22, 24) performed at one atmosphere or less.

Choice of an Index of Toxicity

In order to study pulmonary oxygen tolerance in man, it is necessary to employ a sensitive index that will detect the onset, the degree and the rate

of development of pulmonary involvement before it becomes threatening to the subject. Parameters which have been considered for such a role are the vital capacity, pulmonary diffusion capacity and the alveolar-arterial oxygen difference. Our initial experiments, together with a recent study by Caldwell et al (2), indicated that the alveolar-arterial Po_2 difference was not appreciably affected even when oxygen had produced quite severe pulmonary symptoms. Caldwell and his co-workers exposed 4 normal men to 98% oxygen at 1 atmosphere for periods of 30, 48, 60 and 74 hours respectively. The changes in vital capacities of these subjects during oxygen breathing expressed as percentages of normal control values are shown in Figure 138. A significant reduction of vital capacity occurred in all 4 subjects, and the degree of depression was generally proportional to the duration of exposure to oxygen. However, the magnitudes of alveolar-arterial oxygen differences measured in these same resting subjects just before the termination of each exposure showed no correlation with the duration of exposure to oxygen (Table 70). For example, the oxygen tension difference during oxygen breathing was only 64 mm Hg in a subject with severe symptoms following a 74 hour exposure to oxygen. This alveolar-arterial Po_2 difference approximates that to be expected in normal men acutely exposed to oxygen (6).

Arterial oxygen tensions while breathing air during rest and mild exer-

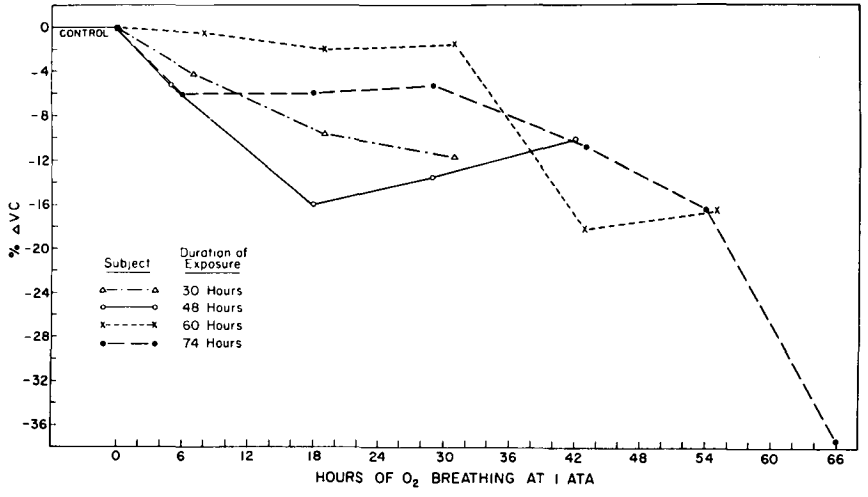

FIG. 138. Change in vital capacity in normal men breathing oxygen at 1.0 atmosphere absolute. Changes are expressed as percent deviations from mean preexposure control values. Total duration of oxygen breathing for each subject is as noted in the figure. After Caldwell et al (2).

TABLE 70

Alveolar-Arterial Oxygen Differences in Normal Men Breathing Oxygen at 1.0 Atmosphere Absolute for 30 to 74 Hours

Duration of exposure for each subject is listed in the table. Each A-a Po_2 difference is the average of 2 measurements performed just prior to termination of oxygen breathing. There is no correlation between duration of exposure and magnitude of oxygen gradient. Also the subject with most severe symptoms and greatest decrease in vital capacity following a 74 hour exposure to oxygen had the smallest A-a Po_2 gradient. Data from Caldwell et al (2).

Duration of Exposure	A-a Po_2 Difference
30 Hours	102 mm Hg
48 Hours	84 mm Hg
60 Hours	108 mm Hg
74 Hours	64 mm Hg

cise were measured after breathing oxygen for 30, 48 and 60 hours. During exercise while breathing air arterial Po_2 was reduced following the 48 and 60 hour exposures, indicating the probable existence of an effect upon the alveolar membrane. However, the magnitude of change was only about 10 mm Hg and was not proportional to the duration of exposure to oxygen.

The pulmonary diffusing capacity for CO was significantly reduced in all subjects who breathed oxygen for more than 30 hours in the study by Caldwell et al, the magnitude of decrease being generally proportional to duration of exposure to oxygen. However, for the purposes of determining the rate of development of toxicity, the analyses and calculations required to obtain this measurement present obstacles in the form of delays which make the CO diffusing capacity a poor choice as an index of a toxic process whose rate of development could suddenly become rapidly progressive. Therefore, after trial and evaluation, change in the vital capacity was selected along with other measurements of pulmonary ventilation as an index of pulmonary oxygen tolerance in man which could be rapidly and accurately measured repeatedly during oxygen breathing and which reflected the onset, degree and rate of development of pulmonary involvement.

Pulmonary Oxygen Tolerance at Two Atmospheres Absolute Inspired Po_2

In order to determine the limits of human pulmonary tolerance for oxygen breathing at 2.0 atmospheres absolute, the rate of development of pulmonary oxygen toxicity was studied in 7 normal men who inspired

humidified 99.8% oxygen continuously at this pressure for 8 to nearly 12 hours (3). Lung function indexes and symptoms were recorded at regular intervals during oxygen breathing. Since determination of tolerance requires production of definite adverse effects, each exposure was continued until a prominent reduction of vital capacity or severe symptoms had been produced.

Subjective Effects

At the start of the exposures all subjects except the two investigators were completely unaware whether they were breathing air or oxygen. No symptoms were experienced until, after intervals ranging from 3 to 6 hours in different subjects, the slightest detectable carinal tickling sensation was noted. This usually was first detected at the end of a maximal inspiration before a vital capacity measurement. Within about one more hour an occasional cough was also precipitated by deep inspiration. The carinal irritation became continuous and gradually increased in intensity in parallel with increasing frequency of cough until about 8 hours of oxygen breathing had passed. From 8 to 10 hours the severity of symptoms became rapidly progressive, and the pulmonary irritation became a constant burning sensation distributed throughout the tracheobronchial tree and was intensified by inspiration. Coughing became uncontrollable, each inspiration was painful and dyspnea even at rest became apparent. The subjective distress of inspiration was manifested in several subjects by a decrease in tidal volume and an increase in respiratory rate. Coughing and the symptoms of tracheobronchitis diminished grossly within 4 hours after the termination of oxygen breathing. Mild dyspnea on exertion was detectable over the following 3 to 4 days in some subjects.

Vital Capacity

The average time course of change in vital capacity in the 7 subjects studied at 2.0 atmospheres is shown in Figure 139 along with an index of the average rate of development of symptoms during oxygen breathing. The decrease in vital capacity appeared to begin soon after the start of oxygen breathing and to progress at an increasing rate as the exposure continued. Oxygen breathing was discontinued after 8 hours in the earliest affected subject and in the remaining subjects between 8 and 12 hours. Accordingly, average changes in vital capacity are not shown on the graph after 8 hours. From a smooth curve drawn through the data it is possible to determine the time required to produce a specific change in vital capacity, such as a 5% or 10% reduction below normal. This quantitative information provides a basis for comparison with other studies which may

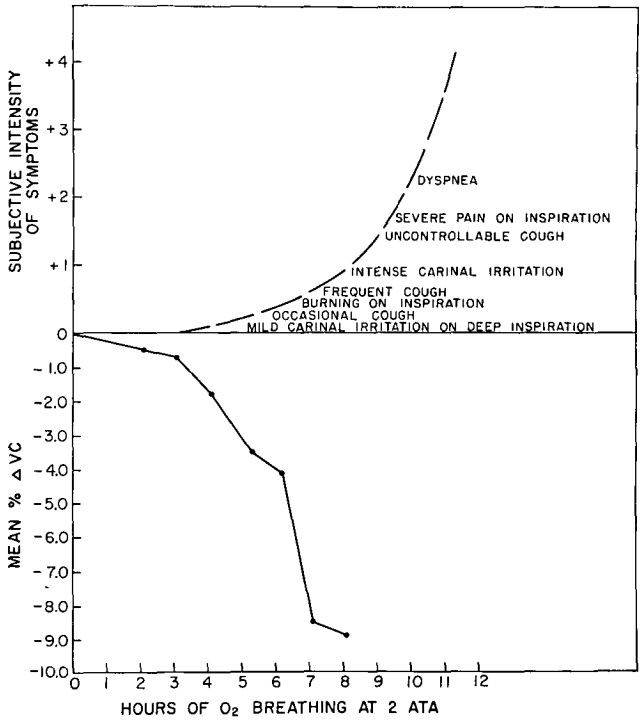

FIG. 139. Rate of development of symptoms and decrease in vital capacity in normal resting men breathing oxygen at 2.0 atmospheres absolute. Change in vital capacity is expressed as percent deviation from an initial control value and represents the average of 7 subjects during the first 8 hours of oxygen breathing. Rate of development of symptoms is represented by a hypothetical curve derived from the pooled subjective reports of all subjects. The most severe symptoms were not experienced by all subjects since these tended to occur, in general, after 9 to 10 hours of exposure.

then together be applied in the construction of a pulmonary tolerance curve.

Changes in the vital capacities of individual subjects were quite variable as is illustrated in Figure 140. The vital capacity data shown are from 3 subjects selected to show the range of responses observed. The graph covers the many hour period of oxygen breathing, 3–4 hours postexposure, and the recovery period during subsequent days. Results are plotted as deviations in milliliters from an initial mean control value ±95% confidence limits. Note that the maximum decrease in vital capacity during oxygen breathing varied from about 150 ml in one subject to about 1600 ml in the subject most affected. Figure 140 also illustrates that, after oxygen breathing was terminated, there occurred a further reduction of vital capacity as great as 650 ml in one subject. Recovery of vital capacity to normal

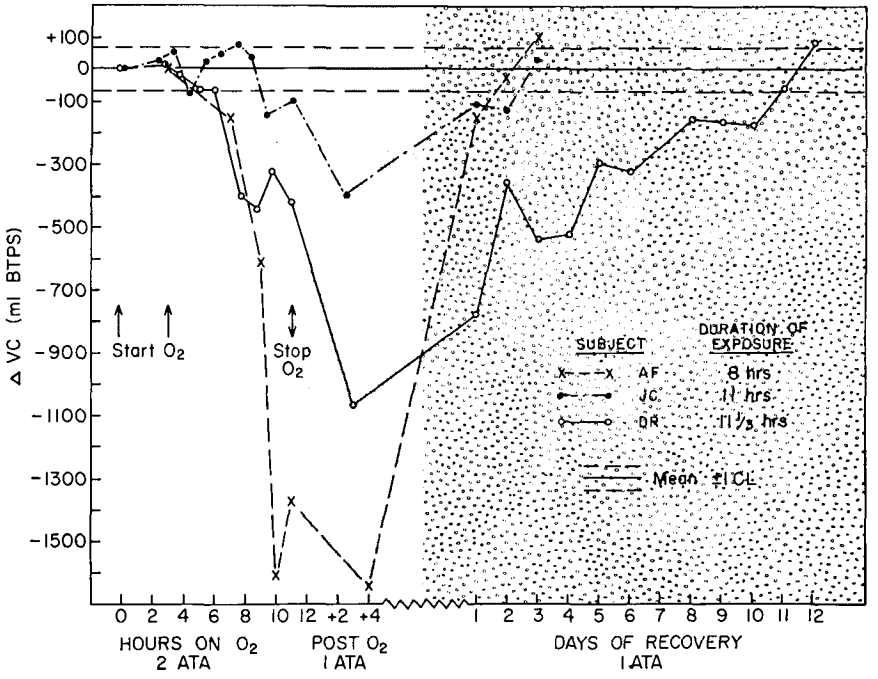

FIG. 140. Change in vital capacity in normal resting men during and after oxygen breathing at 2.0 atmospheres absolute. Results are expressed as deviations in milliliters from an initial mean control value ±95% confidence limits. The confidence limits shown on the graph are those from the subject whose control vital capacities were most variable and therefore represent the maximum for the 3 subjects included. The start of oxygen breathing is plotted at different times for individual subjects to permit the end of oxygen breathing to appear at the same time on the graph for all subjects. Individual durations of exposure are listed in the figure.

then occurred over periods varying from 1 to 12 days following the exposure.

