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MAN IN THE SEA

Volume I

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K.K. Shida
Editors

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Preface

This two-volume book is the product of a truly international effort, with contributions from scholars from 8 countries, who made presentations at the **Second International Symposium on Man in the Sea.** Under the gracious sponsorship of the John A. Burns School of Medicine at the University of Hawaii, this Symposium was organized, in part to bring together world renowned scientists to discuss the current knowledge of human performance in the sea, and to illustrate the importance of international cooperation in diving research. In this period of dwindling funds for research, the gathering of international researchers and the pooling of international resources are of particular significance and value. The costs of facility and expense of operation are such that many would be "locked out" without cooperative programs. Furthermore, the individual programs can more fully benefit from widely available talent.

The **First International Symposium on Man in the Sea** was organized under the leadership of Dr. Suk Ki Hong, then a faculty member at the University of Hawaii. In part, the purpose of that Symposium was to highlight results of our 1975 saturation dive, *Hana Kai II*, a coming-out party, as it were. Since then, researchers from the Department of Physiology have made numerous contributions to the diving literature and many symposia around the world. We have also participated in several major saturation dives in cooperation with Japanese scientists. Organizing an international symposium is one way to foster further cooperation among nations.

In the 13 years which have intervened since the **First International Symposium on Man in the Sea,** there have been countless events and discoveries which validated the initial concept of the pooling of international resources, in the interest of diving research.

The **Second International Symposium on Man in the Sea,** held over four days, November 13-16, 1988, in Honolulu, covered the following topics: Saturation Diving (Compression, Pressure Adaptation, and Decompression), Sports Diving, Hyperbaric Medicine, and Man in the Sea in Manned Submersibles. Volume I is devoted to Saturation Diving, and Volume II, to the remaining topics.

We hope that this Symposium has brought benefit to its participants, and will do so for those who read this book, perhaps bridging the gap between theory and practice, experience and understanding. We are grateful to those who have taken time from their busy schedules for this Symposium.

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Acknowledgements

Diving research at the University of Hawaii began in 1968 with a study on cardiorespiratory functions of divers and climaxed in a 17-day saturation dive of 5 divers at 580 feet in 1975. Later, the research activity expanded to include international cooperative dives. These activities during the last 20 years were generously sponsored by NOAA's Sea Grant Office, Office of Naval Research, National Science Foundation, National Institutes of Health, and local medical associations. Without all of the aforementioned support, the "Human Peformance in the Sea" project, which served as the basis of this symposium, would not have existed.

While Hawaii's reputation and research activities are a necessary ingredient for an international symposium, a symposium cannot ever become a reality without funds. Many organizations and individuals have contributed generously to the operation of this Symposium.

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The splendid cooperation of the publication group at the Sea Grant College Program gave the packaging of the symposium a tremendous boost. We owe it to Mrs. Karen Koki, who produced both the announcement brochure and the Program and Abstract book. The cover photos of both of these publications were taken by Mr. Terry Kerby, a submersile pilot at the Hawaii Undersea Research Laboratory. Dr. Rose Pfund, Associate

Director of the University of Hawaii Sea Grant College Program, gave encouragement and support, and was an important driving force behind the Symposium. On a personal level, the organizers are indebted to many others, including secretaries, and graduate students who labored many hours on the operational details.

Introduction

Man in the Sea represents a range of diversified topics. Volume I spans the three major features of saturation diving, Compression, Pressure Adaptation, and Decompression, and Volume II encompasses Sports Diving, Hyperbaric Medicine, and One-Atmosphere Vehicles.

Saturation Diving — Compression: Compression to increased pressures may result in many adverse effects to the diver such as barotrauma of the lungs, ears and sinus, arthralgias, etc. However, the major problems come with compression exceeding 200 m breathing helium-oxygen (Heliox), hydrogen-oxygen (Hydrox), oxygen-nitrogen-helium (Trimix) or hydrogen-helium-oxygen (Hydreliox). Such compressions, depending on the rate of compression and pressure or depth of the dive, may result in the High Pressure Nervous Syndrome (HPNS). Its symptoms, tremors, dizziness, nausea, vomiting, fatigue, EEG changes, and functional decrements range from mild to debilitating. Research in many countries over more than twenty-five years, has sought to better understand the cause and mechanisms of HPNS. Through animal and human research, the goal has been control of HPNS, for the development of safe and efficient compression at greater depths. This section first discusses animal studies and leads to contributions from 5 countries, France, Germany, Norway, the United Kingdom and the United States. A large number of long and extensive deep dives in these countries are summarized. These include dives on Heliox alone, the value of excursions from saturation and the development and value of Trimix for very deep diving. Substantial American and German works with Trimix enable divers to safely compress to 600 m and carry out an operational 8-hr- day; the French report a major advance, using hydrogen in the Spring 1988 ocean dive to 520 m off Marseille and the impressive Norwegian studies with Heliox to 350 m. The data presented demonstrated remarkable progress in extending the useful working depth of divers from only some 183 m (600 ft) for a few minutes in 1960 to 600 m (1,968 ft) for virtually unlimited time in 1988.

Saturation Diving — Pressure Adaptation: Modern compression procedures have reduced narcosis and HPNS-related performance decrements to a minimum. As a result humans can work sufficiently well in air saturation dives at shallow depths, and in mixed gas at much greater depths. However, complete elimination of these effects is as yet unattainable. Successful adaptation of humans to elevated pressure requires systematic

understanding of biological effects of pressure and gaseous environments, at both organ and cellular levels. Much progress has been made in defining limits of human survivability and adaptabililty in hyperbaric environments through these systematic investigations. Research on cellular function and its potential in enhancing human performance in hyperbaria has not incited much interest in the past, yet it is of paramount importance for long-term biological adaptability. Fortunately, the tide has changed and much enthusiasm is in the offing. "The physiologists have shown that the limits of safe diving have not yet been reached. The engineers have acknowledged that they cannot yet replace man," states Dr. David H. Elliott. Undoubtedly, engineers will continue to build machines and apparatus that reduce risk and facilitate work for humans undersea, while physiologists will move forward learning from experiments, and instruct humans how to better sustain performance in exotic environments. There is still a great deal to be learned about psychomotor skills, cognitive function, sensory performance, and behavior. Knowledge of these is essential to the viability of long-term hyperbaric projects.

Saturation Diving — Decompression: Decompression from a deep saturation dive often takes days or weeks to accomplish. For example, after a 14-day exposure to the pressure equivalent to 300 msw depth, 12 days may be required. When diving depth is doubled, to 600 msw, the decompression time tripled, 33-36 days. Various attempts have been made to shorten the decompression time, but the formulation of practical diving tables is still based mainly on untested hypotheses and trial-and-error. On the theoretical side, significant advances have been made in the areas of bubble nucleation, global testing, and the rigorous application of maximum likelihood statistics, and there is no shortage of algorithms for calculating tables of any depth or duration. On the experimental side, bubble nuclei have been photographed, bubble growth and collapse have been observed, and the role of complement activation in decompression sickness is being investigated. Many problems remain, however, in the collection and analysis of decompression events, in the use of such data to refine decompression theory, and in the testing of decompression tables using animal models and humans, monitored perhaps by Doppler techniques.

Sports Diving: Free diving is an old way of working in the sea. It requires little if any equipment and allows the diver freedom of movement. These advantages are diminished, however, by the human's inability to stay underwater for extended periods. Studies of physiological limits of humans as divers have yielded abundant information. This includes not only general knowledge of the human physiology of breath-

hold diving, but also clinically applicable effects of water immersion and breath-holding, such as diuresis, suppression of paroxysmal supraventricular tachycardia, and promotion of inert gas elimination during decompression. Physiological limitations of humans as divers as well as the applied physiology of free diving are summarized in this section. With increasing popularity of recreational diving, accidents occur more frequently. Accidents associated with free diving (skin diving, or breath-hold diving) are mainly physiological, involving drowning or near drowning. Most free diving accidents can, therefore, easily be avoided by practicing sensible techniques and by knowing and respecting human limitations in the water. Such practice is best exemplified by the professional breath-hold divers. In contrast, those accidents associated with scuba diving are complex, involving problems with equipment, inert gas narcosis, oxygen toxicity and, most troublesome, decompression sickness. Treatments are specific, depending on the nature of the affliction. Actual recording of diving profiles reveals the unreliability of divers' recollections of depth and time. Education of divers to this fact will contribute to improved safety of sports diving.

Hyperbaric Medicine: There has been no better means of treating decompression sickness than recompression either with or without the addition of oxygen. The outcome improves when treatment delay is minimized, and oxygen is added under pressure while staying within the limits of oxygen toxicity. The use of hyperbaric oxygen has also been recognized as an effective adjunct to surgical and medical management of non-diving disorders, such as gas gangrene, carbon monoxide intoxication, chronic osteomyelitis, osteoradionecrosis, soft tissue radionecrosis, bone and skin grafts, and problem wounds. We must direct our attention toward basic research into both the beneficial and deleterious effects of HBO on organ tissues. Otherwise, the use of oxygen under pressure will remain as "a therapy in search of diseases." Whereas the scientific basis for HBO treatment has been proven for some diseases previously treated empirically, and its value in decompression and recompression is well established, much research remains to be done. We must guard against the substitution of enthusiasm for science with claims that we cannot substantiate, lest, as Arntzenius warned in the last century, "that the confidence that treatment deserves might be lost by overemphasizing the value." If we allow that to happen, "A moralist, at least, may say, that the air which nature has provided for us is as good as we deserve." (Joseph Priestly, 1775).

Man in the Sea in Manned Submersibles: Submersibles have expanded our field of vision by bringing the human eye and brain into juxtaposition with the deep ocean. They enable us to undertake detailed sampling and

conduct extensive experiments on the ocean floor with remotely-controlled manipulators. Deep submergence submersibles are now diving to 6,000 meters, allowing studies to be conducted in the deep sea trenches. From the depths of a few hundred meters to three thousand meters along the mid-ocean ridge systems, and along the margin of the Western Pacific basin, submarine volcanoes mark the sites of ongoing hydrothermal mineral formation and exotic mid-water phenomena. Biologists can now observe and sample the complex and fragile faunal populations which exist in these mid-water depths. Sampling delicate fauna, water masses or mineral samples with submersibles, however, requires sophisticated and ingenious systems and manipulators that have to be operated remotely by the observers within. As a result of this requirement, a suite of instruments, manipulators and sensors have been developed for the submersible, making it a true extension of the human eye, the human brain, and the human arm, into the mysteries of the deep ocean environment.

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The Contribution of Animal Experimentation Toward the Development of Rational Compression Schedules for Very Deep Diving

Ralph W. Brauer

I. INTRODUCTION

Contributions of animal experimentation to the formulation of rational compression schedules must necessarily take the form of identification of potentially relevant phenomena and mechanisms, and formulation of guiding concepts and mechanisms, rather than the determination of numerical values of tolerance limits or development of specific pressure/time profile directly applicable to man. Below we shall try to describe what we have been able to achieve over something like twenty years since we first became interested in the problem, and incidentally point up some of the reasons why in relation to the HPNS interspecies extrapolations should be treated with considerable caution.

When the HPNS was first observed and recognized as such in animal experiments, it was taken — or at least we took it — for a coherent entity which entailed a more or less regular progression of manifestations from the onset of fine tremors, through generalized more or less epileptiform, seizures to the development of full-blown maximal tonic or tonic-clonic convulsions (Brauer *et al.*, 1968). This view began to come apart when observations concerning the effect of modifying compression rate (Brauer *et al.*, 1971) and of introducing inert gas narcotics into the compression atmosphere (Brauer *et al.*, 1974) began to reveal substantial differences in the effect of these manipulations upon epileptiform seizures and upon various phases of the tremor stage of the syndrome. It was finally laid to rest by two series of investigations: pharmacologic studies in Keith Miller's laboratory which led those workers to distinguish at least four components showing different combinations of what they termed 'compressibility and solubility properties' of the supposed effective sites (Smith and Miller, 1978). Paralleling this was a series of investigations in our laboratory (Brauer *et al.*, 1981) which showed that the first seizure stage, which we now term "Type I HPNS seizures," and the second, the tonic seizure, stage — "Type II HPNS seizures" — are sharply distinguished by a whole array of properties, ranging from different responses to compression rate manipulation, to differences in their appearance during ontogenetic development and in their genetic background (cf. e.g. Table 1 and for more exhaustive data see Brauer *et al.*, 1975). It became clear then that one had to expect that the clinical picture of the HPNS in a given diving situation might present very different appearances depending upon the compression profile and the compression atmosphere used in each case.

TABLE 1.

HPNS Seizures in CD 1 Mouse — Type I vs Type II

Criteria	Type I	Type II
Clinical	Brief clonic	Tonic-clonic
EEG	Little Change	4-5 Hz spike and dome, post-ictal silence
Heart rate	No Change	80-90% slowing, atropine reversal
Compression rate	K = 11	K = 0 or <0
Phenytoin	Sensitizes	Protects
Reserpine	Sensitizes	No effect
Spinal animal	No seizures below trans-section	Seizures also below trans-section

Abbreviated from Brauer *et al.*, 1981.

Thus, we must recognize that any discussion of the effect of different compression profiles on development of the HPNS needs to define the particular HPNS component to which it is oriented, or else needs to manipulate a number of such components at the same time. One important difference between studies of the effect of different compression profiles upon HPNS development in man and similar studies in animals, is that in man one focuses necessarily upon the total clinical status, and hence by implication upon the mixture of HPNS signs and symptoms of all kinds that converge in an individual, whereas in animal experiments it is possible to concentrate one's attention upon some one well defined endpoint or some one quantifiable manifestation of the HPNS. While this represents a drawback, in the sense that one is making judgments based on less than complete data, this situation permits the investigator using animal subjects to design experiments with some hope of deducing quantifiable relations and testable hypotheses regarding underlying mechanisms.

It is within this framework, then, that I would like to review results obtained in the course of experiments in which the guiding HPNS manifestations were high pressure seizures of the type which we have for some years now referred to as "Type I HPNS seizures." I shall omit from this discussion a review of the important work by Rostain and his collaborators in baboons, because those experiments were designed to replicate, as near as might be, clinical human experiments on relatively large primates and hence did not lend themselves to the kinds of experimental designs that I wish to discuss here.

II. THE END POINT

The characteristics of Type I HPNS seizures which set them apart from "Type II HPNS seizures" in CD 1 mice — and probably in the squirrel

TABLE 2.

Mean Convulsion Threshold Pressures of CD 1 Mice ($He0_2$, Compression Rate — 40 atm/h, type I)

Year	40Pc(I) ata	Year	40Pc(I) ata
1971	99	1982	89.5
1974	98	1983	99
1975	100	1985	93.5
1978	98	1986	91.5
1980	100	1987	95
1981	96.5		

Mean, 96.4; S.D., 3.6; S.E., 1.1 ata.

monkey — are summarized in Table 1 (abbreviated from Brauer *et al.*, 1981). Its suitability as an end point for kinetic studies of the type we are considering here is attested to by the fact that mean seizure threshold pressures measured on the same strain of mouse under the same compression conditions have remained essentially constant in the hands of half a dozen observers working over a period of nearly twenty years (Table 2). As usually conducted in our laboratories, in compressions consisting of 3 atm pressure increments at constant intervals, individually determined seizure thresholds fall on a normal frequency distribution curve with a standard deviation of ± 5.6 atm; thus in our typical experimental design, using eight or nine animals for each point, results can be given with a standard error of about ± 2.0 atm.

A word may be in order concerning scaling of the time coordinate in any comparisons between experiments in mice and potential exposures in human subjects. General physiological considerations suggest scaling to metabolic rate — which is closely akin to scaling to life span, or to heart rate, or to brainbody weight ratios. This leads to a scaling factor between 23 and 30, in which case the compression rates we have used in the mouse would correspond to a range of compression rates from about 0.15 atm/h to 50 to 70 atm/h in man, and thus include pretty much the entire range of mean compression rates encountered in actual diving situations.

III. THE COMPRESSION RATE EFFECT

Initial studies used compressions at a constant rate and carried to the point of seizure onset in each animal, and revealed that in the CD 1 mouse slowing compression rate did indeed result in elevation of mean convulsion threshold pressures (Brauer *et al.*, 1975). Over the range of compression rates from 10 atm/h to 1,000 atm/h convulsion threshold pressures decreased linearly with the logarithm of the compression rate (Fig. 1), i.e. it obeyed the relation:

$$P_c(1) - P_c(2) = k \cdot \log[P_2/P_1] \quad (1)$$

where $P_c(1)$ and $P_c(2)$ are two convulsion threshold pressures observed at the two compression rates P_1 and P_2, and k is a constant which provides a measure of the magnitude of the compression rate effect and will be designated in what follows simply as 'the compression rate effect.'

Using the data of Fig. 1 to calculate for each a series of compression rates the total compression time elapsed from the beginning until the onset of seizures and plotting the results as a function of compression rate, one obtains a line strongly curved toward the time axis (Fig. 2)

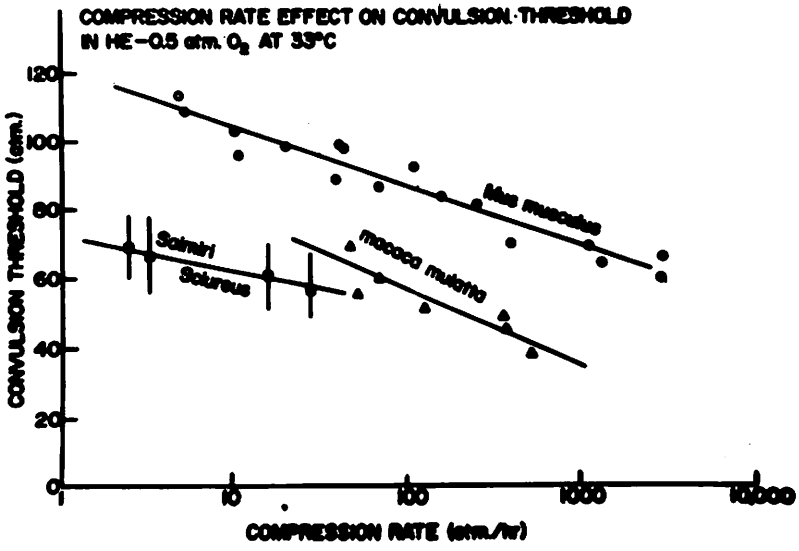


Fig. 1. Effect of variation of compression rate upon mean HPNS Type I convulsion threshold pressures of three mammalian species (HeO_2).

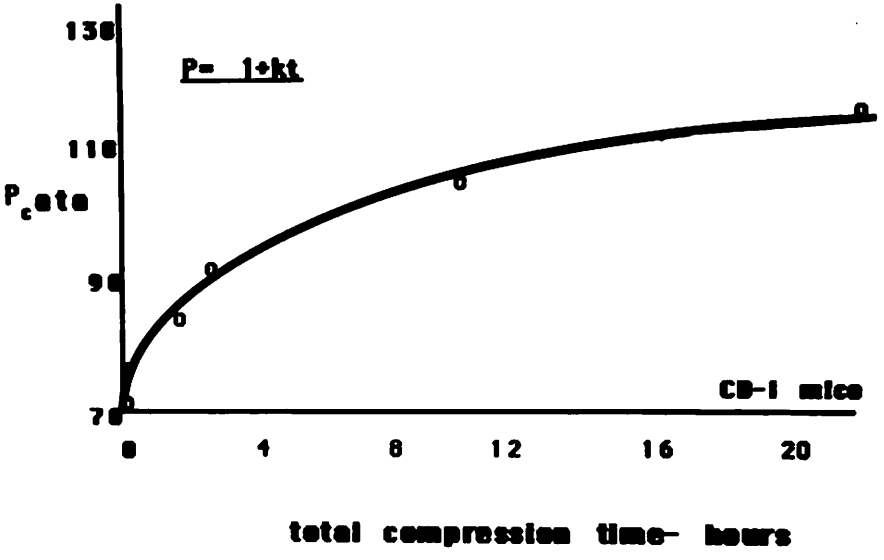


Fig. 2. Mean HPNS Type I seizure threshold pressures observed during compressions at several different but constant rates, plotted as a function of the total elapsed time from beginning of compression to onset of seizures.

reminiscent of what has been termed the exponential compression profile widely utilized in deep diving operations.

As shown by Figure 1, this form of the relation between compression rate and convulsion threshold pressure adequately describes the data over a limited range of compression rates for a variety of other species. As shown by equation (1), the value of k, the compression rate effect parameter, can be computed for these cases from two convulsion threshold pressure determinations, performed at sufficiently different compression rates and thus permits rapid scanning of the degree of compression rate dependence of HPNS convulsions in different biological models (Brauer *et al.*, 1979a). In a series of fifteen vertebrate species, ranging from fish to primates, we found a rather good correlation between mean HPNS convulsion threshold pressures and relative brain development as measured by the allometric constant or encephalization quotient: the least brainy beasts were the most resistant.

On the other hand, the compression rate effect varied from species to species in a highly unpredictable way and with little relation to taxonomic position (Table 3); indeed, for a considerable number of species convulsion threshold pressures were not at all significantly affected by compression rate. Thus it became clear that compression rate dependence cannot be an intrinsic characteristic of the pressure effects leading up to HPNS seizures in all of the vertebrates tested to-date.

TABLE 3.

Compression Rate Effect

Detectable	Not Detectable
Frog	Newt
Turtle	Lizard
Rat	Quail
Mouse (CD 1, AJ)	Hamster (24 to 1000)
Gerbil	Mouse (DBA/2J)
Ferret	Rat (Wistar)
Squirrel monkey	
Rhesus monkey	

Yet, for the majority of species k is clearly greater than zero, so that there is a definite compression rate dependence. In particular, the two primate species with which we have worked show very significant compression rate effects upon HPNS convulsion threshold pressure. The CD 1

mouse shows a value of k intermediate between that for the squirrel monkey and that for the rhesus monkey — an encouraging bit of information which led us to hope that in this respect, as with regard to anesthesia susceptibility, the mouse might prove to be an excellent man (this remains true even after one has introduced the correction for time scaling, since time in these equations appears by itself as the denominator of a fraction under the logarithm, and any scaling factor will consequently be canceled out in the computation of k as the ratio of two threshold pressures).

A. Neuropharmacology

Equation (1) and the simple compression profile upon which it is based were put to a second test in studies seeking to elucidate the neuropharmacologic basis of the compression rate effect (Brauer *et al.*, 1979b). This was based upon the observation that in the CD-1 mouse administration of reserpine (a potent blocker of monoamine neurotransmitters) twenty four hours before the compression experiments abolished the compression rate effect completely: at all compression rates tested such reserpinized animals convulsed at a common low pressure, equal to the convulsion threshold pressure observed in non-reserpinized mice subjected to very rapid compression (1,000 and 1,500 atm/h) (Fig. 3); thus, in the mouse, reserpine does not affect the threshold pressures at which convulsions are elicited by rapid compression, but markedly lowers HPNS seizure threshold pressures elicited by relatively slow compression rates.

Exploratory experiments in sixteen other animal models showed that similar relations are widespread among vertebrates: in our sample a highly significant correlation ($r = 0.82$) was observed between the relative magnitude of the compression rate effect k and the magnitude of the relative reserpine effect (the difference in P_c between control and reserpinized animals devided by P_c in rapidly compressed controls, all measured at a modest compression rate).

These data, therefore, extend the concept already suggested by the existence of a number of species lacking a compression rate effect, i.e. that at least two discrete mechanisms must be involved, one responsible for the causation of HPNS seizures as such, and the other for any effect of variations in compression rate upon the point of onset of such seizures. The reserpine data now suggested a more specific hypothesis, namely that the intrinsic effects of elevation of hydrostatic pressure upon the central nervous system develop very rapidly, while the compression rate effect represents a relatively slowly developing protective response, elicited by exposure to high pressure and blocked by reserpine.

Further pharmacologic tests demonstrated that monoamine oxidase inhibitors as well as precursors of the phenethylamine neurotransmitters

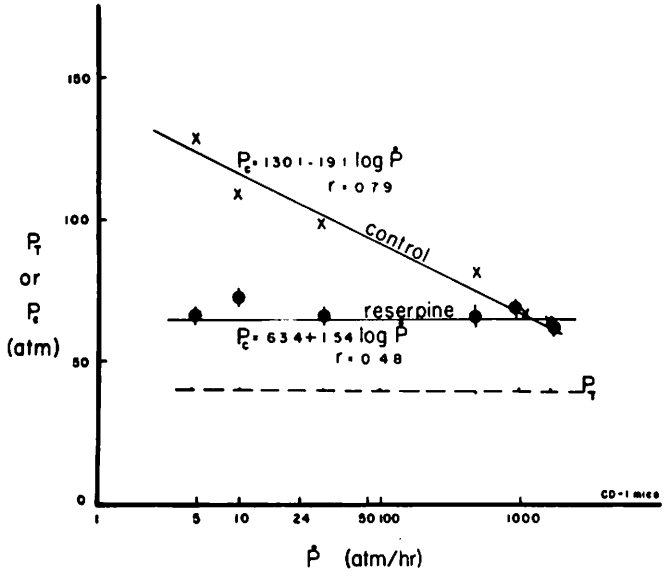


Fig. 3. Effect of reserpine (5.0 mg/kg i.m. 24 hour prior to beginning of compression) upon mean Type I HPNS convulsion threshold pressures at compression rates of 40 and 1000 atm/h in CD-1 mice. P_T represents threshold pressure for onset of fine tremors in the same animals and is included to emphasize that this perimeter is unaffected by reserpine as well as insensitive to variation of compression rate (from Brauer *et al.*, 1979; courtesy of FASEB).

can reverse this effect of reserpine (Fig. 4), as would have been predicted by our hypothesis. The aggregate of our data, therefore, suggested that the compression rate effect was evidence of a dual mechanism of HPNS causation, involving an essentially rate-independent and pressure-dependent mechanism facilitating the onset of HPNS seizures, and a slowly developing and hence compression rate sensitive mechanism involving the release of monoamine neurotransmitters, probably in the central nervous system, and responsible for antagonizing the onset of these seizures.

In light of this concept of the dual mechanism underlying development of HPNS seizures, manipulation of the compression profile thus came to be seen as having the objective of assuring the most rapid development of these compensatory responses possible while incurring a minimum burden of preseizure HPNS effects.

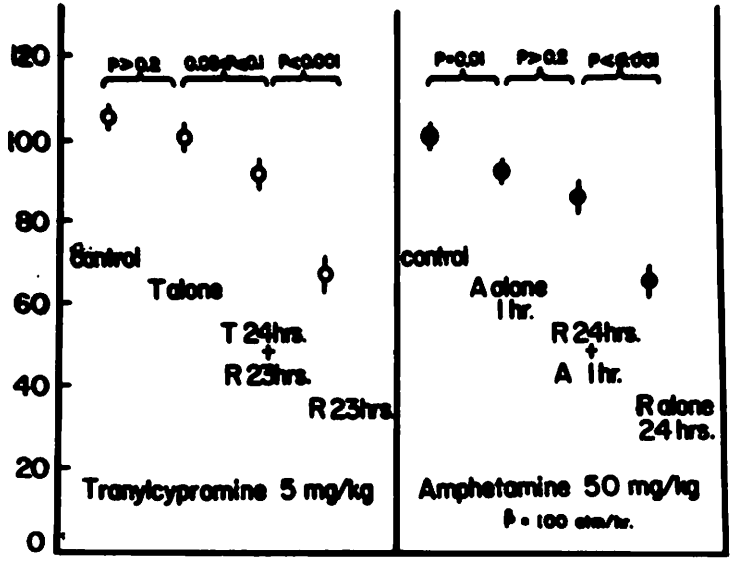


Fig. 4. Effect of monoamine oxidase inhibitors upon modification of HPNS Type I seizure threshold pressures (dP/dt = 60 atm/h) by reserpine in CD-1 mice (from Brauer *et al.*, 1979; courtesy of FASEB).

B. Time and Pressure Factors

The next stage in the development of our ideas on this matter therefore was to seek to extend our knowledge of the kinetics of the development of these reactions. This required the use of compression profiles other than the linear ones studied up to this point, since the total time spent in compression and mean pressure to which the animals had been exposed prior to seizure onset covaried, and hence are inseparable. We now have alternative compression profiles that should allow us to manipulate time and pressure independently of one another.

Such profiles were developed upon the basis of pilot experiments using a three step compression profile (Brauer *et al.*, 1977): in a first step mice were compressed very rapidly to a pressure corresponding to half the convulsion threshold pressure expected for a given linear compression profile; as a second step they were held at that pressure for a period equal to that which would have been consumed in an entire linear compression to seizure onset at a rate chosen for comparison; and finally the experiment

was completed by a second rapid compression step, carrying the animals from the holding pressure to whatever pressure might be required to elicit HPNS seizures. It was found that the final convulsion threshold pressure attained in such a three step compression process was indistinguishable from that which would have been obtained in the linear compression reaching the same pressure in the same total time. Since in the three step compression the rate of approach to the seizure threshold was 1000 atm/h while in the corresponding linear compression it was 60 atm/h or less, we concluded that the rate of compression at which the final threshold is attained has little or no influence upon the eventual convulsion threshold pressure, and that this in fact depends upon some function of pressure and the time spent at various pressures, i.e. the very parameters of the compression profile we proposed to explore.

To delineate the nature of the functional relation between the three parameters, time, pressure, and seizure threshold pressure, we now used the three step compression design, varying independently holding time (0 to 12 hours), and holding pressure (20 to 95 ata) in a matrix design (Fig. 5 and Brauer *et al.*, 1977). Analysis of the resulting set of data revealed two important conclusions:

(1) The rate at which convulsion threshold pressure increased during the early part of any steady pressure sojourn is almost directly proportional to the holding pressure. This implies that the benefits afforded by such compensatory response would accrue most rapidly if the subjects were brought as quickly as possible to the highest pressure compatible with the severity of HPNS symptoms one might be willing to tolerate and then either held at that pressure or compressed further slowly so as to take maximum advantage of the compensatory reactions developing in the pressure exposed animals. This finding confirms the more restricted and qualitative conclusions drawn from the constant rate compression experiments (cf. Fig. 2).

(2) The convulsion threshold pressures approach a definite upper limit as holding times and holding pressures are increased progressively. The value of that limit for the CD-1 mouse, as estimated from the results of (Brauer *et al.*, 1977), was in the neighborhood of 118 ata. More recent experiments in which holding times were increased to up to two weeks — on the basis of the scaling factor suggested above corresponding roughly to men sojourning at pressure for a whole year — reached a limiting threshold only slightly higher than this, about 123 ata. Thus, the benefit to be expected from manipulation of the compression profile alone is likely to prove limited. In the case of the mouse, the scope for this effect is about 50 atm, i.e. from 73 or 74 ata at a compression rate of 1000 to 1500 atm/h to 123 ata for an equivalent compression rate of 0.35 atm/h.

Differential equations were developed to describe the relations between holding pressure, holding time, and convulsion threshold pressure illustrated in Fig. 5 and are currently being explored by optimization techniques for a number of different compression profiles, using as boundary condition 1 and 1% incidence of HPNS seizures.

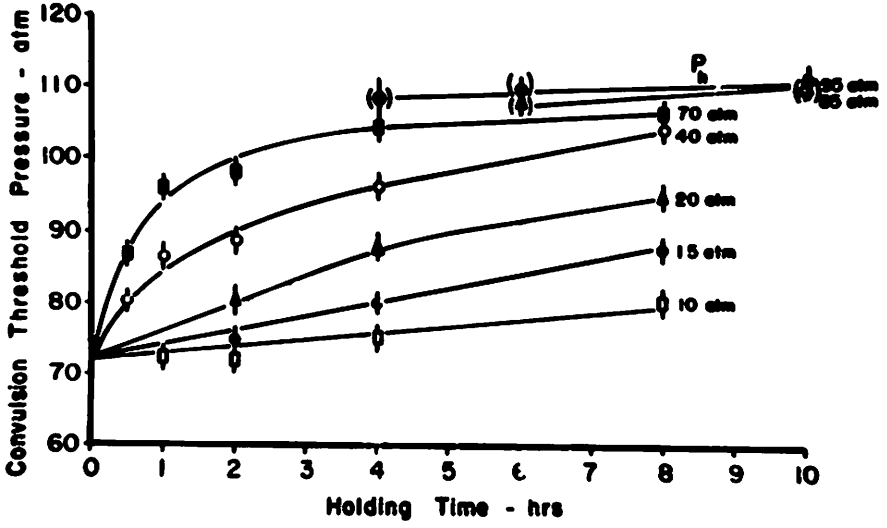


Fig. 5. Mean HPNS Type I seizure threshold pressures in interrupted compression experiments in which holding time and holding pressure could be varied independently of one another. The plot shows the family of curves obtained by selecting a particular holding pressure for each, represented by the figures at the right of each curve, and varying holding time as the independent variable. The two lines at the top resulted from a slightly more complex compression procedure which permitted holding pressures of 85 and 95 ata, respectively (from Brauer *et al.*, 1977; courtesy of the J. Appl. Physiol.)

We explored the possibility of amending the basic procedure by increasing the holding pressure stepwise, paralleling the seizure pressure/time curve shown in Fig. 5. As shown in that figure, in the case of the mouse holding pressures as high as 95 ata proved possible, and allowed the animals to attain seizure threshold pressures very close to the absolute limit. In unpublished experiments we attempted to carry holding pressures to 100 ata or more. So far those experiments have been unsuccessful: most animals we attempted to hold at such high pressures failed to survive and all showed evidence of physical deterioration in overall clinical appearance and progressive weight loss. We have been unable to pursue this matter further, but it has occurred to us that here we may have been encountering for the first time deterioration of pressure

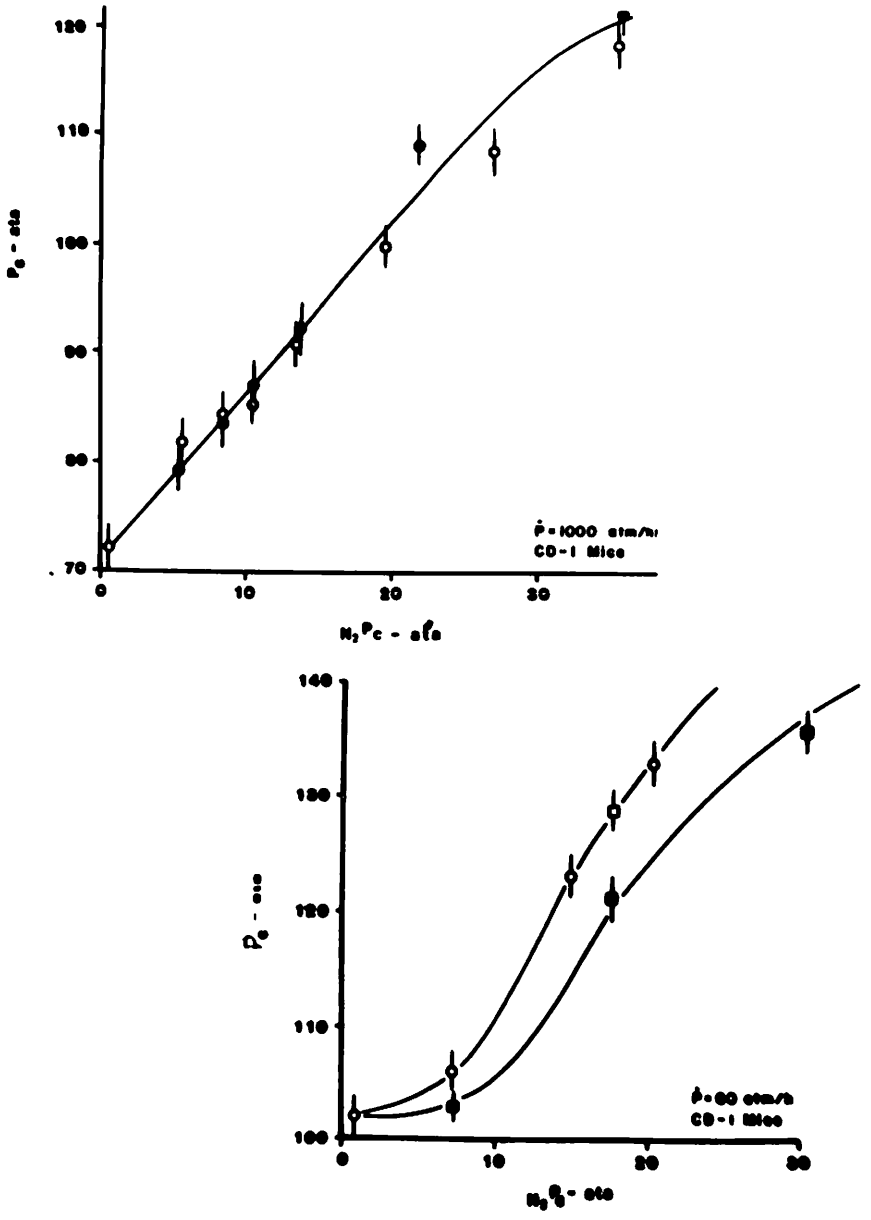
exposed mammals due to pressure effects on replicating cells — perhaps not unrelated to effects already observed in single cell systems and dubbed 'non-class A' effects in a review of inert gas/hydrostatic pressure interactions (Brauer *et al.*, 1982).

