Proceedings

SECOND SYMPOSIUM on UNDERWATER PHYSIOLOGY

February 25-26, 1963
Washington, D. C.

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Prepared for the
Office of Naval Research
Washington, D. C.

by the
Mine Advisory Committee
National Academy of Sciences–National Research Council

Publication 1181
National Academy of Sciences–National Research Council
Washington, D. C.
1963

Price $4.00

Available from
Printing and Publishing Office
National Academy of Sciences
2101 Constitution Avenue
Washington, D. C. 20418

Library of Congress Catalog Card Number: 63-65470

ABSTRACT

These proceedings represent a compilation of those papers presented at the Second Symposium on Underwater Physiology, February 25-26, 1963, sponsored by the Office of Naval Research and the Mine Advisory Committee of the National Academy of Sciences-National Research Council.

The range of interests covered includes oxygen toxicity, decompression and bends, and respiratory problems, with special emphasis on their implications in underwater swimming. Some of the earlier work in these areas of interest has been re-examined in the light of current problems.

This symposium continues and complements the discussions presented in the Proceedings of the First Symposium on Underwater Physiology, National Academy of Sciences-National Research Council Publication No. 377, 1955.

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FOREWORD

In 1955, as part of an attempt to arouse interest in the many problems peculiar to the underwater environment, the Panel on Underwater Swimmers of the National Academy of Sciences' Committee on Undersea Warfare joined with the Office of Naval Research to conduct the first Symposium on Underwater Physiology. Since then the field of diving has attracted considerable attention, in extension of the shallow, self-contained diving begun in the throes of World War II, in attempts to increase the depth of human diving and in efforts to extend the duration of deep diving.

While the practice of diving has spread tremendously during the past decade, neither physiological research nor the engineering of apparatus to permit breathing under water has advanced apace. The volume of medical research has recently increased, but the need and the opportunity to obtain new physiological information still appear as great as they did a decade ago.

The Mine Advisory Committee of the National Academy of Sciences and the Office of Naval Research have sponsored this Second Symposium on Underwater Physiology to again call attention to the unusual, difficult and challenging biomedical problems related to work under positive pressures and beneath the sea. These problems and their solution do not relate merely to success in devising physiological and mechanical means of extending the depth and duration of diving. It is at last being recognized that exposure to positive pressures in laboratory and clinical treatment situations offers useful means of modifying physiological and pathological processes in man. It can be expected that interest in the hyperbaric environment will further increase, quite in addition to the continued concern for improving the capacity of the diver to perform useful work.

This Symposium has provided an opportunity for investigators from several countries, including the United States, Great Britain, Scotland, France, Sweden and Switzerland, to exchange information and concepts. These Proceedings comprise the individual papers presented by this distinguished international group, as well as the discussion of major topics. The active formal meetings were supplemented by demonstrations of diving techniques and equipment displays at the U.S. Navy Experimental Diving Unit.

On behalf of the Mine Advisory Committee and the Office of Naval Research, the Symposium Planning Group would like to express its sincere appreciation for the valuable contributions made by those participating in the scientific sessions. It would also like to recognize with gratitude the diligent and skillful technical editing assistance provided by Miss Eleanor Jones of the University of Pennsylvania Laboratory of Pharmacology, the competent execution of the laborious task of transcribing the manuscripts and discussions by Mrs. Maxine Sheesley of the Mine Advisory Committee Staff, and the valuable assistance provided by Miss Susan Kronheim of the Physiology Branch of the Office of Naval Research in the many details of planning and executing the Symposium.

The Symposium Planning Group

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PRESENT STATUS OF UNDERWATER PHYSIOLOGY

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For our hosts, the Mine Advisory Committee of the National Academy of Sciences and the Office of Naval Research, I welcome all of you to the Second Symposium on Underwater Physiology. May it enjoy the interest and the success of the first symposium[1,1a].

There are many reasons why our combined attention should again be brought to bear upon the physiology of exposure to positive pressure and the underwater environment. Diving is an expanding field of practical endeavor, not only for military purposes, but also in scientific submarine explorations, oceanographic studies and marine biological research activities. While amateur interest in diving has not slackened and will probably be sustained forever, I detect an increasing desire in civilian divers to put their interest in diving to useful purpose.