Other Pulmonary Measurements

Average changes in several indexes of pulmonary function, in addition to the vital capacity, that were measured before, during and after oxygen breathing are listed in Table 71. These include the static volumes, inspiratory capacity and expiratory reserve volume, and the dynamic functions, one second forced expired and forced inspired volumes and maximal flow rates during mid-expiration and mid-inspiration.

Comparison of the measured changes in the static pulmonary volumes reveals that the decrease in vital capacity occurred entirely within the inspiratory component of this lung volume. Change in each of the measured

TABLE 71

Average Changes in Pulmonary Volumes and Dynamics Measured at 2.0 Atmospheres just before Termination of Oxygen Breathing and Repeated at 1.0 Atmosphere about 3 to 4 Hours Later

Measurements were obtained from 7 subjects at 2.0 atmospheres before termination of oxygen breathing and from 6 subjects at 1.0 atmosphere about 3 to 4 hours after return to a normal inspired P_{O_2}. All values in the table are expressed as average deviations in milliliters from initial control measurements.

Measurement	Change Prior to End of O_2 (BTPS)	Change Post-O_2 (BTPS)
Vital capacity (VC)	−529 ml*	−830 ml*
Inspiratory capacity (IC)	−857 ml*	−1078 ml*
Expiratory reserve volume (ERV)	+283 ml*	+360 ml
1 sec. forced expired volume ($FEV_{1\ Sec.}$)	−369 ml	−890 ml
1 sec. forced inspired volume ($FIV_{1\ Sec.}$)	−519 ml	−1242 ml*
Maximal mid-expiratory flow rate ($MMF_{Exp.}$)	+20 L/min.	−52 L/min.
Maximal mid-inspiratory flow rate ($MMF_{Insp.}$)	−56 L/min.*	−170 L/min.*

* Indicates significant changes with $p < .05$.

static volumes increased in magnitude during the first few hours after oxygen breathing was discontinued. Changes in the measured dynamic functions with the exception of the maximal mid-expiratory flow rate showed a similar trend. Chest X-rays taken after each exposure revealed no evidence of pulmonary atelectasis as a mechanism to account for the observed decrease in vital capacity.

Synthesis of Pulmonary Oxygen Tolerance Curves

As stated, a purpose of this study of oxygen toxicity at 2 atmospheres was to provide a basis, along with previous studies by other investigators (2, 4, 9, 10, 18, 19, 20, 21, 22, 24), for the construction of curves predicting the duration of pulmonary tolerance to many levels of elevated oxygen partial pressures. The general concepts underlying the development of oxygen tolerance curves will be discussed in detail elsewhere (16). An example of such a curve, based upon a combination of objective data and these general principles, is shown in Figure 141. It represents predictions of the time required for a 5% reduction below normal vital capacity to occur in normal men breathing oxygen at rest over a large range of oxygen pressures. The curve shown for pulmonary oxygen tolerance is a rectangular hyperbola. This form of mathematical expression has been selected to describe the data, because it has been shown that the relationship between inspired oxygen tension and survival time in *Drosophila* (25), protozoa (25) and mice (7) is well described by such a curve. The derivation of this curve will be further elaborated upon in the following discussion.

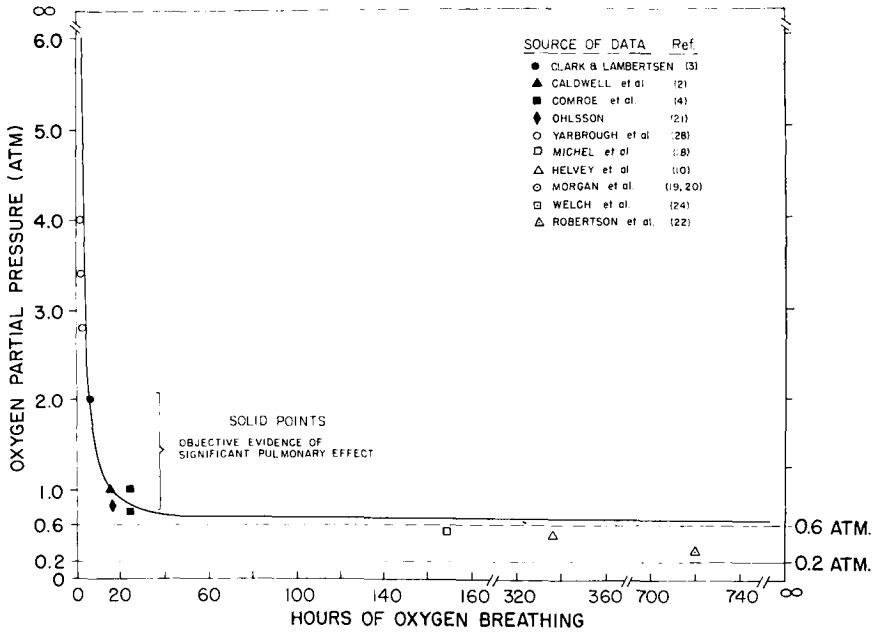

FIG. 141. Pulmonary tolerance curve for normal resting men based upon 5% reduction of vital capacity during oxygen breathing at various partial pressures. The curve is a rectangular hyperbola (7, 25) with asymptotes at zero time and 0.6 atmosphere oxygen partial pressure. The solid symbols have been derived from several studies (2, 3, 4, 21) and represent the times required for an average 5% reduction of vital capacity to occur in normal resting men breathing various partial pressures of oxygen. The open symbols are derived from other studies (9, 10, 18, 19, 20, 22, 24, 28) in which no pulmonary effect was reported or in which the average decrease in vital capacity was less than 5%. Source of the data used for each symbol is identified in the table. Symbols in the table which do not appear on this graph will appear in Figure 142.

Pulmonary Oxygen Tolerance at Oxygen Tensions not Greater than One Atmosphere

Although it appears that no direct study of pulmonary oxygen tolerance in man has been carried out at pressures greater than one atmosphere, a number of studies at lower pressures (2, 4, 9, 10, 18, 19, 20, 21, 22, 24), with purposes ranging from aviation and space medicine to inhalational therapy, have importance to diving and decompression. Many of the findings from these studies are summarized in Figure 142 which is a segment of the overall pulmonary tolerance curve shown in Figure 141. The solid symbols represent data of other investigators (2, 4, 21) from which could be derived the time required for an average 5% reduction of vital capacity to develop in normal men breathing oxygen at rest. The open symbols indi-

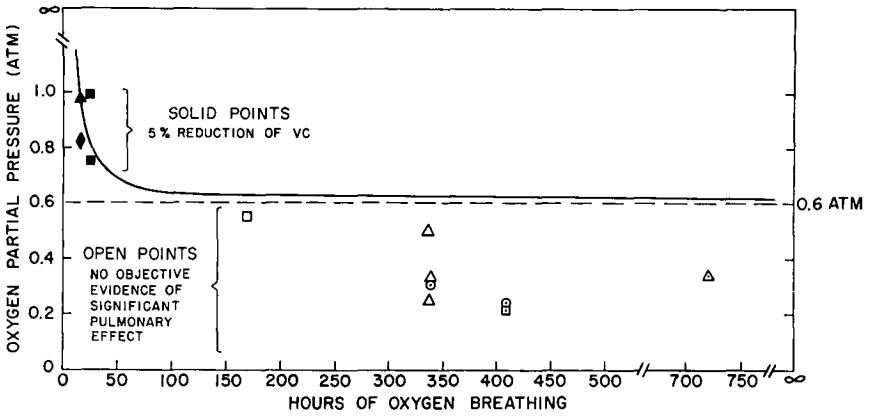

FIG. 142. Pulmonary tolerance curve for normal resting men based upon 5% reduction of vital capacity during oxygen breathing at partial pressures of 1.0 atmosphere or less. This curve is a segment of the overall pulmonary tolerance curve shown in Figure 141 and symbols refer to the same sources of data. The solid symbols are from studies (2, 4, 21) in which objective evidence of a significant pulmonary effect was found. The open symbols are from other studies (9, 10, 18, 19, 20, 22, 24) in which no objective evidence of a significant pulmonary effect could be detected.

cate studies of other authors (9, 10, 18, 19, 20, 22, 24) in which vital capacity was measured but was either not found to be changed or was reduced by an average of less than 5%. A critical decision in constructing a tolerance curve is the choice of the asymptotes for the curve. For our present purposes, 0.6 atmosphere of oxygen was chosen as the horizontal asymptote of the curve (16). The implication of this choice is that a group of normal men breathing oxygen continuously at this partial pressure will never encounter an average reduction of vital capacity exceeding 5%. Although this assumption may well not be justified for an infinite exposure, the assumption is based upon the observations of Helvey et al (10) that men exposed to 0.5 atmosphere of oxygen for 14 days developed no significant pulmonary toxicity. Eventually, as more quantitative information concerning exposures to 0.5 to 1.0 atmosphere of oxygen is obtained, it will become possible to refine the important horizontal asymptote. This will have little effect upon the curve above 2.0 atmospheres.

Pulmonary Oxygen Tolerance at Oxygen Tensions Above One Atmosphere

The curve shown in Figure 143 is the higher pressure segment of the complete pulmonary tolerance curve. The solid symbols at several pressures again represent data from the study at 2 atmospheres (3) and from the several studies (2, 4, 21) in which the time required to produce an average

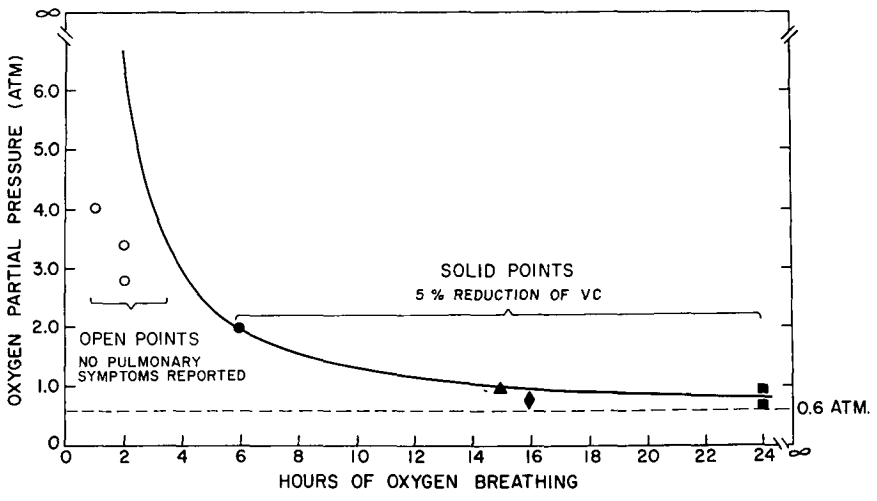

FIG. 143. Pulmonary tolerance curve for normal resting men based upon 5% reduction of vital capacity during oxygen breathing at partial pressures near 1.0 atmosphere and above. This curve is a segment of the complete curve shown in Figure 141 and symbols refer to the same data sources. The solid symbols were derived from the study at 2.0 atmospheres (3) and studies of other investigators (2, 4, 21) previously described. The open symbols represent the duration of oxygen breathing in a study of CNS oxygen tolerance during which no pulmonary symptoms were reported (28).