C. Inert Gas Narcotics

A final skein of investigations pertinent in the present context took off from observations of Rostain (1978) suggesting that the timing of the injection of nitrogen into compression atmospheres had a significant effect upon the magnitude of the protective action of this narcotic gas against the development of the various components of HPNS. In a first series of experiments we compared the effect of nitrogen when injected in a bolus near the beginning of the compression, with its effect when administered continuously in the form of an appropriate helium/nitrogen mix (Brauer and Hinson, 1983). Those experiments showed sharply different results for three components of the high pressure neurologic syndrome in mice. There is a rather dramatic excitement stage (euphoria might seem more appropriate — we termed it 'the student beer party' stage) associated with bolus administration of nitrogen. The total pressure at which this becomes manifest decreases with the partial pressure of nitrogen present at its onset but seems to be unaffected by the timing of nitrogen administration. It comes on equally with N_2 or with N_2O injection, the proportions of their partial pressures at the onset of excitement being as 20:1, rather close to the anesthetic potency ratio for these gases, and seems to us to represent an exacerbation, in the presence of high pressures, of normal patterns of the early stages of inert gas narcosis, and as such is perhaps worthy of further investigation.

With regard to the tremor stage, our data confirmed the observations of Rostain (1978) in that early bolus injection of nitrogen was substantially less effective than continuous administration in elevating the pressure threshold for the coarser tremor stage.

With regard to HPNS seizures the early bolus was significantly less effective in protecting animals subjected to relatively moderate compression rates. With very rapid compression rates, pre-treatment with various nitrogen partial pressures before the beginning compression did not produce results differing in any respect from those attained when nitrogen was introduced with the compression mixture (Figs. 6A and B). These data suggested the possibility that nitrogen might interfere at some stage with development of the compensatory response against high pressures. We sought to explore this possibility by timing bolus injections late in the course of linear compressions. The results showed that nitrogen injected



Figs. 6A and 6B. Comparison of the effect upon ^1P_c of nitrogen when injected early (closed squares) or when injected continuously (open circles) during the course of the compression. A: Compression rate = 1000 atm/h; B: Compression rate = 60 atm/h (from Brauer and Hinson, 1983; courtesy Undersea Biomedical Res.).

near the end of the compression sequence is substantially more effective in increasing HPNS convulsion threshold presure than when it is injected any time before (Fig. 7).

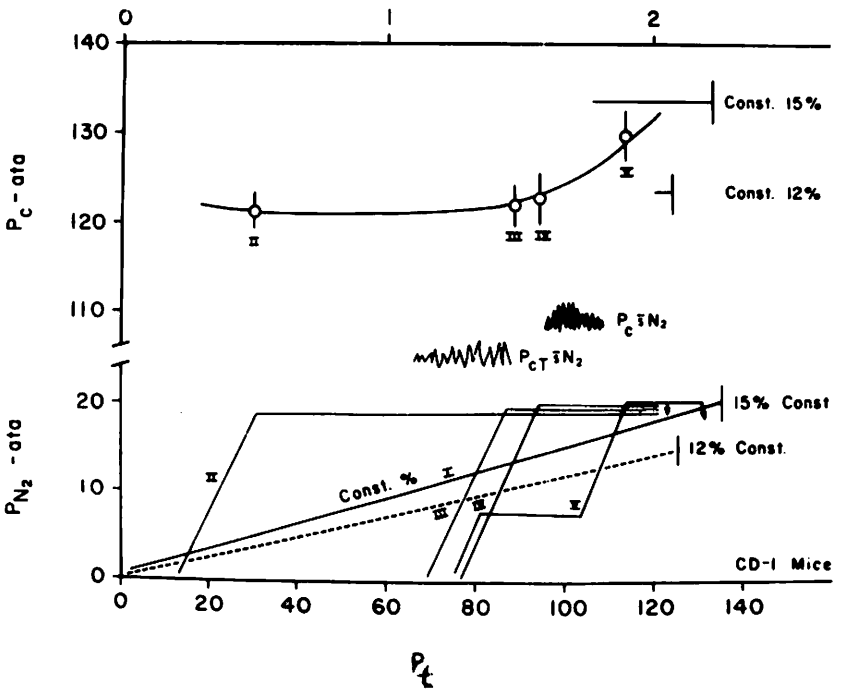


Fig. 7. Effect on $^{I}P_c$ of administration of nitrogen as a bolus beginning at various stages of the compression procedure, and for comparison the effect of comparable total amounts of nitrogen injected continuously throughout the course of the compression. Compression rate — 60 ata/h. Bottom diagram: time course of nitrogen concentration for each of the several Roman figures. Middle: 'wiggly' lines represent approximate zones of onset of fine tremors and the effect of nitrogen thereon. Top: $^{I}P_c$ corresponding to each of the several bolus injections indicated by the Roman numerals, and to comparable amounts of nitrogen administered continuously during the course of the compression (From Brauer and Hinson, 1983; courtesy of Undersea Biomed. Res.).

D. Habituation to High Pressure or to Inert Gas Narcotic

While these results are statistically acceptable, the differences attainable in this kind of procedure were inconveniently small for further exploration and we had to let the matter rest there for some time. Resumption of this study came as a result of studies of the effects of habituation

to inert gas narcotics upon susceptibility to HPNS convulsions (Koblin *et al.*, 1979). Such a procedure resulted not only in marked increase in resistance to narcosis, as had already been shown (Brauer, 1985), but also in a marked lowering of resistance to HPNS seizures. This caused us to become interested in the possibility that in view of the supposed symmetry between the effects of pressure and inert gas narcosis, habituating the animals to high pressure environments might have the opposite effects on those two end points. Trial showed that in this case the supposed symmetry broke down. Pressure conditioning does indeed result in increased HPNS convulsion thresholds but fails to affect susceptibility to inert narcosis in any way (Brauer *et al.*, 1986).

As mentioned above, the maximal pressures attainable in this way did not exceed significantly the maximum attainable by manipulation of compression rates as deduced from our earlier experiments. More interesting in the present context was the observation that in such pressure conditioned animals the compression rate effect had disappeared

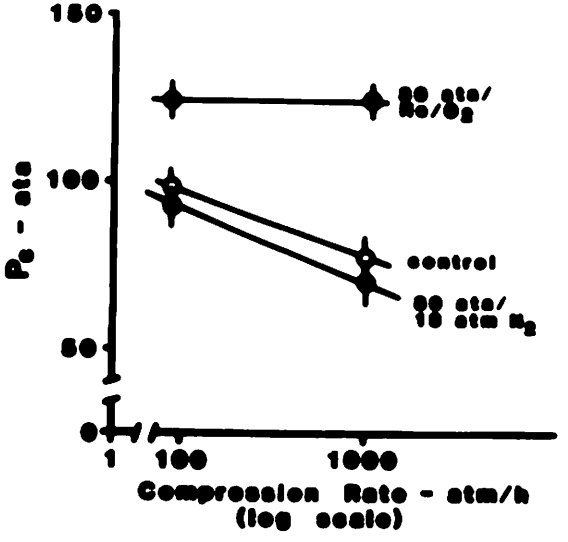


Fig. 8. Effect of pressure conditioning (one week, 80 ata total pressure, heliox) on $^{1}P_{c}$ in CD-1 mice at compression rates of 60 and 1000 atm/h, and absence of these pressure conditioning effects if 18 atm of nitrogen are included in the chamber atmosphere during the conditioning period (from Brauer *et al.*, 1986; courtesy of the *J. Appl. Physiol.).*

altogether. Animals compressed at a rate of 1000 atm/h responded as though their compensatory mechanisms had been fully activated so that they showed convulsion threshold pressures no lower than those of pressure conditioned mice tested by slow compression (Fig. 8). Altogether, the data suggested strongly that what we were calling 'pressure conditioning' in fact merely represented maximal development of the HPNS protective responses we had already explored in the past.

E. Inert Gas Narcosis

We presently showed that the compression rate effect could be blocked by nitrogen or other inert gas narcotics, and that this block cannot be interpreted as a mere summation of the positive effect of pressure conditioning and the negative effect of nitrogen habituation upon HPNS

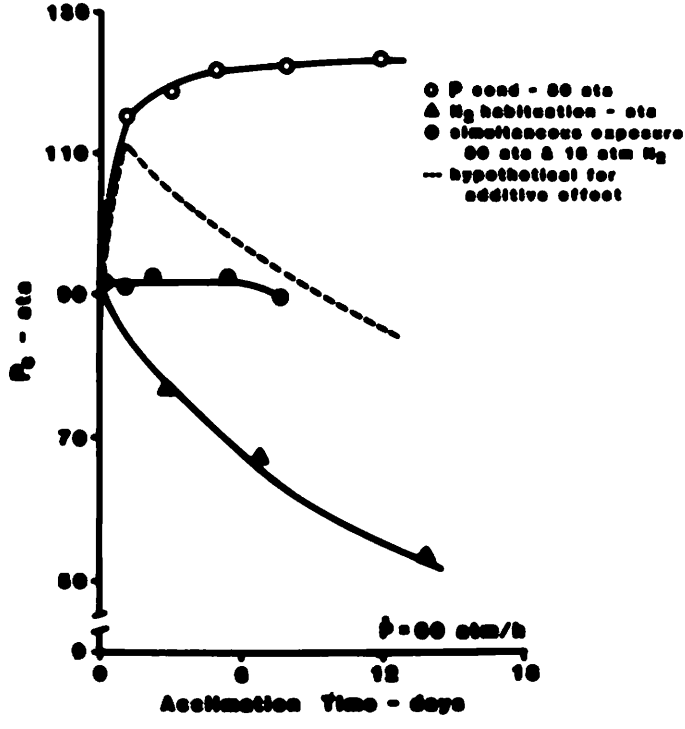


Fig. 9. Time course of development of pressure conditioning, of habituation to nitrogen narcosis, and of pressure conditioning in the presence of 18 atm nitrogen — all in terms of $^{1}P_{c}$. The dashed line represents the hypothetical curve which would result from linear addition of the effects of pressure conditioning and of nitrogen habituation (from Brauer *et al.*, 1986b; courtesy of the J. Appl. Physiol.).

tolerance (Fig. 9, Brauer *et al.*, 1986). Therefore, assembling our several conclusions, we inferred that the effect of nitrogen in this situation must be to block development of the compensatory responses elicited by pressure exposure. If this inference were true, then it would provide a tool to test our hypothesis that pressure conditioning represented merely an extension of the compression rate effect seen in more acute exposures, for in that case inert gas narcotics ought to be capable of blocking the compression rate effect as manifest in acute experiments. This point was therefore tested in experiments in which the inert gas narcotic was injected either at the beginning or very near the end of a three step compression (Fig. 10, Brauer and Dutcher, 1987). Our hypothesis led us to predict in the first place that during rapid compressions, when there would be minimal time for development of compensatory responses, we should see the effects of the gas virtually uncomplicated by any interaction with such compensatory effects, and experiment confirmed this point. Compressing mice pretreated with various partial pressures of N_2 or N_2O at 500 atm/h we found a simple linear relation between partial

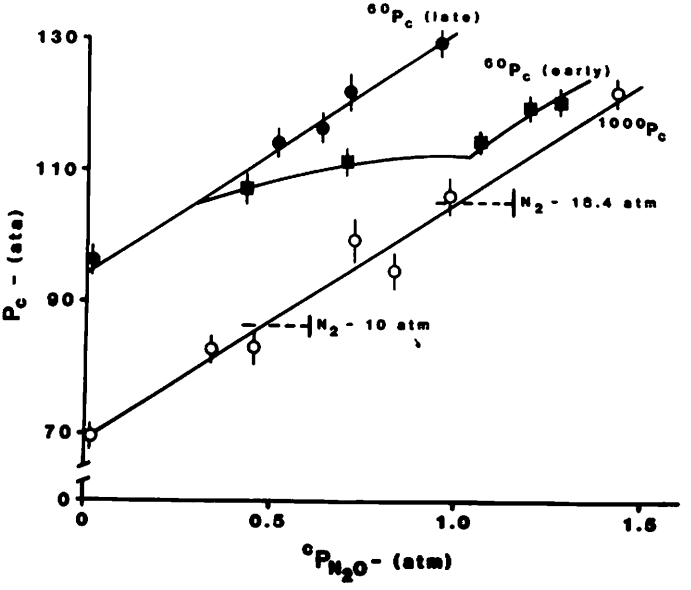


Fig. 10. Effect of inert gas narcosis on the compression rate effect of $^{t}P_c$. Inert gas in the amounts shown on the abscissa was administered either at the beginning of the compression (marked 'early'), or at the beginning of the last 10 atm's of the compression ('late'). The two dashed lines are included to allow comparison of the effectiveness of nitrous oxide with that of nitrogen during rapid compression experiments (from Brauer *et al.*, 1987; courtesy of *J. Appl. Physiol.*).

pressure of inert gas narcotic injected prior to the start and the resulting mean convulsion threshold pressure — thus incidentally providing at least a partial explanation of the non-linear relations between convulsion threshold pressure and inert gas narcotics observed by us and others with slower compression rates in certain mouse strains.

Interrupting the compression at a standard pressure below those producing HPNS seizures and holding them at that pressure for an hour before the final compression step allowed us to inject the narcotic gas either at the beginning or at the near end of the holding stage. As shown in Fig. 10, administration of the narcotic gas near the end, so that it should have no chance to interfere with the development of the compensatory response, once again produced a linear relation between narcotic partial pressure and convulsion threshold pressure, the dose response curve paralleling exactly the slope of that observed with very rapid compression. Early injection of the inert gas narcotic, on the other hand, resulted in convulsion threshold pressures which fell increasingly below those for the late administration series as the amount of narcotic gas used was increased, precisely as predicted by the hypothesis that the inert gas

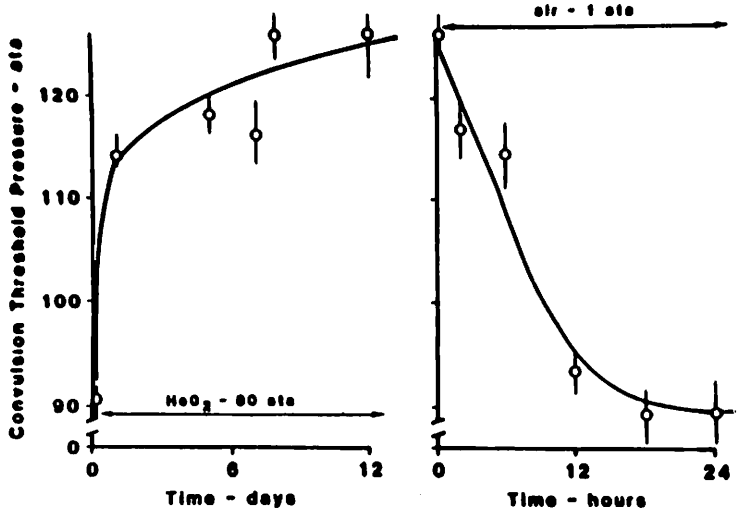


Fig. 11. Time course of accommodation and of loss of accommodation to high pressure. Conditioning: heliox 80 ata, 5 days. Deaccommodation during sojourn in air at 1 ata following decompression (from Brauer *et al.*, 1986a; courtesy of *J. Appl. Physiol.*).

narcotic interfered with development of the compensatory responses antagonizing manifestation of HPNS effects.

In a further test we made use of the observation that the protective effects of pressure conditioning are rapidly dissipated when such pressure conditioned animals are decompressed and held at sea level (Fig. 11). It seemed to us that if our interpretation of the nitrogen effect were correct, then injection of an inert gas narcotic into the chamber atmosphere after the animals had developed their protective response should result in similar rapid dissipation of the protective effect. Experiment has confirmed this prediction (Fig. 12, Brauer and Dutcher, 1987: replacement of the heliox atmosphere after five days at 80 ata with a helium/nitrous oxide/oxygen timix containing nitrous oxide at a partial pressure of 0.9 atm while leaving the total pressure unchanged does indeed result within twenty four hours in significant loss of the protection afforded the animals by pressure conditioning.

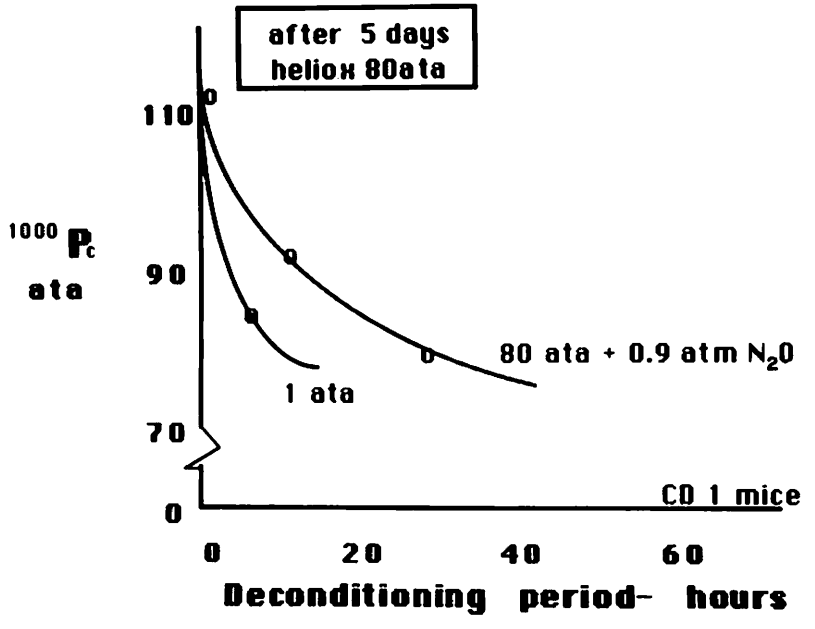


Fig. 12. Time course of reversal of pressure conditioning following five days exposure in heliox at 80 ata, as a result of either decompression and maintenance at 1 ata, or injection of 0.9 atm nitrous oxide while the animals continued to be maintained at 80 ata (from Brauer and Dutcher, 1987; courtesy of the *J. Appl. Physiol.).*

Thus, we conclude that, when using inert gas narcotics as agents to protect divers against HPNS symptoms, it will be necessary to strike a balance between the early injection of these agents so as to maximize the comfort of one's crew, and delaying such injection as long as possible so that the divers might derive maximum benefit from both, their own protective mechanisms and the pharmacological effects of the narcotic gas. We would also infer that replacing an atmosphere containing inert gas narcotics with one devoid of these while still remaining at high pressure could be hazardous and elicit unexpectedly severe HPNS manifestations.

TABLE 4.

The Seven Points

1. HPNS is a compound syndrome; components do not respond identically to manipulations of compression profile or of compression atmosphere.

2. Mean threshold pressure for onset of at least one HPNS manifestation — Type I seizures — decreases in direct proportion to the logarithm of compression rate; consequently the convulsion threshold increases with increasing compression time along a curve strongly concave toward the time axis.

3. In a number of species convulsion threshold pressures are independent of compression rate; this implies that the mechanisms leading to this HPNS symptom are probably independent of the mechanisms underlying the effect of varying compression rate in other species.

4. This compression rate effect in a number of species represents a slowly developing protective response postponing the onset of HPNS seizures, and involves two or more monoamine neurotransmitters.

5. It has been possible to separate time and pressure factors determining the development of this response; during the early stages of its development this proceeds the more rapidly the higher the pressure at which the subject is sojourning; hence accelerating the initial stages of compression as much as acceptable should be advantageous.

6. The data indicate that the extent to which the convulsion threshold pressure can be increased by manipulation of the compression profile alone is limited; the scope of this effect in the mouse is about 50 atm or about 70% of the low convulsion threshold pressure seen with very rapid compression.

7. Inert gas narcotics in concentrations sufficient to significantly affect the onset of HPNS seizures can slow or block entirely the development of the endogenous protective responsible for both, the compression rate effect and the amelioration of HPNS symptoms during prolonged sojourn at pressure; optimal use of these two procedures for amelioration or relief of HPNS symptoms requires a compromise in which the inert gas narcotic is added as late during the compression as is compatible with the level of HPNS symptoms considered tolerable; switching from a narcotically active atmosphere to heliox while remaining at pressure after a substantial pressure sojourn can be expected to result in more severe HPNS symptoms than would be encountered had the sojourn taken place in an atmosphere free of gaseous narcotics.

IV. CONCLUSION

This I believe, is the extent of the contribution which animal studies can make at the present time to the formulation of optimal compression schedules. Table 4 shows a brief summary of the points that seem to me to be likely to affect the design of compression schedules for deep diving as they develop in the future. I think it is worth repeating that, in this area more than in many others, attempts to deduce *quantitative* recommendations for the management of human subjects from animal experiments must be viewed with extreme caution. Our experiments, some of which have been shown above, have made us aware that, in contrast to the situation with regard to inert gas narcosis, with regard to HPNS idiosyncracies of various species and even strains are such that quantitative predictions are hardly admissible. The role of the animal experiments in this context then can only be that of pointing out possible hazards and of suggesting possible mechanisms, leaving the application to man to appropriate studies conducted in that reasonable recalcitrant species.

ACKNOWLEDGEMENT

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2

The Compression Strategy in the Alverstoke Deep Dives Series

Z. Török

I. INTRODUCTION

The Alverstoke deep dives series started in 1975 when the name of this civilian Ministry of Defence research establishment was the "Royal Naval Physiological Laboratory." The nature of the parent organization and the composition of its staff determined the threads that remained consistent throughout. The objective of the work has always been to analyze and define those physiological mechanisms that limit man's effectiveness in a hyperbaric environment. It was assumed that, where possible, systematic scientific experimental work provides the best means of tackling limiting factors, finding solutions to reduce their effects in order to increase both efficiency and safety. Nowhere is this activity better demonstrated than in the field of compression research.

Historically, the work seems to cluster into three phases. The first encompasses 1975 to March 1977 when Dive 6 reached 300 msw simulated depth (Hempleman *et al.*, 1978). With hindsight, this period is best described as the preliminary phase of a much greater program yet to emerge. Though diving to 300 msw was far from routine in 1977, the first 6 hyperbaric experiments at Alverstoke served for the multidisciplinary staff of the Laboratory to establish priorities and to perfect effective methods of working together in this complex and highly demanding field of scientific endeavor. It also served to demonstrate that a more efficient chamber atmosphere conditioning unit was required; its construction held up the experimental program for about a year.

The second phase, between September 1977 and 1982, was the most productive. In a comparatively stable environment, the objective of exploring the limits of usefulness of helium as a diving gas, within the 660 msw limit constituted by the working pressure of the chamber, was firmly established. Available resources set the working pattern to two simulated dives a year, each with two subjects. The most important scientific results concerning man's physiology were described in a conference paper (Török, 1980) and a large detailed report (Hempleman *et al.*, 1980). Work rate linked ventilatory parameters and cardiac output were measured (Winsborough *et al.*, 1981), fundamental hematological changes noted and described, and many changes from the normal in the field of neurology were analyzed (Hempleman *et al.*, 1984). The use of electrical muscle stimulation and Hoffman reflex techniques yielded some insight into the altered states of neuronal excitability during hyperbaric exposure (Harris, 1979). Exacting techniques keeping man's food intake constant during hyperbaric exposures yielded unique insight into alterations in energy and metabolic balance (Garrard *et al.*, 1981).

In 1982 the emphasis of work changed. Experiments into problems of diving deeper than 300 msw could no longer be sustained. The only acceptable task in this field remained the optimization of compression techniques on heliox to 300 msw. Resources available were severely reduced. The third phase of hyperbaric research at Alverstoke comprised three 300 msw simulated dives, one each in 1984, 1985 and 1986. Consolidation rather than new achievement marks this period, which may turn out to be the final one for some time to come.

II. CONTINUOUS VS. STAGED COMPRESSION PROFILES

In 1977 to 1978 a successful compression strategy was formulated that remained in use ever since. In an attempt to dissociate as far as possible physiological changes caused by the rate of change of pressure from those

caused by increased pressure *per se*, two simulated dives were performed to 420 msw maximum pressure. The planned very slow depth-independent compression rate of 60 msw/day was applied in six 10-minute periods at 1 m/min each, 2 hours apart. In the first 420 msw experiment this compression procedure had to be further slowed at around the depth of 250 msw when, due to a throat infection in one of the subjects, a 2-day stay was imposed. No ill effects due to HPNS were seen when the maximum depth of 420 msw was reached after a 9-day total compression period (Fig. 1). In dive 8, the second 420 msw exposure, the slow 60 msw/day compression profile was performed as intended in 7 days. In spite of this long compression phase, during the last 4 hours just as 420 msw was reached, the classical picture of full-blown HPNS developed, with ataxia, tremor, nausea and autonomic changes (Hempleman *et al.*, 1980).

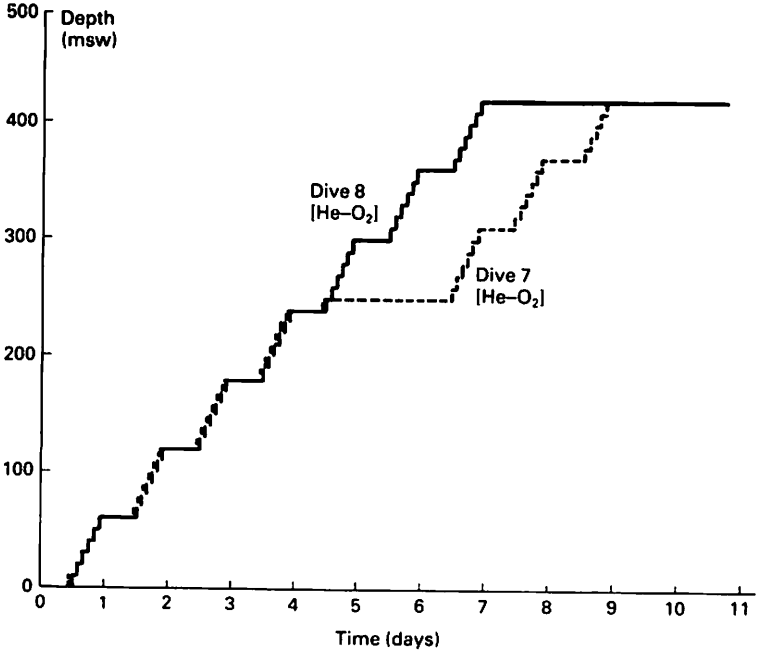

Fig. 1. The compression phase of Dives 7 and 8. The very slow depth-independent compression of 60 msw/day was carried out in six 10-minute periods, 2 hours apart at a rate of 1 msw/min. The extra two days stay at about 250 msw in Dive 7 was imposed due to a throat infection. No ill effects due to HPNS were seen in Dive 7, yet Dive 8 produced unacceptable HPNS at 420 msw, with ataxia, tremor, nausea and autonomic changes.

Since the 9-day compression to 420 msw in Dive 7 was successful, but unacceptably long in practical terms, and the HPNS seen in Dive 8 was interpreted as proving the failure of a very slow linear (depth independent) approach, a radically different technique was tried in Dive 9b (Fig. 2). Compression was carried out at the much faster rate of 5 msw/min during two or three 12-minute periods, 2 hours apart, each day. On successive days 180 msw, 300 msw and 420 msw was reached. The subjects were carefully observed and monitored; indeed, the 2-hour pauses interrupting the day's dose of compression were seen as a concession to safety, against the basic strategy of this compression procedure. When 420 msw was reached on Day 3, changes attributable to HPNS were seen, but the overall state of the subjects was much better than in Dive 8, after less than half the time spent in compression.

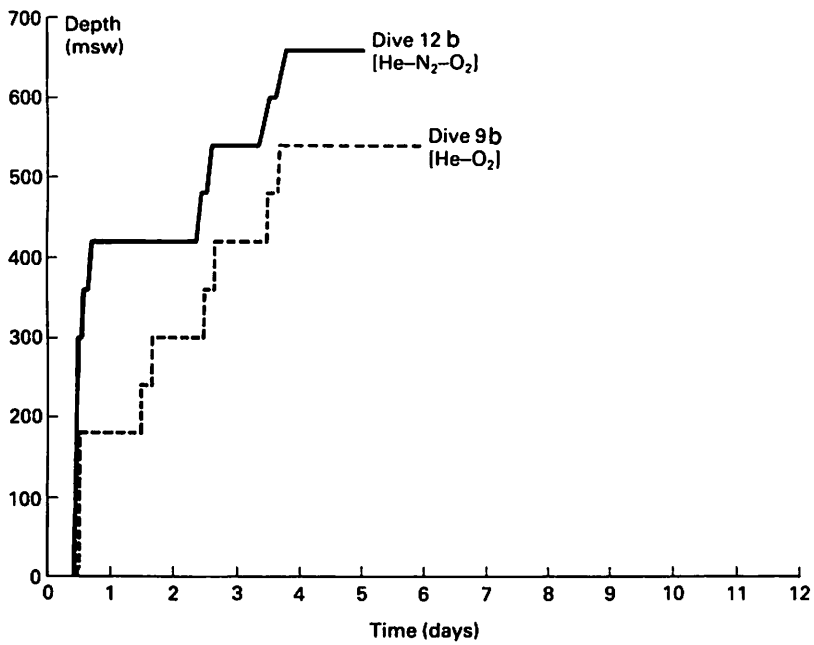

Fig. 2. The compression phase of Dives 9b (Heliox to 540 msw in 1979) and Dive 12 (Trimix to 660 msw) were of nearly the same duration and show similarities of design. Unacceptable HPNS was seen in the heliox dive, the subjects' condition was much worse in the trimix experiment.

On Day 4, 480 msw was reached at 3 msw/min compression rate, and 540 msw the next day, at 1 msw/min. Tremor was pronounced in one subject and, although the subjects were well on arrival, features of HPNS, such as nausea and ataxia apeared some hours later. Lassitude was in evidence, and marked improvement ocurred only some days later on decompression.

III. COMPRESSION RESEARCH ON ANIMALS

Though obvious, a few remarks may not be out of place here on the subject of experiments on animals, isolated organ systems or even cell preparations. The main contribution of these techniques is in elucidating various physiological, or even biophysical, mechanisms of function as these may be altered by high pressure, mass flux of helium particles, or their presence in large numbers in solution at great simulated depths. Models provided in this way may never be ignored; however, their limitations must be borne in mind if damaging mistakes in interpretation are to be avoided. Unlike in the case when a single isolated system constitutes the whole of the experimental preparation in the intact animal most physiological variables may represent the output of several systems, homeostatic or not, in each case. For example, sweat rate or heart rate may respond to an increase in core temperature, or emotional arousal. In an isolated preparation this aspect may have been changed, limiting the range of transferability of apparently applicable information.

Caution must be exercised in inter-species transfer of experimental results, and this is well known to physiologists. In the hyperbaric field this is likely to be compounded by errors concerning magnitude and timescale. There is a tendency for compression experiments on small animals to be performed on a single working day to pressures several times greater than the maximum current human exposures. Some refer to the 50th percentile of the mortality rate as HPNS. This timescale would preclude a steady state to be reached at all, after a compression procedure carried out in human terms both too fast and too far. The relevance of such experiments, especially when setting exposure limits for human divers, is not to be accepted without enquiry.

A recent series of detailed studies emphasized the large, many and systematic changes that correlate with body size in but one organ system, namely respiration (Taylor and Weibel, 1981). It would be surprising indeed if results were transferable from mice to men.

Many parameters of interest in environmental exposure experiments with man relate to his symptoms or effectiveness in a realistic task. These can only be measured in manned trials. In general, it may be stated

that scientific staff at Alverstoke were aware of animal experiments for reasons of their inherent interest in functional or mechanistic terms, and such experiments had nothing to contribute to the design of compression profiles.

IV. PHENOMENOLOGICAL APPROACH TO HPNS

HPNS has lately been approached at Alverstoke as a fundamentally ill-understood phenomenon. The objective was to describe it first, and to collect information about various of its aspects (Török, 1982). The opposite approach would be to assume that the basic causative mechanism is known, and then consider whether each pathological symptom or sign that emerges during compression fits the structure of the hypothesis espoused. It is probably premature to this day to take the second course of action. That stated, it seemed as if by compressing fast (5 msw/min) for two 60 msw pressure increments, some adaptive physiological homeostatic mechanisms had been stimulated or called into action. It seemed as if some mechanism modified the working parameters of the system during the rest of the 24-hour period, to cope with the changes forced on it by the increasing pressure. Inherent in this concept is that such adaptation is not achieved by the slow, gradual increase of pressure experienced by the body during a continuous 1 msw/min compression procedure. This conceptual model is of course pure speculation, but it is compatible with some modern ideas such as catastrophy theory (Zeeman, 1977) or, more generally, the realization of the inadequacies of linear theory applied to biology. Its use was merely the support it seemed to lend to the empirical fact that an environmental change which was much faster, hence a more severe perturbation, seemed to cause less distress, than did a slow environmental change, representing a less steep ramp function.

Another outcome of the above speculative process was the thesis that the most important parameter determining the environmental perturbation is not the compression rate, but its "daily dose." Again, no *a priori* assumption of linearity should be made; the magnitude of the daily dose may well depend on the environmental pressure. The suggestion that it is the daily dose that matters, and not the 12-hour dose, or the pressure increment experienced in any other period, may be supported by the existence of the many and varied diurnal rhythms governing physiological functions of the body. As to which of these are the crucial ones could form the basis of much future research. One may further suggest, by way of explanation, that if the daily dose of compression is the key parameter that will determine the degree of HPNS caused by and therefore the outcome of a given compression profile, historically it was missed for a long

time, because decompression problems and theories dominated much of hyperbaric experimentation. It is generally accepted that the rate of change and not its daily dose is the key parameter in decompression. It is worth mentioning as an aside that in long saturation decompressions the diurnal cyclic variation of much of man's physiological function should not be ignored any longer. It ought to be reflected in a 24-hour cyclic variation of planned decompression rates, slower when divers are asleep at night.