Interest in the interrelated physiological effects of underwater existence is also increasing, at least apace with the expansion in practical applications of diving methods. The peculiar physiological stresses of diving are of evident interest to naval medical laboratories throughout the world. There has been a purposeful and welcome effort by the naval organizations of several countries to advance physiological studies in their own laboratories, and by support of research in universities.

Finally, with the passage of time, investigators have become more and more interested in adapting to positive pressure experimentation the excellent quantitative methods which have been developed for use in sea level studies. Many investigators have discovered that the conditions of diving offer attractive opportunities as tools for physiological research; others are discovering the implications of positive pressure for problems of general medicine[2]. The result of this increase in interest, effort and quantitative study can only be an improvement in the comprehension of the positive pressure environment and in the capacity to work under water.

With these thoughts in mind, where do we now stand in the evolution of diving physiology? Have we truly come a long way from the first shallow penetrations with the lungs full of "held" air or from the primitive efforts to carry a supply of respirable gas beneath the surface? It is worth realizing that while practical progress has been tremendous and physiological advance considerable, even the physiological consequences of breath-holding at various pressures and with various gases have only recently begun to be understood[3,4,5,6]. Very few of the biomedical problems peculiar to diving have been so well studied that we can afford to slacken the pace of their investigation.

Many countries represented here have contributed to our present practical and theoretical information. Years ago, helmeted divers, breathing air compressed to the working pressure, gained tremendously in two important ways from studies by our British colleagues. Haldane cleared the minds of these air-breathing divers by insisting upon the ventilation of their helmets in proportion to the depth of diving[7]; this diminished the high tension of inhaled carbon dioxide which, although unrecognized as such, had been a limiting factor in diving with compressed air. Carbon dioxide still remains important to diving physiology in a great variety of ways.

A second great contribution of English science to diving you also know. This was the successful effort to introduce a logical procedure for decompressing tunnel workers following exposure to compressed air[8]. This theoretical contribution was extended by the subsequent, laborious work of naval laboratories in the United States and England, and led to over a half century of successful diving with compressed air and helium-oxygen mixtures[9,10].

Now, partly because of the practical extension by the French of the use of air-breathing apparatus by free swimmers[11], even compressed air diving provides new problems of decompression physiology which have not been completely solved[12]. These are related to the fluctuating and highly variable patterns of diving depth and also to repeated exposures to increased pressure without complete removal of the excess inert gas accumulated during prior dives. Because of the practical desirability of such forms of exposure, these may forever be among the most common problems of diving medicine.

Thirty years ago, to extend diving depth beyond the levels at which compressed air stupified the diver, gas mixtures other than air were studied and inert gases other than nitrogen were used. This led to the meticulous studies of helium-oxygen mixtures by naval investigators in this country[10,13], the studies with hydrogen in Sweden[14], the practical application of N_2-O_2 diving by the British during World War II, the more recent laboratory studies with nitrogen-oxygen mixtures in England and the United States[15,16], and to a slowly progressing interest in multiple gas mixtures[17,18,19]. Exposures of extreme duration are now also receiving attention[20,21]. We should now be concerned not only with studies of unusual gas mixtures, but also with the problems basic to purposeful alternation of exposure to pure oxygen with exposure to an inert gas-oxygen mixture to improve the rate or safety of decompression[1,19].

Throughout the history of diving, the occurrence of nitrogen narcosis has kept alive the unresolved question of its mechanism. Concepts and studies of inert gas narcosis concern pharmacologists and anesthesiologists as much as they do diving physiologists. Since the earliest recognition of nitrogen intoxication, many concepts of inert gas narcosis have been advanced and subjected to detailed study. In medicine and in diving the mechanism whereby any gaseous agent produces narcosis continues to excite great practical and theoretical interest[22,23,24].