5% reduction of vital capacity could be derived from measurements in normal men breathing oxygen at rest. The open symbols indicate the duration of oxygen breathing in other studies, performed during an investigation of central nervous system oxygen tolerance, in which no pulmonary symptoms were reported (28). The choice of zero time as the vertical asymptote of the curve is based upon the stated reasonable assumption that pulmonary oxygen toxicity will occur almost instantaneously in men breathing oxygen at infinitely high pressures (13, 16).

This curve should actually be considered only one of a family of similar curves which describes the relations of oxygen pressure and time for each degree of pulmonary effect. Various practical circumstances of diving, saturation exposure, decompression or therapy may make it necessary to accept a lesser or greater degree of pulmonary involvement than indicated in the present tolerance curves. With such a family of curves it will become possible to take full advantage of the useful properties of oxygen at increased partial pressures. Examples of such tolerance curves, based upon two different degrees of average reduction of vital capacity, are shown in Figure 144. The curve on the left is a segment of the pulmonary tolerance curve based upon a 5% reduction of vital capacity, and that on the right is based upon a 10% reduction of vital capacity and has been derived in a

similar way. For purposes requiring repeated exposure of the same individual to oxygen at increased partial pressures, it should also become possible to construct additional curves based upon allowance of minimal detectable pulmonary effects and lying to the left of the two curves shown here.

One question of importance relative to these predictions of pulmonary oxygen tolerance is the influence of exercise on oxygen toxicity. Exercise is known to decrease the time required to develop oxygen convulsions or central nervous system oxygen toxicity. However, although the curves shown in Figures 141, 142, 143 and 144 have been derived from studies of pulmonary oxygen tolerance in men at rest, the curves for exercising men may not necessarily be different, since there is no practical indication or evident theoretical reason why exercise should have the same detrimental effects upon pulmonary oxygen tolerance as it does upon the electrical phenomena of central nervous system oxygen toxicity.

In proceeding from this point, several aspects of the predictive curves for oxygen tolerance should be kept in mind. One is that the curves are purely extrapolations for oxygen partial pressures above 2.0 atmospheres. This is a limitation but not a defect of the diagrams, since one of the purposes in studying the effects of oxygen at two atmospheres and in constructing such predictive curves was to aid in the design of further studies of human tolerance to oxygen at increased partial pressures. Second, it must

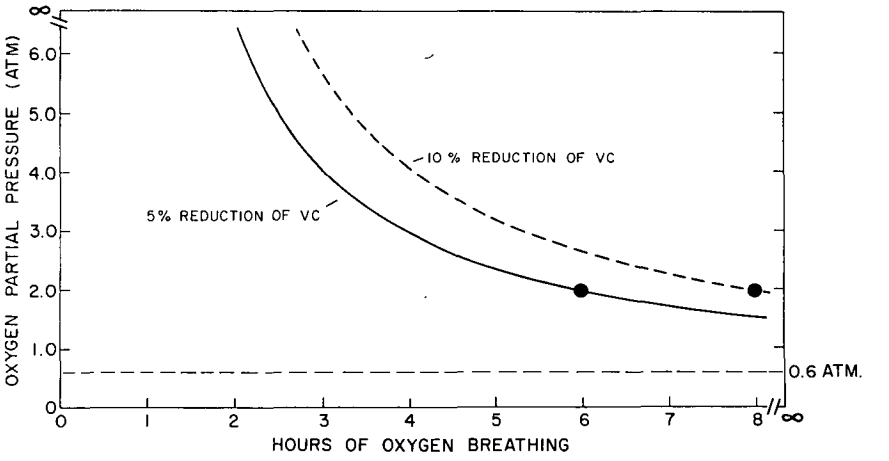

FIG. 144. Pulmonary tolerance curves for normal resting men based upon 5% and 10% reductions of vital capacity during oxygen breathing above 1.0 atmosphere. The curve on the left is based upon a 5% reduction of vital capacity and is a segment of the pulmonary tolerance curve shown in Figure 141. The curve on the right is based upon a 10% reduction of vital capacity and has been derived in a similar way from the study at 2.0 atmospheres (3) and from the data of Ohlsson (21) and Caldwell et al (2).

be realized that the pulmonary tolerance curve expressing fixed reduction of vital capacity in a single individual may fall somewhat to the right or left of an average curve. Finally, the development of curves of this type is essential in evaluating the advantages of intermittent exposure to oxygen and in designing basic and applied studies with alternately increasing and decreasing oxygen pressures in special inert gas-oxygen mixtures (Chapt. 21) (14).

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Artificial Gills for Gas Exchange in Water

Fish obtain oxygen for their metabolic demands by diffusion from the water in which they swim, and eliminate carbon dioxide in the same way. Diffusion takes place, of course, in the gill, where water and blood are in intimate contact, separated mainly by a series of cell membranes. Water in equilibrium with air at sea level has an oxygen partial pressure (P_{O_2}) of 0.2 atm, a value considerably in excess of arterial P_{O_2} in fish blood, and this partial pressure difference causes net diffusion of oxygen into the fish. For carbon dioxide, the partial pressure difference and direction of net diffusion are reversed.

The same physical factors which operate to supply oxygen and eliminate carbon dioxide in fish gills—membranes with appropriate permeability properties, and appropriate partial pressure differences—can be utilized in the design of artificial gills. These devices, which presumably could enable submerged men to obtain oxygen by diffusion from water, would have an obvious utility in the light of current interest in the exploration of inner space. Work on artificial gills has been carried out in several laboratories, and recently a United States patent was awarded to the designer of one (1).

In essence, the problem of obtaining O_2 by diffusion from water reduces to choosing the proper membrane. The desideratum is a membrane which will permit passage of O_2 molecules dissolved in water while restraining liquid water itself. A rather wide variety of materials suitable for such membranes exists, with equally widely-distributed permeability properties, but basically there are two membrane types: 1) continuous membranes which gases penetrate by solution in the membrane substance, and which liquid water cannot pass; 2) membranes which are microporous and hydrophobic. In the latter, gases penetrate through minute pores from which water is excluded by surface tension effects. When a microporous, hydrophobic membrane separates air from water, it functions in effect as a *gas* membrane, that is, gas exchange takes place directly across a gas-liquid interface, with no continuous membrane phase interposed. Both types of

membrane have been used in artificial gills. Robb and his associates, in an extensive series of experiments (2, 3), and Bodell (4) have used silicone rubber membranes, an example of type 1, in artificial gills. In the experiments to be reported here, we have used hydrophobic Millipore filters, an example of type 2, in an artificial gill. The permeabilities of certain membrane materials to O_2, CO_2, and N_2 are compared in Table 72.

Suppose an artificial gill were constructed in the form of a rigid, air-filled box covered with suitable membrane material, a man were placed inside, and the box submerged. In a short time, P_{O_2} in the box would fall to less than 0.2 atm, and P_{CO_2} would rise. If the water surrounding the box is in equilibrium with air, its P_{O_2} would be 0.2 atm, and its P_{CO_2} almost 0. Differences in P_{O_2} and P_{CO_2} between the atmosphere in the box and the surrounding water would cause diffusion of O_2 into and CO_2 out of the box. A steady-state P_{O_2} in the box would be reached when the P_{O_2} gradient from water to air in the box became so steep that oxygen diffusion into the box would exactly equal the oxygen consumption of the man. In principle, then, the respiration of the man would provide the driving forces to make the artificial gill functional. In practice, many variables combine to determine its operating characteristics. It is the purpose of this study to delineate some of the variables important to the function of artificial gill systems.

Methods and Materials

An artificial gill was constructed in the form of a cylindrical lucite chamber, covered on one end with Millipore filter, type RH (Millipore

TABLE 72

Permeabilities of Membrane Materials

The figures in the table $\times 10^{-3}$ represent the volume (STP) of gas per minute which would cross 1 m² of membrane under a partial pressure gradient of 1 atm per cm of membrane thickness.

	O_2	CO_2	N_2	Ref.
Dimethyl silicone rubber	2500	13,600	1170	2
Polyethylene	7	27	2	5
Nylon	0.14	0.25	—	5
Teflon	0.017	—	—	2
Millipore filter, type RH	6750*	135,000*†	3370*	Present studies

* Values given for Millipore membrane are flow dependent and do not represent true permeabilities. However, for comparison they have been calculated from measured gas flux, membrane area, pressure difference, and actual membrane thickness, as if the limiting resistance to gas flux occurred across the membrane thickness. See text for further discussion.

† Calculated from O_2 permeability and the ratio of $\alpha_{CO_2}D_{CO_2}$ to $\alpha_{O_2}D_{O_2}$.

Filter Corporation, Bedford, Mass.). This hydrophobic membrane filter contains an 80% void volume and uniform pores 1 μ in diameter, and is 150 μ thick. The chamber volume was 840 ml, and its membrane surface area was 100 cm^2.

The membrane was supported on a photo-etched stainless steel screen. A Beckman model C-2 paramagnetic oxygen analyzer and a water manometer were connected to the chamber as shown schematically in Figure 145. The oxygen analyzer was calibrated directly in mm Hg P_{O_2}, using room air at several negative pressures. The atmosphere in the chamber was circulated through the oxygen analyzer at 250–300 ml/min by a diaphragm-actuated pump. Water was circulated over the membrane surface with a submersible pump, whose intake could be measured with stopwatch and graduated cylinder. Rate of flow of water over the membrane was varied by changing resistance in the outflow line.

In certain experiments, 150–200 gm bullfrogs were enclosed in the air-filled chamber, and submerged in air-equilibrated water. The changes in P_{O_2} and total chamber pressure (P) were followed as functions of time. When steady values of P_{O_2} and P were obtained, the chamber atmosphere was sampled and analyzed for CO_2 by the method of Scholander (6).

Results

Gas Fluxes

For measurements of net gas fluxes, the chamber was flushed and filled with N_2, submerged in air-equilibrated water at room temperature, and the changes in both P_{O_2} and P were followed as functions of time. Figure 146

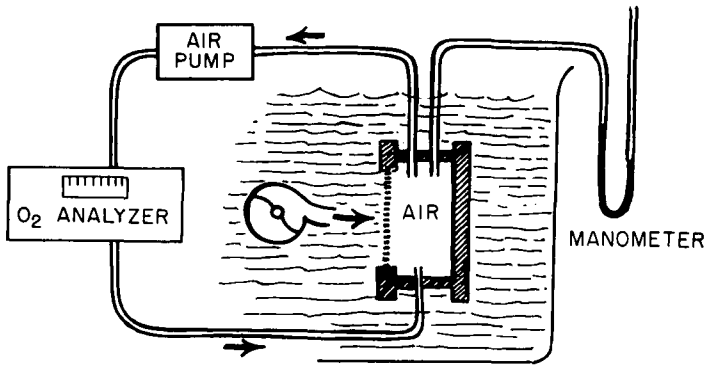

FIG. 145. Schematic drawing of the artificial gill system. Water was pumped over the membrane surface through large bore tubing connected directly to a lucite plate (not shown) bolted to the chamber in such a way as to form an 8 mm deep channel over the membrane.