It may be interesting to note a simple practical feature of the work at Alverstoke that helped the emergence of the staged compression concept. In operational diving the objective of compression is simply to approach the diving site, whereas in the Physiological Laboratory one performed the compression in order to study and minimize its effects, namely HPNS. Experiments were to be conducted before maximum depth was reached, in order to monitor the safety of the procedure during previously untried exposures of man to high pressures. That meant measurements during compression. Many transducers would not provide a stable output whilst pressure is increasing, and some have to be calibrated for each pressure level. The 2-hour "stages" on the compression profiles after each 60 msw pressure increment were first introduced for this purpose.

V. THE MAGNITUDE OF THE COMPRESSION STEP

The magnitude of the 60 msw increments was defined on the basis of minimum measurable departure from a normal baseline of some neurophysiological parameters. It may be a performance decrement in a standardized psychomotor task, an increase in postural or action tremor, a change in the gain of the vestibulo-ocular reflex or in the structure of the EEG power spectrum. It may be the spontaneous apearance of an eye movement pattern such as gaze nystagmus or opsoclonus, or a symptom reported by the subject on systematic questioning or spontaneously. The central point here is that the magnitude of the increment of compression would be increased until it produced some minimal measurable change such as the above. A fundamental deficiency of this approach is that the increment is a function of the sensitivity of the particular measurements taken. For example, the technique remained practically useless until due regard was given to indicators of the state of the vestibular sensory system. The objective must be to identify all changes elicited, and then, using a just acceptable change in the variable that matters, whichever one that happens to be, to command a halt to further environmental stress. It must be realized in the light of the above that the Alverstoke practice of two 60 msw increments a day, 2 hours apart (three on the first

day) is a very crude approximation to the ideal, and that further fine tuning must be eminently feasible. Most of this information was obtained during the earlier dives.

VI. THE DEPTH THRESHOLD FOR HPNS

HPNS, regarded as the strain, has a threshold with respect to the stress causing it. This threshold was defined at Alverstoke using the above technique. The earliest significant change is the spontaneous apearance of opsoclonus, a random disjunct eye movement pattern with amplitude of only a few degrees of arc visual angle. Since this is just below the resolution of electro-oculographic technique (EOG) of recording eye movement, it is best detected by using the Baranay spectacles: illuminated goggles with 30 diopter lenses in front of the subject to prevent visual fixation. Opsoclonus is more specific than gaze nystagmus for this purpose, and preceded EEG spectral changes. It is seen at around 160 msw during compression, practically never before that pressure is reached. It effectively set the first day's dose of compression at 180 msw. There were three simulated dives in the deep dives series at Alverstoke in 1979, called training dives 9a, 10a and 10b, to 180 msw, supporting the above conclusion concerning the threshold. The 180 msw portion of deeper exposures provided compatible data.

VII. 540 MSW ON HELIOX: DIVE 13

Further staged compressions along the pathway pointed to by the 540 msw 1979 Dive 9b (Fig. 2) were conducted such as Dive 11 to 300 msw, and the important Dive 13, again to 540 msw (Fig. 3). During the staged compression of this simulated dive, on consecutive days 180 msw, 300 msw, 420 msw, 480 msw and 540 msw equivalent pressure was reached. With one additional day's work planned at 420 msw in order to complete a rather extensive program of experiments, target depth was reached on Day 6. Compression rates were 5 msw/min to 420 msw, 1 msw/min to 480 msw and 0.5 msw/min to 540 msw. There are four different items of information available about the subject's state after this experimental compression. First, for what it is worth, there was the rather subjective consensus of the chamber control team, those in charge, and of course the subjects themselves. There were only minimal features of HPNS present, and the view recorded at the time states that a lockout of divers from a diving bell in the sea would be possible in that state of health and well-being. This applied to the time on arrival, or any time later, as there was no deterioration, unlike in Dive 9b, the previous 540 msw exposure. Secondly,

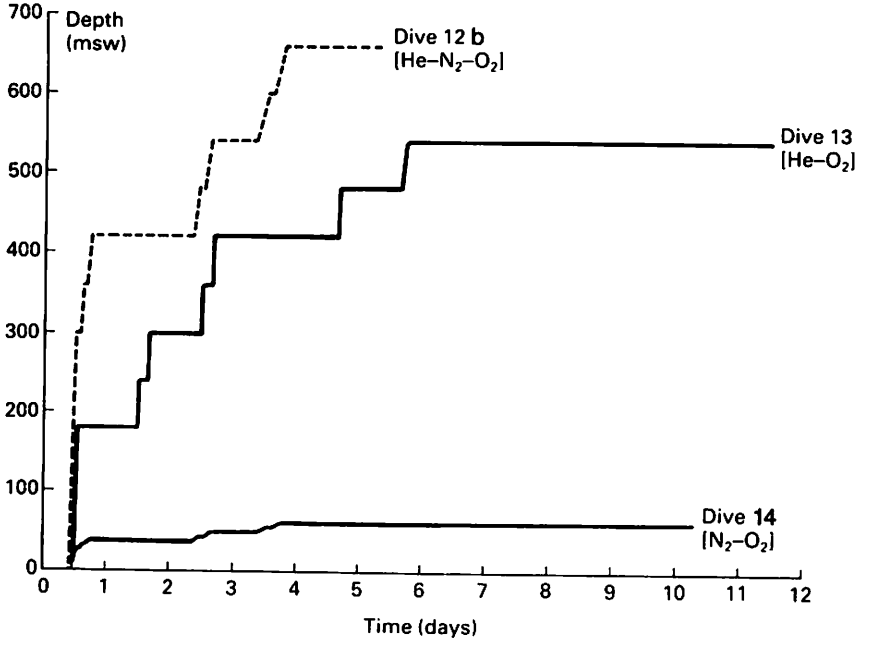

Fig. 3. Three experiments comparing the effects of compression to 540 msw on heliox with those of trimix to 660 msw. The same subjects took part in Dives 12b and 13, the trimix exposure being both deeper and shorter, thus potentially more severe. The Dive 14 profile followed the time course of nitrogen partial pressure in Dive 12b exactly, without added helium (Török, 1984a).

measurements of postural hand tremor indicated levels not exceeding three times the subject's own normal physiological tremor, in amplitude terms (Török, 1984a). In normal subjects, this increase is not very much, perhaps hardly noticeable, and the subject's manual dexterity remained as good as ever. Thirdly, a set of cognitive performance test results (Logie and Baddeley, 1983) told a different story: decrements of about 30% were seen — for example, in the mental arithmetic test on arrival at 540 msw. Lastly, the structure of the EEG power spectrum (Fig. 4) also changed markedly the theta to alpha ratio showing 4 to 10 times increases (Török, 1984a). Though the elegant French work on this subject (Rostain *et al.*, 1981) established the lack of correlation between EEG spectral changes and performance in a general, predictive sense, the above finding does indicate that some aspects of brain function changed as a result of the compression.

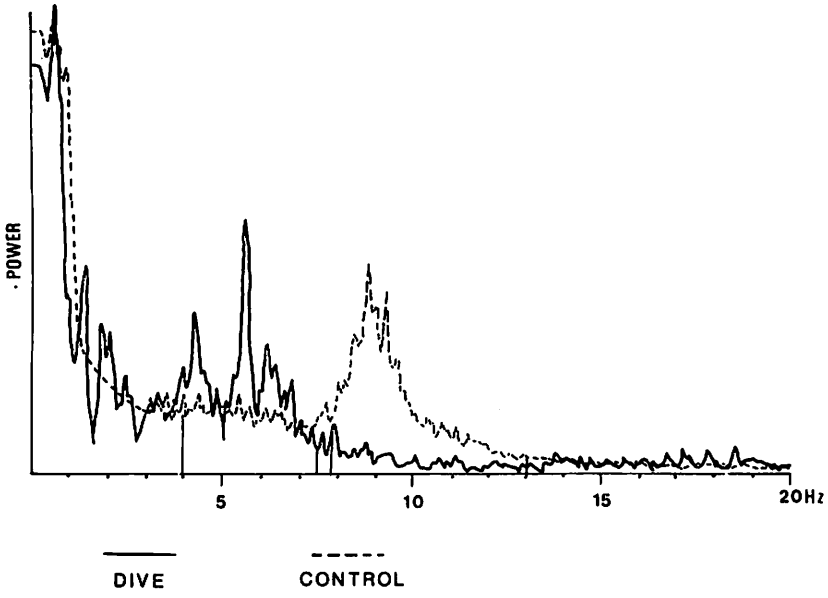

Fig. 4. Power spectral estimates of EEG from the same subject, illustrating typical HPNS changes: increase of power in the theta range (4-8 Hz) and decrease in the alpha range (8-13 Hz) of frequencies. This is a consistent change of low operational significance, as it does not correlate with performance decrements (Rostain *et al.*, 1981).

VIII. COGNITIVE TESTS

The point referred to above is so fundamental that in a laboratory of applied physiology it is impossible to consider the efficiency of various compression procedures without measuring the subject's cognitive and psychomotor performance. A large change in any neurophysiological variable seen on compression may be irrelevant for practical purposes. Intuitively one may wish these did not occur, but this view changes nothing. There is no doubt about the direct operational relevance of performance decrements. The bulk of this work was carried out by the MRC Applied Psychology Unit at Cambridge, to their usual high standards (Lewis and Baddeley, 1981). Ten pencil-and-paper tests were selected with the objective of monitoring all the cognitive performance factors that could possibly be affected. Of these, the Stroop test scores, semantic processing and the speed and accuracy of mental arithmetic correlated

with pressure *per se*. Performance scores were obtained about 24 hours after maximum depth was reached; this experimental design would therefore miss short-term rate-of-change-of-pressure effects.

Most pencil-and-paper tests measure either the speed of performance of an already well practiced task, or its accuracy. The overall averaged slowing was 7% and the increase of error rates about 12% measured across the 10 tests in the depth range 300-540 msw, when 100% was defined as the subject's own pre-dive control value. Though averaging scores of many different tests in this way is probably quite unjustifiable, the undoubtedly rough impression given is that these results are of the same order as, and certainly not worse than, similar tests yielded elsewhere after many different compression procedures (Török, 1984b). The acceptability of a given decrement of the cognitive test performance of working divers in an occupational health sense, as the reviewer pointed out, is a completely different question.

In order to pinpoint the hyperbaric exposure to helium as the cause of the cognitive decrements measured, other variables like cumulative sleep deficit, or significant mood changes due to perhaps social isolation in the chamber (the caging effect) have to be excluded. This was done as part of the above study by obtaining the subject's own daily estimate of his sleep quality that night, and also of his mood. The use of opposite adjectives with an analogue bar to be marked by the respondent yielded quantitative data; the essentially subjective nature of the information so obtained must not be overlooked. Test scores correlated poorly with both estimates, increasing the probability of a causal relationship between pressure and decrements in cognitive performance. Though the potential was there, the work relating to mood and sleep quality did not, in the event, provide information for the evaluation of compression procedures.

IX. 660 MSW ON TRIMIX

In 1980, following the conspicuous success of the 650 msw simulated dive at Duke University, called 'Atlantis II' (Bennett *et al.*, 1982), the decision was made at Alverstoke to use what seemed the best technique at the time for the next simulated dive, namely trimix, containing 10% nitrogen in the inert gas. After a short 180 msw experiment, Dive 12b was performed at Alverstoke in November 1980. On the first day, 420 msw was reached using the successful Atlantis II "fast" compression procedure. After a day's work at that pressure, the two subjects were compressed to 540 msw on Day 3, and to 660 msw on Day 4.

The last two days compression conformed to the pattern of arithmetic established earlier. A graphical comparison of Dive 12b with Atlantis II

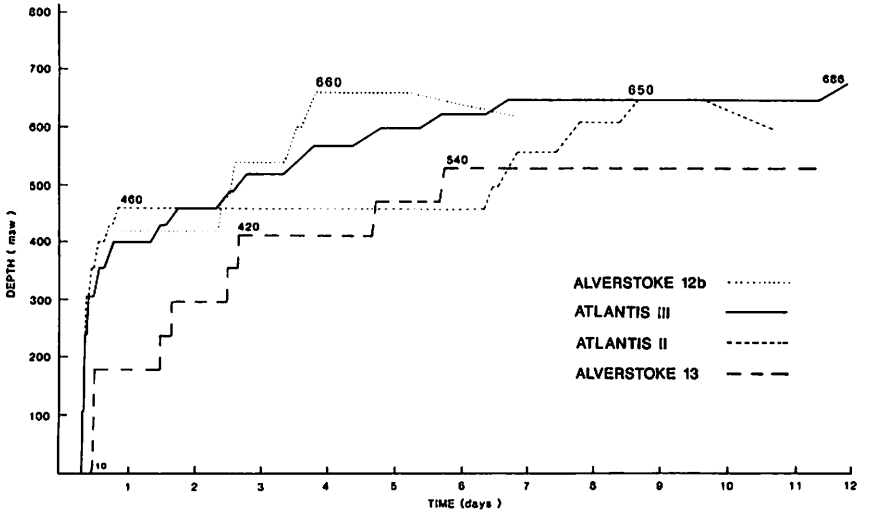

Fig. 5. Comparison of the compression profiles of four experimental deep dives. The early stages of Dive 12b follow Atlantis II, designed at Duke. Both Atlantis dives proceeded deeper than initially planned, with very good results, contrasting sharply with those in Dive 12b. The subjects' condition was excellent in Dive 13 on heliox, the compression to achieve this took longer than in the three trimix exposures illustrated.

(and Dives 13 and 14) is made on Fig. 5. A difference perhaps more significant than our present state of knowledge suggests, was the oxygen partial pressure: PO_2 was 0.5 bar at Duke, and 0.4 bar in Alverstoke, in both cases in order to conform to previous work, in absence of strong indications to the contrary. There were no convincing reasons to suggest that a PO_2 = 0.4 bar is inadequate at 660 msw.

In Dive 12b, on arrival at 420 msw, the subjects gave the impression of being under the influence of nitrogen narcosis. Their performance in any task was poor with marked inability to concentrate. Their approach was clearly "one step at a time," concentrating on a minute part of their job, completing it first, then going on to the next. They stopped frequently, even in well practiced procedures, just waiting for instructions. Their mood was subject to rapid and large changes triggered by insignificant events: they were fragile in this sense. They were unable to perform the cognitive pencil-and-paper tests at all. Since they were cheerful and cooperative at the time, and, in fact, made one or two feeble attempts, zero scores were recorded (Logie and Baddeley, 1982). This occurred on two more occasions during the dive, including two days later at 660 msw.

They were frequently euphoric, and had no useful and coherent recall later of what happened to them in the first few hours on arrival at 420 msw.

Recovery was dramatic after a night's sleep and on the fourth day 660 msw was reached. There were very few features of their behavior attributable to nitrogen narcosis at 540 msw, their condition being close to normal on arrival at 660 msw. A few hours later there was a sudden deterioration in their condition, marked by somnolence, lassitude, poor concentration and performance, myoclonic jerks, nausea and vomiting in one subject, and some dyspnoea. On the following day, in spite of all this, their morale was high. Their co-operation and rapport with colleagues outside the chamber was excellent though not very effective, and very little useful work was completed. When it was established that no significant improvement occurred during the day, decompression was started, since there seemed very little cause to spend the second day of the planned two days bottom time in this unproductive way. This decision was borne out by later events, namely that marked improvement was only seen several days later in decompression.

X. HELIOX OR TRIMIX?

The temptation was very strong at this point to consider the signs and symptoms encountered in this experimental exposure in terms of some blend of nitrogen narcosis on one hand and of HPNS on the other. After all, the maximum nitrogen partial pressure was PN* = 5.6 bar which, in terms of compressed air diving, (as opposed to in terms of the critical volume hypothesis (Simon *et al.*, 1975), is way beyond the acceptable.

In Dive 14, therefore, compression with nitrogen followed the time course of the nitrogen partial pressure encountered during the previous 660 msw exposure. Helium was not used, and the result was a 61 msw nitrox saturation dive (see Fig. 3). It may well be argued from an analytical standpoint that this experimental exposure should have been performed before Dive 13, not after it. On the basis of the emerging data, namely EEG and postural tremor, a quantitative and objective comparison was carried out of the effects of heliox (Dive 12b), nitrox and trimix. This work has been published (Török, 1984a) but its conclusions may be worth repeating here.

Firstly, high gas pressure, most of which was represented by helium (540 msw in Dive 13, 660 msw total in Dive 12b), was accompanied by approximately equal increases in postural tremor to a level of about three times the subject's own normal control value. The changes in the structure of the EEG power spectrum were numerically greater in trimix (see

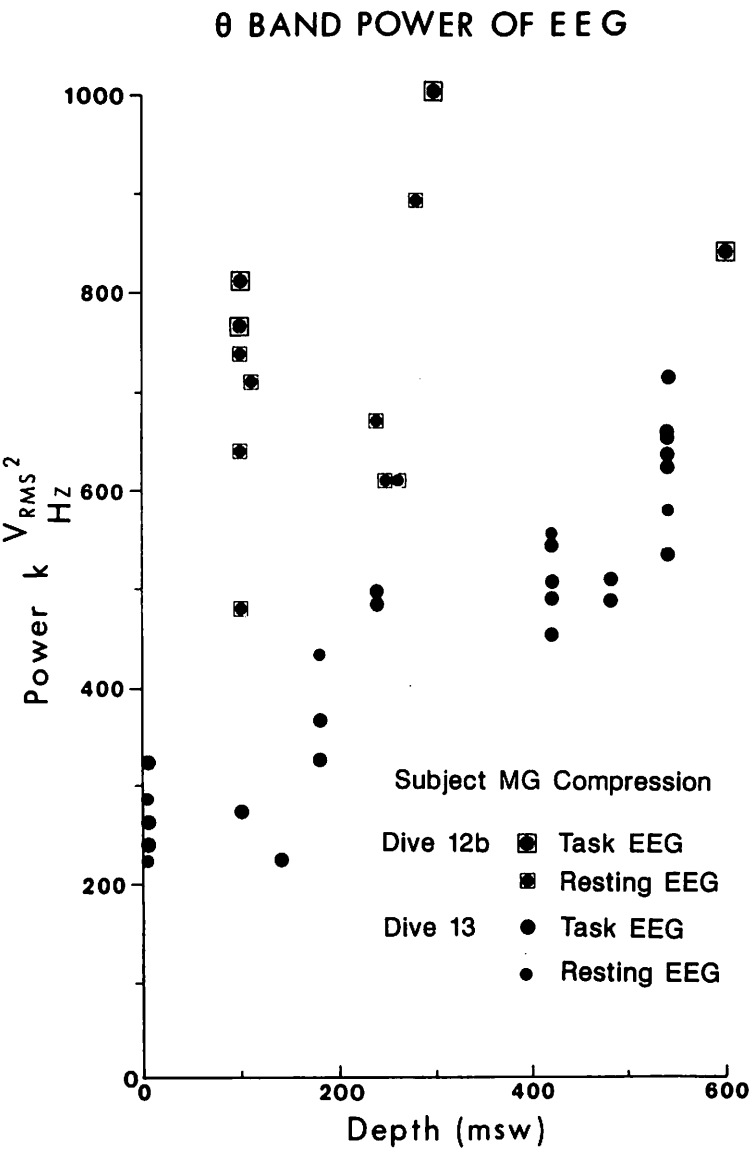

Fig. 6. Theta band (4-8 Hz) power of EEG of the same subject during compression on heliox (black discs) and trimix (boxed black discs), as a function of depth. The brain function of this man as indicated by his EEG, was altered more during his exposure to trimix than to heliox. Though this finding is clear, its significance is not.

Fig. 6). Secondly, nitrogen on its own at partial pressures of up to 5.6 bar (Dive 14) did not cause significant changes in either tremor or EEG. Finally, it was clear that nitrogen, when added to helium (Dive 12b) at a concentration capable on its own to modify behavior (i.e., a pharmacologically active dose), did not lessen the magnitude of these changes. Observation of the subject's condition and comparison of cognitive performance scores (Logie and Baddely, 1982) were compatible with the thesis that nitrogen and high pressure interacted positively to produce some of the augmented effects, causing a modified HPNS, as previously predicted elsewhere (Roth, 1975).

It must be emphasized that the above refers to one particular deep trimix exposure at Alverstoke, and is not a general comparison of the merits of trimix with heliox as diving gases. The success of at least two of the Atlantis experiments, and more recently the German series (Bennett *et al.*, 1987), tell a different story about trimix. Further evidence will no doubt emerge with time.

XI. THREE DIVES TO 300 MSW (1984-1986)

From the point of view of experimental work carried out during the compression, and also the consistency of the compression profile with principles of the design strategy established earlier, these three simulated dives undoubtedly belong to the "Deep Dives Series," constituting its third, probably the last phase. After 1982 simulated dives at Alverstoke could no longer be justified on grounds of studying physiological changes. Dives to 300 msw were performed in order to test equipment at that pressure, the compressoin itself remaining available for experimental work with the stated objective of optimizing the profile.

The number of days spent at maximum pressure was two, five and eleven days respectively, according to the amount of equipment-orientated work, some of it in the 3 m deep water-filled part of the chamber complex. Earlier simulated dives of the series were carried out in a much smaller 2-compartment chamber capable of higher working pressures. There were 3 subjects in each dive, seven different men, as two took part in two experiments each. Three were professional Royal Navy divers. In contrast, no military divers took part in Phases 1 and 2 of the series.

Oxygen partial pressure was $PO_2 = 0.4$ bar throughout, except during decompression of the 1986 dive. In the 1984 and 1985 dives decompression was carried out at the depth-independent rate of 26 msw/day, the gas being released in the form of a steady "bleed," monitored with a flow meter, during 14 hours out of each 24. The faster 28 msw/day decompression rate used in earlier dives has been shown to be unacceptable. For reasons mentioned above, the subjects were not decompressed whilst asleep.

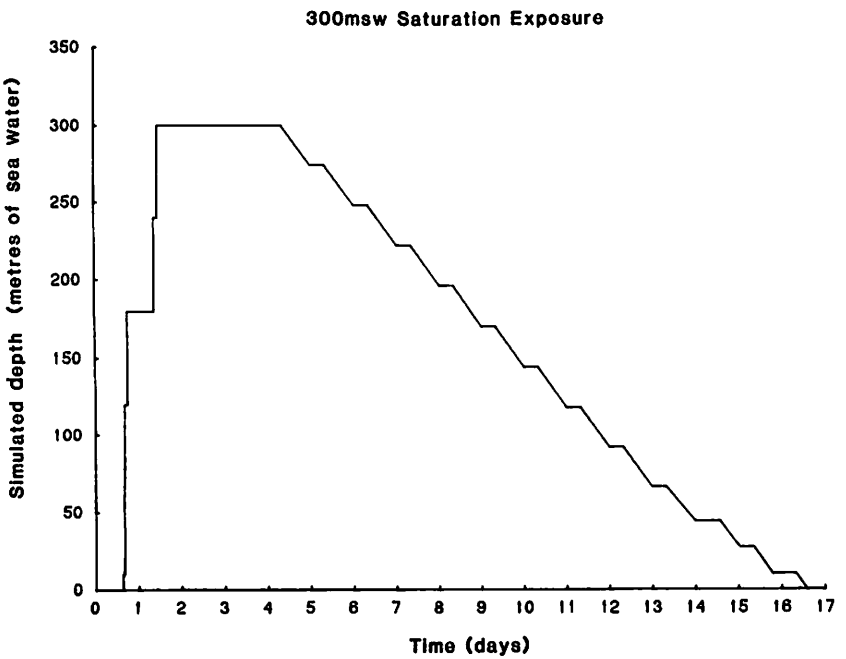

Fig. 7. Dive profile of the 1984 300 msw experiment. The 20 hours compression phase was identical in all three 300 msw dives, comprising 5 msw/min compression rates, two-hour long "stages" at 120 and 240 msw, and a 15-hour overnight stay at 180 msw.

The compression procedure (Fig. 7) was identical in all three dives. About 30 minutes was spent at 10 msw whilst chamber atmosphere was flushed with helium to bring down the nitrogen partial pressure to below 0.02 bar and to establish the PO_2 = 0.4 bar. This procedure has also been consistently carried out in all the Alverstoke oxyhelium exposures of the series, an important part of the design strategy by excluding an experimental variable, namely nitrogen effects. Compression was then carried out at a rate of 5 mws/min, with "holds" or "stages" of 2 hours at 120 msw, 15 hours overnight at 180 msw, and 2 hours at 240 msw. Total compression time is just short of 20 hours on this profile.

As in previous dives, the subjects were monitored almost continuously during this time (excluding overnight). Semistructured interviews and simple techniques of clinical examination were used, such as the finger-to-nose test of ataxia and tremor, or examining the eyes with Barany spectacles for signs such as nystagmus and opsoclonus. EEG and tremor recordings were made, and the gain of the horizontal vestibulo-ocular

reflex measured using sinusoid stimuli on a pivoting stool. Questionnaires on mood and sleep quality were used twice daily, and pencil-and-paper tests of cognitive performance applied as in Phases 1 and 2 of the Deep Dives Series.

From the above 9 man-dives with 7 different subjects, a consistent picture can be said to have emerged. Signs and symptoms of HPNS were seen, but they were acceptable in each case. At 120 msw nothing untoward could be detected. Tremor started to increase on arrival at 180 msw in five man-dives out of nine, in each case returning to normal overnight. At 240 msw increases from this baseline were slight, less than that seen at 180 msw on arrival. On arrival at 300 msw postural tremor was increased in all subjects, 300% being a representative figure. One subject had a normal tremor about twice as much as that seen in most others at 300 msw. This man increased his postural hand tremor to about 800% of his own normal control value. The significance for the normal population of this unusual finding is difficult to assess.

Of the minor symptoms and signs of HPNS, opsoclonus was present in two subjects at 180 msw and on six occasions at 240 msw. Nothing else untoward could be detected at 180 msw, with arthralgia in shoulders and wrists noted by three men in all. At 240 msw one subject had symmetrical gaze nystagmus with some ataxia, reporting some sliding vertigo on head movement and a perceptible delay in visual fixation; all the other subjects were free of symptoms.

At 300 msw only minor symptoms and signs were experienced, all symptoms resolving in one or two hours. Two men reported the above visual symptoms, and had accompanying ataxia. Nobody had nausea, one reporting slight epigastric "queaziness." Balance while standing on one leg deteriorated in two subjects, with a third man feeling unsteady but his performance remaining quite normal. There were no symptoms referrable to the autonomic nervous system. The four instances of opsoclonus noted at 300 mw perhaps represented an improvement upon the six times it was noted at 240 msw. The significance of this account is clearly in the fact that even with careful systematic observation nothing worse than the above could be noted or reported during and after the 20-hour compressions to 300 msw.

Six tests of cognitive performance were used at 180 msw, 240 msw, and on arrival and again 24 hours later at 300 msw in the 1984 and 1985 dives. These were arithmetic adding, grammatical reasoning, visual search, number similarities, semantic processing and the manikin test of spatial orientation (Logie and Baddeley, 1982). Taking the 1984 dive scores as typical, the 300 msw-on-arrival scores averaged out at -3% across the 3 subjects, with each subject's mean pre-dive performance taken

as 100%. The second testing session at 300 msw yielded a mean score of 102.4%, both well within normal variability. The severe methodological limitations of amassing scores in this way have been pointed out before (Török, 1984b) and cannot be ignored. Inspection of the individual scores indicated maximum decrements of −22% and −18% in arithmetic adding on arrival at 300 msw, at the same time as the manikin test improved 117% and 130% in different men. Probably very little additional useful information may be gleaned from further such analysis at 300 msw, the keynote seems to be no significant change.

XII. SUMMARY

Important features of the Alverstoke compression strategy are the following. The depth-time profile is staged, with the daily dose of compression rather than its rate in msw/min being considered as important. The objective of the designed compression profile was to allow minimal transient signs and symptoms of HPNS to develop such that the subjects are free of them again in a few hours after arrival. Tremor, EEG, pencil-and-paper performance tests, the gain of the vestibulo-ocular reflex, signs elicited with techniques of clinical neurological examination, and symptoms obtained by systematic questioning served as the main criteria in the design process. The subjects were, with five exceptions out of 27, technical and scientific staff of the Laboratory and were reporting any unusual symptoms, however small. The HPNS itself was approached phenomenologically, i.e. as seen, its signs and symptoms were not screened against those predicted by an espoused theory. Empirical data obtained elsewhere from manned experimental compressions were taken into account, but animal experiments and their various associated theories played a minor and indirect role only. The diving gas was heliox with only two exceptions where trimix with 10% nitrogen produced unacceptable results. The oxygen partial pressure was kept constant in all compressions at PO_2 = 0.4 bar, with nitrogen in the heliox dives below 0.02 bar, regarded as a contaminant and flushed out at 10 msw over half an hour or so at the start of the compression.

In a single 540 msw exposure the subjects had only minimal signs and symptoms of HPNS after a six-day staged compression (Fig. 3). More recently nine man-dives were performed to 300 msw where after the 20-hour staged compression profile (Fig. 7) the subjects were practically unaffected as described above. The compression rate used as 5 msw/min.

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3

Development and Evaluation of Compression Procedures for Deep Operational Diving

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I. INTRODUCTION

Following demonstration in resarch dives, such as Predictive Studies III at the University of Pennsylvania in the early 1970s, that man has sufficient ventilatory capacity to perform useful work at very great depths (Strauss *et al.*, 1976; Wright *et al.*, 1972; Lambertsen, 1976; Peterson and Wright, 1976; Strauss *et al.*, 1976; Lambertsen *et al.*, 1977), the most critical problem for practical deep diving operations became that of compressing men to depth in sufficiently good condition for them to safely and effectively perform to their potential. One important obstacle to such performance has been a group of debilitating effects commonly referred to as the high pressure nervous syndrome, or "HPNS" for short (Bennett, 1982).

In order to develop and validate an operational procedure for compression to great depths, finding a way to minimize or eliminate HPNS within the bounds of a practically useful schedule was made an important objective in a series of loosely associated dives conducted, in part, at the Institute for Environmental Medicine of the University of Pennsylvania in Philadelphia, Pennsylvania, U.S.A., and at the Norwegian Underwater Technology Center in Bergen, Norway. These are summarized in Table 1 and Table 2 which list research dives, and operational or operational validation dives, respectively.

TABLE 1.

Development and Verification of Practical Capability for Deep Compression (Research Dives)

Predictive Studies IV	
Phase I Institute for Environmental Medicine University of Pennsylvania Philadelphia, Pennsylvania, U.S.A. 1200 fsw - 370 msw 1975 4 Divers	Phase II Institute for Environmental Medicine University of Pennsylvania Philadelphia, Pennsylvania, U.S.A. 1600 fsw - 490 msw 1975 4 Divers
Deep Ex	
Dive I Norwegian Underwater Institute Bergen, Norway 980 fsw - 300 msw 1980 6 Divers	Dive II Norwegian Underwater Institute Bergen, Norway 1630 fsw - 500 msw 1981 6 Divers

As a result of this extended research and development program, procedures have been derived which have enabled men to be compressed to 450 msw with heliox gas mixes in condition to safely and effectively work in the water about 48 hours after leaving the surface. While reports about some of the individual dives have been previously published, no general overview has ever been presented. This paper, therefore, describes the progress in practical compression procedures made over the course of these related programs. Special attention is given to the specific procedures used, and the subjective and general performance results obtained with them. The results of quantitative measures are also considered, but only one measure, long-term memory (evaluated through a word:word association test, is discussed in detail. This measurement appears to correlate

more closely with the subjective findings than do any of the other objective parameters which were measured as a part of these programs.

For more detailed accounts of the specific dive operations and the performance studies which were conducted, readers are referred to the prior publications on these dives. A selection of these is listed in the appendix of this paper.

TABLE 2.

Development and Verification of Practical Capability for Deep Compression (Operational Dives)

Deep Dive Development Project	
Welding Qualification Dive 1 Comex, Marseille, France 980 fsw - 300 msw 1983 6 Divers	Onshore Verification Dive 1 NUTEC, Bergen, Norway 1140 fsw - 350 msw 1983 6 Divers
Onshore Verification Dive 2 NUTEC, Bergen, Norway 1140 fsw - 350 msw 1983 6 Divers	Welding Qualification Dive 2 Comex, Marseille, France 980 fsw - 300 msw 1983 8 Divers
Fjord Dive Onarheims Fjord, Norway 980 fsw - 300 msw 1983 20 Divers	
Diving and Subsea Intervention Studies	
Onshore Verification Dive NUTEC, Bergen, Norway 1470 fsw - 450 msw 1985 6 Divers	
Oseberg T-Project Diving and Repair Program	
Onshore Trial Dive 1 NUTEC, Bergen, Norway 1180 fsw - 360 msw 1986 6 Divers	Onshore Trial Dive 2 NUTEC, Bergen, Norway 1180 fsw - 360 msw 1986 6 Divers
Onshore Trial Dive 3 NUTEC, Bergen, Norway 1180 fsw - 360 msw 1986 6 Divers	

II. RESEARCH DIVES

A. Predictive Studies IV

Within the research category, Predictive Studies IV (PS IV) was conducted to investigate several aspects of HPNS including impact of

TABLE 3.

Scope of Physiological and Performance Studies During Predictive Studies IV

Central Nervous System Function
Perceptual, Cognitive and Psychomotor Performance
Somatosensory Evoked Response
Clinical and Sleep Electroencephalograms
Neuro-muscular Function
Intentional and Postural Tremor
Muscle Strength
Nerve Conduction Velocity
Auditory and Vestibular Function
Balance
Vestibular Stimulation
Audiometry
Visual Function
Visual Evoked Response
Visual Studies
Eye Tracking
Ocular Fixation
Thermal and Metabolic Measurements
Respiratory Gas Pressures
Respiratory Gas Exchange
Ventilatory Rate and Pattern
Exercise
Skin and Rectal Temperatures
Inspired and Expired Gas Temperatures
Cardio-Pulmonary Function
Electrocardiogram
Cardiac Output
Circulatory Reflex
Diaphragmatic Electromyogram
Esophageal Pressure
Pulmonary Function
Biochemical, Endocrinological and Hematological Studies
Underwater Work Performance
Speech Generation and Distortion

compression rate and compression depth on onset, the influence of exercise, and the extent and rate of recovery or adaptation. It was also intended to demonstrate in-water work capability at great depths and to progress towards deep operational diving. The approach adopted for studying HPNS was to purposely provoke the syndrome and then to follow its effects in time over a broad range of physiological and performance functions. The scope of these measurements is given in Table 3.

In order to provoke HPNS repeatedly, the dive plan called for a rapid, staged compression to 1200 fsw with daily, rapid excursions to 1600 fsw. Helium-oxygen gas mixes were utilized throughout, and it was planned to vary the excursion descent rate as necessary to adjust the degree of HPNS which occurred. Measurements of the many parameters being studied were taken in modules which were repeated periodically before, during and after the compressions.