In all of these investigations, whether of bends, narcosis, carbon dioxide effects, or respiratory problems, the physiological effects and toxicity of oxygen itself run as a web of connecting threads. My memory is remarkably clear

concerning one brief episode in the long-term evolution of diving. This was the period of extensive practical use of oyxgen in diving[11] and of studies of pure oxygen effects on man in Italian, British and U.S. laboratories during World War II[25,26] Out of these efforts came considerable information concerning the tolerance of men to increased Po_2, but this information is, even now, so incomplete that diving with oxygen alone and with inert gas-oxygen mixtures is handicapped. Recent studies with inert gas-oxygen mixtures have again focused attention upon carbon dioxide and oxygen by indicating that incapacitating, carbon dioxide autointoxication can occur even when nitrogen-oxygen mixtures are used in open-circuit breathing systems during strenuous work[27]. Such observations offer partial excuse for the still evident uncertainty regarding the roles and interactions of carbon dioxide and oxygen producing what twenty years ago was aptly labeled "Shallow Water Blackout"[28].

For a time the diminished use of pure oxygen in peacetime diving resulted in an unfortunate lack of attention either to the important implications of high oxygen pressures to other forms of diving or to the physiological gains in decompression by inspiring gas mixtures with low or zero tensions of inert gas. Increased interest in the application of oxygen decompression to shorten or improve the safety of air or mixed gas diving will require continued study of the physiological as well as the toxic effects of oxygen.

It is evident that while most of the individual problems of the underwater environment are now well recognized, they are not yet adequately solved. Today, with renewed interest in extending the capacity of man for extra-atmospheric existence, it should be emphasized that the research required for penetration of the seas of this earth deserves attention at least comparable in quality and degree to that for human existence in the space beyond earth's atmosphere. This is an increasingly exciting field of work. Research in underwater physiology is no longer the slowly moving stepchild of medical research. Questions and the methods of answering them are springing out of many civilian and military laboratories, and, as already mentioned, the implications of some of these studies to general medicine and surgery are being recognized.

With this renewed interest, what is the state of our information and our concepts? What do we know and what experiments should now be done? Let me join you in the audience, give attention to our first session, and find out.

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TISSUE INERT GAS EXCHANGE AND DECOMPRESSION SICKNESS

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Current ideas on tissue saturation with inert gases were largely initiated by Haldane[1] in his attempt to construct successful decompression schedules. Since then much further practical work has been carried out by Jones and his associates[2] using radioactive tracer techniques, and a very detailed mathematical treatment of various tissues of differing capillary densities appears to lend convincing support to the present ideas. This analysis was performed by Roughton[3] and the basic model used was a central cylindrical capillary responsible for a concentric cylinder of tissue. In brief, the position now reached with these ideas may be summarized as follows:

> The inert gas which is supplied to the tissue disperses itself uniformly over the tissue space because diffusion is very rapid between the capillaries, and hence the inert gas tension of the blood being removed is truly representative of the whole tissue inert gas partial pressure. Defining:

P_o = inert gas tension of blood supplying tissue

P = inert gas tension of blood leaving tissue

V = rate of blood supply per unit tissue volume per minute

S_B = solubility of inert gas in blood

we see that

P_oVS_B = rate of supply of inert gas to tissue

PVS_B = rate of removal of inert gas from tissue

and from this

$(P_o - P)VS_B$ = rate of accumulation of inert gas in tissue.

Also defining

S_T = solubility of inert gas in tissue

$S_T(dP/dt)$ = rate of change of gas content in tissue.

Since the rate of accumulation must equal the rate of change in tissue content we have the equation:

$$S_T(dP/dt) = (P_o - P)VS_B$$

letting $k = VS_B/S_T$ and solving we have

$$P = P_o(1 - e^{-kt}).$$

Thus the rate of saturation of a tissue depends only upon the blood perfusion, V, and the ratio of the solubility of inert gas in the blood to its solubility in tissue, S_B/S_T. On this theoretical basis most analyses of whole body uptake and elimination of inert gas have taken place.

In a paper from Groupe d'Etudes et de Recherches Sous-Marines at Toulon[4] after reviewing the practical and theoretical discussions regarding tissue inert gas exchange the author decides to support the perfusion mechanism and to reject any place whatsoever to diffusion mechanisms. It is my intention to try to demonstrate that this can only be regarded as an incorrect appraisal of the true situation.