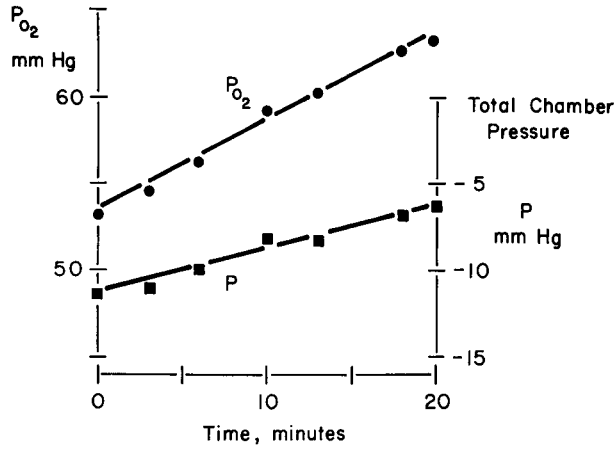

FIG. 146. Changes in chamber P_{O_2} and total pressure P with time, followed with the O_2 analyzer and water manometer. Experiments were usually done at slight negative pressures to hold the membrane firmly in place.

shows in part the result of one such experiment. Notice that P_{O_2} rises more quickly than P, an indication that O_2 enters the chamber more rapidly than N_2 leaves. Because only two gases are involved, both O_2 and N_2 fluxes and permeabilities may be computed from such experimental data.

Figure 147 demonstrates the importance of stirring to O_2 flux. The initial portion of the curve was obtained by measuring increase in chamber P_{O_2} in unstirred water. At the point marked "jets on" the water pump was switched on, and a jet of water directed at the membrane surface. The rate of rise of P_{O_2} immediately increased 16-fold, and returned to its previous value upon switching off the pump. A systematic investigation of O_2 permeability of the system as a function of water flow over the membrane yielded the data shown in Figure 148. The linear velocities shown on the abscissa are average velocities, calculated from measured volume flow rates and average cross-sectional area of the channel through which water flow

TABLE 73

O_2 Flux as a Function of Number of Membranes, at a Single Flow Rate

The values in the table are in ml O_2 (STP)/min/m²/atm. n = Number of measurements.

	O_2 FLUX
1 membrane	281 ± 61 s.d. (n = 12)
2 membranes	275 ± 25 (n = 12)
3 membranes	300 ± 32 (n = 9)

over the membrane surface took place. The O_2 permeability was calculated as follows:

$$K_{O_2} = \frac{dP_{O_2}}{dt} \cdot \frac{V}{(P - P_{H_2O})} \cdot \frac{1}{A} \cdot \frac{760}{\Delta P_{O_2}} \quad (1)$$

where

K_{O_2} = O_2 permeability, $cm^3/min/m^2/atm$

$\frac{dP_{O_2}}{dt}$ = rate of increase of chamber P_{O_2} with time, mm Hg/min

V = volume of chamber and connections, cm^3

P = total chamber pressure, mm Hg

P_{H_2O} = vapor pressure of water at chamber temperature, mm Hg

A = membrane area, m^2

ΔP_{O_2} = average O_2 partial pressure difference between water and chamber over time dt, mm Hg.

The N_2 permeability was computed in a similar manner, and the ratio of K_{N_2} to K_{O_2} was found to be 0.50 ± .04 (s.d.) at all flow rates.

The rise in K_{O_2} with water flow rate suggests a relatively slow-moving or "stagnant" layer of water, a so-called boundary layer, on the surface of the membrane. In order further to elucidate this possibility, O_2 fluxes were

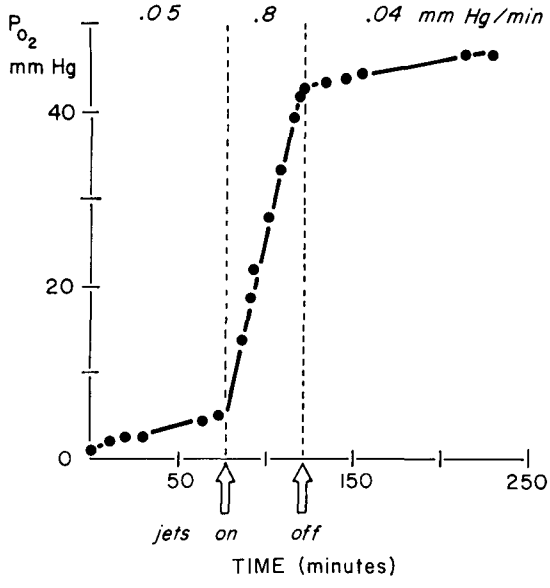

FIG. 147. Time rate of change of chamber P_{O_2}, with and without stirring

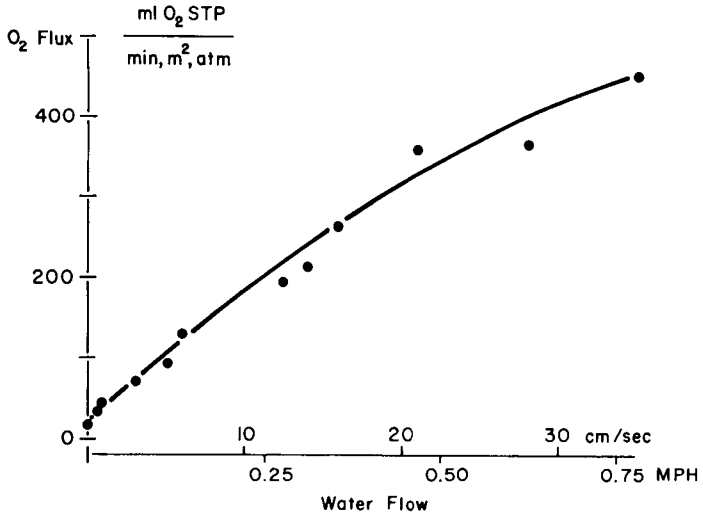

FIG. 148. Oxygen permeability of the gill membrane as a function of water flow

measured at a fixed water flow but using several membranes stacked in series. Table 73 shows the O_2 permeability of the system measured with one, two, or three membrane thickness. It seems fair to conclude that the membrane itself plays a negligible role in controlling O_2 flux in these experiments, and by inference, that the boundary layer on the membrane surface offers the most important resistance to O_2 diffusion into the chamber. It is possible to compute the *effective* thickness of this boundary layer as the thickness of an absolutely stationary layer of water on the membrane which offers the same diffusion resistance as the actual boundary layer, in which water velocity increases asymptotically with distance from the membrane. The geometrical correlate of this idealization is shown in Figure 149. ΔX, the effective thickness of the boundary layer, is given by the following

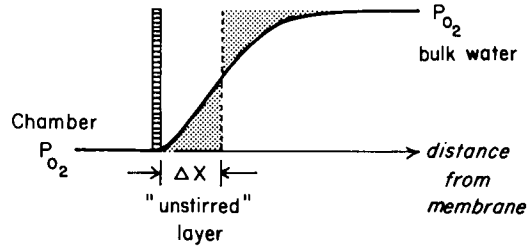

FIG. 149. Schematic drawing of the P_{O_2} gradient in the vicinity of the membrane; ΔX was chosen so that the shaded areas are equal.

expression, which is simply a rearrangement of Fick's law of diffusion for the steady state:

$$\Delta X = \frac{(A)(\alpha_{O_2})(D_{O_2})(\Delta P_{O_2})}{J_{O_2}} \qquad (2)$$

where

A = membrane area, cm^2
α_{O_2} = solubility of O_2 in water, $cm^3/cm^3/atm$
D_{O_2} = diffusion coefficient of O_2 in water, cm^2/sec
ΔP_{O_2} = O_2 pressure difference between bulk water phase and chamber atmosphere, atm
J_{O_2} = observed O_2 flux into chamber, cm^3/sec

In Figure 150, values of ΔX computed from equation (2) are plotted against water flow rate. Table 74 contains the values of α and D used for the computation. The effective thickness of the boundary layer changes from nearly 300 μ to 10 μ as the water flow goes from 0 to 40 cm/sec. However, even a 10 μ layer of water constitutes a relatively large diffusion barrier when compared with a 150 μ thick membrane whose pores are largely air-filled. It is only necessary to realize that the ratio of the diffusion coefficient of O_2 in air to that in water is nearly 10,000 to 1 to appreciate this fact. A layer of still air 150 μ thick and 100 cm^2 in area would transfer nearly 90 liters of O_2 per minute for a steady ΔP_{O_2} of 1 atmosphere.

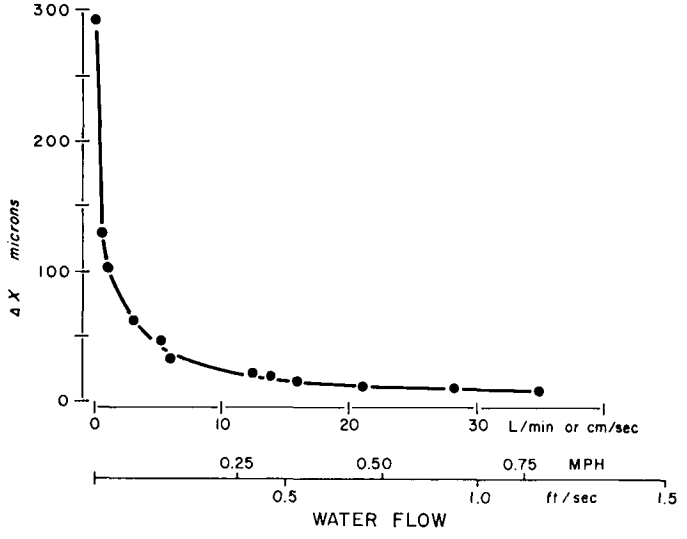

FIG. 150. The effective thickness, ΔX, of the boundary layer as a function of water flow past the membrane. ΔX was calculated as described in the text.

TABLE 74

Values of the Diffusion Coefficients and Solubilities in Water of O_2, N_2, and CO_2 at 20° C

Taken from the Handbook of Respiration, D. S. Dittmer and R. M. Grebe, eds., W. B. Saunders Co., Philadelphia, 1958.

	$D \times 10^5$, 20° C CM²/SEC	α, 20° C ML/ML/ATM	$\alpha D \times 10^7$ CM²/SEC/ATM
O_2	2.28	.0310	7.06
N_2	2.08	.0155	3.23
CO_2	1.58	.878	139

Animal Experiments

Bullfrogs, 150–200 grams in weight, were enclosed in the air-filled chamber and submerged. P_{O_2} and total pressure in the chamber fell in a roughly exponential manner as a function of time, and were relatively steady after 200–400 min. Figure 151 shows a representative experiment. Total chamber pressure always became negative by an amount almost exactly equal to the steady-state difference between P_{O_2} in the outside water and P_{O_2} plus P_{CO_2} in the chamber. Steady-state P_{CO_2}'s in the chamber usually were less than 2 and never greater than 8 mm Hg. Table 75 contains steady-state data for the frog experiments.

Discussion

It is useful to divide artificial gills arbitrarily into two classes: 1) those with rigid walls, fixed volumes, and internal pressures held constant and close to 1 atm; such gills might function in submarines for example; 2) those which contain a collapsible element, so that their internal pressure must be the hydrostatic pressure in the water around them, whatever the depth. The present experiments were done using a rigid system, and will be discussed first. Some of the results are applicable to collapsible artificial gill systems, as well; they will be treated subsequently.