In order to establish decompression procedures for the planned 400-fsw excursions from 1200 to 1600 fsw, a preliminary dive with saturation at 800 fsw and excursions to 1200 fsw was conducted. This Phase I dive also provided an opportunity to refine the monitoring techniques and to evaluate the planned compression schedule (Table 4). This procedure was derived following discussions with French scientists who, based on their deep dive experience concurred that such a compression time frame would produce an appropriate degree of HPNS. Two men were studied simultaneously, and a total of four men participated in the Phase I dive. All were commercial divers who were fit and healthy.

With the planned compression (Table 4), no symptoms of HPNS were noted after the rapid descent to 800 fsw. After a two-hour hold at 800 fsw, the subsequent compression to 1200 fsw produced distinct symptoms in three of the four divers. These symptoms included headache, dizziness,

TABLE 4.

Compression Rate Profile for Predictive Studies IV, Phase I

Depth (fsw)	Compression Rate (ft/min)	Compression Duration (min)
0-400	20	20
400-600	10	20
600-800	5	40
800	-	120
800-1000	20	10
1000-1100	10	10
1100-1200	5	20

concentration difficulty, incoordination and nausea, but were generally mild and fully recovered from upon return to 800 fsw. Subsequent excursions to 1200 fsw produced no symptoms of note and the divers seemed highly competent.

Because the HPNS developed during the Phase I dive was mild, the compression rates for the Phase II dive of PS IV were increased as shown in Table 5. As before, two men were compressed simultaneously, and 4 men were studied altogether. Two of these men had been participants in the Phase I dive, and again, all were fit commercial divers.

TABLE 5.

Compression Rate Profiles for Predictive Studies IV, Phase II

Depth (fsw)	Compression Rate (ft/min)	Compression Duration (min)
0-400	32	12.5
400-600	16	12.5
600-800	8	25
800	2 Hour Hold	
800-1000	20	10
1000-1100	10	10
1100-1200	5	20
1200	22 Hour Hold	

	Initial Excursion		Later Excursions	
	Rate (ft/min)	Time (min)	Rate (ft/min)	Time (min)
1200-1400	20	10	40	5
1400-1500	10	10	20	5
1500-1600	5	20	10	10

The results of the two compressions conducted from the surface with the Phase II schedule were dramatic and not fully expected. As indicated above, the intent in this operation was to provoke HPNS. This was to be done not only on the initial compression to 1200 fsw, but also on excursions from 1200 to 1600 fsw each day for some days after the initial descent. Based on an earlier USN dive to 1600 fsw (Spaur, 1974), substantial symptoms were expected during the excursion descents to 1600 fsw. It had to be considered possible that an excursion from 1200 to 1600 fsw at the rate planned, particularly one of the first excursions for any individual,

would cause such severe symptoms of HPNS that the compression would have to be aborted short of the target depth.

The inital compressions from sea level to 800 fsw during the Phase II dive produced mild symptoms in 3 of the 4 subjects, but these had all resolved by the time compression was resumed. The subsequent descent to 1200 fsw produced marked symptoms of HPNS in all subjects, however. These included such typical findings as headache, nausea, vomiting, dizziness, fatigue, somnolence, tremor and myoclonic jerks. The response of each of the individuals was different, but all required about two hours of rest in which to recover before carrying on with the test protocol.

After a night of rest at 1200 fsw, only minor symptoms remained, so the compression to 1600 fsw was commenced. Though plans had been made to stop at some intermediate depth if any of the subjects became severely affected by HPNS, this was not necessary. Over the course of the first (i.e., 40-minute) compression from 1200 to 1600 fsw, the two subjects were not only not incapacitated by HPNS, but had no marked change in condition. As a result, the compression rates were doubled and the compression time was halved to 20 minutes on the two following days, but there was still no important impact of compression from 1200 to 1600 fsw. Based on these findings, the second two divers were compressed from 1200 to 1600 fsw in 20 minutes on their first excursion. Again, this produced no deterioration in the condition of the subjects, nor did two subsequent excursions.

During the PS IV, Phase II excursions, no critical functional or performance decrements were found in any of the divers. Tremor was found to increase during periods of descent, but returned to initial values quickly after a stable depth was established. It was not an operational consideration. Sensitive psychometric parameters such as long-term memory also deteriorated to some extent during the excursions. These changes became less prominent in the course of the saturation, though. In general, the divers functioned in a reliable and competent manner throughout the operation. Routine preparations required substantially longer periods at 1200 and 1600 fsw than they had at the surface, however.

At the end of the bottom phase, all 4 divers made excursions to 1600 fsw and carried out a brief, timed work performance program in the wetpot using commercially available UBA. The task was to rig, unbolt and remove a heavy valve-choke from a scaled-down wellhead assembly, then reassemble the system and remove the lifting rigging. The work was performed in warm water and required an average oxygen consumption of about 2.0 liters/minute over a 10 to 12-minute period. At 1600 fsw, the 2 divers using the superior piece of breathing equipment performed with a proficiency equal to the best sea-level trials. The other 2 divers were slower,

but except for one period when the valve-choke twisted in the rigging, these men still performed within the general time frame required for the task at sea-level pressures.

The results of Predictive Studies IV, then, were somewhat disappointing from the research standpoint. While marked HPNS was produced, the adaptation to it was very quick and sufficient to prevent rapid 400-fsw descents from provoking further, marked symptoms. From the operational standpoint, however, the results suggested that a relatively fast, staged compression profile with a heliox gas mix might provide sufficient management of HPNS to permit efficient and effective manned subsea intervention at depths to 1600 fsw (ca. 500 msw). In addition, the dive demonstrated that men in a stable thermal environment were capable of performing useful in-water work over limited time periods at depths to 1600 fsw.

B. Deep Ex

By the early 1980s, research dives had progressed to depths as deep as 2250 fsw (Bennett *et al.*, 1982). Open-sea operational dives, however, were only infrequently deeper than 200 msw. Thus, a great gap existed between the depth man had been exposed to under highly controlled conditions and the depth range he routinely worked at in the open sea. In planning for future offshore petroleum resources development, therefore, oil companies, particularly in Norway, became interested in identifying both the existing capability of divers to work at deep depths, and those areas of procedures and diver life-support equipment which required upgrading to increase the practical working depth. To this end, two dives were conducted at the Norwegian Underwater Institute (NUI, later renamed the Norwegian Underwater Technology Center (NUTEC)), in Bergen. These dives were Deep Ex I to 300 msw and Deep Ex II to 500 msw.

The general objectives of the two dives were similar to each other, and except for some specialty research programs such as lost-bell survival and high-pressure TIG welding, the dive contents were similar. The scope of the psychometric studies and other monitoring relevant to HPNS which was conducted in the dry during the Deep Ex dives, and also during the subsequent operational validation dives conducted at NUTEC, are given in Table 6. The primary objectives of the two Deep Ex dives were, as suggested above, to determine the adequacy of procedures (e.g., compression, decompression, vertical excursions) and diver life-support equipment (e.g., UBA, thermal protection gear) for use in practical deep diving operations. The dives were also intended to demonstrate the in-water

work capability of man at great depths under realistic open-sea conditions (i.e., cold water for extended work periods). The scope of the in-water work program is given in Table 7.

TABLE 6.

Psychometric and Related Monitoring During Dives Conducted at NUTEC (Studies in the Dry)

Measurement/ Test	Dive ID: Depth (msw):	DXI 300	DXII 500	3DP1 350	3DP2 350	DSIS 450	OTP 360
EEG (Spectral Analysis)		X	X	X	X	X	X
Tremor		X	X	X	X	X	X
Microtremor						X	X
Finger Oscillation Speed		X	X	X	X	X	X
Hand Grip Strength		X	X	X	X	X	X
Visuomotor Speed		X	X	X	X	X	X
Reasoning		X	X	X	X	X	X
Arithmetic		X	X	X	X	X	X
Perceptual Speed		X	X	X	X	X	X
Long-Term Memory		X	X	X	X	X	X
Operational Test			X	X	X	X	
Hidden Patterns			X	X	X		
Visual Digit Span		X	X	X	X		
Time Reproduction		X					
Visual Reaction Time		X	X	X	X	X	
Finger Dexterity		X	X	X	X	X	
Manual Dexterity		X	X	X	X	X	
Arm-Wrist Speed		X	X	X	X	X	
Pursuit Coordination Test		X	X				
Static Control Test		X	X				
Status Questionnaire		X	X	X	X	X	X

With respect to compression, several different approaches were taken during the Deep Ex dives. One was to use a staged descent profile with heliox gas mixes; another was to use a staged descent profile with a nitrogen-helium-oxygen trimix; the final approach was to convert the divers from trimix to heliox after reaching bottom depth.

In Deep Ex I, the same time-depth profile was planned for both the heliox and trimix compressions. This schedule was adapted without major change from the Predictive Studies IV, Phase II time-depth profile and is given in Table 8. Each compression was made with a group of three men. The heliox group consisted of one experienced commercial diver, one student and one electronics technician; the trimix group consisted of two experienced commercial divers and one physiologist. The trimix composition

TABLE 7.

Psychometric and Related Monitoring During Dives Conducted at NUTEC (In-Water Studies)

Measurement/ Test	Dive ID: Depth (msw):	DXI 300	DXII 500	3DP1 350	3DP2 350	DSIS 450	OTP 360
Valve Assembly/Disassembly		X	X	X	X	X	X
Heavy Flange Assembly/Disassembly			X	X	X	X	X
Finger Dexterity			X	X	X	X	
Manual Dexterity			X	X	X	X	
Hand-Wrist Speed			X	X	X	X	
Visual Reaction Time			X	X	X	X	
Operational Test			X	X	X	X	
Visual Digit Span			X	X	X		
Arm Ergometer				X	X	X	X
Trapeze Swimming				X	X	X	X
Emergency Drills				X	X	X	X
Status Query		X	X	X	X	X	
Length Estimation		X					
Time Estimation		X					
Weight Estimation		X					
Roughness Estimation		X					

TABLE 8A.

Deep Ex I Trimix Compression Schedule

Depth (msw)	Rate (msw/min)	Planned Time (min:sec)	Actual Time (min:sec)	Elapsed Time (min:sec)
0-125	6.0	20:50	20:50	20:50
125	-	1:10	1:10	22:00
125-188	3.0	21:00	21:00	43:00
188	-	1:00	1:00	44:00
188-250	1.5	41:20	41:20	85:20
250	-	180:40	180:40	266:00
250-275	6.0	4:10	4:10	270:10
275	-	0:50	0:50	271:00
275-288	3.0	4:20	4:20	275:20
288	-	0:40	0:40	276:00
288-300	1.5	8:00	8:00	274:00

employed had 10% nitrogen as then advocated by Dr. Peter Bennett (Bennett *et al.*, 1981).

During the heliox compression (Table 8B), two of the subjects, both of the non-commercial divers, became markedly affected by HPNS starting at about 210 msw. They suffered from vertigo and nausea when they moved their heads and became unable to perform scheduled tasks after arrival at 250 msw. The third subject in this group, the experienced commercial diver, was unaffected.

TABLE 8B.

Deep Ex I Heliox Compression Schedule

Depth (msw)	Rate (msw/min)	Planned Time (min:sec)	Actual Time (min:sec)	Elapsed Time (min:sec)
0-125	6.0	20:50	20:50	20:50
125	-	1:10	1:10	22:00
125-188	3.0	21:00	21:00	43:00
188	-	1:00	1:00	44:00
188-250	1.5	41:20	41:20	85:20
250	-	180:40	520:40	606:00
250-275	6.0	4:10	4:10	610:10
275	-	0:50	0:50	611:00
275-288	3.0	4:20	4:20	615:20
288	-	0:40	0:40	616:00
288-300	1.5	8:00	8:00	624:00

Both the affected heliox divers were allowed to rest and sleep. After extending the hold at 250 msw from the planned 3 hours to 8 hours and 41 minutes, the two men were sufficiently recovered to resume scheduled tasks and proceed on to 300 msw. No further deterioration due to HPNS occurred and the men were in good condition after a night of sleep at 300 msw.

The three divers compressed on trimix had an essentially uneventful compression (Table 8A). The only noticeable effect was a marked euphoria which was particularly noticeable in the non-commercial diver and was attributed to narcosis. This euphoria did not cause any major problems in the operation, but did require extra effort to be expended in managing that particular individual during some of the performance studies.

The gas switch from trimix to heliox was executed as planned a day after the divers arrived at 300 msw. It took 75 minutes to complete, and the nitrogen was lowered from 9.5% to 3.5%. The two commercial divers

reported no symptoms, whatsoever, following the gas switch. The non-commercial diver, however, reported flu-like symptoms (i.e., mild nausea and aching muscles) starting about 7 hours after the switch. These symptoms disappeared overnight. They may have been related to an exchange-rate counterdiffusion syndrome as described by Harvey and Lambertsen (1978), though the theoretical inert gas pressure transients were not particularly large.

Clearly the trimix compression in Deep Ex I was much easier on the men, but following adaptation of the heliox divers, all participants were in good condition at 300 msw. Tremor, however, was distinctly lower when trimix was being breathed. It was of operational significance in only one diver, though, and this man had been found to have a relatively great degree of tremor under normal circumstances on the surface.

Among the psychometric measurements, long-term memory was most affected by compression to 300 msw. Performance tended to normalize with time at depth, however, though in the Trimix Group, psychometric parameters such as long-term memory and reasoning returned to baseline values only after the switch to a heliox gas mix.

In Deep Ex II, the approaches to compression were similar to those utilized in Deep Ex I. Different time-depth schedules were used for trimix and heliox, however. The trimix schedule (Table 9) was one proposed by

TABLE 9.

Deep Ex II Trimix Compression Schedule

Depth (msw)	Rate (msw/min)	Planned Time (min:sec)	Actual Time (min:sec)	Elapsed Time (min:sec)
0-108	9.0	12	12	0:12
108	-	10	10	0:22
108-240	3.0	44	44	1:06
240	-	10	10	1:16
240-300	1.5	40	40	1:56
300	-	120	240	5:56
300-350	0.5	100	100	7:36
350	-	120	129	9:45
350-400	0.25	200	200	13:05
400	-	120	535	22:00
400-440	0.125	320	320	27:20
440	-	120	120	29:20
440-470	0.1	300	300	34:20
470	-	120	120	36:20
470-500	0.1	300	300	41:20

Dr. Peter Bennett based on his experience in the Atlantis dive series. Trimix with 10% nitrogen was utilized. The heliox schedule (Table 10) was again based on the Predictive Studies IV experience, but the intermediate stop depth was reduced from 250 msw to 216 msw in order to try to minimize development of initial symptoms of HPNS. Three men were compressed in each group.

TABLE 10.

Deep Ex II Heliox Compression Schedule

Depth (msw)	Rate (msw/min)	Planned Time (min:sec)	Actual Time (min:sec)	Elapsed Time (min:sec)
0-108	6.0	18	18	0:18
108-162	3.0	18	18	0:36
162-216	1.5	36	36	1:12
216	-	180	180	4:12
216-296	5.0	16	16	4:28
296-336	2.5	16	16	4:44
336-376	1.25	32	32	5:16
376	-	1174	1259	26:15
376-440	8.0	8	8	26:23
440-472	4.0	8	8	26:31
472-500	2.0	14	14	26:45

The Trimix Group in Deep Ex II included the commercial diver and the electronics technician from the Heliox Group in Deep Ex I, as well as one of the commercial divers from the previous Trimix Group. These three men were affected very differently by the compression. One had narcosis starting at about 240 msw and mild, transient HPNS on arrival at 300 and 500 msw. He made a lockout into the wet pot on trimix at 500 msw and performed competently, but slowly.

Another man, the commercial diver who had been unafffected during the Deep Ex I heliox compression to 300 msw, had moderate symptoms of HPNS at 300 msw and euphoria from 200 msw until he was no longer breathing trimix at 500 msw. He served as the backup diver for the lockout, but despite his considerable professional experience and the importance of this activity, he proved to be unreliable.

The third man, the electronics technician, became very dizzy and nauseous starting at 240 msw. He was not fully conscious at 300 msw and the compression was extended by 2 hours at that depth and by 7 hours at 400 msw in response to this man's serious symptoms of HPNS. He improved somewhat over the period of compression from 400 to 500 msw

but was not in condition to lock out for some time after arrival at bottom depth.

The gas switch from trimix to heliox was commenced on Dive Day 4, about 1.5 days after arrival at 500 msw. It was made over a twenty-four hour period to minimize the possibility of difficulties due to exchange-rate counterdiffusion. During the gas switch, tremor in all three subjects became more prominent, but psychomotor and cognitive performance, particularly long-term memory (Table 11A) and perceptual speed, improved. Immediately after the gas switch, there was no apparent problem in any of the divers. Later in the evening as they tried to sleep, however, two of the men had visual and auditory hallucinations and the other had marked myoclonic jerking in his legs. While these symptoms resembled those of withdrawal from a narcotic agent, their nature has not been identified. In any case, the condition had passed by morning and did not reappear.

The compression on heliox (Table 10) also had a very different impact on each of the divers. One man, an experienced professional diver who had participated in the Trimix Group in Deep Ex I, had only mild, transient symptoms of HPNS on reaching 376 and 500 msw. These disappeared during the overnight holds, and this man performed with greater proficiency and stamina than any other diver during lockouts in the wetpot.

The other 2 men in the Heliox Group were professional divers with less experience than the others who were participating in the dive. One of these men had some unsteadiness approaching 376 and 500 msw, and this did not completely resolve during the overnight holds or prolonged stay at 500 msw.

The third man, the least experienced professional diver, had debilitating dizziness when he moved his head upon reaching 500 msw. This did not prevent him from doing useful work. As with the other affected diver in the Heliox Group, this man's condition did not improve over time at 500 msw. It must be noted that the deviation from the planned compression schedule at 376 msw with heliox occurred because of operational considerations. It was not a purposeful delay due to HPNS.

Following 4 days at 500 msw, when it was apparent that the conditions of the impaired heliox divers would not improve, and after a problem related to the sealing of several chamber hatches had been cleared up, the two men were decompressed at the rate of 2 msw/minute to 445 msw. After only 20 msw of ascent, the men noted a marked improvement, and they were very much better upon arrival at 445 msw. After remaining at this depth for the balance of the day and holding overnight at 465 msw, the men were returned to 500 msw. The diver who had the debilitating dizziness was normal. The other diver was improved but still had some unsteadiness.

TABLE 11.

Index of Long-Term Memory Results from Deep Dives Conducted at NUI/NUTEC

Key:

Long term memory was assessed with a word:word association test. The divers were given 30 seconds to study the ten word pairs and then were asked to recall associated words 15 minutes later.

The index used here is the decrement in long-term memory divided by the decrement representing one standard deviation of the average sea-level, pre-dive results. A value of 1.0 or less, therefore, is indicative of a result not significantly different than normal. A value of 0.0 would be the same as the pre-dive control value.

R Measurement made upon reaching depth indicated (msw)

L Measurement made before leaving depth indicated (msw)

P Measurement made around time when divers passed through depth indicated (msw)

A Measurement made while at depth indicated (msw)

GS Measurement made during gas switch from trimix to heliox

D Dive day when measurement took place

A. Deep Ex II — 3 Divers, Trimix Group — Compression given in Table 9

R300 D1	R350 D1	R440 D2	R500 D2	A500 D3	A500 D4	GS500 D4	GS500 D5	GS500 D5
3.2	3.7	4.0	4.3	4.5	4.4	4.5	2.8	2.2

B. Deep Ex II — 3 Divers, Heliox Group — Compression given in Table 10

R216 D1	R376 D1	R500 D2	A500	A500
0.0	2.6	1.9	2.5	1.0

C. 3DP Onshore Verification Dive 1 — 6 Divers — Compression given in Table 12

P100 D1	R216 D1	L216 D1	R296 D1	R350 D2	A350 D2	A350 D3	A350 D4	A350 D6
1.3	1.9	1.6	1.5	2.4	2.5	1.1	1.4	0.6

D. 3DP Onshore Verification Dive 2 — 6 Divers — Compression given in Table 13

R100 D1	R200 D1	R300 D1	L300 D2	R350 D2	A350 D3	A350 D4	A350 D5	A350 D6	A350 D7	A350 D9	A350 D11	A350 D13
1.0	1.2	1.8	1.3	1.9	1.4	0.8	1.2	1.2	1.2	0.8	0.9	0.8

E. DSIS Onshore Verification Dive — 6 Divers — Compression given in Table 14

R100 D1	R200 D1	L200 D1	R300 D1	L300 D1	R350 D2	R400 D2	L400 D2	R450 D2	A450 D3	A450 D8
0.5	1.8	1.6	1.7	2.0	0.2	3.4	1.8	2.3	0.5	0.2

F. Oseberg-T Project Trial Dives — 18 Divers — Compression given in Table 15

R80 D1	R160 D1	R240 D1	L240 D2	R320 D2	L320 D2	R360 D2
0.5	1.5	1.1	0.9	1.0	0.9	1.0

With respect to tremor, even on heliox, only one of the six divers had difficulties which had significance at an operational level. This was the same individual who had similar problems at 300 msw during Deep Ex I and who normally had a relatively large amount of tremor at the surface.

While many of the measured psychometric parameters normalized during the stay at 500 msw, decrements in some, such as long-term memory (Table 11B), improved only slowly. In addition, a number of parameters including long-term memory were more markedly affected in the Trimix Group than in the Heliox Group. This finding was in general agreement with the subjective view of the divers. The Heliox Group seemed to be more reliable and to perform tasks more proficiently than the Trimix Group, even after the gas switch.

Among the conclusions drawn from the Deep Ex dives were that trimix did not prevent HPNS but did induce operationally significant narcosis; that while heliox compressions were not entirely satisfactory as done, they did seem to offer a likely approach for getting divers to deep depths in an efficient manner to perform practical work. Based on the results, it appeared that a stop shallower than 216 msw and an overnight hold at a depth shallower than 376 msw during heliox compression would be beneficial.

III. OPERATIONAL AND OPERATIONAL VALIDATION DIVES

In 1982, activities were begun offshore Norway which required at least back-up diving capabilities to depths of 300 msw and deeper. These projects included the laying of a pipeline across the Norwegian trench at a depth of 300 msw, and the development of a gas and oil field with water depths as great as 400 msw. In order to ensure a safe and effective capability for manned subsea intervention in support of these programs, Norwegian oil companies initiated several deep diving projects. These projects utilized the facilities and capabilities developed at NUTEC to conduct onshore operational validations of procedures and diver personal equipment.

A. Deep Dive Development Project

The objectives of the Deep Dive Development Project (3DP) were to validate the procedures and equipment of two diving service contractors to support pipe laying activities and perform welded pipeline repairs at depths to 300 msw. Diver personal equipment (e.g., UBA, thermal protection suits) and dive procedures were demonstrated in two onshore simulated dives (one for each contractor) at a depth of 350 msw. These dives

were 50 msw deeper than the program depth in order to provide some margin of safety when going from the controlled environment of an onshore chamber system to the more hostile environment of the open sea.

In addition to the two onshore verification dives mentioned above, three other operations, all to 300 msw, were done by one of the diving contractors as part of the 3DP program. Two of these operations were onshore welding qualification dives, the third was a full-scale pipeline repair demonstration done in a fjord in western Norway.

The compression schedule utilized by the diving contractor for the single onshore verification dive (Dive 1) is given in Table 12. This schedule was based on the Deep Ex experience. It used helium-oxygen gas mixes, and the hold at 216 msw was lengthened to allow a greater period of adaptation during the approach to 350 msw. The compression, performed with 6 experienced commercial divers, was generally uneventful. All divers reported some minor, transient symptoms of HPNS in the depth range from 150 to 216 msw. These included nausea, dizziness and concentration difficulties, none of which had any operational impact. These initial symptoms had all cleared after 4 hours at 216 msw, but several divers reported further mild, transient HPNS symptoms during the subsequent compressions to 296 and 350 msw. There was again no operational impact, however, and no symptoms were reported during the bottom period at 350 msw.

From the standpoint of objective evaluation of cognitive, psychomotor and sensory performance, some decrements were detected during compression, particularly in long-term and short-term memory. These either normalized or progressed toward normal during the bottom period. As shown in Table 11C, long-term memory for the group of divers remained just below the normal performance range for some days, but eventually

TABLE 12.

3DP Onshore Verification Dive 1 Compression Schedule (Heliox)

Depth (msw)	Rate (msw/min)	Event Time (min)	Elapsed Time (hr:min)
0-108	6.0	18	0:18
108-162	3.0	18	0:36
162-216	1.5	36	1:12
216	-	480	9:12
216-296	5.0	16	9:28
296	-	720	21:28
296-350	2.5	22	21:50

improved to normal levels on Dive Day 6. The compression schedule utilized by the other diving contractor, Comex, for the second 350 onshore verification dive (Dive 2), the two 300 msw welding qualification dives, and the 300 msw fjord dive is given in Table 13. This procedure also utilized heliox gas mixes and was based on the considerable deep diving research conducted over many years in France.

TABLE 13.

3DP Onshore Verification Dive 2 Compression Schedule (Heliox)

Depth (msw)	Rate (msw/min)	Event Time (min)	Elapsed Time (hr:min)
0-100	1.0	100	1:40
100	-	120	3:40
100-200	0.5	200	7:00
200	-	120	9:00
200-300	0.33	300	14:00
300	-	720	26:00
300-350	0.165	300	31:00

In the onshore verification dive, the operation in which the divers were most closely observed, the compression was again generally uneventful. A few divers reported some concentration difficulties and poor memory on reaching 200 msw, but the rest of the compression was unremarkable. With respect to objective measures, long-term and short-term memory were most affected, and there were impairments in some of the other functions in individual divers. These decrements normalized or progressed toward normal during the stay at 350 msw. For the group of divers, long-term memory remained very close to one standard deviation below the sea-level average during most of the bottom phase of the dive (Table 11D).

On the dives to 300 msw conducted by Comex as part of the 3DP program, the compressions were also uneventful. In the welding qualification dives, the welders executed satisfactory welds to very exacting test standards. In the fjord dive, the pipeline repair demonstration was completed successfully and, in general, within a time frame simlar to that required by the same work at shallower depths. Only removal of the concrete coating on the pipe required greater time than usual, and this was attributed more to the newness of the coating than to any inefficiency of the divers.

Because of individual variability and the small number of divers (6) compressed to the same depth (350 msw) with each schedule, only a superficial comparison can be made between the two compression protocols utilized during the 3DP program. There were qualitatively fewer symptoms reported with the schedule given in Table 13 (Dive 2), however; about the same or, perhaps, slightly less functional decrements; a tendency for normalization to be faster at 350 msw. In the work activities in the wet-pot, the performance of the divers compressed with the schedule given in Table 13 was also less affected.

The results of the dives conducted as part of the 3DP program, therefore, seemed to support the conclusions of the Deep Ex Dives. Efficient and effective compressions to 300 and 350 msw were conducted with heliox gas mixes, and shallower intermediate holding depths seemed to provide for a somewhat less stressful compression with better management of HPNS. Shortly following the 3DP Fjord Dive, Comex began routine operations at depths to 307 msw off the coast of Brazil and this depth has now become routine for a number of diving service contractors.

B. Diving and Subsea Intervention Studies

The general objectives of the Diving and Subsea Intervention Studies (DSIS) program were similar to those of the 3DP program, but only one diving contractor was involved and the target depth for practical operations was increased from 300 msw to 400 msw. Procedures and diver life-support equipment were to be developed, validated and demonstrated in an onshore dive simulation at 450 msw. As before, a 50-msw depth margin was provided for safety when employing the same procedures and equipment in an open-sea dive setting.

The compression schedule utilized in the DSIS onshore verification dive is given in Table 14. On the first day of compression, this protocol called for a moderate rate of travel (1.0 msw/min), progressively longer intermediate stops at 100 and 200 msw, and an overnight hold at 300 msw. On the second day of compression, the compression rate was reduced to 0.5 msw/min, and the depth changes between stops were decreased from 100 to 50 msw. The progressively longer holding periods after depth changes were maintained as on the first day, however. A twelve-hour overnight hold was specified before the divers began lockout activities at 450 msw.

Despite the satisfactory result obtained with the compression profiles utilized during the 3DP program, the results with the DSIS compression profile were markedly better. There were a few sporadic and transient symptoms of HPNS reported by the six experienced commercial divers

TABLE 14.

DSIS Onshore Verification Dive Compression Schedule (Heliox)

Depth (msw)	Rate (msw/min)	Event Time (min)	Elapsed Time (hr:min)
0-10	1.0	10	0:10
10	-	20	0:30
10-100	1.0	90	2:00
100	-	120	4:00
100-200	1.0	100	5:40
200	-	300	10:40
200-300	1.0	100	12:20
300	-	720	24:20
300-350	0.5	100	26:00
350	-	120	28:00
350-400	0.5	100	29:40
400	-	300	34:40
400-450	0.5	100	36:20
450	-	720	48:20

who participated in the operation, but none of these was prominent or of any operational significance. On the bottom, the divers appeared strikingly normal as they went about their activities. The times required for task preparation and other routine activities were no longer at 450 msw than they had been during training at sea level. With respect to objective evaluation of performance in the dry, all measures including long-term memory were within the normal range when the divers were ready to start in-water activites on Dive Day 3 (Table 11E). For in-water activities, the pacing of work efforts due to ventilatory limitations produced some increase in time over sea-level values, but cognitive and psychomotor test results were normal.

C. Oseberg T-Project Diving and Repair Program

The final industrial deep diving development program carried out at NUTEC was the Oseberg T-Project Diving and Repair Program. As with the other oil-industry-managed projects, the objectives of this program were to have a diving contractor develop and demonstrate procedures and equipment for performing practical subsea work at high pressure. In this case, the target depth was 360 msw. As an additional objective in this project, a number of divers were to gain experience in working at high pressure through a series of onshore trial dives. Three dives were conducted,

and each dive involved six divers. Twelve of these divers were experienced commercial divers; six of them were Royal Navy saturation divers.

The compression profile utilized in the Oseberg program is given in Table 15. As with the DSIS profile, it was a derivation from prior experience at NUTEC as well with consideration given to other published compression experience. The Oseberg schedule utilized heliox gas mixes with progressively decreasing descent rates and progressively increasing holding periods throughout the compression. This pattern is similar to that successfully utilized with trimix in a number of very deep dives conducted at Duke University in the United States and at GKSS in Germany. Additionally, the depth changes between holding depths were less than in the DSIS schedule.

TABLE 15.

Oseberg T Project Trial Dive Compression Schedule (Heliox)

Depth (msw)	Rate (msw/min)	Event Time (min)	Elapsed Time (hr:min)
0-15	3.0	5	0:05
15	-	20	0:25
15-80	3.0	22	0:47
80	-	60	1:47
80-160	1.5	53	2:40
160	-	180	5:40
160-240	0.67	120	7:40
240	-	480	15:40
240-320	0.33	240	19:40
320	-	600	29:40
320-360	0.167	240	33:40

In general, the results of the Oseberg compressions were similar to the DSIS compression. The divers had few mild, transient symptoms of HPNS and performed well during the various dive activities. The results of the Oseberg dives, therefore, further confirm that staged compressions conducted with heliox gas mixes provide suitable management of HPNS to allow safe and effective manned subsea intervention at depths from 300-450 msw. In addition, these results help to demonstrate that there is a range of staging depths and descent rates which provide satisfactory compression for divers breathing heliox gas mixes.

IV. OBSERVATIONS AND CONCLUSIONS

Based on the results of the dive programs described here, a number of conclusions have been drawn with respect to the compression of divers to high pressure for the performance of practical work. In addition, some observations have been made which, though lacking sufficient trials to have scientific validity, may help to provide some insight into HPNS and how it may be best dealt with in operational diving. These observations and conclusions are presented below.

- Adaptation to HPNS becomes essentially complete at depths of 300 msw and shallower, regardless of the degree of HPNS elicited by the compression.
- Adaptation to HPNS does not necessarily occur at depths deeper than 300 msw, but the point at which adaptation becomes dependent on the compression procedure has not been determined. It may well vary with the individual.
- Compression to at least 450 msw for operational dives can be conducted efficiently and effectively with helium-oxygen gas mixes. An appropriately staged compression profile is the means by which this can be accomplished.
- There is insufficient experience with various profiles in the studies described here to establish what the best compression rates and staging depths are. These, too, may vary from diver to diver. There would seem to be some latitude in acceptable values for rate of compression between stages and for the depth interval between stages, however.
- Based on the similarities of effective compression procedures utilizing heliox and trimix, it would appear that the time-depth profile and not the breathing gas mix is the critical factor in determining the result of that compression.
- From the standpoint of open-water, operational dives, helium-oxygen gas mixes would seem to be superior to nitrogen-helium-oxygen gas mixes for a variety of reasons including narcosis, breathing gas density, diver respiratory heat loss, speech unscrambler function, decompression efficiency and gas management. Nitrogen in the breathing gas does suppress tremor but was not found to prevent other manifestations of HPNS in Deep Ex II.
- Once divers have adapted to high pressure, rapid descents to depths at least 120 msw deeper can be well tolerated.

- Professional divers seem to be less sensitive to high pressure effects than non-divers. This could be due to adaptation or a natural selection process.
- Tremor has not proven to be an operational problem in deep heliox dives. It would appear that individuals with greater tremor at the surface are the ones with greater tremor at depth. Thus, it may be possible to screen out individuals with the highest risk of incapacitating tremor in deep heliox dives.

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APPENDIX

Publications on Compression Aspects of Dive Programs Discussed in this Paper

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4

The French Deep Diving Scientific Program on Oxygen-Helium, Trimix and Oxygen-Hydrogen Gas Mixtures

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I. INTRODUCTION

Man's penetration of the sea to ever greater depths has in recent years become an economic necessity on a global level. Industrial deep diving can only be conceived of within a complex technical and logistic system.

The diver's biological parameters are modified as a function of the ever greater pressure exerted on him as he progresses deeper and deeper. To be able to work effectively under water, divers must remain under pressure for several weeks. Long periods of confinement in hyperbaric chambers pressurized to the same depth as the subsea worksites necessitate special technology systems: comfortable chambers, strict environmental controls (pressure, temperature, relative humidity, pollutants), compression and decompression procedures and highly perfected breathing gas mixtures. Before being "saturated" for a long duration, divers must undergo extremely thorough medical examination and physical fitness tests. Thereafter they must have checkups every year, or every six months for those over 40 years old.

At present most underwater work below 50 msw depth is carried out in saturation on helium-oxygen mixture, heliox. An average of 700 to 1200 saturations are performed by COMEX divers every year, cumulating since 1976, 30,000 hours at work and 400,000 hours under pressure.

Beyond 250 msw two factors limit the diver's efficiency: the neurological effects of the pressure (high pressure nervous syndrome, or HPNS), and ventilatory problems due to the density of the gas mix at high pressure. Since 1968, to overcome these two factors COMEX has undertaken a research program, the most extensive in the world, on deep experimental and validation diving with heliox, helium-nitrogen-oxygen (trimix) and hydrogen-oxygen (hydrox) or hydrogen-helium-oxygen (hydreliox) breathing gas mixtures.

II. METHODS

A. Environments

Since its creation in 1964, COMEX's hyperbaric experimental center has been continuously under development. The main simulation facilities to perform the experimental deep diving program, was "EMS 800" and "HYDROSPHERE." "EMS 800" is composed of three living and working spheres and one living chamber type 2400 with lock. "HYDROSPHERE" is a versatile, 5 meters i.d., working habitat with its interior divided into two parts by a removable floor. The lower zone is used for diving and testing equipments and materials under conditions simulating tropical to arctic waters. A lock type 2000 and a living chamber type 2500 are connected to hydrosphere.