Let us suppose that a subject commences suddenly to breathe a pressure of inert gas of magnitude P_o atmospheres and that previous to this time he had no inert gas whatsoever in any part of his body. It is clear from very simple considerations that after a few minutes of breathing the new gas pressure there will exist certain parts of the body where the concentration of the inert gas is high and certain parts of the body where the concentration is non-existent or very low. The existence of concentration gradients will cause dissolved gas to flow down the gradients. Such flow will be largely influenced by diffusion mechanisms and one must decide whether such inter-tissue diffusion flow is going to compete in any way with the perfusion flow of dissolved gas into the respective tissues. Resorting to microscopic situations such as those examined by Roughton will not prove very effective as a means of yielding quantitative considerations. Consequently a new model for discussion will be proposed. It must of course be realized that all these models represent completely idealized situations and are constructed solely for the purpose of extracting very gross information.

Represented in Figure 1 are two tissues of very different vascularities. The vascular tissue ends abruptly at a flat surface and a relatively poorly vascularized tissue commences. Suppose that the perfusion of these two tissues began some minutes ago with blood at a gas tension P_o atmospheres. Suppose further that there exists a uniform gradient of concentration from this highly vascular region to a plane 1 cm. inside the slow tissue, AA' on the diagram. Consider a slice of tissue at AA' of the length 1 cm. and with a cross section measuring 1 mm. x 1 mm. This will be considered as a piece of poorly vascularized tissue the center plane of which is 1 cm. away from a high concentration P_o. If both the very vascular and poorly vascular tissues are of a "watery" nature it can be stated that at body temperature approximately 1.0×10^{-5} cc. of nitrogen will flow per sq. cm. per atmosphere pressure gradient through the plane AA' per minute. The amount therefore flowing through the section on the diagram will be 1/10 of this, i.e., 1.0×10^{-6} cc. of dissolved nitrogen per minute per atmosphere pressure. The amount reaching the tissue via the blood stream can also be estimated. Taking 1 capillary per cubic millimeter there will be 10 capillaries

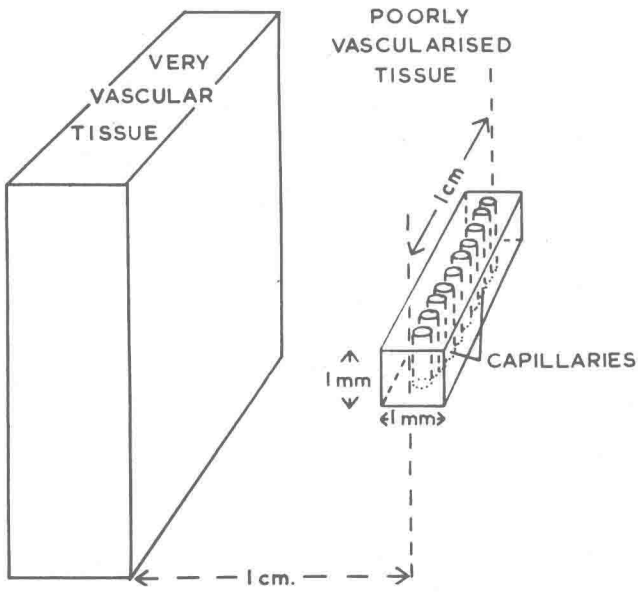

Figure 1. Tissue Saturation with Inert Gas Perfusion-Diffusion Complex Situation.

in the slice of tissue under consideration. Suppose each of these are 8 μ in diameter and that the flow of blood down them is 1 mm per second. Taking the solubility of nitrogen in blood as 0.012 cc per cc of blood per atmosphere pressure it is seen that the rate of arrival of nitrogen via the blood flow in P_o x 3.6 x 10^{-7} cc per minute. Examination of these figures suffices to show that the diffusion gradient is supplying gas molecules which for a 1 atmosphere per cm pressure gradient would require a P_o value of nearly 3 atmospheres. In such situations as this one the inter-diffusion processes will tend to dominate the kinetics. The poorly vascularized tissue will have rapid and slow components to its uptake curve, with the slow components predominating, whereas the vascular tissue will have fast and slow components with the rapid components dominating. This then will be the general picture derived from an examination of this particular type of tissue situation. When the vascularity of the two tissues does not differ by a great deal, or when both tissues have large perfusion rates then the part played by inter-diffusion will become very much less important, and will only be noticeable at the interface between the two different capillary densities. When the vascularity of a tissue is non-existent and the adjoining tissue is a highly vascular one, then provided the avascular tissue is 3 or 4 mm thick, this tissue will be entirely diffusion limited for its uptake and elimination of inert gases. Such a situation occurs in the cartilage associated with knee joints, where the completely avascular layer of cartilage is overlaid with the very vascular synovial membrane, or again there is the relatively vascular spinal cord which treads its way through cartilagenous discs, teninous inserts and bone. In fact these latter situations look to be exactly the sort of situations with which one is principally concerned in decompression sickness research. The main troubles which occur as a result of inadequate decompression are pains in and around joints, particularly knee joints, and in the more severe cases there are paralyses undoubtedly caused by emboli in, or close to, the spinal cord.