The Rigid Artificial Gill System

Nature anticipated a gill based on a hydrophobic, microporous membrane several million years ago. The aquatic insect *Aphelocheirus aestivalis*, native to the British Isles and the continent, possesses a "plastron" or hair pile consisting of minute, very closely-spaced hydrophobic hairs which form, in effect, a water-impermeable, gas-permeable membrane over the openings of the tracheal system. This system of hairs is exactly analogous in its function to the Millipore membrane used in the present experiments. (For a comparison of dimensions, see Fig. 152.) When the insect dives beneath the surface,

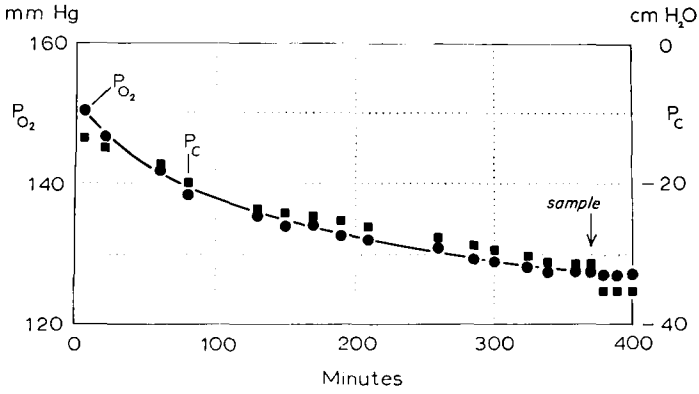

FIG. 151. Chamber P_{O_2} and total pressure P as a function of time after submersion of a 122 gm bullfrog enclosed in the gill chamber. At 370 min., a sample was withdrawn for CO_2 analysis.

TABLE 75

Steady-State Values (mm Hg) Recorded in Chamber During Frog Experiments

The difference between the atmospheric and chamber pressure is theoretically equal to the difference between water P_{O_2} and the sum of chamber P_{O_2} and P_{CO_2}.

EXPT. #	BAROMETRIC PRESSURE	TOTAL CHAMBER PRESSURE	CHAMBER P_{O_2}	CHAMBER P_{CO_2}
1	737	710	126	1.9
2	731	713	125	1.4
3	747	705	125	1.8
4	742	685	114	2.4
5	743	669	88.5	1.67
6	730	590	20	8.2

air remains trapped in the hair pile. Surface tension at the tips of the hairs keeps the pressure in this trapped air film near one atmosphere, and *Aphelocheirus* is able to remain submerged indefinitely, using its hair pile as a gill to obtain O_2 by diffusion from water. Thorpe and Crisp have extensively described the respiratory function of the hair pile, which they term "plastron respiration," in a series of excellent papers (7, 8, 9).

It is informative to project the results of our experiments onto a scale which might be useful to man. Our maximum measured O_2 permeability was 450 ml O_2 (STP)/min/m^2/(atm ΔP_{O_2}). If P_{O_2} in the chamber atmosphere is allowed to fall to 100 mm Hg (equivalent to an altitude of about 10,000 ft), and the water flowing past the membrane has a P_{O_2} of approximately 150 mm Hg, an O_2 flux of about 30 ml O_2 (STP)/min/m^2 will result. A man at rest, consuming 240 ml O_2 (STP)/min, would require a membrane

surface of 8 m^2 to meet his need for O_2. In strenuous exercise, oxygen consumption ($\dot{V}_{O_2}$) may rise to 10 times this amount, requiring an 80 m^2 membrane. If P_{O_2} in the water flowing past the gill remains fixed at 150 mm Hg, the desired P_{O_2} in the chamber atmosphere and $\dot{V}_{O_2}$ will determine the area of membrane. This relation is shown graphically in Figure 153. The family of lines has as a parameter ΔP_{O_2} in mm Hg, which has been also translated into oxygen pressure in the chamber atmosphere, here labelled $P_{I_{O_2}}$.

Since O_2 permeability depends on water flow rate (Fig. 148), we have computed P_{O_2} in the chamber as a function of flow rate in our system for a

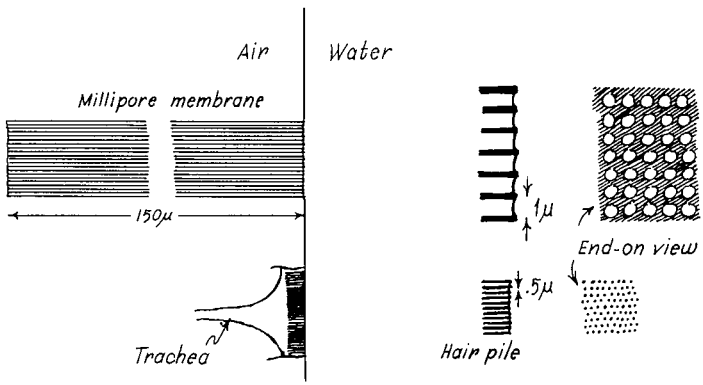

FIG. 152. Schematic drawing comparing a Millipore membrane (above) with the hair pile of *Aphelocheirus* (below). The Millipore structure is in reality much more complex than shown.

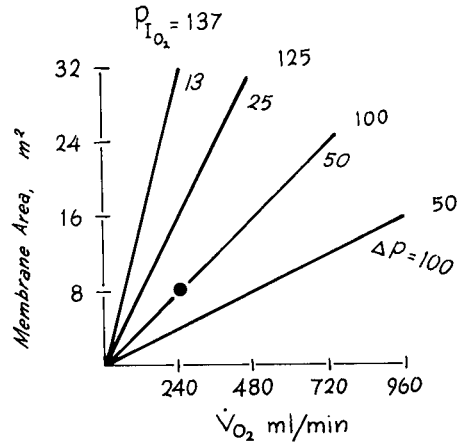

FIG. 153. Membrane area plotted against oxygen consumption. P_{IO_2} stands for oxygen partial pressure in the chamber, and ΔP, for the difference between water P_{O_2}, taken as 150 mm Hg, and chamber P_{O_2}.

given $\dot{V}_{O_2}$ and membrane area, and plotted the results in Figure 154. The second ordinate represents arterial hemoglobin saturation for corresponding inspired oxygen tensions (10).

The experiments done with bullfrogs in the chamber demonstrate that CO_2 accumulation in the chamber will not limit the performance of our artificial gill. This conclusion is consonant with the ready solubility of CO_2 in water. Theoretically, CO_2 should traverse a water layer 20 times faster than O_2 for equal partial pressure differences, as comparison of the values of αD in Table 74 will show. The relation between the steady state P_{CO_2} and P_{O_2} in an artificial gill containing a man may be computed from the following considerations.

$$J_{O_2} = (K_{O_2})\ (A)\ (\Delta P_{O_2}) \tag{3}$$

and

$$J_{CO_2} = (K_{CO_2})\ (A)\ (\Delta P_{CO_2}) \tag{4}$$

where

J = flux of gas into or out of chamber
A = membrane area
K = permeability of the membrane.

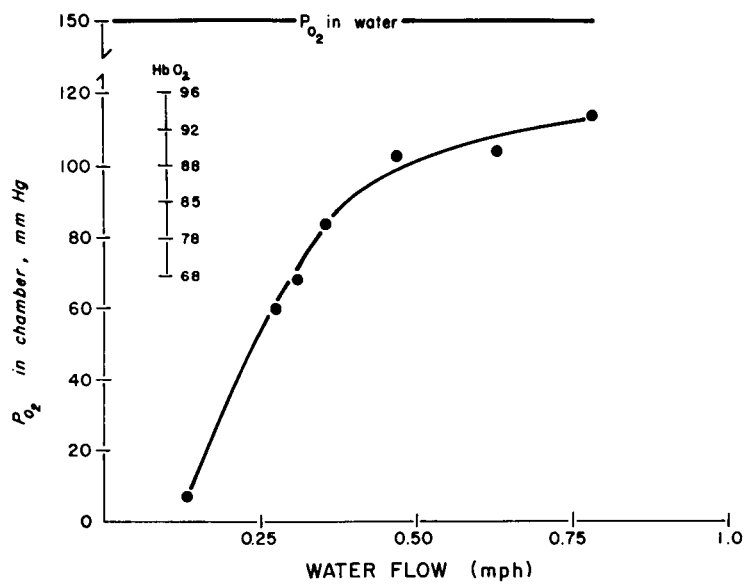

FIG. 154. Chamber P_{O_2} vs. water flow rate for a 10 m² membrane and an oxygen consumption of 240 ml (STP)/min. % HbO_2 in man for a corresponding P_{O_2} in inspired air is shown as a second ordinate.

In the steady state

$$J_{O_2} = \dot{V}_{O_2}\text{, the } O_2 \text{ consumption}$$

and

$$J_{CO_2} = \dot{V}_{CO_2}\text{, the } CO_2 \text{ production.}$$

But

$$K_{O_2} = \frac{(\alpha_{O_2})\ (D_{O_2})}{\Delta X}$$

and

$$K_{CO_2} = \frac{(\alpha_{CO_2})\ (D_{CO_2})}{\Delta X}$$

Thus

$$\frac{\dot{V}_{CO_2}}{\dot{V}_{O_2}} = R = \frac{(\alpha_{CO_2})\ (D_{CO_2})\ (\Delta P_{CO_2})}{(\alpha_{O_2})\ (D_{O_2})\ (\Delta P_{O_2})} \tag{5}$$

where

R = respiratory gas exchange ratio.

If we assume that R is approximately 1,

$$\Delta P_{CO_2} = \frac{(\alpha_{O_2})(D_{O_2})}{(\alpha_{CO_2})(D_{CO_2})} \cdot \Delta P_{O_2}\text{,} \tag{6}$$

or

$$20\ \Delta P_{CO_2} \cong \Delta P_{O_2} \text{ at } 20^\circ \text{ C} \tag{7}$$

Thus for a 20 mm Hg fall in chamber P_{O_2}, P_{CO_2} will rise by only 1 mm Hg. Figure 155 shows a graph of equation 7, in which P_{O_2} and P_{CO_2} in water have been chosen as 150 and 0 mm Hg, respectively. The points represent data from Table 75. Comparison between theory and experiment is made somewhat uncertain by the small number of experiments, but agreement is sufficiently good to show that chamber P_{CO_2} levels present no problem to the successful function of our artificial gill.

Water Flow Requirements

Water flow has previously been regarded as a variable which controls gas fluxes into or out of the artificial gill through its influence on the thickness of the boundary layer. In addition, water flow must be considered in relation to the oxygen which it transports to the membrane surface. Water at 20° C contains about 30 ml O_2 (STP)/liter/atm, or 6 ml/liter at 0.2 atm P_{O_2}. If

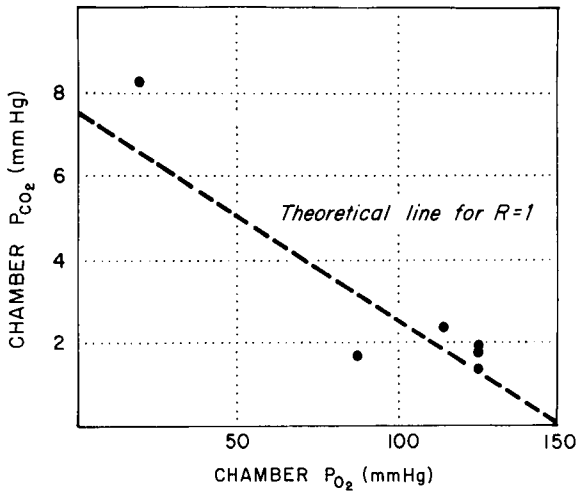

FIG. 155. $P_{O_2} - P_{CO_2}$ diagram for the steady-state chamber atmosphere in the bullfrog experiments. The R-line is theoretical and was drawn from equation 7. The points are experimental values taken from Table 75.