All these chambers are connected up with monitoring equipment with a large number of hull penetrations for all standard physiologic, electric, hydraulic or pneumatic measurements.

B. Animal Experiments

The experiments on the *Papio papio* monkeys (5-10 kg weight) were carried out in a horizontal cylindrical hyperbaric chamber with a volume of 3.8 m^3 which is designed to have two animals (one in a restraining chair and the second in a cage). This chamber allowed the introduction of water and food for the animals by means of a lock. Organic waste was evacuated daily. The system for the regeneration of the breathing mixture was exterior to the chamber; i.e., the gas circulated through a series of filters (sodalime, silica gel and activated charcoal) and subsequently reintroduced into the chamber. This made it possible to control the atmosphere during the experiment with good precision.

C. Hydrogen

The hyperbaric facilities of the COMEX Research Center, particularly the chambers, were not initially intended for hydrogen use. We thus had to adapt them to this new diving technique.

Hydrogen diving could only be considered after an extensive study for the risks relevant to the handling of hydrogen and its use in the chamber systems. The flammability threshold of hydrogen in air at atmospheric pressure is 4%, so the risk must be prevented from any local formation of hydrogen pockets. Hydrogen is a fast diffusing gas and tends to leak through cylinders, piping and chambers. A system of hydrogen sensors must be implemented to detect the leaks and a powerful ventilation must be installed to collect and evacuate them. To study the fire risk inside the chamber system, COMEX carried out tests to determine what would be the safe limits for using of hydreliox mixtures at different depths. The flammability threshold of hydrogen in heliox was found to range from 5.5% at 16 ATA to 43.5% at 76 ATA. During compression, hydrogen must be injected deeper than 200 msw, and during decompression, all hydrogen must be removed before reaching 200 msw.

Hydrogen produced for industrial use cannot be directly used for diving operations because of the pollutants it contains. COMEX had to work out specifications for a "diving quality hydrogen."

A new gas regeneration system was designed to automatically control the temperature and relative humidity in the hyperbaric chambers, scrub pollutants (CO_2 and hydrocarbonic agents), and reoxygenate the gas

while automatically maintaining the partial pressure of oxygen in the hydrogen mixture.

D. HPNS

To analyze and quantify the HPNS, the most usual methods used are tremor, EEG, and performance measurements.

1. Tremor

Tremor is measured by means of an accelerometer. The captor is placed on the middle finger of the dominant hand. The tremor is measured during the "epreuve du serment" which is repeated several times a day at fixed times both during the dive and during periods of predive at atmosperic pressure. The signals are recorded on analog magnetic tapes and analyzed by computer with a program which gives the amplitude of the signal, its power spectra and frequency (Gourret *et al.*, 1984).

2. EEG

For EEG study the electrodes (platinum wire) are implanted on the fronto-polar, central, mid-temporal and occipital areas of the right hemisphere with a fifth electrode serving as a ground. The EEG activities are analyzed in different states:

- Wakefulness during rest with the eyes open and closed, a test carried out for 10 to 15 min several times a day at fixed times.
- Wakefulness during intellectual activity.
- Sleep with two additional electrodes placed on each side of the eyes to record ocular movements.

The EEG activities are recorded on electroencephalographs and also on analog magnetic tapes. The EEG traces are read and interpreted while the magnetic recordings are analyzed off line on computer in order to obtain power spectra in each frequency band: Delta 1-4Hz, Theta 4-8 Hz, Alpha 8-14 Hz, Beta 1(14-22 Hz), and Beta 2(22-40 Hz).

E. Psychomotor and Intellectual Tests

The psychomotor and intellectual tests for evaluation of divers are:

1. Manual Dexterity

Each subject is given a board measuring 54 cm by 12 cm, drilled with 100 holes 1 cm in diameter and arranged in four columns. At each end of

the board there is a receptacle containing 50 cylinders 4.4 cm long and 0.9 cm in diameter. At a given signal the subject takes pegs from the left-hand receptacle with his right hand and fits them as quickly as possible into the holes, starting at the extreme right of the board. He then works from the opposite end with his left hand. The observer notes the time taken to place pegs with each hand and calculates the average number of pegs per minute.

2. Visual Choice Reaction Time

Whenever a red or green light is flashed the subject reacts by pressing a button on the side corresponding to the side of the light. A series lasts two minutes and is preceded by about 30 seconds of practice. Each series consists of 31 red or green signals which appear in a random order with random intervals between them. The subject uses a single finger poised midway between the two buttons. Performance is assessed by the median in 100ths of a second for 31 correct responses.

2. Number Ordination

Rey's test entails putting into numerical order figures listed out of order in groups of 7. The experiment lasts ten minutes, and the subject is asked to note how far he has completed the task at the end of each minute (the time being given by the tester). Performance is measured by the average number of figures correctly put in order per minute.

III. RESULTS

Since 1975, six series of man and animal experiment dives have been carried out in the chambers of COMEX's hyperbaric center or the FRENCH NAVY's center. The man's dives are summarized in Table 1.

The evolution of this work leading to operational compression procedures for open sea dive demonstration at great depths, JANUS IV 501 msw in 1977 and HYDRA VIII, 5334 msw in 1988, is reported here.

A. CORAZ SERIES

In 1975, four human dives were performed at 300 msw with a compression in four hours (Fig. 1). These dives were conducted with different concentrations of nitrogen to determine the effect of N_2 on man during rapid compression. The N_2 concentrations used were:

TABLE 1.
French Experimental Dives Deeper than 200 msw

Experiment	Year	Depth msw	Diver	Breath. Gas	Compres.	Bottom Time	Decompress.	Chamber Total Time	Work At Depth
PLC1 CX	1968	335	2	TRIMIX	2h	17min	94h 37	96h 57	in water
PLC2 CX	1968	266	2	TRIMIX	1h 20	30min	974h 45	99h 35	in water
PLC3 CX	1968	300	2	TRIMIX	1h 05	20min	90h 50	92h 15	no
PHYSALIE I CX	1968	335	2	TRIMIX	1h 53	10min	97h 33	99h 35	in water
PHYSALIE II CX	1968	360	2	HELIOX	1h 55	5min	144h 31	116h 31	no
PHYSALIE III CX	1968	365	2	TRIMIX	2h 03	4min	138h 34	140h 41	no
PHYSALIE IV CX	1968	300	2	TRIMIX	3h	10min	103h 40	106h 50	no
PHYSALIE V CX	1970	520	2	HELIOX	74h 28	1h 37	208h	284h 05	no
PHYSALIE VI CX	1972	610	2	HELIOX	176h 58	1h 20	233h 10	411h 28	dry
SAGITTAIRE I CX	1971	300	4	HELIOX	163h 54	2h 24	128h	435h 54	dry
SAGITTAIRE II CX	1972	500	2	HELIOX	49h	100h	189h 30	338h 30	dry
SWECOM	1972	300	4	HELIOX	77h	44h 20	124h	245h 20	in water
SAGITTAIRE III CX	1973	300	4	HELIOX	112h 28	360h	165h	637h 28	dry
SAGITTAIRE IV CX	1974	610	2	HELIOX	260h	50h	231h	541h	dry
CORAZ I CX	1974	300	3	TRIMIX	4h	72h	151h	227h	in water
CORAZ II CX	1975	300	2	TRIMIX	4h	81h	136h 35	221h 35	in water
CORAZ III CX	1975	300	2	TRIMIX	4h	35h	136h 35	175h 35	in water
CORAZ IV CX	1975	300	2	HELIOX	4h	81h	136h 35	221h 35	in water
JANUS II-PHASE I CX	1970	200	3	HELIOX	1h 10	192h	112h	305h 10	in water 250msw
JANUS II-PHASE IIA CX	1970	200	3	HELIOX	5h 40	144h	92h 50	242h 3	in water 250msw
JANUS II-PHASE IIB CX	1970	200	3	HELIOX	11h 38	144h	95h 50	251h 28	in water
JANUS II-PHASE III CX	1970	200	3	HELIOX	7h 50	184h	102h	293h 50	open sea 250msw

JANUS III A CX	1974	390	3	HELIOX	49h	144h	170h	363h	in water
JANUS III B CX	1974	395	3	HELIOX	49h	144h	205h	398h	in water
JANUS IV-PHASE II CX/GISMER	1976	400	8	TRIMIX	24h	216h	202h	442h	in water 480msw
JANUS IV-PHASE III CX/GISMER	1977	430	6	TRIMIX	30h	144h	185h	359h	open sea 501msw
79/131 CX/GISMER	1979	450	4	TRIMIX	38h	48h	245h	331h	dry
ENTEX 5 GISMER/CX	1981	450	4	TRIMIX	38h	288h	315h	641h	dry
ENTEX 8 GISMER/CX	1982	450	4	TRIMIX	38h	288h	315h	641h	in water
C.E.H. CONSTANZA/CX	1981	300	4	HELIOX	21h 40	8h	198h 20	228h	in water
ENTEX 9 GISMER/CX	1983	450 610	2	HELIOX	38h(450m) 95h(610m)	144h(450m) 57h(610m)	550h	984h	dry and in water
ENTEX 11 GISMER/CX	1986	450	4	HELIOX TRIMIX	38h	288h	315h	641h	in water
HYDRA IV CX	1983	300	6	HELIOX HYDROX	108h	64h	256h	428h	in water
HYDRA V CX/GISMER	1985	450	3+3=6	HYDRELIOX	38h	120h(3) 192(3)	465h(3) 348h(3)	660h(3) 681h(3)	dry and in water
HYDRA VI CX/GISMER	1986	500	8	HYDRELIOX	86h	95h	429h	640h	dry and in water 520msw
HYDRA VII CX	1987	260	4	HYDROX	88h	63h	183h	342h	no
HYDRA VIII CX/GISMER	1988	500	6	HYDRELIOX	94h	185h	419h	698h	open sea 520-534m
37 Experiments			**121 men**			**172 Days**		**586 Days Spent Under Pressure**	**23 Dives With In Water or Open Sea Tests**

CORAZ I	:9%
CORAZ II, III	:4.5%
CORAZ IV	:0%

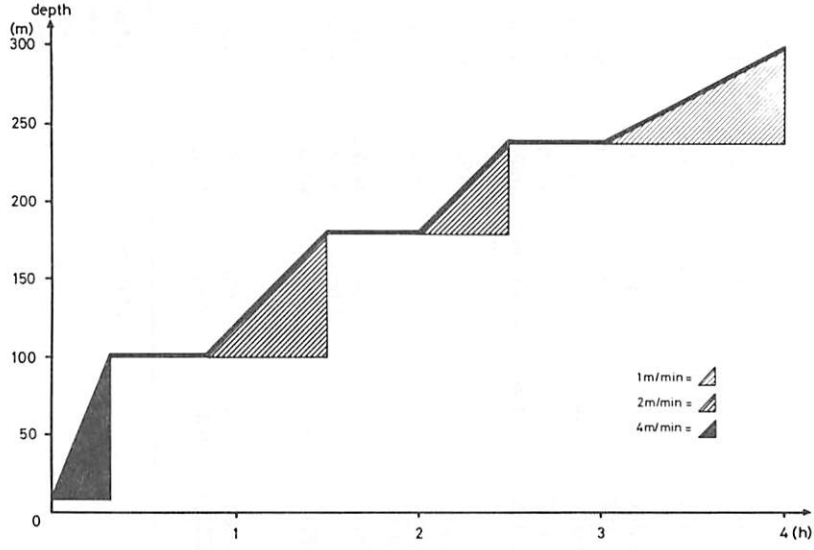

Fig. 1. The compression profile for the CORAZ I, II, III, IV experiments was maintained constant; only the percentage of nitrogen in the breathing mixture differed (2.8 ATA N_2 for CORAZ I, 1.4 ATA N_2 for CORAZ II AND III and no N_2 for CORAZ IV). The compression rate was 4 msw/min to 100 msw; 2 msw/min from 100 to 240 msw; and 1 msw/min from 240 to 300 msw. The compression was halted for 30-min periods at 100, 180, and 240 msw.

Nitrogen decreased the HPNS clinical symptoms and increased the performance (Fig. 2) but EEG modifications were more important.

B. CORASIN Series

Following these human dives, a long series of animal dives were carried out, using the *Papio papio* monkey (1975-1977) Ten dives were conducted (Table 2). Seven of which at 600 msw with two hours compression and two animals per dive. From this series of experiments, the results were as follows:

- An exponential compression profile was selected rather than a linear profile;
- A compression with short duration stages seemed better than a continual compression;

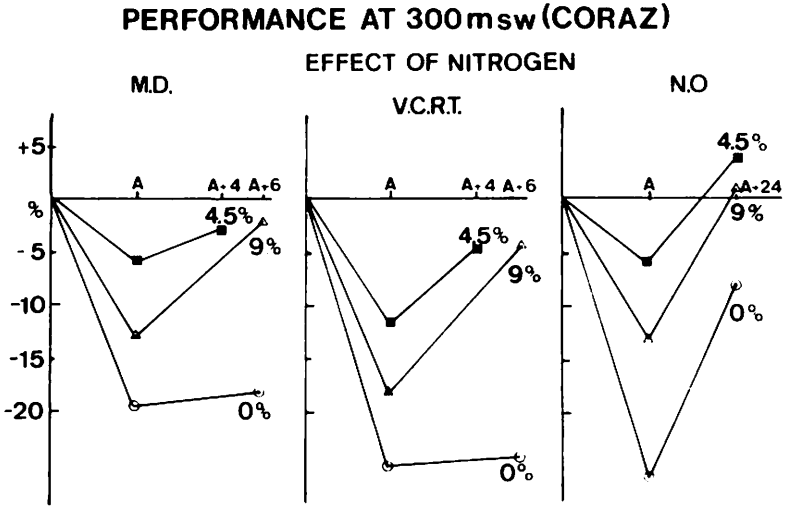

Fig. 2. Influence of the proportion of nitrogen in the breathing mixture on the performance at arrival at 300 msw and after 4 or 6 hours spent at this depth (CORAZ series).

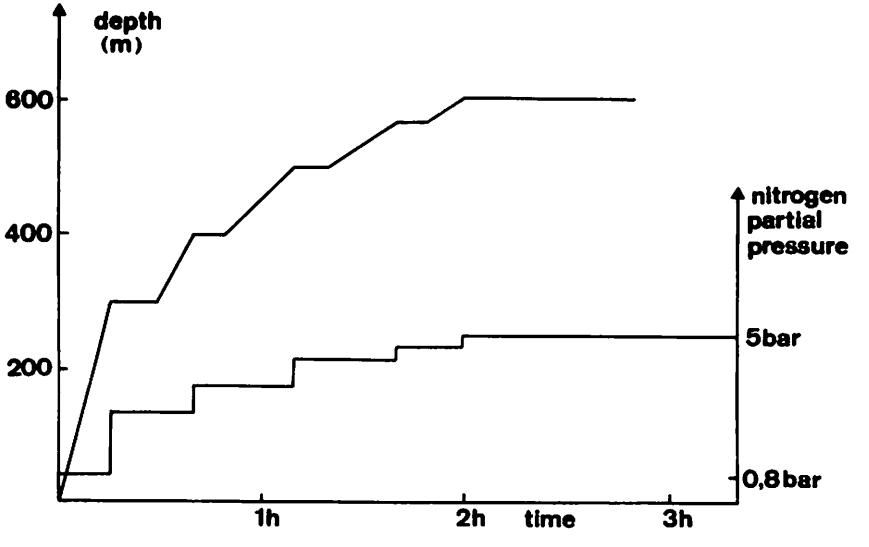

Fig. 3. Compression profile and N_2 introduction procedure in CORASIN VIII dive.

- progressive addition of N_2 during compression (Fig. 3) reduced the behavioral signs of HPNS.

TABLE 2.

Characteristics of Dives CORASIN I-X in Three Groups

CORASIN	Depth in m	Compression	Time of compression	N_2	Po_2 mbar
		Series I. Effect of N_2 on HPNS			
I	800	Linear (200 m/h)	4	8% beginning of compression	210
II	600	Nonlinear, stages at intermediate depths	3	4% beginning of compression	300
III	600	Nonlinear, stages at intermediate depths	2	8% beginning of compression	400
		Series II. Compression Profile			
IV	600	Exponential, stages at intermediate depths	2	8% beginning of compression	400
V	600	Exponential, no stage	2	8% beginning of compression	400
X	600	Exponential, stages at intermediate depths	2	8% beginning of compression	400
		Series III. N_2 Injection Procedures			
VI	600	Exponential with stages	2	8% saturation before the compression	400
VII	600	Exponential with stages	2	8% end of compression	400
VIII	600	Exponential with stages	2	8% injection during compression	400

Each series uses 6 baboons; CORASIN IX is not reported here

An extrapolation of this method was successfully conducted at 1000 msw: CORNELIUS I with 6.4% of N_2 (6.5 ATA). This procedure compression was adapted for man.

C. JANUS IV

In phase I, test dives to 180-220 msw with rapid compressions were used for selecting the divers. Two saturation dives on He-N_2-O_2 mixture (trimix 4% N_2, Fig. 4) were carried out.

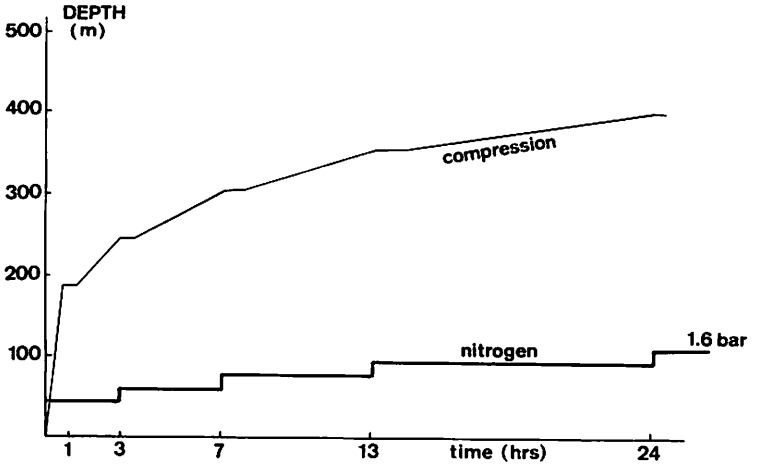

Fig. 4. Compression curve and additions of N_2 for fast exponential compression extrapolated from monkey (experimental series CORASIN) to human for JANUS IV. Curve is characterized by initial fast speeds that then were rapidly decreased.

- JANUS IV, phase 2 (1976), onshore dive at 400 msw with 11 excursion dives at 430-445-460-480 msw with 8 subjects.
- JANUS IV, phase 3 (1977), offshore operation at 430 msw with 5 excursion dives at 460 msw and one to 501 msw with 6 subjects. The total time spent in water was 10 hours to carry out a mechanical pipe line connection at 460 msw.

We observed an important increase of EEG modifications in the first rapid compression phase from surface to 300 msw during onshore dive. We therefore reduced the compression speeds of this phase during the open sea-dive.

D. CORNELIUS/RESO Series

Between 1977 and 1980 two series of monkey dives were conducted at COMEX (Fig. 5): five CORNELIUS dives and four RESO dives with two *Papio papio* monkeys per dive. During these dives the depth of 100 msw was reached: CORNELIUS III and IV (Fig. 6).

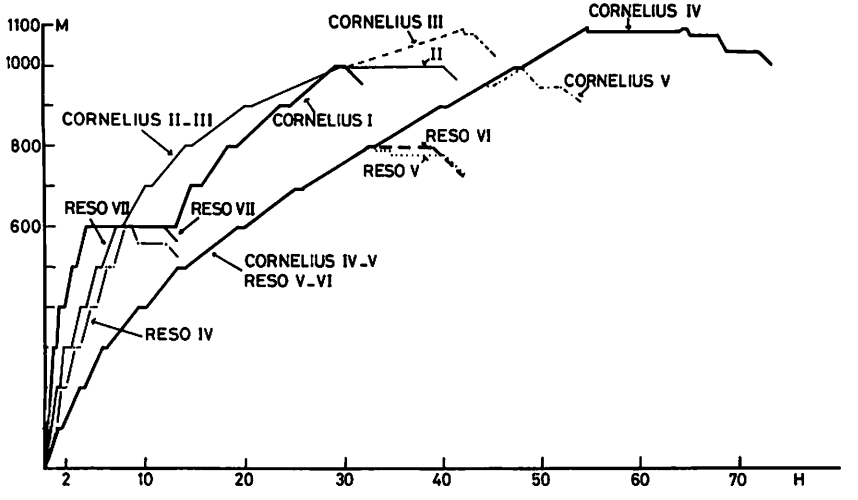

Fig. 5. Compression profiles for the CORNELIUS and RESO series of dives.

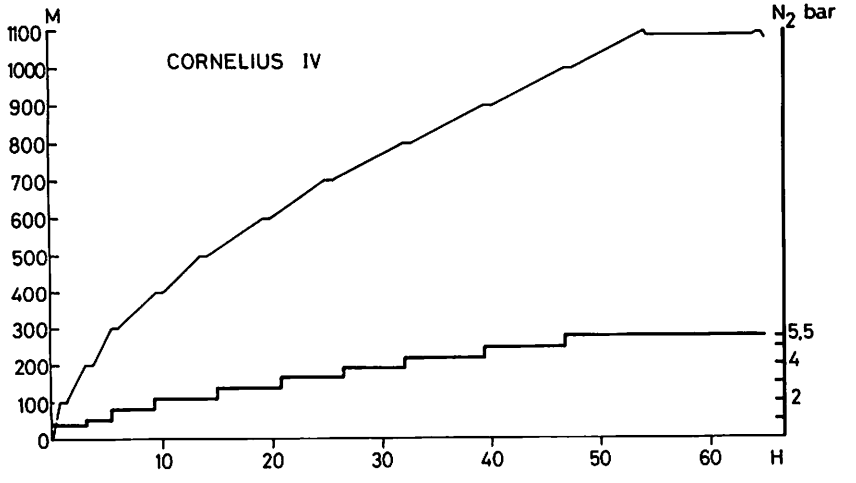

Fig. 6. Compression method in the monkey *Papio papio:* compression profile with intermediary stages every 100 msw and procedure for nitrogen additions to readjust the level to 5.5% (i.e. 5.5 bars at 1000 msw).

From the Janus IV results we have tested, between 0 and 600 msw, slower speeds than the ones used in CORASIN Dives: 40 min stops every 100 msw with N_2 additions before each stop.

These new compression profiles confirmed the beneficial effect of N_2 on HPNS clinical symptoms without EEG modifications up to 800 msw. However, we pointed out new disturbances occurring at this depth.

There was a general depression of EEG activity and, deeper than 1000 msw, motor disturbances (hypertonus spasms and shaking), palpebral clonus and eye movements associated with peaks of EEG activities localized in the posterior region of the skull that sometimes evolved toward an epileptic seizure localized in this region.

E. DRET/ENTEX Series

Based on the animal dives, a human simulated dive at 450 msw was carried out in 1979: DRET 79/131, with 8 subjects. The duration of compression was 38 hours with speed decreasing with depth. Stops lasted 2.5 hours at 100, 200, 300, 400 msw with 3.5 msw of N_2 adds before each stage; 4.8% N_2 at 450 msw (Fig. 7) No HPNS clinical symptom was observed and theta EEG activity increase was reduced.

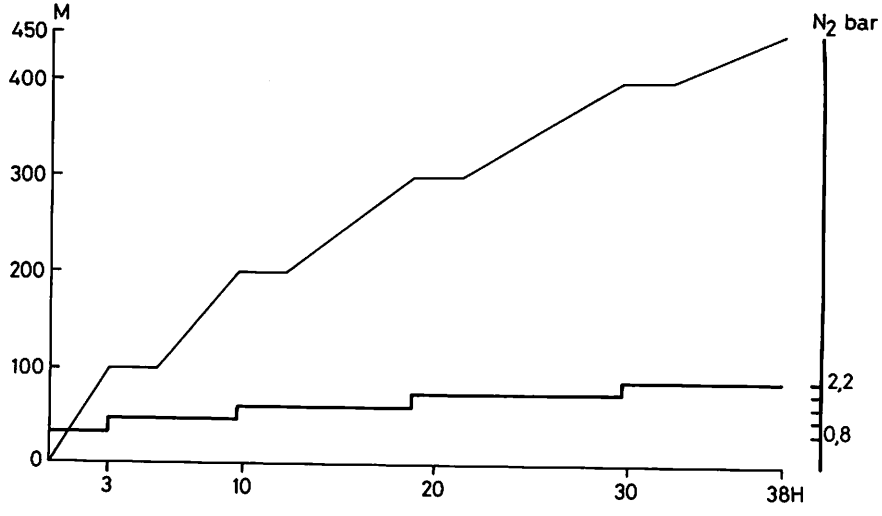

Fig. 7. Compression curve and additions of N_2 for slow exponential compression extrapolated from monkey (experimental series CORNELIUS) to human for DRET 79/131, ENTEX 5,8,9,11 and HYDRA V,VI. Curve is characterized by slow speeds at the start that become progressively slower with depth.

The same compression procedures were used in the ENTEX series which took place at the FRENCH NAVY hyperbaric center in Toulon.

- ENTEX 5 (1981): 12 days at 450 msw — 4.8% N_2 — 4 divers;
- ENTEX 8 (1982): 12 days at 450 msw — 4.8% N_2 — 4 divers;
- ENTEX 9 (1983): 6 days at 450 msw, 57 hours at 610 msw — 0% N_2 — 2 divers;
- ENTEX 11 (1986): 12 days at 450 ms — 6 days with 0% N_2 and then 6 days with 4.8% N_2 — 4 divers;

During this long saturation stay from 6 days to 12 days we observed performance and EEG modifications which reach their maximum intensity during the first 24 hours at pressure, regress and stabilize at a level which is always greater than at the surface. The recovery seems to be better with nitrogen than without.

F. HYDRA Series

A new gas mixture, hydrox (H_2-O_2) or hydreliox (H_2-He-O_2) is developed since 1983 by COMEX for a best anti-HPNS effect.

- **Hydra IV, 1983.** Six divers breathed hydrox at 120, 150, 180, 240 msw during 30 minutes to 6 hours in dry or wet conditions and hydreliox at 300 msw during 30 to 45 minutes. These exposures permitted, for the first time, to describe the "Hydrogen narcosis" on man.
- **Hydra V, 1985,** was the first hydrogen saturation dive to 450 msw with 6 divers, 38 hours compression, identical to those of preceding dives, ENTEX 5, 8, 9, 11 on helium or trimix (Fig. 8). At 450 msw, gas mixture was: 54.3% H_2 (P_{H_2} = 25 ATA), 44.8% He, 0.9% O_2. Tremor, EEG (Fig. 9) and psychometric test results have showed that 25 ATA of H_2 at 450 msw can neutralize considerably HPNS without narcosis symptoms.
- **Hydra VI, 1986.** During this second onshore saturation dive on hydreliox a depth of 500 msw was reached with an excursion dive at 520 msw. It was carried out also at the COMEX hyperbaric research center in Marseilles with 8 subjects. The same compression profile as Hydra V's, was used until 450 msw (Fig. 10).

At 500 msw, the gas mixture was: 47% H_2 (P_{H_2} = 24 ATA), 50.6% He, 1.6% N_2, 0.8% O_2. This saturation dive was mainly oriented toward underwater activities in order to test new individual diving equipment and to prepare the open sea dive demonstration Hydra VIII. As in Hydra V, we observed the anti-HPNS effect of hydrogen, shown by an absence of

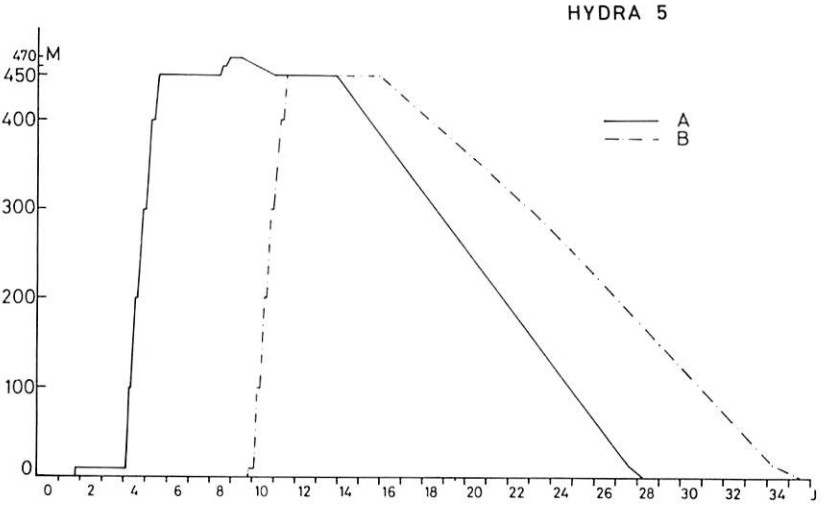

Fig. 8. Profiles of the 2 dives performed with H_2-He-O_2. Solid line = group A. The shift from H_2-He-O_2 to He-O_2 was performed 72 h after the beginning of the stay at 450 m. A compression to 470 m was performed to eliminate the counter diffusion problems that occurred during the shift. *Broken line* = group B, the 2nd dive which began 10 days after the first. To avoid counterdiffusion problems, decompression was performed by progressive elimination of H_2 until 200 m, then in He-O_2.

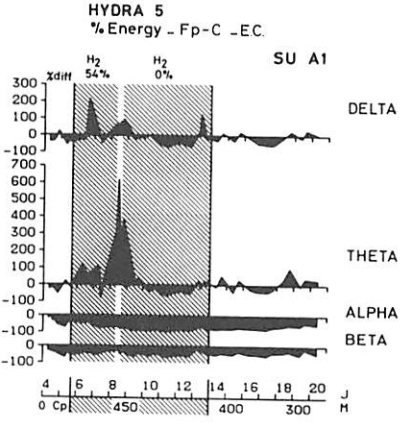

Fig. 9. Evolution of power spectra of EEG activities in the fronto polar central lead (Fp-C) of one subject during the dive HYDRA V up to 450 msw.
X axis: the depths in msw (M) and the days (J).
Y axis: The increase of the power expressed as a percentage difference from control values. From top to bottom, the increase in the power of delta frequency band (1-4 Hz), of theta (4-7 Hz), alpha (8-14 Hz and beta 1 (14-22 Hz). The hatched zone represents the stay in hydrogen-helium-oxygen and in helium-oxygen. The white part inside the shaded area represents the shift from 54% to 30% H_2 and from 30% to 0% H_2.

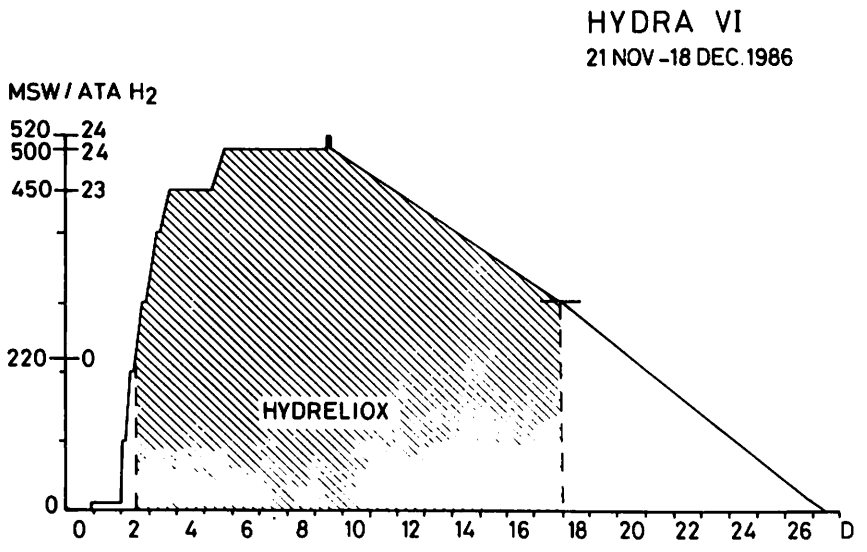

Fig. 10. HYDRA VI dive's profile. Compression curve until 450 msw was the same as the one used in HYDRA V. P_{H2} at 450 msw was 23 ATA and 24 ATA at 500 and 520 msw. Decompression between 500 and 300 msw was performed by progressive chemical elimination of H_2.

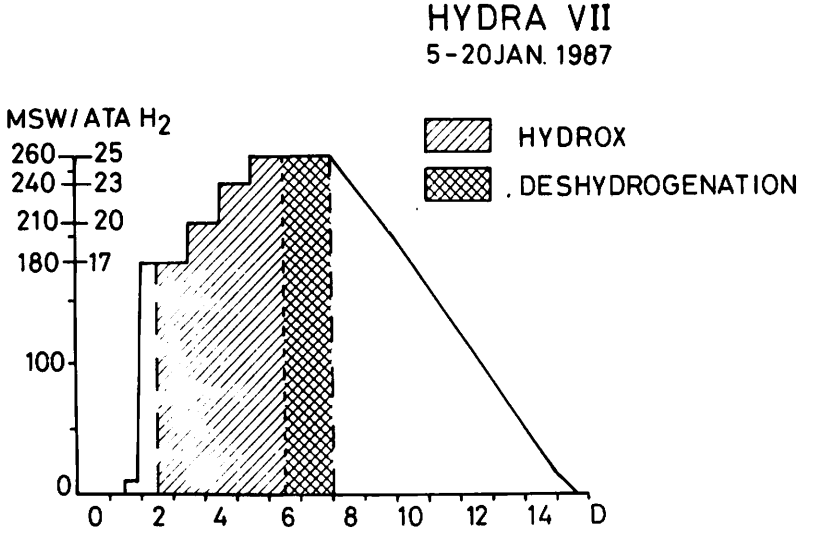

Fig. 11. HYDRA VII dive's profile. After the switch from heliox to hydrox at 180 msw, the depth was reached step by step until 260 msw with 25 ATA P_{H2}. H_2 was progressively eliminated by chemical process "dehydrogenation" at 260 msw.

tremor and an ease and dexterity in underwater work. Twenty-two dives were carried out in the cold pool chamber, all new equipment was tested successfully.

- **Hydra VII, 1987.** To determine the hydrogen narcosis threshold in hydrox saturation, 4 divers were compressed up to 260 msw (P_{H2} = 25 ATA) in 4 days (Fig. 11).

At 180 msw, 15-30 min after sudden switch from heliox to hydrox (17 ATA H_2) the divers felt a slight narcosis, but it disappeared rapidly and without further narcotic effect at 20, 23 and 25 ATA of hydrogen. This experiment proved that the gas gradient plays an important role in the onset of narcosis, just as in HPNS.

- **Hydra VIII, 1988.** This offshore dive was designed to demonstrate the feasibility of hydrogen diving.

This operation was performed in the Mediterranean sea with the DSV ORELIA at 520-534 msw depth with 6 divers selected from HYDRA V, VI and VII. A new slower compression profile was tested (Fig. 12). At living depth: 500 msw, the gas mixture was hydreliox: 49% H_2 (P_{H2} = 25 ATA), 48.6% He, 1.6% N_2, 0.8% O_2.