Thus the idea formed that perhaps in decompression sickness the main mechanism was a diffusion limited one. Initially this was also apparently well supported by the following experimental evidence. If one takes a large animal such as a goat as the experimental subject then the manifestations of decompression sickness which occur after inadequate decompression are very similar to those shown by man, i.e., they get a pain in a limb (a bend) which causes limping,

or in more severe cases they get emboli in the spinal cord causing paralysis of the hind legs. Now if a goat is rapidly compressed to a pressure P feet of sea water, is held there for a time t minutes, and then is decompressed in 150 seconds back to atmospheric pressure, it is possible to choose P and t, which are of course independent variables, such that for a given t there is a P value which just produces a mild bend on return to atmospheric pressure. This value of P is called the bend threshold for this particular animal for this particular t value. In Figure 2 can be seen the curves obtained from doing hundreds of such threshold

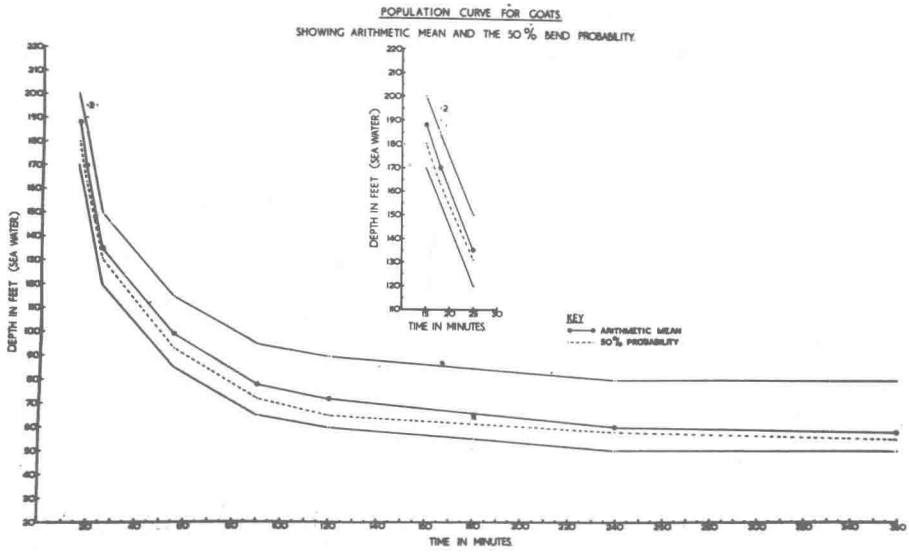

Figure 2.

dives on very many different goats. The two outer black lines represent the limits of the population. The bottom line represents the most sensitive results obtained and the upper line represents the most resistant results. In between (also a continuous black line) is shown the arithmetic mean. It can be seen that the arithmetic mean is nowhere near the middle of the range of sensitivities and hence it is correctly deduced that for a given duration of exposure the sensitivity of the population is not distributed normally but in a very skew manner. Most animals are close to the average but a few highly resistant animals give a tail to the distribution. In view of the skewed nature of the distribution the median average goat will be discussed. It is immediately apparent and not in the least surprising that for a short t there corresponds a large P value, and that for a large t there is a comparatively small P value. This suggests that perhaps a constant quantity of excess gas is involved in producing the threshold bends observed in all these animals. If now this idea is coupled with a diffusion-like inert gas saturation process then a relationship of the form $P_t^{1/2} = K$ is to be expected, provided the t value is not too great. As can be seen from Table I $P_t^{1/2}$ is quite constant over a considerable range of t values. The P value used is that for the median average goat. Thus it would appear that there exist good