TABLE 76

Water Flows at 20° C through Artificial Gill Required for Known Oxygen Consumptions ($\dot{V}_{O_2}$) and Differences between Oxygen Pressure in In-flowing and Out-flowing Water

In-Flowing P_{O_2} − Out-Flowing P_{O_2} (mm Hg)	Water Flow (L/min) Required for a $\dot{V}_{O_2}$ of:	
	240 ml/min	2400 ml/min
10	600	6000
50	120	1200

we require that water passing through the gill lose no more than 10 mm Hg P_{O_2} while supplying 240 ml O_2/min to the man in the gill, a water flow of about 600 liters/min is required. Table 76 shows the large water flows required for two different oxygen consumptions and P_{O_2} differences between in-flowing and out-flowing water.

In addition to the problem of gross O_2 supply, P_{O_2} in water leaving the gill must be maintained above P_{O_2} in the chamber itself, or the driving force for O_2 diffusion from water into gill will be diminished. A diminution in O_2 gradient at any given point along the membrane must necessarily cause a fall in O_2 flux into the gill. Thus water flow in our gill system plays two related roles: one of mixing, and one of supply.

In summary, Figure 156 is a rather fanciful projection of a rigid gill system designed for fish-watching in the Niagara River. The 6 mph current

flowing over an 8 m^2 membrane should be more than adequate to provide a man at rest with a proper chamber atmosphere.

The Collapsible Gill

It may be profitable to speculate on the characteristics of an artificial gill system operating at ambient pressure, whatever the depth, rather than a fixed pressure of 1 atm. The permeability characteristics of the gill membrane are not affected by this change, but certain of the driving forces are changed drastically. Let us define our system as follows: 1) We shall require a membrane surface area of 80 m^2, which is large enough to supply a $\dot{V}_{O_2}$ of 2.4 l(STP)/min at a chamber P_{O_2} of 100 mm Hg. Note that by fixing area and specifying $\dot{V}_{O_2}$, we have also fixed P_{O_2} in the gill atmosphere. $\dot{V}_{O_2}$ has been chosen at 2.4 l(STP)/min to accommodate the needs of a man in heavy exercise. An 80 m^2 membrane will transmit approximately 17.6 liters N_2 (STP)/min/atm. If the gill is operating at a depth of 99 ft, or approximately 4 atm absolute pressure within the gill, P_{N_2} and P_{O_2} will be 3.9 and 0.13 atm, respectively. However, the surrounding water is in equilibrium with O_2 and N_2 partial pressures prevailing at the surface, and therefore will have a P_{O_2} of 0.2 atm, and a P_{N_2} of 0.8 atm. This situation is shown schematically in Figure 157. A ΔP_{N_2} of 3.1 atm exists between gill atmosphere and surrounding water, which will produce an N_2 loss of 54 l(STP)/min. Obviously, this N_2 loss will be accompanied by continuous collapse of

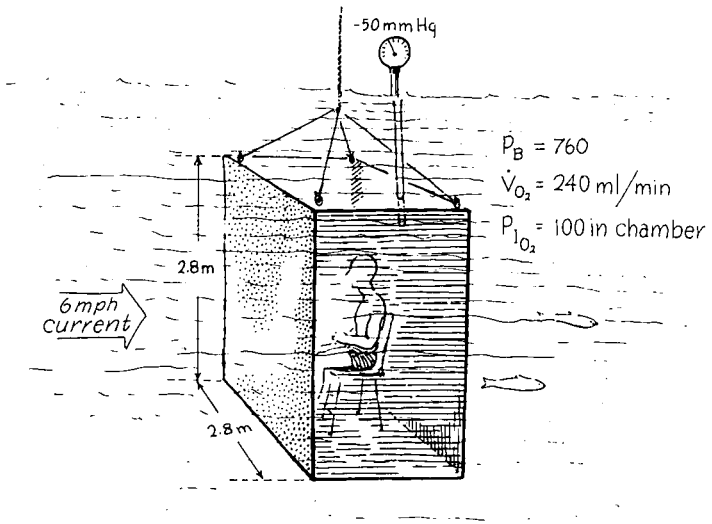

FIG. 156. Man in a rigid gill system, submerged in a swiftly-flowing river. The pressure in the box is 50 mm Hg below atmospheric; an 8 m^2 membrane supplies 240 ml O_2 (STP)/min at a P_{O_2} of 100 mm Hg.

the gill system unless it is compensated by addition of N_2 at a rate equal to the loss. Calculations of the N_2 loss rate (or rate of N_2 addition necessary for a stable gill volume) have been made at other depths and the results plotted in Figure 158. Interestingly enough, nature has again provided us with a prototype of the collapsible gill system. Some aquatic insects such as *Corixa*, the water boatman, carry with them on their dives below the surface a thin film of air which adheres to their abdomen. Since they lack a hair pile, this air film will be nearly at ambient pressure, whatever the depth of the dive. The air film serves *Corixa* as a gill, for as O_2 is removed from it by diffusion into the trachea of the insect, it is replaced by O_2 diffusing from the water. The Danish physiologist Ege was aware of this process as long ago as 1918 (11). However, by the same process described for a collapsible gill, N_2 leaves the air film and it shrinks until its surface area is no longer

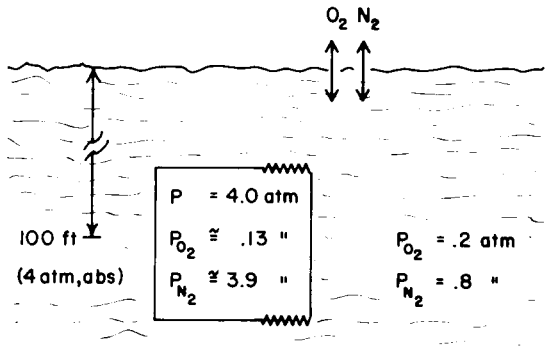

FIG. 157. Collapsible gill system. Chamber pressure is equal to the hydrostatic pressure, whatever the depth.

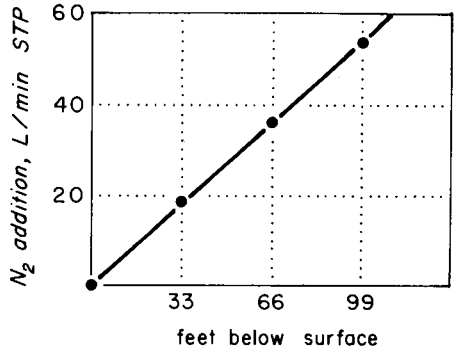

FIG. 158. Nitrogen addition necessary to maintain constant volume in a collapsible artificial gill as a function of depth.

large enough to supply the insect with O_2 by diffusion. Now *Corixa* must return to the surface to replenish not its O_2 but its N_2 supply (12).

The Blood-Perfused Artificial Gill

At least two solutions exist to the problem of N_2 or inert gas loss from a collapsible gill system. One lies in the design of a membrane whose permeability to N_2 or inert gases is very low compared with its O_2 permeability. The second lies in eliminating the gas phase in the artificial gill system altogether. This solution would require direct blood perfusion of a gas-permeable membrane in contact with water, exactly as is the case with fish gills. Robb and his coworkers (3) have speculated on this possibility, and have recognized the physiological difficulties inherent in such an approach. Avoiding the potential heat loss from a blood-perfused gill will require a very efficient counter-current heat exchanger, such as that found in the flipper of a seal, or a membrane combining low thermal conductivity with high O_2 permeability, or both. If we regard our Millipore membrane as a layer of dead air 150 μ thick, its thermal conductivity would be 6×10^{-5} cal/sec/cm/° C. Let us assume an average temperature difference of 10° C between blood flowing on one side of a gill membrane and water on the other. For an 80 m^2 membrane, 0.0150 cm thick, the initial rate of heat loss would be 1900 kcal/min, an insupportable drain even in a man performing vigorous work, whose heat production might be 10 kcal/min. The second problem to be overcome in the design of a blood-perfused gill deals with CO_2 loss. If we assume for simplicity that P_{O_2} and P_{CO_2} come to equilibrium during the gas exchange between blood and water flowing over the gill, then blood gas tensions will be a function of metabolic rate, gill water flow, and solubility of CO_2 and O_2 in water. Since CO_2 is 28 times more soluble in water at 20° C than O_2, one can predict that a man who maintains an arterial O_2 tension of 100 mm Hg will perforce have an arterial CO_2 tension of 2 mm Hg, a level which our acid-base economy is not prepared to tolerate (13). Both the CO_2 and temperature problems apply, of course, to fish gills as well as blood-perfused artificial gills, and fish have chosen over the millenia not to strive against the inexorable laws of diffusion and heat flow. They have remained poikilothermic, and have adjusted their bicarbonate system to live contentedly with an arterial P_{CO_2} of 2 mm Hg.

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Panel on

Physical and Cellular Mechanisms

W. O. FENN, *Chairman*

Dr. CLARK

Dr. DOEBBLER

Dr. PAGANELLI

Dr. PHILP

Dr. ROSENBAUM

Dr. SMITH

Discussion

CHAIRMAN FENN: The question has been asked about the variable humidity, in studies of pulmonary oxygen toxicity. Dr. Clark, was the oxygen in your experiments humidified?

DR. CLARK: We humidified the gas by bubbling it through a hospital oxygen humidifier. We measured the relative humidity of this gas and it ranged from 70 to 80 per cent.

DR. SCHAEFER: I would like to ask Dr. Clark at what time of day were the experiments on reduction of vital capacity in pulmonary oxygen toxicity performed. One has to take into consideration that even during the day, let alone during the night, you have a cycle of variation of about ten per cent in the vital capacity.

DR. CLARK: We didn't take daily variation into account. These measurements were done over a finite period of time, ranging from eight hours to about twelve hours. The subjects were trained very thoroughly in performance of vital capacity to show that they could duplicate their vital capacity within a 100 cc range on three to five separate tries. With this training the results indicated that as oxygen breathing continued there is a progressive decrease in vital capacity. No upward trend occurred. I am not aware of the magnitude and nature of this daily variation.

DR. SCHAEFER: The daily variations are related to the sleep/wakefulness cycle and they vary individually but they are on the order of ten per cent and the magnitude depends at what time you make this measurement.

CHAIRMAN FENN: I understand, Dr. Clark, that your theoretical curves were rectangular hyperbolas, which I suppose means that you kept the product of time and intensity constant and did not take into account any

concurrent rate of recovery which may be going on at the time when oxygen toxicity is being built up.

This, I suppose, is all right at least for the pulmonary symptoms where the rate of recovery seems very slow, but I wonder whether the same kind of an equation would work for the pressure-duration curve describing oxygen tolerance of the central nervous system. I suppose the recovery must be more rapid there just as the rate of development is more rapid.