Six dives to 520 msw and one dive to 534 msw were performed (Fig. 13). Each dive duration in water was from 15 minutes to 4 hours 15 minutes with two divers on working site and one diver inside the bell. Twenty six hours of underwater work were carried out. A pipe line connection was easily made by the divers at 520 msw on hydreliox (47% H_2) with good

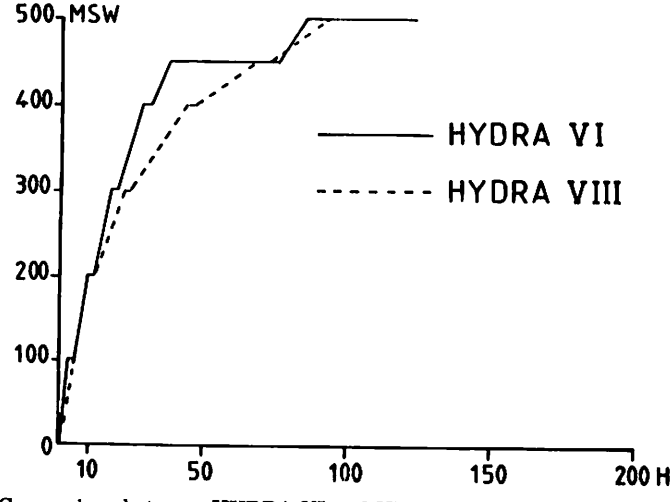

Fig. 12. Comparison between HYDRA VI and HYDRA VIII compression profiles. Speeds used for HYDRA VIII, from 20 to 500 msw, were slower.

manual dexterity and performance similar to that of 150-200 msw heliox depth. The monitoring of the diver's breathing rate, gas, hot water and central temperatures showed normal variations.

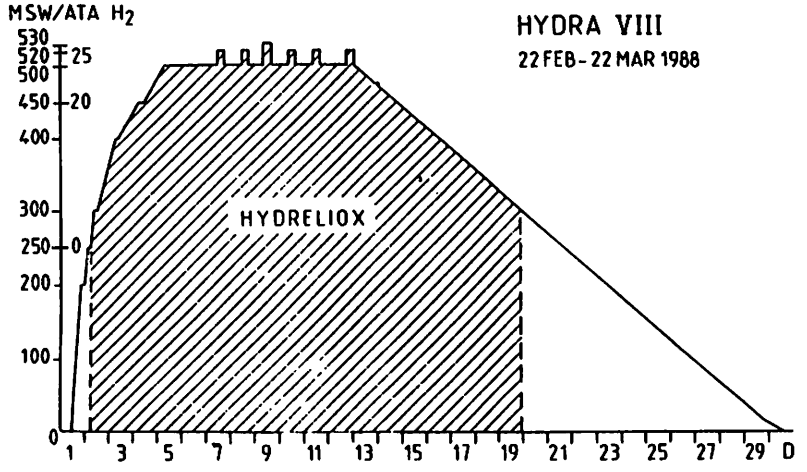

Fig. 13. HYDRA VIII general profile. Compression with H_2 from 250 msw to 500 msw (P_{H2} = 25 ATA at 500 msw.) Dehydrogenation between 500 and 300 msw.

IV. DISCUSSION

From these six big series of experimental dives, several aspects of HPNS appear.

A. Characteristics of HPNS in He-O_2 Mixture

HPNS is composed of neurological disturbances and electrophysiological changes, the most important of which are shown in Table 3. Most of these symptoms have been described in animals exposed to high pressures of helium (Brauer, 1975; Halsey, 1982).

B. Influence of Variations of Pressure

The compression and the type of compression play a large part in the appearance of HPNS, both in the intensity of its diverse symptoms and in the magnitude of the changes of performance.

TABLE 3.

HPNS in man in a helium-oxygen mixture from 200 to 610 msw.

Neurological symptoms	Electrophysiological changes
Nausea, vertigo	EEG changes : Increase in theta waves
Tremor (8-12 Hz)	Decrease in alpha waves
Fasciculations, myoclonus	Microsleep
Dysmetria	Sleep disruptions : Increase of awake periods, stages 1 and 2 ; decrease of stages 3 and 4 ; unstability of REM period
Drowsiness	Changes in evoked potentials and cortical excitability cycles
Decrease of psychometric performance	Changes in reflexes

TABLE 4.

HPNS in animal models (rats and monkeys) in helium-oxygen mixture up to 1000 msw.

Neurological symptoms	Electrophysiological disruptions
Tremor (10-14 Hz)	EEG changes : Increase of slow waves, paroxystic activity, epileptic seizure
Muscular hypertonus	Changes in evoked potentials, cortical excitability and reflexes (monkeys)
Myoclonus	
Muscular spasms	
Convulsions	

The very first deep dives with He-O_2 were performed with very fast rates of compression: 180 msw/hour in PHYSALIE I to IV (1968). They induced disturbances in the central nervous system beyond 200 msw and the depth of 365 msw was not exceeded because these were too severe (Brauer *et al.*, 1969; Fructus *et al.*, 1969). Subsequent experiments were carried out with slower speeds of compression and depths of 457, 500 or 610 msw were reached (Bennett and Towse, 1971; Bennett, 1975; Fructus *et al.*, 1976; Rostain and Naquet, 1974). These experiments have shown that the depth at which the symptoms of HPNS occur tends to increase while their intensity tends to decrease if compression follows a slow exponential time course interrupted by stops at intermediate depths. HPNS is enhanced by continuous and/or rapid compression.

For the sensori-motor tests and the intellectual tests, the results are also in favor of a relatively slow compression. At the same time the psychomotor disturbances can bring about various problems (vertigo, tremor, sleepiness, articular pain, etc.) which in turn can limit the diver's activity once he has arrived at the bottom. In so far as a compression syndrome exists, a slow compression is justified since the symptoms only slowly disappear. Certain functions are more sensitive to the speed of compression and recovery is not the same for all of them (Fig. 14).

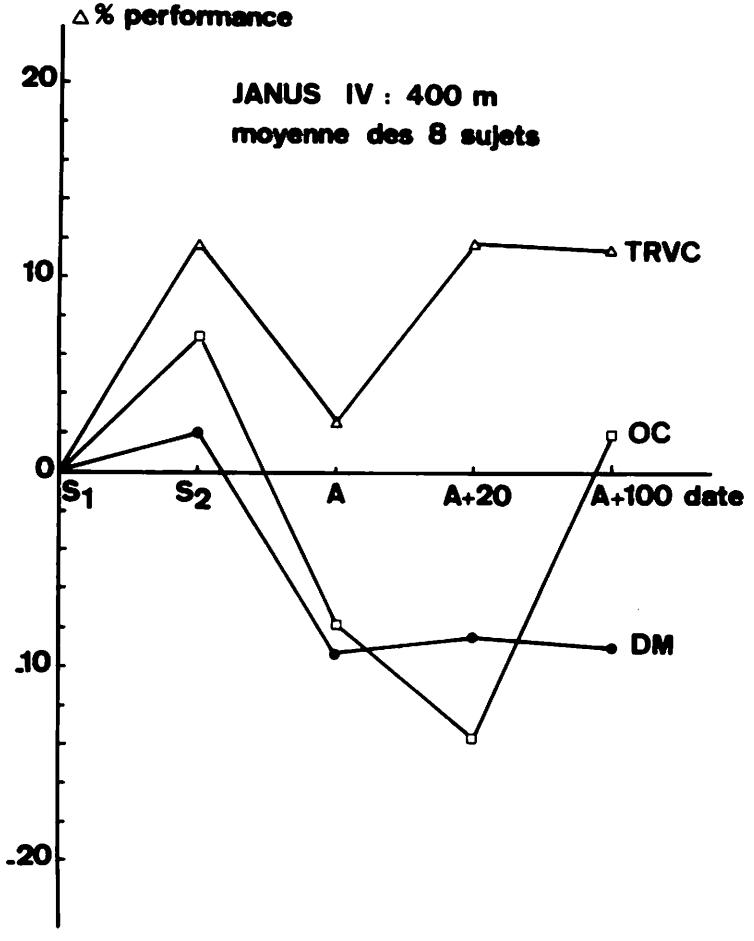

Fig. 14. Variation of performance during a stay at 400 msw (mean for 8 subjects). S1 and S2 represent the surface tests. A is the first test at maximal depth. DM is used for Manual Dexterity. TRVC. for Visual Choice Reaction Time, OC for Number Ordination.

One must therefore assume that before a diver is operational it is necessary to add to the time of a "rapid" compression the time necessary to recover. So this period of time is available (compression plus recovery) to carry out a slower compression which disturbs the subjects less. But the lengthening of compression time does not resolve all the problems; even a compression of 10 days to reach 610 msw, does not bring changes of relative importance. Thus, it is desirable to find an antagonist to the effects brought about by the compression and this antagonist might be included in the breathing mixture itself.

C. Influence of the Respiratory Mixture

Nitrogen, which is narcotic under pressure, might in a helium-oxygen mixture reduce or suppress HPNS in animals (Brauer, 1975; Miller, 1972) and in man (Bennett *et al.*, 1974. Sixteen professional divers have performed several dives using the same compression method (DRET-ENTEX 5, and 8) (Fig. 7).

The neurological symptoms were reduced and even suppressed: little or no tremor was recorded; no dysmetria or fasciculation were observed. The EEG changes were low intensity and the synergistic effect of nitrogen and pressure on EEG changes was not recorded. The average decrease of performance for the sensori-motor tests was upon arrival at 450 msw 10% for manual dexterity and 8% for visual choice reaction time, while the intellectual test of number ordination showed a loss of 15% (Table 5).

TABLE 5.

Mean Performance Variations Function of the Breathing Gas Mixtures.

Mixture	HeO_2	$He\text{-}N_2\text{-}O_2$	$H_2\text{-}He\text{-}O_2$
Manual Dexterity	−20%	−10%	−5%
Visual Choice Reaction Time	−20%	− 8%	−5%
Number Ordination	−28%	−15%	−3%

The performance, even though modified to a fairly marked extent was much less so than in a mixture without nitrogen. The use of helium-nitrogen-oxygen mixture under similar conditions (Bennett *et al.*, 1982) has

enabled men to reach the depth of 686 msw in pressure chamber. However, the studies which were carried out with trimix in *Papio papio* monkeys and in man have shown that the effects of N_2 are more complex than simple antagonism. (Naguet *et al.*, 1975; Rostain *et al.*, 1980). Nitrogen, even if a "good" narcotic, is relatively heavy and can induce problems in pulmonary ventilation at great depths by increasing the density of the respiratory mixtures and reducing ventilatory flow.

Another "inert gas" is possible: hydrogen. Indeed, hydrogen has a low density in comparison with helium. It also has a narcotic potency which reduces strongly the HPNS symptoms. If one compares the results obtained with the three mixtures (heliox, trimix, hydreliox), the improvement of symptoms is better with hydreliox than trimix or heliox (Table 6). However, the EEG changes were similar to those recorded with other mixtures. But the performance was less affected in the tests of manual dexterity (−5%) and reaction time (−5%) while the decrease in the number ordination was much less (only 3%) (Table 5). The effect of the addition of a gas having narcotic properties appears quite clearly, and the use of hydrogen modifies the psychomotor and intellectual disturbance considerably.

TABLE 6.

Median values of the increase of middle finger tremor at the beginning of the stay at 450 msw expressed as a percentage difference from predive values.

$He-O_2$	$He-N_2-O_2$	H_2-He-O_2
97%	43%	7%
(n = 6)	(n = 13)	(n = 6)

Data were obtained during dives performed with the same compression curve and various breathing mixture. The increase of tremor is significant (Mann Whitney U test) for the results obtained in $He-O_2$ ($P < 0.05$) or in $He-N_2-O_2$ ($P = 0.05$) versus that obtained in H_2-He-O_2.

D. Effect of Duration of the Stay

An operational dive necessitates a stay at pressure of increased duration. It is thus important to know how much acclimatization will take place and how man will withstand life at pressure. Several prolonged stays have been carried out at 300, 400 and 500 msw in $He-O_2$ and other gas mixtures.

In a He-O_2 mixture at 300 and 400 msw, neurological symptoms which are generally significant when arriving at depth differ according to the subject. The symptoms having reached maximum intensity during the first 24 hours (Fig. 14) which could diminish but persist throughout the duration of the stay, diminish then markedly increase, or diminish and disappear only at 300 msw.

The EEG modifications which also reach their maximum intensity during the first 24 hours at pressure regress and stabilize at a level which is always greater than at the surface, or alternatively show a secondary increase during the second part of the stay. The sleep disturbances are most noticeable during the first days, with a partial amelioration sometimes noted for certain sleep stages from the 5th or 6th day. In all cases a return to values close to those obtained at the surface occurs during the decompression. With the helium-nitrogen-oxygen mixture the stays of 12 days at 450 msw showed similar changes.

E. Effect of Changing the Composition of the Breathing Mixture at Constant Pressures

1. Changing from He-O_2 to He-N_2-O_2

During the ENTEX 11 dive, we studied the effects of introducing nitrogen in the helium-oxygen mixture on the 6th day at 450 msw. Nitrogen was added until the concentration was 4.8% (2.2 ATA). The measurements made in helium-oxygen and then in He-N_2-O_2 showed a lessening of neurological symptoms (especially tremor) and a improvement in psychometric performance. Sleep seemed to be less disturbed in the presence of nitrogen, although it was difficult to be certain that this improvement in sleep was not simply that which normally occurs between the 5th and 6th night of a stay at pressure during a dive. However, the EEG modifications did not change significantly after the introduction of N_2. Thus, one again sees the beneficial effects of nitrogen on the clinical symptoms and psychometric performance.

2. Changing from H_2-He-O_2 to He-O_2

During the HYDRA V dive, we studied the effects of changing from a hydrogen-oxygen mixture (H_2 = 54%) to a helium-oxygen mixture at 450 msw. It was necessary to know what the practical effects of such a change would be in order to enable hydrogen to be used in future offshore diving.

The results obtained were quite dramatic. As we have seen previously, the hydrogen-helium-oxygen mixture prevents the onset of the clinical

symptoms of HPNS. However, the EEG changes were the same as those seen with other mixtures at this depth. Switching from H_2-He-O_2 to He-O_2 was carried out in two steps. Firstly the concentration of H_2 was reduced from 54% to 30%, and 8 hours later was reduced from 30% to 0%. The sudden change of breathing mixture produced severe isobaric HPNS in all the subjects. Tremor appeared within 3 hours of the first switch 80-140% increase). The theta activities in the EEG increased after the first reduction (56% to 30%) and increased again after the second switch (30% to 0%); the increase in theta activities exceeded 400% (Fig. 9) (Rostain *et al.*, 1987b). Twenty four hours after the second switch to 0% hydrogen, the EEG changes became less, but tremor continued throughout the period in He-O_2.

It is worth noting that, resulting from the isobaric HPNS, isobaric counterdiffusion also developed, which necessitated a 20 msw recompression (Gardette, 1987; Masuel, 1987). The appearance of isobaric HPNS during the change in mixtures might be due to the removal of the narcotic gas which suppressed or masked the clinical symptoms. It might also be due to the sudden increase in the partial pressure of helium, which was equivalent to a rapid compression. In any case, this procedure of suddenly changing the mixture to a higher percentage of helium must be avoided. The return to He-O_2 mixture must be carried out during the decompression, with progressive elimination of hydrogen (Gardette, 1987). This should avoid problems of isobaric HPNS and counter-diffusion.

F. Individual Susceptibility of Deep Divers to HPNS

Experimentation, both in human and animal, has shown that there are important individual differences in susceptibility to the hyperbaric environment (Bennett, 1975, Rostain & Naquet, 1974; Rostain and Naquet, 1978, Rostain *et al.*, 1980). Thus for the same depth and a given compression, the intensity of the symptoms may be greater in some subjects than in others. Likewise, some individuals may have more symptoms than others.

It thus appears that certain subjects are more resistant than others to the effects of the hyperbaric environment. In addition, it seems that this susceptibility is a stable characteristic for each subject and that a given subject presents the same symptoms for several identical exposures to high pressure. Even though the reasons for these individual differences are still unknown, we wished to determine the degree of susceptibility to HPNS so as to avoid the most sensitive subjects having to dive at depths greater than 300 msw.

It was thus necessary to find a method to identify such divers. It is possible that those symptoms found at great depths could be reproduced at lesser depths by using a very rapid speed of compression. During bounce dives, with a very fast compression (10-15 min to 180 msw : 1080 msw/h to 720 msw/h) certain subjects showed symptoms of HPNS (Rostain *et al.*, 1980). We then wished to know if the divers who display the greatest disturbances would also do so during deeper dives to more than 300 msw.

As a result of the increase in the EEG activities of the theta frequency, 50 subjects were divided into three groups:

Group 0: no significant increase (less than 10%) — 9 subjects

Group 1: a significant increase (between 10% and 100%) — 31 subjects

Group 2: an increase greater than 100% — 10 subjects.

The EEG changes resulting from rapid compression to 180 msw constitute stable data because they were found to occur even with intervals of several months in those subjects who repeated the dive. Sixteen subjects from the three groups participated in the dives to 450 msw. The results obtained in this last group can be summarized as follows: the reproducibility of our classification into three groups between the test dives and that to 450 msw was confirmed for the EEG changes when the breathing mixture at 180 msw was the same as that used for the dive to 450 msw (Fig. 15).

But there is no relationship between variations in performance between 0 and 180 msw and between 10 and 450 msw. In the same way there is no strict relationship between the decrease in performance and that of the increase in theta frequency activities. This absence of correlation, which has already been reported during previous dives (Naquet *et al.*, 1984; Rostain & Charpy, 1976) raises the problem of the meaning and importance of certain HPNS symptoms which we have considered. It is important to note however, than an alteration in the central nervous system can be masked in psychometric tests by a supplementary effort which allows the maintenance of performance.

It should also be noted that there is no systematic relationship between the results of the different psychometric tests. This is not surprising since they measure different functions. Thus there is probably no point in searching for fine correlations between the decrease in performance of one psychometric test and the size of the increase in slow EEG activities which is the expression of another function. We have to consider a wider and behavioral level in seeking to discover if EEG modifications are accompanied, in the majority of cases, by a drop in performance, without trying to link the intensity of one to another.

Finally, we all need to consider the possibility that the EEG modifications, even though we do not yet know their meaning, may be the early

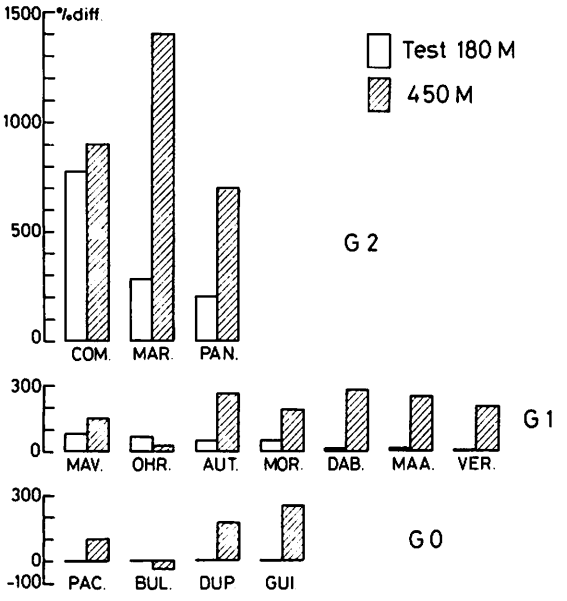

Fig. 15. Evolution of the power of theta band EEG activities. Fourteen subjects are presented according to their group classification: group 2 (three subjects: COM, MAR, PAN); group 1 (7 subjects: MAV, OHR, AUT, MOR, DAB, MAA, VER); group 0 (4 subjects: PAC, BUL, DUP, GUI). For each subject columns represent the increase in theta activities in anterior region of the skull, expressed as a percentage difference from control values: at 180 msw (white bars) during the test dives at 180 msw with rapid compression; at 450 msw (hatched bars) on arrival at the bottom after a compression in 38 hours with 4.8% nitrogen added during compression every 100 msw. The Spearman's rank correlation (non parametric) gives 0.72 P = 0.01 for relation between values at 450 msw and those of test dives at 180 msw.

signs of much more serious nervous events. Indeed, results obtained from the baboon *Papio papio* under hyperbaric conditions (Rostain, 1973; Rostain, 1980; Rostain *et al.*, 1984a; Rostain *et al.*, 1984b), show that some epileptic seizures can occur at depths of about 1000 msw, and more generally convulsions are observed in several animal species (Brauer *et al.*, 1974; Brauer *et al.*, 1979; Halsey, 1982). However, one cannot yet be confident that those subjects which display the largest increase in slow EEG activities will be the most predisposed to epileptic seizures under hyperbaric conditions. These considerations show that it is not easy to determine

criteria allowing us to choose the "best subjects" for deep diving and subsequent work. However the large EEG modifications recorded after a compression in 15 minutes to 180 msw may be, at present, one of the elements to be retained in order to determine the sensitivity of the diver to great depths.

G. Origins and Mechanisms of HPNS

The neural origins and the mechanisms of HPNS are still little known. In order to try to explain the events which occur at pressure, various authors have proposed the hypothesis of hypoxia (Bennett, 1966, Chouteau and Imbert, 1971; Hyachinthe *et. al.*, 1973) or have postulated that there are disturbances of the membrance structure (Bennett *et al.*, 1975; Miller, 1975) or of the energetic process (Rostain and Charpy, 1976).

Recent electrophysiological studies have shown that the cerebellum is probably not the origin of hyperbaric tremor (Fagni, 1981; Fagni, 1987; Kaufmann *et al.*, 1978) but that the spinal cord is affected by the hyperbaric environment and could produce, in the spinal animal, rhythmic muscular activites, but which differ from those recorded in the intact animal (Fagni, 1981; Fagni, 1987; Fagni *et al.*, 1982; Kaufmann *et al.*, 1979). This suggested a role for the higher nervous centers in the etiology of hyperbaric tremor.

The muscular spasms and myoclonus without electroencephalographic changes of a paroxystic type (spikes, spike and wave) seen in the rat and in the baboon *Papio papio* (Rostain *et al.*, 1984a; Rostain *et al.*, 1986) suggests that they have a noncortical origin. The muscular disturbances could originate in the peripheral nervous system or in the lower part of the brain (spinal cord, brain stem) and could be similar to the non epileptic myoclonus described by Hallet *et al.* (1977). In support of this hypothesis, the results of Kaufmann *et al.* (1979) in the spinal rat and those of Fagni *et al.* (1982) on the spinal cat show that the spinal cord plays a role in HPNS. In addition, Brauer *et al.* (1981b) have shown with 5-deoxyglucose that Type I seizures in the mouse (which are similar to muscular seizures in the baboon *Papio papio* (Rostain *et al.*, 1980) would have a sub-cortical origin found in the ventral region of the thalamus, the posterior hypothalamus and the pontine and medullar reticular formation.

All these studies have demonstrated the complexity of HPNS. The variables of the hyperbaric environment have differential actions on the different nervous structures which react according to their own sensitivity (Rostain *et al.*, 1980). In general, the results obtained during experiments

carried out both in animals and man suggest that there is some dysfunction of numerous biochemical mechanisms. Thus, in the baboon *Papio papio* the epileptic seizure localized in the posterior region of the cortex in a helium-nitrogen-oxygen mixture, while generalized and of tonic-clonic type in the absence of nitrogen, could be linked to hyperexcitability of this region in relation to a change in the level of gamma amino butyric acid (GABA); an inhibitory neurotransmitter. Similar phenomena have been observed in photosensitive baboons when the level of this neurotransmitter is modified by pharmacological manipulations (Meldrum and Horton, 1974; Meldrum *et al.*, 1979).

Again, in the baboon *Papio papio*, changes in cortical excitability recorded during the study of somatic evoked potentials could also be related to disturbances of the GABAergic system, as could cycles of excitability. The reduction in vigilance, and sleep disturbances (which in the baboon can become total sleep deprivation at depths greater than 1000 msw) suggest the possibility of disruption of the noradrenaline-serotonin system, in so far as it can be implicated in the regulation of vigilance. Likewise, the increase of tremor could be related to an increase in catecholamines (increase in physiological tremor) (Mardsen, 1978). The disturbances of the monoamines could be related to behavioral changes and hallucinatory type episodes.

In other respects, the study of reflexes carried out on the baboon *Papio papio* and on man (Fagni *et al.*, 1980; Harris, 1979a; Harris, 1979b; Harris and Bennett, 1983; Hugon *et al.*, 1980) demonstrate a certain number of variations which suggest that there are disturbances of the cholinergic system at least in the peripheral nervous system. Therefore, the study of HPNS mechanisms and neurophysiological effects of compression proceeds via a neuropharmacological and neurochemical approach associated with an electrophysiological study of the nervous structures likely to be implicated in the appearance of HPNS. Such studies have been undertaken by various laboratories to try to both alleviate diverse symptoms of HPNS and to identify the neurotransmitters which could be implicated. We have been particularly interested in amino acid neurotransmitters and in monoamines (Forni and Rostain, 1984; Meldrum *et al.*, 1983; Rostain and Forni, 1987; Rostain *et al.*, 1984c; Rostain *et al.*, 1986; Wardley-Smith *et al.*, 1986).

V. CONCLUSION

In deep diving, the modifications observed for behavior performance and electrophysiology depend not only on the depth attained, but also on the speed of compression and the breathing mixtures. The results which

we have obtained in man and animals alike demonstrate the importance of the speed and the type of compression in relation to the intensity of various HPNS symptoms.

Dives with mixtures other than helium-oxygen have become sufficiently numerous to enable us to draw conclusions about various points. The trimix mixture is efficient and does not add phenomena due to narcosis. The amount of nitrogen in the trimix must be about 5% until a depth of 500 msw, i.e., a partial pressure of 2.5 bars. The introduction of hydrogen into the respiratory mixture reinforces this idea that HPNS symptoms can be reduced without increasing narcosis. It does not seem that subjects can be compressed to very great depth in heliox, even with a slow compression rate, without causing major disturbances. The use of trimix made up of nitrogen or hydrogen thus seems necessary to reduce several HPNS symptoms. Nevertheless, the use of nitrogen or hydrogen do not reduce EEG changes. Their use have shown that the action is more complex than simple antagonism. Further studies on the nervous system, neurotransmission, at the cellular and molecular levels are necessary to gain our knowledge on the complexity of HPNS and to establish rational scientific bases for new progress in human deep diving.

The results of the use of hydrogen as a diluent of oxygen, either along or in combination with helium, are definitely positive. The gas constitutes a new solution to life and work under pressure once certain technical problems have been overcome, and the handling techniques mastered. By virtue of its lightness and its anti-HPNS effects it affords to the deep diver much greater comfort than heliox. A diver breathing hydrogen will be more efficient, less tired and more comfortable, thus much safer while working in the water.

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5

The Value of Trimix 5 to Control HPNS

P.B. Bennett and H. Schafstall

I. INTRODUCTION

The abililty of man to be able to dive very deep and yet remain functionally normal has been the subject of much basic and applied research in several countries over the past twenty or thirty years (Bennett, 1982; Enseleit and Curley, 1987; Lemaire and Rostain, 1988). This paper will concentrate therefore on the more recent American and German work which has developed to the point where working divers may more or less routinely be compressed to depths of 600 m or 1967 ft and probably deeper (Bennett & Towse, 1971; Bennett *et al.*, 1988).

II. OXYGEN-HELIUM DIVING

It was not until after World War II that substitution of helium-oxygen for compressed air in deep diving, to circumvent the narcosis produced by the nitrogen, stimulated research into diving deeper than 300 ft. Considerable surprise was thus evoked in the early nineteen sixties at the then seemingly remarkable achievement of a young Swiss mathematician, Hannes Keller, who first reached 1000 ft, both in the pressure chamber and ocean for brief periods after rapid compressions of one or two hours (Keller and Buhlmann, 1965).

At the time, this was considered all the more remarkable, as rapid compressions with helium-oxygen to 600 ft and 800 ft in 1964 in England had indicated some new and unusual signs and symptoms (Bennett, 1965; Bennett, 1967; Bennett and Dossett, 1967). These British Navy dives resulted in performance decrements in arithmetic ability and manual dexterity, accompanied by tremors of the hands and arms, dizziness, nausea, vomiting and excessive fatigue. The severity of 800 ft precluded the likelihood of divers reaching 1000 ft under such conditions and still be fit to work.

A little later Brauer *et al.* (1968) in the USA and Miller *et al.* (1967) reported similar signs and symptoms terminating in convulsions in animals exposed to very high pressures of oxygen-helium. Eventually the phenomenon was termed the High Pressure Nervous Syndrome (HPNS).

HPNS is characterized by signs and symptoms resulting from the effects of the pressure itself and the rate of its application or compression. These are dizziness, nausea, vomiting, postural and intention tremors, fatigue, somnolence, myoclonic jerking, stomach cramps, increased EEG slow wave activity (6-8 Hz, theta) and decreased fast wave activity (8-11 Hz, alpha), decrement in intellectual and psychomotor performance and poor sleep with vivid dreams or nightmares (Hunter and Bennett, 1974).

Nevertheless, in 1968 the U.S. Navy carried out the fiirst 1000 ft saturation dive at the then new Duke University Medical Center Hyperbaric complex at the F.G. Hall Laboratory (Overfeld *et al., 1969;* Shaefer *et al.*, 1970; Summitt *et al.*, 1971). Compression involved a linear rate of some 40 ft/hr (24 h total time), 77 hr and 30 min at 1000 ft and a 284 hr 50 min decompression. There were no tremors, mental decrement or other adverse effects of pressurization compared with the HPNS effects of the 100 ft/min English dives to 600 ft and 800 ft. Clearly rapid compression with helium-oxygen to such depths was at least one of the causative factors.

Even so, the Swiss group, under Professor Buhlmann, continued to carry out relatively rapid compressions of only 60 min to 1000 ft and with the excursions to 1150 ft involving heavy work underwater for up to 2 hours with only minimal signs or symptoms of HPNS (Buhlmann *et al.*, 1970). Conversely, Brauer, in conjunction with French researchers experienced severe and debilitating HPNS during a 2 hr compression to 1150 ft, which led to the suggestion of an "HPNS Barrier" at some 1200 ft (Brauer, 1968).

Subsequent British, French and American research (Bennett and Towse, 1971; Bennett and Towse, 1971b; Fructus and Rostain, 1978; Morrison and Florio, 1971; Rostain and Naquet, 1978), however, showed no evidence for such a barrier but noted the greater the depth and more rapid

the compression, the more severe was the HPNS and there was considerable individual susceptibility. It also became clear that, in addition to a very slow compression it was advantageous to use several stages of up to 24 hours at interim depths to reduce the effects of each compression phase and permit adaptation.

Thus at the University of Pennsylvania, Institute of Environmental Medicine in 1971, divers were compressed at increasingly slower rates and with stages of between 2 to 4 days at 400 ft, 700 ft, 900 ft and 6 days at the final depth. Rates for the 10 day compression were 31 ft/min to 400 ft, 5 ft/min to 700 ft and to 900 ft and 2.5 ft/min to 1200 ft. Although a small but consistent increase in overall magnitude of tremor occurred during compression no gross compression tremors were observed and there were no important functional problems, EEG or other HPNS changes (Lambertsen, 1976).

In 1975 Predictive Series IV at the University of Pennsylvania (Lambertsen 1976; Spencer *et al.*, 1979) examined the value of excursions from a shallower depth after a one hour compression to 800 ft breathing oxygen-helium which produced arthralgias but little HPNS. The first of six subsequent excursions to 1200 ft in only 40 min using 20 ft/min for 800-1000 ft, 10 ft/min for 1000-1100 ft and 5 ft/min for 1100-1200 ft resulted in headache, dizziness, slight nausea, shakiness, uncoordination and difficulty concentrating. However, it is interesting that subsequent excursions elicited little difficulty. Other Swiss and French work reported similar success with such excursions.

A second phase of this study involved a 3½ hour compression to 1200 ft and after a 22 hour stage, excursions in 40 min to 1600 ft. This rapid compression similar to the earlier Brauer dive to 1150 ft in 2 hours (Brauer, 1968) resulted in nausea, vomiting, fatigue, tremors, exhaustion, intermittent increased EEG theta activity and other adverse indications of HPNS with some recovery after 2 hours. After 22 hours an excursion to 1600 ft in only 40 min elicited various decrements in performance efficiency, visible tremors, feelings of tenseness, muscle fasciculations, increased EEG theta and decreased alpha. However, subsequent compressions were better and it was possible to reduce the compression time to a remarkable 20 min, without causing much HPNS and carry out underwater work at an oxygen consumption of 2 L/min. Clearly, though, such methods are unlikely to be used routinely for future deep diving due to the HPNS present.

A little later in 1979 the U.S. Navy carried out a dive to 1800 ft (549 m) which together with British and French work pointed to a potential limit for deep helium-oxygen diving (Spaur, 1980). During this dive, after nearly 4 days of compression with rates mostly of 30 ft/hr except for the

last 200 ft at 15/hr and 40 ft/hr to the 1000 ft depth and long stages at 890 ft, 1000 ft, 1400 ft and 1520 ft, severe HPNS nevertheless occurred.

This was in spite of the use of various methods developed in the 1970's to minimize signs and symptoms of HPNS such as preselection of the divers, a slow exponential rate of compression with stages etc. (Bennett, 1975; Bennett, 1980). While these methods did appear quite effective to about 1500 ft, at greater depths the HPNS was often debilitating and alternative methods were required. It was to this end that the use of nitrogen with heliox to form TRIMIX was proposed by Bennett, and first tested in the 1970's in divers at Duke University Medical Center, and eventually in 1981 to 686 m (2250 ft).

III. TRIMIX (HELIUM/NITROGEN/OXYGEN)

The potential value of TRIMIX arose from the work of Johnson and Flagler (1950). This showed that pressure *per se* was very effective in reversing the effects of narcosis. Thus tadpoles anesthetized with ethyl alcohol would resume the conscious state and return to swimming at increased hydrostatic pressure even though the same anesthetic dose was present. Later Bennett, *et al.* (1967) reported that increased pressures of nitrogen, argon and carbon dioxide caused a fall of the surface tension of a phospholipid monolayer. Conversely helium and neon induced a rise (Fig.1).

The fall of surface tension was equated to expansion of neuronal cell membranes and narcosis and the rise, to constriction and signs and possibly symptoms of HPNS.

In 1971 Lever *et al.* also reported such pressure antagonism of nitrogen narcosis in mice by compression to 150-200 ata with helium. This led Bennett to hypothesize that if such nitrogen narcosis can be antagonized by pressure (high helium pressures — which is synonymous with HPNS) then the reverse should also apply. Thus small amounts of nitrogen added to helium-oxygen to give TRIMIX ($He/N_2/O_2$) should allow great depths or pressures to be reached without causing any change in membrane surface tension and therefore neither narcosis nor HPNS.

In 1973 the concept was first tested in human divers at the F.G. Hall Laboratory with rather high nitrogen percentages of 25% and 18% and rapid compressions of some 33 min to 305 m. This resulted in some protection against HPNS but signs and symptoms of nitrogen narcosis.

A mathematical model, based on the Gibbs absorption equation was therefore used in an attempt to better quantify the amount of nitrogen required (Simon *et al.*, 1975). This in 1974 permitted proof of the hypothesis in 33 min compression to 1000 ft by five divers (Bennett *et al.*,

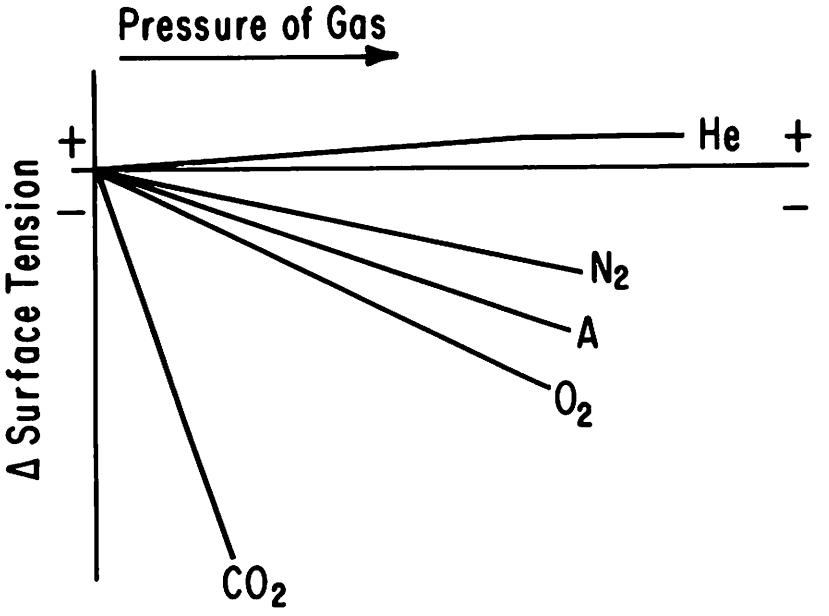

Fig. 1. Changes in surface tension of an egg phospholipid monolayer exposed to increased pressures of helium (He), nitrogen (N_2), argon (A), oxygen (O_2) and carbon dioxide (CO_2). Helium causes a rise in surface tension while other gases induce a fall.

1975) breathing TRIMIX 10 (10% nitrogen in heliox). There was no performance decrement, no tremors, nausea or fatigue and no sign of nitrogen narcosis. However, underwater work was performed for 44 min in 13.3°C water, with the diver in a heated suit, who noted mild euphoria. It was therefore planned in the late 1970's to explore the value of TRIMIX more extensively in a very deep diving series termed ATLANTIS during which a record simulated depth of 2250 ft was obtained (Bennett and McLeod, 1984).

A. Atlantis

The so called ATLANTIS series of 4 deep dives was developed at the Duke University hyperbaric facilities to compare the effectiveness in controlling the debilitating signs and symptoms of HPNS by use of exponential rates of compression with pauses or stages for adaptation and the addition of 5% or 10% nitrogen to helium-oxygen. An intensive series of

pulmonary, psychometric, hematologic and other tests were made as well as data on the most effective decompression procedures (Bennett and McLeod, 1984; Bennett *et al.*, 1982).

An extensive amount of information was obtained on human physiology at such great depths (Andersen and Bennett, 1981; Bennett, 1967; Bennett *et al.*, 1981; Harris and Bennett, 1983; Harris and Bennett, 1984; Logue *et al.*, 1986; Parmentier *et al.*, 1985; Salzano *et al.*, 1981). On the basis of this research it was concluded that it is possible for men to dive to 600 m and beyond using a slow exponential compression with stages and a TRIMIX breathing mixture containing 5% nitrogen throughout.

Thus the least signs and symptoms of performance decrements were seen with the slow compression and 5% nitrogen rather than the faster rates and 10% nitrogen (Figs. 2 and 3).

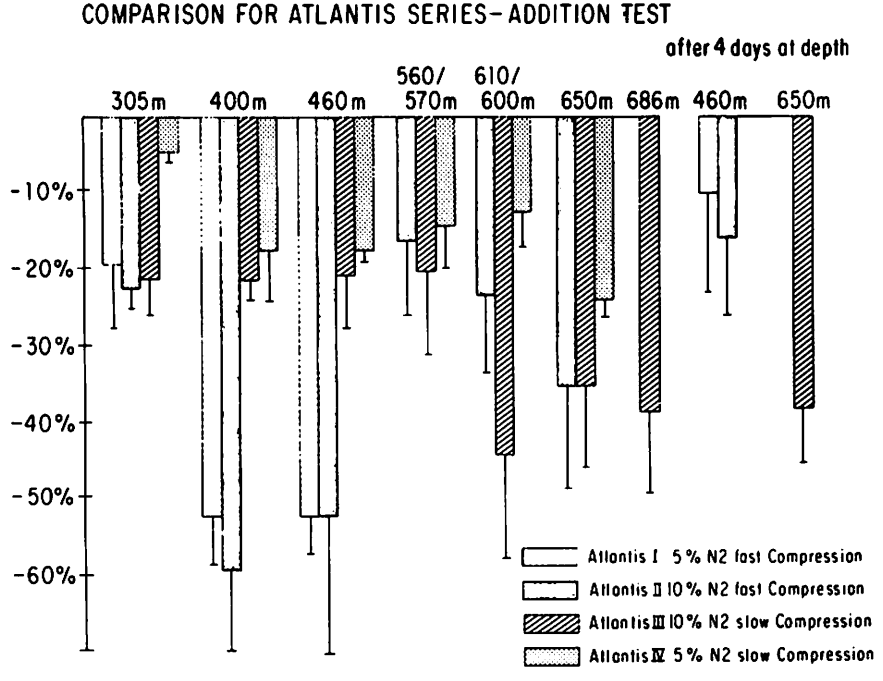

Fig. 2. Comparison of the mean percentage of decrement and SEM of 3 divers performing an arithmetic test during ATLANTIS I, II, III and IV. The advantage of slow compression with TRIMIX 5 (5% nitrogen) is apparent.

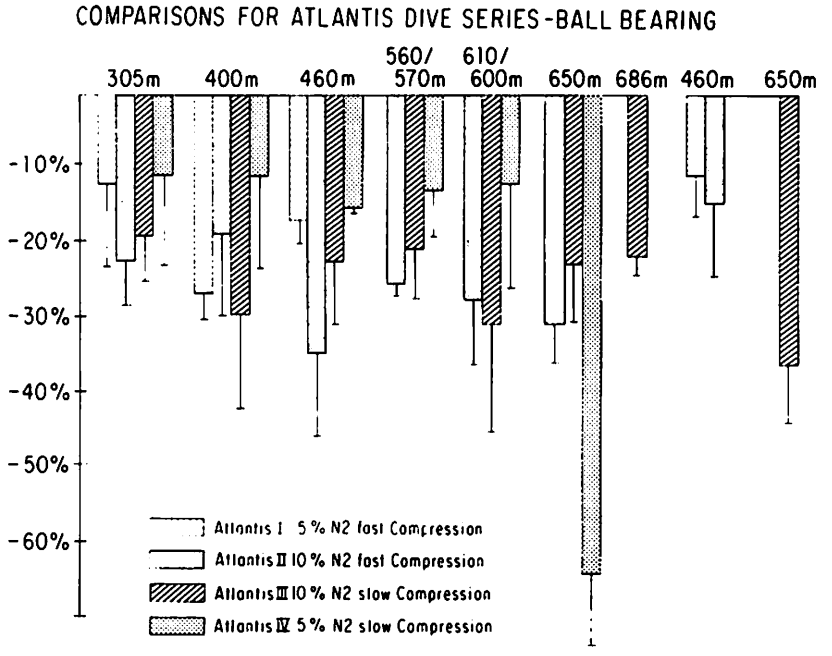

Fig. 3. Comparison of the mean percentage decrement and SEM of 3 divers performing the ball bearing test of fine motor dexterity. As with Fig. 2 the advantage of slow compression with TRIMIX 5 (5% nitrogen) is clear except for the data at 650 m.

The efficacy of this method for control of the adverse effects of HPNS has been substantiated by French work (Lemaire and Rostain, 1988) described also at this symposium and by collaborative research between Duke and the GKSS research laboratories in Germany at Geesthact near Hamburg. Using the new German Underwater Simulator (GUSI) from 1983 to 1986, 14 operational type dives were made by 13 international divers at depths from 300-600m (985-1967 ft).

B. Duke/GUSI TRIMIX Research

For optimal relief from HPNS or nitrogen narcosis it was decided to use TRIMIX 5 (5% nitrogen, 0.5 atm oxygen and remainder helium) throughout including the decompression. The compression profile chosen was adapted from ATLANTIS IV. A series of dives were then planned,

each with 3 or 4 divers, from 1983 to 1986 which would gradually go deeper using the same compression profile (Table 1). In this way the compression profile was repeatedly tested.

The actual dives made, the dates, number of divers and duration are shown in Table 2. The divers were not especially selected and included divers from Germany, England, France, and the United States. Many had

TABLE 1.

Duke/GUSI Compression Profile to 600 m with Trimix (N_2 5%/0.5 bar 0_2/He rest)

Travel 0 m - 180 m	= 5 m/min (36 min)
Stop at 180 m	= 2 hr
Travel 180 m - 240 m	= 3 m/min (20 min)
Stop at 240 m	= 6 hr
Travel 240 m - 300 m	= 1.5 m/min (40 min)
Stop at 300 m	= 2 hr
Travel 300 m - 350 m	= 0.5 m/min (1 hr 40 min)
Stop at 350 m	= 9 hr
Travel 350 m - 400 m	= 0.25 m/min (3 hr 20 min)
Stop at 400 m	= 2 hr
Travel 400 m - 430 m	= 0.125 m/min (4 hr)
Stop at 430 m	= 2 hr
Travel 430 m - 460 m	= 0.125 m/min (4 hr)
Stop at 460 m	= 12 hr
Travel 460 m - 490 m	= 0.100 m/min (5 hr)
Stop at 490 m	= 2 hr
Travel 490 m - 520 m	= 0.100 m/min (6 hr 40 min)
Stop at 520 m	= 13 hr
Travel 520 m - 550 m	= 0.075 m/min (6 hr 40 min)
Stop at 550 m	= 13 hr
Travel 550 m - 575 m	= 0.05 m/min (8 hr 20 min)
Stop at 575 m	= 16 hr
Travel 575 m - 600 m	= 0.05 m/min (8 hr 20 min)

TABLE 2.

GUSI/Duke Dives 1983-1986

Dives	Date	Dive Days	No. of Divers	Man Days
GUSI 1 125/300/150 m	23 Nov 1983 to 16 Dec 1983	24	4	96
GUSI 2 150 m	12 March 1984 to 21 March 1984	10	3	29
GUSI 3 300/150 m	7 May 1984 to 27 May 1984	21	3 (300 m) 3 (150 m)	86
GUSI 4 400/200 m	2 Sept 1984 to 29 Sept 1984	28	3 (400 m) 3 (200 m)	135
GUSI 5 450/265 m	14 Nov 1984 to 14 Dec 1984	31	4 (450 m) 4 (265 m)	173
GUSI 6 450/265 m	23 April 1985 to 24 May 1985	32	4 (450 m) 4 (265 m)	198
GUSI 7 500/450/300 m	6 Nov 1985 to 10 Dec 1985	35	4 (500 m) – (450 m) 4 (300 m)	280
GUSI 8 600/360 m	20 March 1986 to 1 May 1986	43	4 (600 m) 4 (360 m)	344
Totals		224	51	1341

made only shallow dives prior to this series while others were experienced commercial divers. Predive extensive clinical and psychological tests were made including long bone x-rays, full head EEG, CAT scan, neurological, etc. (Holthaus and Bennett, 1985). These were repeated yearly. In addition careful immediate pre- and post-dive medical examinations were made.

In order to ascertain the presence or not of HPNS and the fitness of the divers to carry out their welding or other work, various tests were conducted. These included a subjective symptom check list, neurological examination, EEG with fast fourier frequency analysis, muscle strength tested by dynamometer and body weight data. Blood morphology and urine electytrolytes were obtained in some of the dives together with ergometric measurements up to 160 watts.

A clinical psychological test battery, especially of memory and vigilance, was made by Dr. Goeters of DFVLR during the 500 m and 600 m dives. Four tests were used; test KBT required steady and coordinated use of perception, speed, memory capability and calculation; test MEK measured the visual memory; test UZA measured the memory capacity for auditory perception and the CLE test quantified the memory capacity for acoustically transmitted information.

The decompression procedures developed by Dr. Vann were based on evaluation of 1055 previous helium-oxygen man decompressions and 189 nitrogen-oxygen decompressions (Vann, 1984). The equation utilized was $R = K \cdot PIO_2$ where R is measured in m/hr or fsw/hr, PIO_2 is in atm (or bars) and the proportionality constant is in mph/atm or fph/atm. It was found necessary to reduce K as the depth increased. The decompression tables for depths to 686 m (2250 ft) are shown in Table 3.

TABLE 3.
Provisional Duke Saturation Decompression Schedules (msw)

Saturation Depth, msw	K fph/ atm	Rate of Ascent, min/(0.5 msw) Until 14 msw	14 to 9 msw	9 to 6 msw	6 to 3 msw	3 to 0 msw	Decompression Time Day	Hr
0 - 30	12.0	17	21	25	30	40	0	22
30 - 60	11.0	18	23	27	33	43	1	17
60 - 90	10.0	20	25	30	36	47	2	18
90 - 120	9.5	21	26	31	38	50	3	18
120 - 150	9.0	22	28	33	40	53	4	21
150 - 180	8.5	24	29	35	43	56	6	7
180 - 210	8.5	24	29	35	43	56	7	7
210 - 240	8.0	25	31	37	45	59	8	15
240 - 270	8.0	25	31	37	45	59	9	16
270 - 300	7.5	27	33	39	48	63	11	13
300 - 330	7.5	27	33	39	48	63	12	16
330 - 360	7.0	29	36	42	52	67	14	20
360 - 390	7.0	29	36	42	52	67	16	1
390 - 410	6.5	31	38	45	56	73	18	0
410 - 450	6.5	31	38	45	56	73	19	18
450 - 480	6.0	33	41	49	60	79	22	10
480 - 510	6.0	33	41	49	60	79	23	19
510 - 540	5.5	36	45	54	66	86	27	11
540 - 570	5.5	36	45	54	66	86	28	23
570 - 600	5.0	40	50	59	72	94	33	20
600 - 630	4.5	44	55	65	80	105	39	1
630 - 686	4.0	50	62	73	90	118	48	6

Oxygen — 0.5 atm partial pressure deeper than 14 msw
— 21% from 14 msw to surface
Nitrogen — Not more than 5% deeper than 15 msw
— Not more than 0.79 atm partial pressure at less than 150 msw
Helium — Balance

This series of dives confirmed the efficacy of the use of TRIMIX 5 with appropriate exponential compression rates and stages. There was little or no HPNS and the divers arrived at depth fit and able to carry out successfully extensive welding and other work to 600 m. There were no visible tremors or undue fatigue. One diver at 500 m vomited after breakfast the day after arrival but he then developed a viral infection with increased temperature and was taken off work.

TABLE 4.

GKSS/DFVLR Test KBT (Goeters/Kirsch) for Perception Speed, Memory, and Calculation

Depth	Mean	SEM	T-Test
Pre-Dive	79.25	±26.17	—
500 m (1985)	47.00	±23.19	1%
278 m	70.50	±27.04	—
Post-Dive	97.00	±28.52	—

The performance tests in general showed little change except at 500 m and 600 m. In fact only the KBT test showed a significant decrement at 1% level (Table 4). At 600 m the decrement was more general in nature involving both the KBT and CLE tests with significant levels of 5% and 1% respectively (Tables 5 and 6). However, this was not indicated in the ability of the divers to carry out their work, although greater concentration was required. Obligate mouth breathing often began deeper than 450 m.

TABLE 5.

GKSS/DFVLR Test KBT (Goeters/Kirsch) for Perception Speed, Memory, and Calculation

Depth	Mean	SEM	T-Test
Pre-Dive	94.33	±36.35	—
600 m	59.33	±34.39	5%
510 m	65.67	±40.99	5%
Post-Dive	90.66	±41.47	—

Although no increased theta activity was seen in the EEG, the usually seen reduction of alpha activity at increased pressures, was sustained. Body weight also declined as with previous deep oxygen-helium dives (Table 7). The dynamometer tests at 500 to 600 m showed an average reduction of 3% to 13% in peak strength with little change in duration.

TABLE 6.
GKSS/DFVLR Test CLE (Goeters/Witt) for Memory Capacity and Auditory Information

Depth	Mean	SEM	T-Test
Pre-Dive	207.67	±11.69	—
600 m	151.33	±30.09	1%
510 m	170.67	±34.96	—
Post-Dive	188.33	±29.53	—

TABLE 7.
Body Weights (kg) During 600 m Dive

Depth	S1	S2	S3	S4	Mean
Control	95	81	76.5	93	86.4
599 m	92.3	79.1	74	88	83.4
474 m	91	76.8	74.3	86	82.0
441 m	91	76.8	72.8	85.9	81.6
360 m	89.8	75.7	72.1	84.7	80.4
259 m	89.1	76.7	73.0	84.5	80.8
134 m	88.8	75.3	73.3	84.3	80.4
Surface	90.0	77.5	73.8	84.0	81.3

Three cases of decompression sickness occurred during the 50 man dives. During GUSI 7, one of the divers at 7.8 m complained of sleep difficulty. A 300 m diver reported knee pain twenty minutes later. Treatment involved 3 x 20 mins oxygen with complete resolution and return to schedule after 6 hrs.

During GUSI 8 another diver also complained of knee pain at 40 m and was treated with oxygen as above. The third case, another 600 m diver showed foot drop, muscular weakness and sensory deficit during his post-dive physical. He was recompressed to 18 m for 24 hours with oxygen therapy and fully recovered. It is noteworthy that this diver had indicated some evidence of foot drop in his pre-dive physical.

IV. CONCLUSION

The data indicates a useful method to attain very great depths to carry out underwater work. However, pressure is still causing some effects and the true mechanisms by which TRIMIX is able to control some of the more deleterious effects of HPNS has yet to be ascertained.

The obligate mouth breathing and respiratory data from the ATLANTIS series also give strong support to the use, where feasible, of

hydrogen as the narcotic instead of nitrogen, although a much higher percentage than 5% is appropriate (Rostain *et al.*, 1988). Alternatively it may be possible to use helium-oxygen and control the HPNS pharmacologicaly with a suitable narcotic. Whatever method is chosen it, however, remains clear that TRIMIX has a vital part to play in the ability of man to explore and work in the deep ocean. Just how deep these methods will permit man to safely dive remains to be elucidated.

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6

Natriuresis and Hypoxic Signs at Pressure — Cellular Considerations

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I. INTRODUCTION

Since pressure is "thermodynamic state" variable it has rather ubiquitous effects on systems, organ and cellular physiology. Recently, the impact of pressures from 2 to 1000 ATA on cellular transport systems has been extensively reviewed (Jannasch *et al.*, 1987). There are several phenomena however which are routinely experienced by human divers during deep saturation dives e.g. H.P.N.S., natriuresis and diuresis, bradycardia, and hypoxic signs during normoxia. The purpose of this communication is to assess the cellular mechanisms which may underlie or contribute to, two of these disturbances, namely, natriuresis and apparent hypoxia in a normoxic or slightly hyperoxic environment.

II. PRESSURE NATRIURESIS

Since the development of the saturation diving technique in the middle 1950s by the U.S. Navy, many simulated (dry) deep saturation dives have been conducted throughout the world. In practically all of these dives a significant increase in daily urine flow (by 500-1000 ml/day) was

observed at high ambient pressure, even in the absence of cold stress. This phenomenon has been referred to as hyperbaric diuresis. Although it was first reported by Hock *et al.* in 1966, the exact mechanism underlying this important phenomenon is still unknown. Despite such a sustained diuresis there was no evidence to indicate that the daily fluid intake increased correspondingly (Bennett and Gray, 1971; Schaefer *et al.*, 1970). The latter findings rule out greater fluid intake as a cause for this diuresis.

During the Hana Kai II dive (Hong *et al.*, 1977) a comprehensive study of body fluid balance was conducted. These studies suggested the hyperbaric diuresis was due to an observed 35% reduction in insensible H_2O loss and a 40-50% suppression of antidiuretic hormone. Although urine osmolality is generally decreased during the diuresis, both the osmolal clearance and the fractional excretion of osmotic substances increased suggesting that the tubular reabsorption of osmotic substances was also inhibited.

Clear evidence for such inhibition of tubular reabsorption of osmotic substances, especially Na^+, was obtained more recently in three U.S.-Japan cooperative saturation dives, Seadragon IV (1979) (Nakayama *et al.*, 1981), Seadragon VI (1984) and New Seatopia (1985), at 31 ATA. The usual hyperbaric diuresis associated with reduction in plasma ADH level and urinary excretion of ADH was again observed, but, in contrast to previous shallower dives, there was a significant natriuresis in the face of constant creatinine clearance. For instance, in the most recent New Seatopia dive, the daily Na^+ excretion increased from predive level of approximately 160mEq/day to nearly 300 mEq/day during the first 3 days at 31 ATA, after which it decreased somewhat and leveled off at about 220 mEq/day. What is more remarkable is the fact that this hyperbaric natriuresis is present in the face of increased plasma renin and aldosterone. This indicates the presence of aldosterone-independent natriuretic mechanism(s) at pressure. It thus appears that an inhibition of the tubular reabsorption of Na^+ is at least partly responsible for the development of a hyperbaric diuresis.

The isolated amphibian skin or urinary bladder preparation has been used extensively as a "model" epithelium for studies on active Na^+ transport and contributed to the understanding of the underlying cellular mechanisms. The toad skin can be easily isolated from the body, and the Na^+ transport characteristics can be studied *in vitro* by measuring the short-circuit I_{SC} which is equal to the net rate of active Na^+ transport across the epithelium (Ussing and Zerahn, 1951).

According to the current cellular model (Macknight *et al.*, 1980) Na^+ enters the toad skin cell passively across the apical (mucosal) membrane

and is actively extruded from the cell across the basolateral (serosal) membrane through a mechanism involving the Na, K-ATPase. This net Na^+ transport across the cell generates a relatively high transepithelial electrical potential difference that reflects the low passive permeability of the tissue to ions. The passive movement of ions is presumably through the "tight junctional" complexes which have nearly equal Na^+ and Cl^- permeabilities. Some actively transported Na^+ leaks back to the mucosa through the junctions, while Cl^- moves from mucosa to serosa in response to the Na^+-generated serosa-positive electrical potential.

Antidiuretic hormone (ADH) produces, after a latent period of 3-5 min, a rapid increase in I_{SC} in this tissue which reaches a maximum in about 20 min and is sustained for about one hour. It is generally held that the increased Na^+ transport in response to ADH is mediated through intracellular cyclic AMP (cAMP). As first postulated by Orloff and Handler (1962), ADH stimulates adenylate cyclase activity in the basolateral membrane which increases cAMP in the cell; cAMP then increases the permeability of the apical membrane to Na^+ through mechanism(s) yet to be identified. Exogenous cAMP and theophylline also increase Na^+ transport.

Aldosterone also increase Na^+ transport but its mode of action is distinctly different from that of ADH. The increase in Na^+ transport does not occur until 30-90 min after the skin or bladder is exposed to aldosterone. Once initiated the response may last several hours. Edelman and associates (1973) have demonstrated, in a series of elegant studies, that the stimulation of Na^+ transport by aldosterone involves entry of the hormone into the cell, binding to a cytoplasmic protein, transformation to an active complex, migration of this active complex to the nucleus, binding of the complex to specific nuclear sites and activation or depression of transcription resulting in induction of synthesis of specific proteins. However, the mechanism by which aldosterone-induced proteins effect an increase in Na^+ transport is still unclear, although it is recognized that this mechanism involves increased entry of Na^+ to the cell and increased metabolism related to Na^+ extrusion from the cell (Macknight *et al.*, 1980).

Recently, Edelman and his associates (1973) indirectly assessed the effect of ADH and aldosterone on the apical membrane Na^+ permeability (P^a_{Na}) in the toad urinary bladder by using current-voltage (I-V) analysis of the K^+-depolarized preparation. In this preparation, the basolateral membrane is depolarized by raising the K^+ concentration of the serosal bathing medium and the transepithelial resistance can be almost entirely attributed to the apical membrane resistance. Therefore, one can calculate P^a_{Na} from the I-V relationship. It was concluded from these studies

that both ADH and aldosterone increased P^a_{Na} by 68% and 126%, respectively (Li *et al.*, 1982; Palmer *et al.*, 1982). Moreover, power density spectral analyses conducted in the same studies led to the conclusion that the effect of ADH and aldosterone on P^a_{Na} is not due to an increase in the single channel conductance but to an increase in area density of conducting Na^+ channels. In other words, these hormones seem to recruit new Na^+ channels. In a subsequent study by Garty and Edelman (1983) who used the enzyme trypsin to expose Na^+ channels, it was concluded that ADH-induced channels may involve either fusion of channel-containing vesicles with the apical membrane or recruitment from some other channel precursor pool whereas aldosterone-induced channels are presumably present in the apical membrane before stimulation by this hormone.

Gottlieb and Cymerman (1970) and Gottlieb *et al.*, (1968) have investigated the effects of elevated pressure of O_2, He, N_2, Xe, Kr and N_2O on active Na^+ transport (as measured by I_{SC}) across frog skin, and concluded that the high partial pressures (12-65 ATA) of specific gases involved (and not pressure *per se*) were responsible for the inhibition of Na^+ transport observed in O_2, Xe ($\approx$15 ATA), Kr ($\approx$64 ATA), and N_2O ($\approx$15 ATA). Helium or N_2 produced no inhibition at a pressure of 130 ATA, while frog skin may have a sensitivity to increased P_{O_2} similar to that found in mammals. An inverse relationship was found between the P_{O_2} and time required for initiation of a decrease in I_{SC}. However, no direct measurements of the effects of hydrostatic pressure alone could be made in their experimental system. It should also be noted that these authors *assumed* that I_{SC} represents active Na^+ transport under high pressure, which was not verified.

Since Na,K-ATPase is implicated in the active transport of Na^+, Gottlieb *et al.* (1976) also investigated the effects of elevated pressures of O_2, He and N_2 on rat intestinal Na,K-ATPase activity. They found significant inhibition of the enzyme under moderate pressures of O_2 (5-10 ATA) or N_2 (5 ATA) but significant stimulation at higher pressures (>30 ATA) of O_2 or N_2. On the other hand, helium induced a monotonic inhibition of activity as the pressure was raised to 21 ATA. A qualitatively similar biphasic effect of O_2 and N_2 pressures on Na,K-ATPase activity was observed in the rat heart (Gottlieb *et al.*, 1976) and beef brain (Hermick and Gottlieb, 1977). The interpretation of these data is very difficult unless the hydrostatic pressure effect is factored out. Nevertheless, it is evident that there is no correlation between the observed effects of various gas pressures on I_{SC} and Na,K-ATPase activity.

More definitive studies on the effect of hydrostatic pressure *per se* on the permeability characteristics of the isolated frog skin were carried out

by the Pequeux group in Belgium. In their first study (Pequeux, 1976a) they observed that a pressure of 100 Kg/cm^2 ($\approx$100 ATA) produced a reversible, sustained increase in transepithelial potential difference (Δ PD $\approx$20 mV). In a subsequent study, Pequeux (1976b) observed that such an increase in the transepithelial PD reaches a maximum ($\approx$30 mV) at 200-300 ATA and is reduced at higher pressures; at pressures higher than 500 ATA the PD irreversibly decreased. Since this increase in PD at relatively modest pressure (100 ATA) was accompanied by a parallel increase in I_{SC} and was abolished when Na^+ in the outside bathing medium was replaced with K^+, Mg^{++}, Li^+ or choline, they concluded that pressure increases the Na^+ permeability of the outer barrier of the skin. In support of this conclusion, Pequeux (1976a) also observed that the frog skin Na,K-ATPase activity is not significantly affected at 100-250 ATA while it decreases markedly at 500 ATA (50%) and 1,000 ATA (80%). Brouha *et al.* (1970) also reported that 10 mU/ml oxytocin in the bathing medium increased PD even at 100 ATA (oxytocin has an effect similar to ADH on Na^+ and water transport across the frog skin). Based on the rationale that pressure may alter the state of ionization of the membrane components (e.g., proteins) and hence the structure and activity of the transport mechanism, Pequeux (1976b) also studied the effect of medium pH on the pressure-induced increase in PD across the frog skin. However, he observed that the pressure effects (100 ATA) remain rather similar at each pH value, indicating that pressure-induced ionization changes cannot be solely responsible for the passive permeability modification. While these studies are important in that pressure is used as a tool to study the structure of the cell membrane in relation to function, there are several critical problems with the technique and design of their studies: 1) there is no description in their papers of how they maintained the O_2 supply to the tissue during exposure to high pressure, 2) the tissue was exposed to pressure for ony 2-5 min in most experiments, and 3) there are no measurements of Na^+ fluxes to indicate that I_{SC} indeed represents the net Na^+ flux under pressure. In order to address these issues and further explore the cellular mechanisms of the natriuresis we have examined the effects of hydrostatic pressure on active Na absorption by the *in vitro* short-circuited toad skin.

The results of a typical experiment illustrating the entire time course is shown in Fig. 1 (Hong *et al.*, 1986). The baseline I_{SC} increased transiently during the first 10 min after the start of compression and then decreased continuously until it leveled off at approximately 40 min. The initial transient increase in I_{SC} ($\approx$20% of the precompression level) under pressure was generally accompanied by an increase in the temperature of the bathing medium. We have subsequently determined that the initial

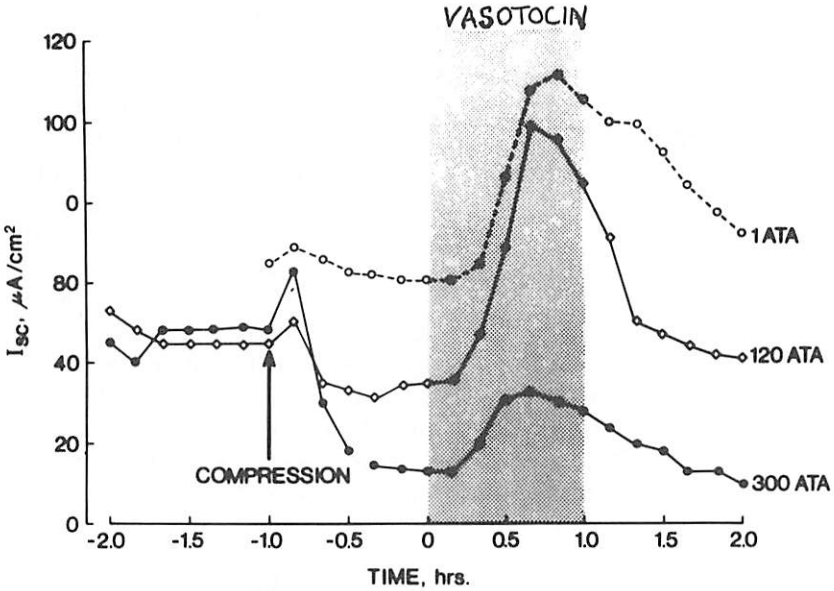

Fig. 1. Typical experiments illustrating changes of short-circuit current I_{SC} under influence of pressure and vasotocin. Vasotocin was added to inside bathing medium at a concentration of 100 mU/ml during the l-h period (shaded area).

increase in I_{SC} may be in part attributable to adiabatic heating. On the other hand, the magnitude of reduction in I_{SC} observed at 60 min under pressure was pressure dependent, increasing from 15 $\mu A/cm_2$ ($\approx$20% reduction) at 50 ATA to 30 $\mu A/cm^2$ ($\approx$60% reduction) at 300 ATA. The transepithelial resistance (R) calculated from PD/I_{SC} tended to increase initially and at 60 min under pressure.

As shown by previous investigators, the I_{SC} across the toad skin was completely inhibited by the addition of 10^{-4} M amiloride to the medium bathing the other surface of the skin at 1 ATA (Fig.2) (Goldinger *et al.*, 1986). Since amiloride specifically blocks Na^+ channels in the apical (or outer) membrane of the epithelium, the above result indicates that the I_{SC} is entirely due to the active transport of Na^+ across the toad skin. Moreover, when amiloride was added to the medium bathing the outer surface of the skin exposed to 100 ATA for 100 min, I_{SC} was again reduced to a near zero value (not significantly different from zero) (Fig. 2). This indicates that no transepithelial ion currents have been introduced by high hydrostatic pressure and also that the reduction in I_{SC} observed

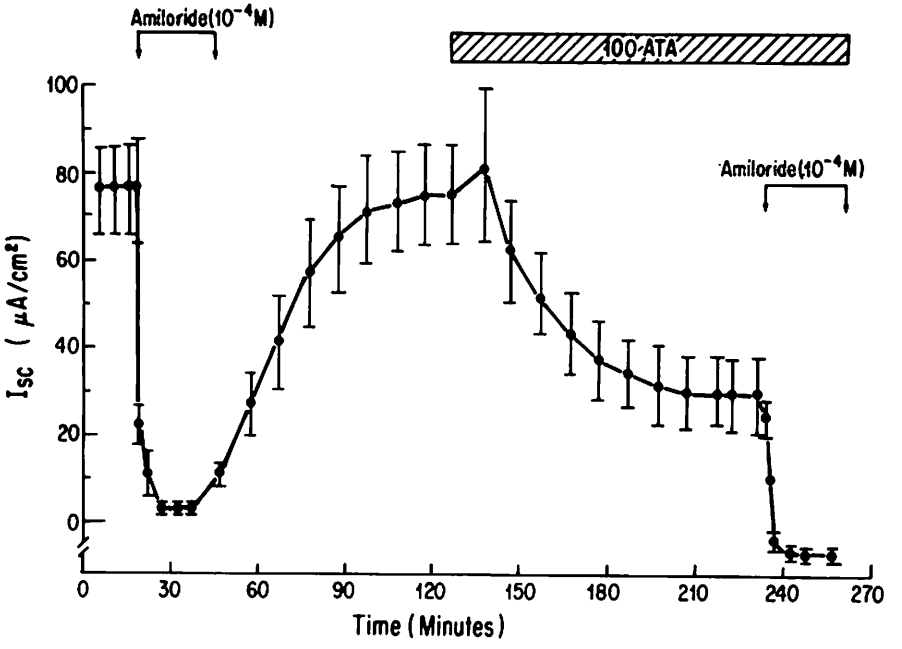

Fig. 2. Time course showing the influence of pressure in the presence and absence of amiloride on I_{SC} (short-circuit current) in toad skin. Data are $\bar{x} \pm$ SEM from three toad skins.

during the steady-state phase of the hyperbaric exposure is most likely due to the inhibition of active Na^+ transport.