DR. CLARK: This is very possible. The reason that we based the shape of this curve upon a rectangular hyperbola was related to the studies of Gershman, Williams and Beecher, and Cleveland, in which Gershman showed that survival times of mice were hyperbolically related to the pressure of inspired oxygen. Williams and Beecher showed that the same relationship held true for Drosophila. Cleveland's work shows the same pattern for protozoa. This type of curve is a straight line on a log-log plot. By taking advantage of this we could construct such a curve from relatively few data points.

As far as the central nervous system tolerance curve is concerned, we derived data from the U. S. Navy studies of Yarbrough et al and also Donald's studies in England, pooled it and determined the time required to develop a ten per cent incidence of central toxicity (an incidence of CNS toxicity in ten per cent of the subjects). By this means we obtained three solid points of information which, like the pulmonary findings, also fell on a straight line in a log-log plot. That curve is described by Dr. Lambertsen (Chapt. 21).

DR. LUNDGREN: I would like to ask Dr. Clark how were the measurements of vital capacity made? It is known from experience in pilots that the limiting factor in vital capacity reduction might be pain. This is eliminated if the man makes a forced inspiration so that the collapsed alveoli dilate.

This implies that part of the explanation for the variation of vital capacity could be variation in pain sensitivity of the subjects. I would also like to ask whether you have any idea what kind of change lies behind the reduction in the experiments at two atmospheres.

As you might know, it has been shown by Rahn and Farhi that the likelihood of developing atelectasis when you work with high oxygen pressures is much smaller than when you work with oxygen at low ambient pressures.

DR. CLARK: Our subjects were highly motivated and were "vocally encouraged" during the performance of their vital capacity measurements. It is true there was pain and this probably had a degree of influence in various subjects. Dr. Lambertsen and I were two of the subjects and in my own case, near the end of the exposure to oxygen breathing at two atmos-

pheres, it was very painful to inspire. However, my vital capacity was decreased by only about three to four per cent. Three to four hours later the symptoms had greatly subsided. Then, although I felt a great deal better, my vital capacity was at this time decreased by ten per cent. For this reason I do not think that pain is the answer. In some subjects it may contribute, but I do not think it did to a great extent in our series.

As for your question about the mechanism of the decrease, we do not think it was atelectasis, at least at the stage of the process we studied. We could not, in our preliminary studies, routinely measure the alveolar-arterial oxygen tension gradient. Caldwell did this in his four subjects and one subject who had a 37 per cent decrease in vital capacity had a normal alveolar-arterial Po_2 difference of 64 mm Hg during oxygen breathing. The two subjects from whom we obtained arterial blood had no increase in alveolar-arterial Po_2 either.

We think that the decrease in vital capacity must be related either to edema or to some type of reduction of volume of the larger respiratory passages.

Dr. Bennett: I know that Dr. Smith has done experiments which definitely contradict the hydrate theory of narcosis. Would he like to comment on this?.

Dr. Doebbler: I have been talking with Dr. Smith and believe that, except for a very few individuals, there really seems not to be a disagreement in the views that have been taken concerning the merchanism of inert gas narcosis.

What has been said up to the present emphasizes the correlations of narcotic properties with various observed physical properties of gases. It seems very likely that one might ultimately arrive at an explanation that would account for and would incorporate several viewpoints into an actual mechanistic view.

As an example I can point out that it seems rather obvious to everyone working with inert gases at cellular levels that the phenomena of narcosis are membrane-related. In this case these effects are going to be related to some action within lipid-like phases.

One may be dealing also with interactions with water and we feel quite strongly that there may be a definite primary effect of the gas on the water that simply provides a mechanism or a driving force for putting the gas molecules into certain hydrophobic regions of the cell. This goes back to the fact that water is an extremely associated liquid and consequently the involvement of water here may be simply a means of providing a driving force for the process of getting gases into lipid sites where they actually produce a biological effect.

Dr. Smith: I think it is clear that the anesthetic pressures of most gases

correlate with virtually every physical property: ideal solubility, polarizability, ionization. If you write down any physical property you will find that, except for the fluorine compounds, they are in rough agreement with the anesthetic pressures.

Then if you look at the fluorine compounds, you find that they do not lie on the ideal solubility plots first used many years ago. That is why, although their mechanism of narcosis may of course be different, I believe that their agreement with the lipid solubility theory and not with the hydrate theory and not with ideal solubility, and not with polarizability, is perhaps some evidence that the lipid solubility theory is on a slighty closer level than most other correlations. That is really all one can say from physical data of this sort.

DR. BRAUER: There is one other exception in that hydrogen, like the fluorine compounds, also does not fall on your plot.

We have done a series of experiments with monkeys in hydrogen, using electroencephalograms as the end point. You have to go to fairly high pressures to see effects and we have been operating in the vicinity of 120 to 150 atmospheres.

At that point with helium, you begin to get indications of narcosis. At least you see delta wave development and we will have to go to higher pressures yet to see whether the picture in helium will follow the picture with nitrogen where the delta wave development is rather promptly followed by subsidence of the voltage and development of narcosis.

With hydrogen at the greatest pressures we have used so far, we have not seen any indication of narcosis. Therefore, at the present time I think it is safe to state that hydrogen anesthesia certainly comes very far beyond the point of nitrogen narcosis. It falls far out of line and our data lead us to suspect strongly that hydrogen may prove considerably less potent as an anesthetic than helium.

DR. BOND: We have been very interested in permiselective membranes for saturation diving work, not for obtaining oxygen from sea water, but from the point of view of the possibility of concentrating the CO_2 inside the habitat to a level at which sea water CO_2 scrubbing would be efficient.

We are concerned about loss of helium through such a system. I know you have been working with Robb and his associates. Would you estimate whether we could afford a helium loss through their new permiselective membranes?

DR. PAGANELLI: I'm afraid I can't. I do not know the relative permeabilities of their latest membrane to helium and to carbon dioxide. In our case we are dealing with a millipore membrane which really isn't permiselective. It is a sieve, and the reason we use it and can get away with it is because it is hydrophobic. The only selectivity we get is that which is given by the different solubilities and diffusion coefficients of the gases.

Interestingly, the silicone rubber membrane of Robb and the millipore membrane turn out to have about the same selectivities for oxygen and carbon dioxide, almost by chance. The solubilities and diffusion coefficients come out to be just about in the same order.

DR. TROELL: I would like to ask the panel a question about oxygen toxicity and intestinal movements. Some years ago I did some experiments with plastic abdominal windows in rabbits. Through the abdominal windows you could see very nicely the movements of the intestines, and you had the ability to see derangement of peristalsis.

We put the rabbits in a compression chamber with 100 per cent oxygen at 280 feet. Then after about an hour, the intestinal movements completely disappeared and there was complete standstill, a paralytic ileus. We removed the pressure and the movements started immediately, we put on the pressure again and the movements stopped, rather quickly. Then we went up to 380 feet and the movements stopped after 20 or 30 minutes. Why did the intestinal peristalsis stop?

DR. ROSENBAUM: Do you think the effect was of nervous origin?

DR. TROELL: We can't answer that. I could see constriction of vessels.

DR. ROSENBAUM: If I were called on to give the etiology of oxygen toxicity in an intact mammal, I would say it was largely of nervous origin. Even the effects of oxygen on the lung appear to be neurogenic. If you look at lung from the point of view of the pathologist you can find no direct effect of oxygen on lung tissue, including atelectasis. The atelectasis seems to be the result of a degassing phenomena that takes place. It is independent of an effect of oxygen per se on pulmonary epithelium.

If I were asked now to state the etiology of pulmonary oxygen toxicity, I would say it was a left heart block due to nervous effects resulting in a pulmonary edema-like situation, with the nervous system being responsible for the prime effect. I would not be at all surprised if the intestinal effect you observed was nervous in origin.

DR. MACKAY: Dr. Troell, activity in the bowel is dependent on very many things. It is very sensitive, even to the emotional state of the animal. When we have humans and animals swallow small radio transmitters and monitor such things including activity patterns, I can assure you that the increase or decrease of activity depends on almost everything.

DR. NOGUCHI: I have had some experience with oxygen effects on tissue cultures. I have used 100 per cent oxygen, using one atmosphere and twenty psig for exposures of 24 to 72 hours and at this point I am not certain whether there is any sensitivity difference among various strains of tissue culture cells. I wonder, Dr. Rosenbaum, have you found any difference in the sensitivity of different cells to oxygen toxicity?

DR. ROSENBAUM: Oh yes. There are different strains of cells which re-

spond differently to levels of oxygen up to one atmosphere. We have experimentally used only two strains of cell cultures, but a number of different organ cultures. Most of our experience has been with the intact animal and the cells of the nervous system seem to be the most affected in an intact animal. I don't mean morphologically affected since you cannot see such changes readily in the intact animal. This is why we began using cell cultures.

DR. LAMBERTSEN: As we discuss various indirect effects of high oxygen pressures, it is wise for us not to forget that oxygen has many effects and at many sites. Mention has been made of central nervous system, psychological and circulatory influences of oxygen as being responsible for the pulmonary toxicity of oxygen.

What is now extremely important is that we not obscure the clear fact that oxygen directly affects cells in the lungs too. Oxygen poisoning of the lungs is a real and direct event, due to high oxygen pressure in the respiratory passages. The lung epithelial membrane in man or animals is exposed to the highest oxygen pressure of any cells in the body. When one breathes oxygen for a long period of time these cells receive the greatest dose of oxygen. The effects on the human lung are so prominent that there is no mistaking that there is a direct effect of oxygen on that membrane. If you breathe chlorine or bromine you will have no doubt that there is an effect on that lung membrane. The effect of oxygen feels very much the same, so there is a direct toxicity. There are of course other secondary or contributory effects but these are not in themselves damaging. These indirect factors should only modify the gross event of pulmonary oxygen toxicity and should not be confused with the primary toxic event.

DR. BEAN: Regarding oxygen effects on peristalsis, you can demonstrate very readily that in an isolated preparation exposed to high oxygen pressures, intestinal movements stop completely. That is so promiment that it almost looks like the effect of cyanide and suggests that there exists an effect of high oxygen resembling that of hypoxia.

I think Dr. Rosenbaum has a good point concerning the effects of oxygen on the lungs. I do not deny that there is a direct effect on the lung but I do know that in animals which convulse, and therefore increase the influence of the sympathetics on the lungs, you can get a very, very marked gross effect on the lung which you do not see without the effect of convulsive seizure. Therefore there is something which is subconvulsive which may effect the lung but there is also a direct effect.

DR. ROSENBAUM: The problem is very difficult to study. I have no doubt there are effects at the cellular level. In our hands, at least, it has

been virtually impossible to demonstrate morphologically any pathological changes that would be due to oxygen toxicity.

One of the problems of cells in the organism is you have means of recovery, you have various redox systems which tend to offset local oxidations. Cells are far more resistant in vivo than in vitro.

A second problem is that, with routine pathological staining methods you cannot detect bona fide effects due to oxygen toxicity.

DR. DOWELL: I would like to ask Dr. Rosenbaum if he thinks that HeLa cells are a good preparation since they show a higher rate of glycolysis and a less sensitive control mechanism in the Pasteur effect.

DR. ROSENBAUM: Any cell or tissue culture is a compromise when you want to extrapolate to the intact organism. I cannot answer your question. A tissue culture cell is an abnormal cell to begin with. Any normal cell of non-pathological origin would be abnormal once placed in tissue culture.

DR. DOWELL: My assumption is that one of the earliest stages of the signs of oxygen toxicity would be in the control between glycolysis and the citric acid cycle.

DR. ROSENBAUM: Well of course the SH-dependent enzymes in the citric acid cycle are certainly affected, as shown by the classical experiments that go back to Dickens, Stadie and Haugaard.

DR. LEITH: Dr. Paganelli, with appropriate structural support to maintain a hydrostatic pressure gradient, do you suppose that the artificial gill system could work at great depths? Should the Navy be building submarines out of cintered bronze covered with plastic film?

DR. PAGANELLI: It certainly would work. I do not know how many men you could support with it, but it is theoretically possible.

DR. BENNETT: To get back to the subject of pulmonary damage at the higher pressures, I agree with Dr. Bean that it seems to be related somehow to the onset of the convulsions. I also agree that the evidence seems quite clearcut that there is a direct effect of oxygen on the lungs.

DR. RAHN: I would like to ask Dr. Fenn to review for us very briefly any effects of pressure per se which would affect a warm-blooded animal, not in terms of enzymes but in terms of whole tissue preparations. Do we have any evidence for warm-blooded animals?

CHAIRMAN FENN: I would say we should not expect effects at ordinary diving pressures. If we go beyond 1,000 or 2,000 feet then we may begin to get effects of hydrostatic pressure itself.

At 1,000 feet the possibility of getting a helium narcosis seems to be just about borderline. You might and you might not. But the possibility of getting some effect of hydrostatic pressure is also just about borderline. So, if you are on the bottom at 1,000 feet and if there are any symptoms, you

would not know which effect to attribute them to. You can not tell what the cause is from the nature of the effect.

Very little information is in the literature about any pressures less than 100 atmospheres. That is why I showed our findings at 41 atmospheres and I mentioned one at 7 atmospheres. However, that is all the information there is, so there is very little likelihood that pressure will have any effect at ordinary diving depths.

Most of the work on the physiological effects of high pressures has been done with lower organisms or cold-blooded animals. The work on nerves and muscles of toads and frogs, however, seems applicable to warm-blooded animals. Human red blood cells can be made spherical by very high pressures and some Russian authors have shown changes in the staining of isolated brain and gland tissues of mice when exposed to pressure. All of these observations, however were made at pressures far beyond the range of interest to divers.

DR. RAHN: Unless we go to hydrogen.

DR. BRAUER: There is in considerations of oxygen toxicity a fascinating interplay between oxygen toxicity, anoxia and some of the inert gas phenomena. Bennett and his colleagues have brought out some of this in studies of drug effects as protectants.

With regard to these interactions, we were interested in the effect of adaptation to hypoxia on the susceptibility to oxygen toxicity. You can altitude-adapt rats and mice to altitudes in the 18,000 foot range within a few weeks. We have done enough work to be sure that this type of adaptation does indeed provide very remarkable protection against at least the pulmonary phase of oxygen toxicity.

The results are something like this: rats will survive about 36 hours in an atmosphere containing nitrogen plus 1.06 atmospheres partial pressure of oxygen. If you altitude adapt these same animals to 18,000 feet for four weeks the animals will survive for seven days or longer in one atmosphere of oxygen in nitrogen. When you sacrifice it prematurely, it clearly fails to show severe lung injury. The animal is not one that can survive a collapsed lung but an animal in whom the lung has not developed oxygen toxicity.

In mice we have carried this one step further. We know that in altitude adaptation there are CNS effects, most prominent of which perhaps is the decreased CO_2 susceptibility. There are the decreased CO_2 equilibrium levels. These are dissipated rather rapidly whereas adaptation of the enzyme chain and hematological chain does persist.

We have data on mice that were altitude-adapted and then removed from the altitude chambers and allowed to remain in the laboratory for a week. At the end of that time the CO_2 adaptation is pretty well dissipated whereas the enzyme and hematologic adaptations persist.

We have then challenged these animals with oxygen and the indications at present are that the resistance to oxygen toxicity persists and well outlives the CO_2 effects. At present, therefore, the indications are that the enzyme or the hematologic effects of altitude acclimatization do indeed afford quite nice protection against the pulmonary phases of oxygen toxicity.

DR. ROSENBAUM: Neonatal rats are remarkably resistant to both anoxia and oxygen toxicity. A newborn rat can be put in water for six or seven hours and he will be perfectly all right when removed. If he is put in 100% oxygen at a single atmosphere, he will survive for 21 days and come out of it perfectly all right. An adult rat would survive only 48 to 50 hours at the most.

Newborn guinea pigs are not so resistant. They die very much like adults and the remarkable fact is that when you examine the lung of newborn guinea pigs and compare it with the lung of a newborn rat, it is virtually a different organ.

Apparently, depending upon the degree of maturation at birth, whether you have a premature birth as in the case of a rat or a full-blown adult in the case of the guinea pig, something takes place in the lung which may indicate relationship between anoxia and hyperoxia.

DR. SALTZMAN: Would Dr. Rosenbaum relate this observation of immaturity protecting the animal in one area from oxygen toxicity to the observations of retinal vulnerability in immature animals to high oxygen tensions?

DR. ROSENBAUM: I cannot.

DR. BEHNKE: Dr. Clark, it seems to me that the time is long past when you could use one point for a predictive curve and use a parameter as labile as vital capacity to obtain information with any meaning. What you have with your one point curve I think, is a prediction for each of the subjects that you used. There was wide variability in them and it seems to me that the other point at six-tenths of an atmosphere was not established. I wish we knew whether individuals could breathe oxygen at six-tenths of an atmosphere.

I think the time has come to use many parameters for such studies, including sensitivity tests, bio-chemical measurements of serotonin and other tests and to start with oxygen at 100 mm Hg pressure and go up by 100 or 200 mm Hg at a time, in steps up to 4,000 mm Hg. Then give us a curve. A predictive curve at this time is of no help to you, I can assure you.

DR. CLARK: As I said, the six-tenths of an atmosphere asymptote shown was an assumption based upon the data which now exists. We do not believe that no effect at all will be produced by continuous, indefinite exposure at six-tenths of an atmosphere. We think there will probably be some pul-

monary effect. We purposely set it higher than the two week long study by Helvey at five-tenths of an atmosphere to get into a region where we would see a significant pulmonary effect in a finite time.

Vital capacity may be considered a labile measurement and we wish we had a better one, but if the subject is very well trained it doesn't have to be a labile measurement. There are changes from day to day but on a given day a trained subject, I think, can reproduce his vital capacity fairly accurately.

DR. LAMBERTSEN: Whether this predictive analysis makes sense depends, Dr. Behnke, upon what you are after. We were trying to develop a predictive curve to give ourselves, others within our own laboratory, and still others outside it, a guide which would permit the design of oxygen tolerance experiments to test such a curve. For this purpose I am not shocked by what you called a one point curve, since the predecessor of this predictive curve was drawn before there were any points at all.

The predictive curve was a no-point curve until the present series of experiments was done and the comparative analysis of these and other studies carried out.

One of our most important questions has been the relation between the oxygen tolerance of the lung and that of other tissues such as the brain. We know, without quantitative criteria, that if you breathe oxygen at high tensions you will convulse, if you breathe them at low tensions you will get pulmonary damage. We must determine the pressure-time relationships for these and other forms of oxygen toxicity. Prediction based upon analysis has to be carried out to find the points of pressure most likely to provide the information that will help resolve these questions.

Out of our initial analysis came the decision that two atmospheres of oxygen pressure would give the greatest likelihood of long periods of oxygen exposure without having convulsions or severe pulmonary damage.

DR. BEHNKE: I thought this curve dealt with pulmonary damage and we need a curve relating to pulmonary damage. However, one question is whether the pulmonary damage is directly proportional to pressure. One point of Dr. Clark's work that seemed impressive was that perhaps at two atmospheres one can safely breathe oxygen only half as long as at one atmosphere. You seem to get a doubling effect. Generally at four atmospheres, for example, the pulmonary effect does not appear to be four times greater than at one atmosphere. However, we carried the experiments at four atmospheres only to about 45 minutes before collapse occurred.

MR. HEMPLEMAN: I would like to ask Dr. Philp if he has any comments at all on the work of Waldo who showed that there was a significant correlation between the static serum surface tension and the susceptibility to

aviators bends. He also found that by dehydration he could alter the static serum surface tension and also alter sensitivity to bends.

DR. PHILP: I think it is possible that the effect of surface tension may be involved, but probably not the only one. When you are dealing with dehydration you are dealing with a multiplicity of effects, one of which is the reduction of fluid volume, another relates to changes in viscosity as well as surface tension, possibly others to changes in clotting, and there are certainly general debilitating effects.

I think it is quite likely that the surface tension theory may well be involved, as may one of these factors in the effects of dehydration.

C. J. LAMBERTSEN

Summary

The usefulness of man in systems for exploring the deep seas and space is periodically questioned by many engineers and scientists who believe that unmanned apparatus and machines are capable of accomplishing detailed exploration. Man is considered to be unnecessary. Devices already exist which automatically can "see," can hear, can calculate, can measure temperature, light, radioactivity, magnetism, pressure, hardness, and elasticity, can sense direction and velocity and rate of change of direction and velocity, can perform certain chemical analyses, and can even test for the presence of simple life forms. However, limitations in the ability to adapt such devices to deep sea or space exploration indeed requires that the role of man as a direct contributing part of the system be carefully appraised.

Not only has it been stated that man would be unnecessary for deep submarine and space exploration, but that the presence of man would actually decrease the chance of carrying a mission to a successful conclusion. This attitude arises from the recognition that specialized devices, supplies, and special structural features are required to sustain man in a useful state during submergence or a prolonged flight through space. It is sometimes considered that such "life-supporting" systems detract from the likelihood of overall mission success.

The objections to the direct use of man in deep submergence and in space exploration appear logical but are not entirely so. It is necessary to consider that in each case the total task will be carried out by a great variety of methods. There will continue to be tasks which will be more appropriately carried out by means of unmanned, instrumented vehicles. However, there will also remain other aspects of exploration, or even rescue, which no machines yet conceived can carry out alone. No man-made mechanical apparatus has yet been designed to use judgment in the face of the unexpected. Man has created complex and wonderful forms of programmed equipment and electronic computers but it remains true that the only computer capable of all functions such as remembering, recognizing, learning, thinking, reasoning, judging, integrating, reacting, communicating and logically altering a previously programmed sequence of events is man himself. Man has been jokingly called the cheapest computer to mass produce, but it has required a period of development measured in millions of years to reach his present high state of effectiveness. Recognizing the

many attributes of highly trained man, it is important to search for ways in which man can increase the possibility of successful operations, rather than to assume that he will interfere with achievement of success.

It should not be necessary any longer to consider whether man is required in deep undersea or deep space operations. Man should be intentionally utilized as a distinct asset, insofar as he can improve the quality of the total effort, can decrease the lag between now and the time when even more advanced exploration begins, or can decrease the cost of the program.

Open Sea Saturation Dives to Date

Conshelf 1

September 1962, 2 men for 7 days at 35 feet. Cousteau group project.

Man in Sea

September 1962, 1 man for 24 hours at 200 feet. Link project.

Conshelf 2

July 1963, 5 men for 1 month at 33 feet and 2 men for 7 days at 85 feet. Cousteau group project.

Man in Sea

June 1964, 2 men for 49 hours at 432 feet. Link-University of Pennsylvania project.

Sealab I

July 1964, 4 men for 11 days at 192 feet. U. S. Navy project.

Conshelf 3

September 1965, 6 men for 22 days at 330 feet. Cousteau group project.

Sealab II

September 1965, 28 men for 15 or 30 days at 205 feet. U. S. Navy project.

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