In order to firmly establish the pressure effect on the active Na^+ transport process itself, the unidirectional fluxes of radioactive Na^+ ($^{24}Na^+$) across the toad skin were determined at 1 ATA and 90 ATA (Goldinger *et al.*, 1986). The Ussing chamber was modified to allow measurements of Na^+ flux during simultaneous measurement of I_{SC}. Because of technical limitations, the influx (from apical to serosal) and the outflux (from serosal to apical) were determined in different skins, short-circuited and exposed to 1 ATA first and then to 90 ATA. The mean value of I_{SC} at 1 ATA was 58 μA/cm² compared to Na^+ influx of 55, while the mean I_{SC} at 90 ATA was 43 μA/cm² compared to Na^+ influx of 40. Thus exposure of the skin to 90 ATA reduced both I_{SC} and Na^+ influx by 28%. (The outflux averaged only 0.1 μA/cm², representing less than 2% of the simultaneously measured I_{SC}.) These results establish, for the first time, the ionic

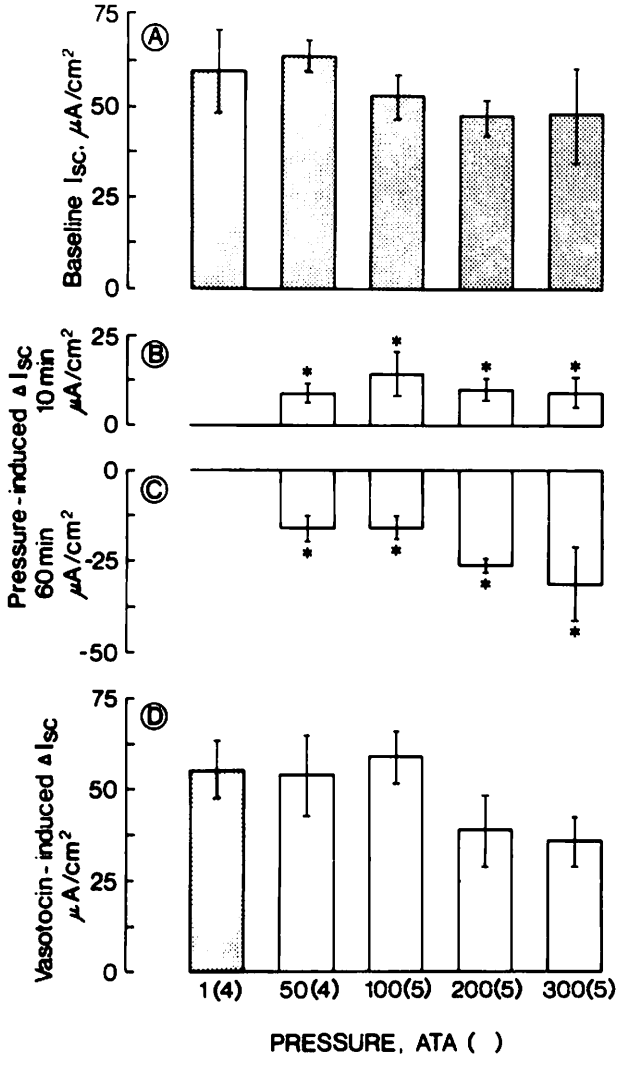

Fig. 3. Summary of short-circuit current I_{SC} responses to various levels of hydrostatic pressure and vasotocin: A. Base-line I_{SC} (at 1 ATA) immediately before compression, B. magnitude of transient increase in I_{SC} during first 10 min of compression, C. magnitude of decrease in I_{SC} observed at 60 min under pressure, D. magnitude of peak response to vasotocin. Each bar represents the mean (± SE) of the number of experiments indicated in parentheses after each pressure value. Shaded and open bars represent value obtained at 1 ATA and high pressures, respectively.

basis of I_{SC} at high pressure and allow us to conclude that active Na^+ transport is indeed inhibited by high hydrostatic pressure.

Typical experiments illustrating the stimulatory effect of vasotocin (an amphibian neurohypophysial hormone that is functionally analogous to the mammalian antidiuretic hormone) on I_{SC} are shown in Fig. 3 (Palmer, 1985). In these experiments, a supramaximal dose of vasotocin (100 mU/ml) was added to the medium bathing the inner surface of the skin exposed to various pressures for 1 h. Although the basic pattern of I_{SC} response to vasotocin was the same at all pressures, the magnitude of the peak response to vasotocin (ΔI_{SC}) decreased from 60 $\mu A/cm^2$ at 1-100 ATA to 35-40 $\mu A/cm^2$ at 200-300 ATA ($0.05<p<0.10$) (Fig. 3). Since the vasotocin effect is known to be mediated by cAMP, the above effect of pressure on the vasotocin effect could be attributed to either the pressure-induced inhibition of cAMP production or pressure-induced alteration of the cAMP effect on the Na^+ transport across the apical membrane under high pressure.

In order to differentiate these different possibilities, the direct effect of cAMP itself on I_{SC} was investigated at 300 ATA. As shown in Fig. 4, 1.0 mM cAMP added to the serosal bathing medium increased I_{SC} to the same level at both 1 and 300 ATA. These observations suggest that a hydrostatic pressure of 200-300 ATA might have interfered with one of the steps involved in the formation of cAMP. In addition, the fact that the overall Na^+ transport across the toad skin can be stimulated under high pressure by increasing the passive entry of Na^+ into the epithelial cell (across the apical membrane) by adding vasotocin or cAMP clearly indicates that the serosal membrane Na,K-ATPase activity (which represents the active transport step) can be activated readily even under high pressure when the supply of substrate (i.e., Na^+) is increased. It thus appears that the inhibition of base-line Na^+ transport observed under pressure may be primarily due to a decrease in the apical membrane Na^+ permeability rather than an inhibition of the Na,K-ATPase.

Although it is ideal to use techniques utilizing isotope tracers or intracellular microelectrodes for the measurement of membrane permeability, it is difficult to use them under high hydrostatic pressure. Fortunately, P^a_{Na} can be determined by transepithelial current-voltage (I-V) measurements, which has been readily adapted to our existing Ussing chamber apparatus at pressure. In this method, the K^+ concentration of the serosal bathing medium is elevated so that the K^+ permeable basolateral (serosal) membrane depolarizes, causing this membrane resistance to become very small with respect to the apical membrane. The preparation is then effectively reduced to an apical membrane barrier, so that P^a_{Na} can be determined by a Goldman-Hodgkin-Katz analysis from transepithelial

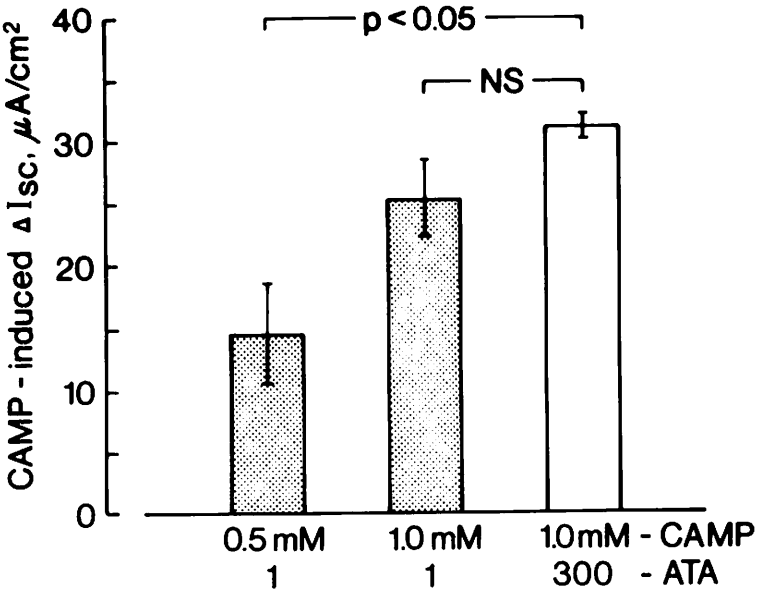

Fig. 4. Stimulatory effect of dibutryryladenosine-3',5'-cyclic monophosphate (cAMP) on short-circuit current I_{SC} at 1 and 300 ATA. Each bar represents the mean (± SE) of 3 experiments.

I-V measurements. Briefly, short duration voltage pulses are passed through the tissue by a computer driven voltage clamp and the current response is recorded. This process is repeated through a series of voltage and current amplitudes and an I-V plot is constructed by the computer. Amiloride is then added to the mucosal bath to inhibit I_{Na} and the process is repeated. An I_{Na}-V plot is then constructed by the computer from the difference in the pre-amiloride and amiloride I-V values.

Since the accuracy of these measurements depends on the ability of serosal bath K^+ elevation to depolarize the cells, Wilkinson *et al.*, (1985) measured the apical membrane potential directly with microelectrodes in the "split-skin" preparation at 1 ATA. In this preparation the basolateral membrane is exposed by removal of the corium of the tissue with the enzyme collagenase (Fisher *et al.*, 1980). When the K^+ concentration of the serosal medium of these tissues was raised from 5 to above 110 mM the membrane potential depolarized from -57 ± 5 mV to -13 ± 3 mV and the apical membrane fractional resistance increased from 0.93 ± 0.01 to

0.97 ± 0.01 in eleven impalements. Under these conditions, P^a_{Na} determined from transepithelial I-V analysis averaged 4.53×10^{-7} cm/sec, while P^a_{Na} determined by microelectrode measurements in the same tissues averaged 4.96×10^{-7} cm/sec. In other words, P^a_{Na} determined by transepithelial I-V analysis in K^+-depolarized tissues is a reasonably good estimate of P^a_{Na} in toad skin.

Having thus validated the above indirect technique in our hands, we applied it to the measurements of P^a_{Na} at 1 and 100 ATA in the same skins. Table 1 shows the apical membrane Na^+ permeability and intracellular Na^+ activities measured at 1 and 100 ATA. 100 ATA of hydrostatic pressure reduced both P^a_{Na} (by 40% which was very similar to the % inhibition of I_{SC} observed at this pressure) and $[Na^+]_C$ (Wilkinson *et al.*, 1987).

TABLE 1.

Apical Na^+ Permeabilities (P^a_{Na}) and Intracellular Sodium Activites $(Na^+)_C$

Condition	P^a_{Na} (nm/sec)	I^o_{Na} (μ A/sec)	$(Na^+)c$ (mM)
1 ATA (0 time)	72 ± 7	38 ± 7	6.0 ± 0.6
100 ATA (2 hrs)	28 ± 3	16 ± 2	1.8 ± 0.4

Values represent means ± SEM for the indicated number of skins n = 19.

P^a_{Na} was calculated from the short-circuit Na^+ current (I^o_{Na}), mucosal solution Na^+ activity $(Na^+)_O$, and $(Na^+)_C$, using Fick's law of diffusion. $(Na^+)_C$ was calculated from the Na^+ reversal potential (V_{Na}) and $(Na^+)_O$ using the Nernst equation. $(Na^+)_O$ was always 84 mM.

These results are consistent with a pressure induced decrease in apical membrane permeability to Na^+. Such a decrease could be a direct effect of pressure on apical membrane channels or a pressure induced breakdown in mechanisms which normally regulate those channels. The biphasic nature of the response and slow onset (60 min) suggests the latter possibility. It is clear from the literature that the apical membrane permeability is highly regulated. The need for such regulation is to maintain cell homeostasis during transepithelial ion transport. If the intracellar Na^+ is to be maintained constant under a variety of circumstances then the Na^+ pump rate at the basolateral membrane must match the Na^+ entry rate at the apical membrane. Thus there must be communication between the two membranes leading to regulation of P^a_{Na} (Schultz, 1983). While the exact mechanism of the regulation of P^a_{Na} has not been described, there is a considerable amount of evidence that P^a_{Na} is regulated by intracellular Ca^{++} which in turn is regulated by Na^+:Ca^{++} exchange (Chase and Al-Awqqati, 1983; Palmer, 1985). Hypothetically, the biphasic

nature of the pressure effect may be explained by an increase in apical Na^+ permeability followed by a pressure induced alteration in the normal compensatory response leading to the closure of apical channels. Obviously, the exact mechanism of the pressure effect on Na^+ transport awaits further experimentation.

III. "APPARENT" HYPOXIA AT PRESSURE

The observations of Chouteau on goats (1974) and Rokitka and Rahn (1978) on deer mice suggests that breathing normoxic gas mixtures (Po_2 = 0.2 ATA) at high pressure results in impaired performance, indicative of hypoxia. Human divers evidently also experienced discomfort since while normoxic He-O_2 gas mixtures were used in early saturation dives to relatively shallow depths, subsequent dives at higher pressure have generally used slightly hyperoxic gas mixtures. The apparent hypoxia at pressure probably represents an ensemble response including, for example 1) alveolar hypoventilation or impaired alveolar capillary exchange, 2) subclinical anemia associated with clearance of abnormal red cells or 3) a pressure induced alteration in the oxygen dissociation curve. The latter could be caused by a direct effect of pressure on intrinsic heme-oxygen affinity, altered binding of ATP or DPG or a Bohr response to changes in pH. Kiesow (1973, 1974), using human erythrocyte suspensions *in vitro*, reported a left shift of the oxygen dissociation curve at pressures up to 100 ATA (Kiesow *et al.*, 1973; Kiesow, 1974). This observation has been confirmed by Wells in erythrocyte lysates (Wells, 1976) and most recently by Reeves and Morin (1986), who reported an increase in O_2 affinity in whole blood and erythrocyte suspensions. In the latter investigation great care was taken to control for pressure sensitive buffers and pressure sensitive O_2 solubility. Stolp *et al.* (1984) found a left shift in oxygen dissociation curve in three divers compressed to 65.5 ATA during the Atlantis IV dive.

Thus, the *in vivo* measurement appears to be consistent with *in vitro* predictions. The mechanism of the left shift has been less well studied. As discussed by Reeves and Morin (1986) the left shift could be accounted for by a pressure induced change in the ionization of hemoglobin, raising intracellular pH. Protonation of the histidine groups in peptide chains, a process favored by pressure ($\Delta V = -18$ ml/mol), would decrease the net negative charge on hemoglobin and therefore change the red cell Donnan equilibrium. Such a change would alkalinize the red cell and result in a left shift in O_2 dissociation curve. This possibility was considered of minor consequence, since hemolysates and whole cells showed the same changes in P_{50}, suggesting a direct effect of pressure on heme-O_2 affinity. We have

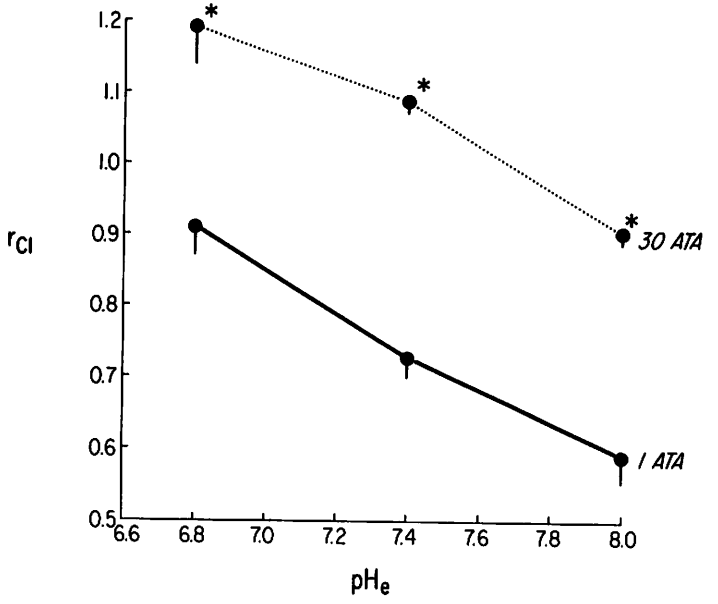

Fig. 5. Donnan ratio (r_{Cl} = $[^{36}Cl]_i/[^{36}Cl]_o$) in human erythrocytes as a function of medium pH at 1 and 30 ATA. Shown are means ± SEM, n = 4. *significantly different at $p<0.05$.

however, directly measured the chloride (^{36}Cl) distribution ratio (the Donnan ratio) (Goldinger *et al.*, 1981a; Goldinger *et al.*, 1981b) in red cell suspensions compressed from 1-30 ATA. As shown in Fig. 5 the Donnan ratio increased at pressure independent of pH. For reasons discussed above, such a change in the Donnan ratio would be expected to result in a left shift of the dissociation curve. The reasons for the discrepancy between these observations and those of Reeves are unclear. In the Reeves and Morin (1986) study no effect of pressure on P_{50} was observed at pH > 7.4. Since a change in the Donnan ratio would result in an increased pH in the cellular preparation but not the hemolysate, this might preclude seeing a difference between whole cells and hemolysates. Regardless of the mechanism, the overwhelming evidence suggests pressure causes a decrease in P_{50}. Both Stolp *et al.* (1984) and Reeves and Morin (1986) discussed the physiological consequences of such a change. Both groups of investigators concluded that the change in P_{50} was small and could be

readily compensated for, particularly in regard to O_2 delivery to muscle. As discussed by Stolp *et al.* (1986) however, there are changes, particularly in liver, which have been shown to be sensitive to changes in P_{50}, e.g. bile flow and redox state (Bakker *et al.*, 1976a; Bakker *et al.*, 1976; Versmold *et al.*, 1975). In this regard, one of the most consistent observations in human divers (reported in 7 different dives) is the elevation of serum transaminases which is normally pathognomonic of liver dysfunction (Goldinger *et al.*, 1987). Furthermore changes in red cell morphology, e.g. acanthocytes commonly seen in liver disease have been reported at pressure (Paciorek *et al.* 1984). Table 2 shows the serum enzyme profiles in two saturation dives. The liver may be extremely sensitive to small changes in oxygen delivery since its circulation is primarily via the portal vein. Lemasters *et al.* (1982) have reported reversible, focal changes in liver structure under hypoxic conditions leading to liver enzyme release. Doran and Garrard (1984) and Doran *et al.* (1985) have reported substantial evidence of compromised liver function at pressure. It is tempting to speculate that these observed changes in liver function are associated with decreased O_2 delivery, however, clearly such a hypothesis would require extensive investigation.

TABLE 2.

Serum Enzyme Profiles

	Seadragon IV (1978)			Seadragon VI (1984)		
Enzyme	Predive n=4	31 ATA n=16	Postdive n=4	Predive n=8	31 ATA n=8	Postdive n=8
SGPT	18.5±4.0	45.2±6.0*	49.0±17.6	7.88±0.58	18.9±4.0*	15.0±3.8
SGOT	15.7±3.1	30.8±4.3*	26.0± 7.8	16.1±1.4	24.4±3.9**	20.6±2.4
LDH	159.0±7.1	175.8±5.8	150.0± 7.6	110.6±6.6	117.3±9.3	109.6±6.8
ALP	57.0±4.7	68.7±3.5**	80.2± 6.5*	135.0±9.6	154.0±3.7**	153.1±4.3
CK	85.7±18.5	84.2±9.6	72.2±10.7	107.0±8.1	123.0±20.1	78.7±6.6*

Values are X ± S.E.M. in U/l at 37°C

Data were analyzed using Student's t Test

* $p<0.05$

** $p<0.01$

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7

U.S.-Japan Cooperative Diving Research (1973-1985)

S.K. Hong

I. HISTORY

The first joint meeting of the Diving Physiology and Technology Panel of the U.S.-Japan Joint Cooperative Program on Development and Utilization of Natural Resources (UJNR) was held in Tokyo on October 11 and 12, 1972. At that time, specific areas were identified which were to receive emphasis during a continuing program of cooperation. The meeting was concluded with the following note: "We should promote the exchange of information in these areas leading to future cooperative programs relating to the application of diving technology and physiology to marine resource development, caisson work, the fishing industry and basic medical science." However, no specific recommendations regarding implementation of this idea were made.

Since the University of Hawaii (UH) was very actively involved in broad-spectrum marine-oriented research, including "Human Peformance in the Sea", it occurred to some of us that we should take initiatives in developing a cooperative research program with Japan. The mere

fact that Hawaii is geographically and culturally closest to Japan than any other part of the U.S. had convinced us even more. When we brought our interest to the attention of Dr. Motohiko Matsuda, then the Director of Research and Development of the newly founded Japan Marine Science and Technology Center (JAMSTEC), who visited Hawaii at the end of October, 1972, to attend the 2nd "Inner Space Pacifica", we were pleasantly surprised to learn that he, too, had the same interest. Shortly after this preliminary contact between us, Dr. Matsuda returned to Hawaii in December, 1972 to formally discuss the plan. A tentative plan for 5-year Cooperative Research on Diving Physiology between UH and JAMSTEC was thus generated.

The underlying philosophy of this cooperative plan was to pool all resources existing on both sides in order to improve and facilitate the on-going diving research programs on each side. For this purpose, both groups agreed to plan several cooperative saturation diving experiments that would be jointly designed, carried out and evaluated. Three such experiments were carried out during 1973-1975.

At the third meeting of the UJNR Panel on Diving Physiology and Technology again held in Tokyo in July 1975, the scope of the UH-JAMSTEC Cooperative Diving Research Program was newly designated as the U.S.-Japan Cooperative Diving Research Program to solicit participation of non-UH or non-JAMSTEC affiliated scientists. At the same time, the U.S. Panel designated myself as the U.S. coordinator of this program while Dr. Matsuda was designated by the Japanese panel as my counterpart. Subsequently, Dr. Matsuda retired in 1984 and was succeeded by Dr. Hideaki Nakayama. In 1985, Dr. Motohiko Mohri joined the JAMSTEC as Director of Diving Research and became the third Japanese Coordinator of the U.S.-Japan Joint Research Program. In the meantime, I also requested that Dr. Yu-Chong Lin of the University of Hawaii be designated as the new U.S. Coordinator as of 1989 when the currently planned U.S.-Japan joint projects are expected to be completed.

Although the original plan was for 5 years (i.e., 1973-1978), this cooperative program is still on-going as of 1988 and is considered to be one of the most active U.S.-Japan cooperative research programs sponsored by the UJNR. Since 1973, six saturation dives (one in Hawaii and five at JAMSTEC) were conducted under the U.S.-Japan Cooperative Program, which led to the publication of 25 scientific papers (Table 1). Overall, 10 institutions and 47 investigators in the U.S. and Japan have actively participated in this program during the last 15 years (Table 2).

TABLE 1.
Profiles of Six U.S.-Japan Cooperative Research Dives Conducted During 1973-1985.

Number	Code Name	Year Conducted	Saturation Pressure (ATA)	Bottom Time (days)	Special Remarks	Publications*
1	Seatopia	1973	7	7	Conducted in Japan	Matsuda *et al.*, 1975a; Matsuda *et al.*, 1975b; Nakayama *et al.*, 1978
2	Hana Kai II	1975	18.6	17	Conducted in Hawaii Dry Dive	Dressendorfer *et al.*, 1977 Hong, 1978 Hong *et al.*, 1977a Hong *et al.*, 1977b O'Reilly, 1977 O'Reilly *et al.*, 1977 Smith & Hong, 1977 Smith *et al.*, 1977 Webb *et al.*, 1977
3	Seatopia	1975	11	17	Conducted in Japan Included immersion in 15°C water (resting)	Matsuda *et al.*, 1978
4	Seadragon IV	1979	31	14	Conducted in Japan Included immersion in 35°C water (resting)	Claybaugh *et al.*, 1984 Matsuda *et al.*, 1981 Nakayama *et al.*, 1981 Ohta *et al.*, 1981
5	Seadragon VI	1984	31	7	Conducted in Japan Dry Dive	Arita *et al.*, 1987 Claybaugh *et al.*, 1987 Goldinger *et al.*, 1987 Konda *et al.*, 1987 Matsui *et al.*, 1987 Nakayama *et al.*, 1987 Sagawa *et al.*, 1987 Shiraki *et al.*, 1987
6	New Seatopia	1985	31	17	Conducted in Japan Included immersion in 26°C water (exercising)	Manuscripts in preparation

*excluding abstracts

TABLE 2.

Participating institutions and investigators

U.S.A.		Japan	
Univ. of Hawaii —	Claybaugh	JAMSTEC —	Itoh
	Dressendorfer		Kirigaya
	Dwyer		Matsuda
	Hong (until 1975)		Mohri
	Hayashi		Murai
	Johnson		Nakayama
	Kurata		Naraki
	Lin		Takeuchi
	McDonough		Taya
	Moore		
	Morlock	U.O.E.H.* —	Konda
	O'Reilly		Matsuoka
	Pegg		Park
	Respicio		Sagawa
	Smith		Shiraki
	Strauss		
	Yelverton	Tokai Univ. —	Kuwahira
			Ohta
SUNY at Buffalo —	Farhi		Tamaya
	Goldinger		
	Hong (since 1975)	Nagoya Univ. —	Matsui
	Lundgren		Murata
	Morin		Seo
	Paganelli		Tamura
Webb Associates —	Troutman	Tsukuba Univ. —	Arita
	Webb		
		Jikei Med. College —	Saiki
U.S. Navy —	Frattali		Sudoh
Total	4 institutions 25 investigators		6 institutions 24 investigators

* University of Occupational and Environmental Health, Kitakyushu, Japan

II. MAJOR AND SPECIFIC OBJECTIVES

The overall objective of this U.S.-Japan Cooperative Diving Research Program was to examine the effects of prolonged hyperbaric exposure on various physiological systems. Based on this premise, we tried to avoid the development of the high pressure nervous syndrome (HPNS) as well

as decompression sickness by adopting a rather conservative rate of compression and decompression. Moreover, we had a minimum 7-day bottom time so that one could assess if any adaptation to the hyperbaric environment develops.

The following physiological functions have been investigated: energy balance; 2) heat exchange; 3) water exchange, especially renal function; 4) electrolyte balance, especially Na; 5) endocrine functions, especially the antidiuretic hormone (ADH) and renin-aldosterone systems; 6) cardiopulmonary functions, including the determinations of the maximal aerobic power, orthostatic tolerance, and cardiovascular fitness; and 7) certain cellular functions. All six dives were conducted using hyperbaric chambers under thermoneutral and slightly hyperoxic (Po_2 = 0.3-0.4 ATA) conditions. Helium was exclusively used as the diluent gas in all dives.

III. HIGHLIGHTS OF SPECIFIC ACCOMPLISHMENTS

A. Energy and Heat Balance

In some of the saturation dives conducted earlier before our program, it was recognized that the divers cannot maintain their energy balance during hyperbaric exposure. For instance, the divers involved in a University of Pennsylvania dive lost 4.0 kg during 17 days of exposure to pressure ranging from 13 to 37 ATA despite a high daily caloric intake (3,500 kcal/day) in the absence of any cold stress (Webb *et al.*, 1977). However, the mechanisms underlying such a failure to maintain body weight under high pressure were entirely unknown. Since the body weight is not only controlled by the dietary intake but is also determined by the state of the body fluid balance, it became necessary to carefully monitor the state of body fluid balance in assessing the mechanism of the body weight loss under high pressure.

In four U.S.-Japan cooperative diving experiments, we measured the body weight at 0700 h (after emptying the urinary bladder and before breakfast) while monitoring the body fluid balance. As summarized in Table 3, the changes in body weight in our studies were very modest. The body weight actually increased slightly at 7 ATA while it decreased by 0.7-1.0 kg at 31 ATA. In other words, our studies show that the divers are indeed able to maintain their energy balance at pressure up to 31 ATA. Why, then, did body weight decrease so markedly in the above cited University of Pennsylvania dive? The answer to this question is still unclear. The slight reduction in body weight observed in our dives reached a maximum during the first 3-5 days under high pressure and was accompanied by increased hematocrit and plasma protein concentration (Shiraki

TABLE 3.

Changes in body temperature and body weight during saturation dives

Pressure (ATA)	Chamber Temp. (°C)	Max. ΔTre (°C)	Max. ΔTsk (°C)	Max. ΔBW (Kg)	Caloric intake (kcal/day)	Reference
7	28-29	−0.2	−1.0	+0.3	~ 3,000	Matsuda *et al.*, 1975a
	25-26	−0.2	−1.8		~ 3,000	Matsuda *et al.*, 1975a
18.6	30-31	0	+0.2	−0.8	~ 3,440	Webb *et al.*, 1977
	27	0	−2.3		~ 3,800	Webb *et al.*, 1977
31	31.5 ± 0.5	0	−0.1	−1.0	~ 2,600	Konda *et al.*, 1987
	31 ± 0.2	0	−1.0	−0.7	~ 2,700	Nakayama *et al.*, 1981

et al., 1987). These findings indicate that the observed reduction in body weight may be attributed to a mild dehydration. In fact, the urine flow increased markedly during the early phase of hyperbaria in the absence of any increase in fluid intake (Hong *et al.*, 1977; Nakayama *et al.*, 1981; Shiraki *et al.*, 1987). As discussed below, this early hyperbaric diuresis is greater in magnitude than the diuresis observed during the steady state phase of hyperbaric exposure, and seems to induce a mild dehydration. Actual estimates of the daily energy expenditure by a means of 24-hr monitoring of O_2 consumption and/or CO_2 output also showed no significant increases during hyperbaric exposure (Webb *et al.*, 1977), thus indicating that there appears to be no energy imbalance to account for the reduction of body weight.

Although it has been recognized that the rate of body heat loss is markedly increased in the hyperbaric He environment, the exact level of the thermoneutral temperature is yet to be defined. In our dives, we measured both the rectal (T_{re}) and the mean skin (T_{sk}) temperatures of the divers during hyperbaric exposure while changing the environmental temperature. The data summarized in Table 3 show that small decreases in the environmental temperature under high pressure resulted in marked increases (~10-fold) in the degree of reduction of the mean skin temperature, indicating that the comfort temperature zone is very narrow in the hyperbaric He environment. Our data indicate that a thermoneutral temperature is clearly about 29°C at 7 ATA and increases to 30-31 and 31.5°C at 18.6 and 31 ATA, respectively.

B. Fluid Balance

Significant increases in urine flow were observed in practically all saturation dives conducted earlier, some of which were carried out in the presence of subtle cold stress. Although a similar hyperbaric diuresis was observed even in the absence of cold stress, the mechanism of this non-cold-related hyperbaric diuresis was very vague when we undertook our first dive in 1973. Since the urine flow represents only one avenue of body fluid exchange and is influenced by other factors such as the fluid intake and insensible and fecal water output, it required a systematic design of the study to delineate the mechanisms of the hyperbaric diuresis. Therefore, we adopted a comprehensive approach to the problem and investigated the patterns of daily water and electrolyte (Na and K) balance and of changes in water- and salt-regulating hormones. In fact, our studies represent one of the most comprehensive approaches to the problem and they have contributed much to the understanding of the mechanism of the hyperbaric diuresis.

With the onset of compression, the urine flow slowly increases reaching a maximum during the first 1-3 days at saturation pressure, and then it decreases somewhat to a steady-state level which is still significantly above the predive level. This diuresis is reversed during the decompression period, indicating that the diuresis is clearly pressure-dependent. As shown in Fig. 1, this diuresis is always accompanied by a decrease in urine osmolality, the rate of excretion of osmolal particles (U_{osm}). Despite this reduction in urine osmolality, the rate of excretion of osmolal particles ($U_{osm}V$) often increases significantly during exposure to a steady state pressure above 20 ATA or during the early phase of exposure to a pressure below 20 ATA (Hong *et al.*, 1977; Nakayama *et al.*, 1981). Such an increase in the excretion of osmolal particles is mostly due to the increased excretion of Na, K, inorganic phosphate (P_i) and urea (Hong and Claybaugh, 1989). In contrast to these increases in the excretion of osmolal particles, the plasma osmolality remains unchanged or decreases slightly; consequently, the osmolal clearance increases during dives, at least in part, accounting for the observed hyperbaric diuresis. However, the negative free water clearance relative to the osmolal clearance always decreases, clearly indicating that the hyperbaric diuresis is also, in part due to the increased excretion of free water. The rate of excretion as well as the plasma clearance of endogenous creatinine either remains unchanged or slightly decreases during hyperbaric exposure, indicating that increased excretions of osmolal particles and of free water are primarily due to inhibition of the tubular reabsorption of these substances.

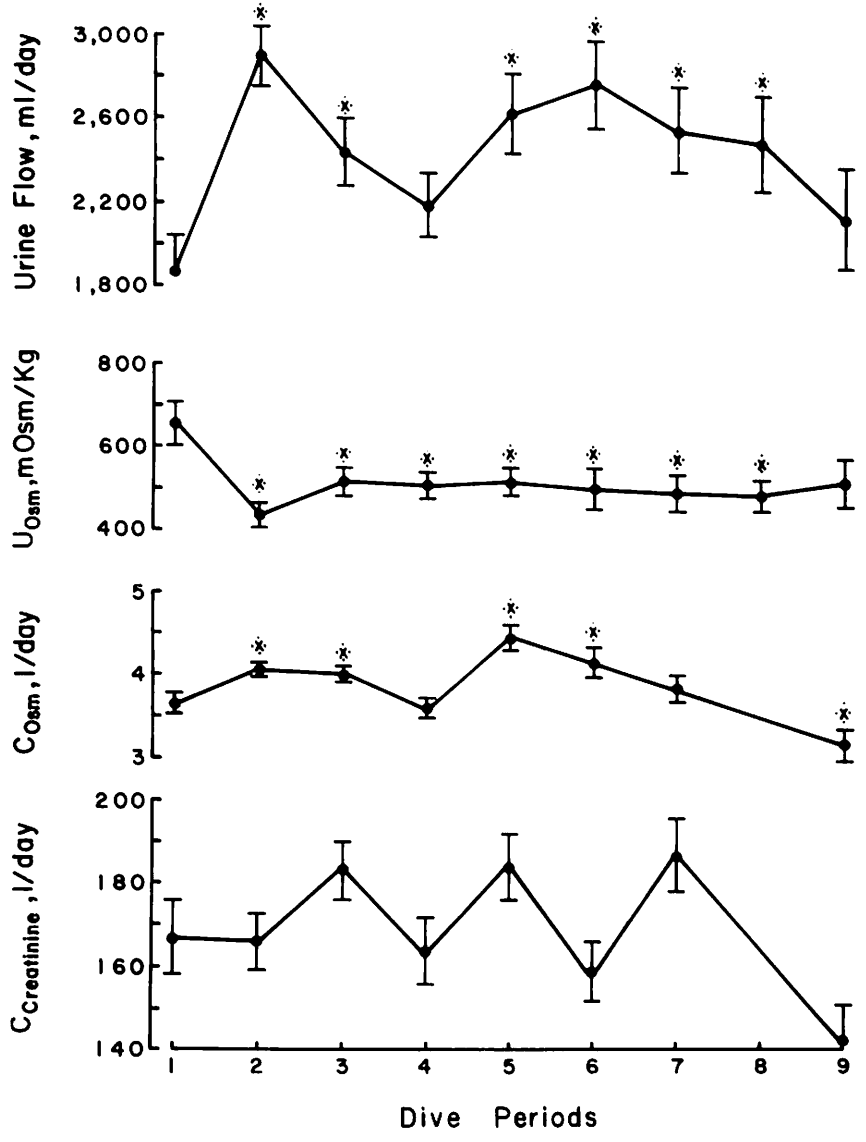

Fig. 1. Urine flow, urine osmolality (U_{osm}), osmolal clearance (C_{osm}), and endogenous creatinine clearance ($C_{creatinine}$) during the course of a dry saturation dive at 18.6 ATA. Periods 1 and 9 represent pre- and postdive 1 ATA control, respectively; periods 2-5, 18.6 ATA, 30-31°C; period 6, 18.6 ATA, 25-27°C; periods 7 and 8, decompression. Each period has 3 days. Vertical bars represent ± 1 SE. * indicates significant difference ($p<0.05$) compared to respective predive control. From Hong *et al.*, (1977) with permission.

Despite the presence of the sustained diuresis during a prolonged exposure to high pressure, there is no corresponding increase in the daily fluid intake to counteract the diuresis. In fact, the daily fluid intake tends to decrease slightly under high pressure. These observations led us to speculate that the divers must be progressively dehydrated under high environmental pressure. Since the average increment in daily urine flow during hyperbaric exposure over and above the predive level is approximately 500 ml/day, it was anticipated that the body weight would decrease by approximately 7 kg (= 500 ml/day x 14 days) during a 14-day exposure to high pressure. However, in one dive at 31 ATA for 14 days, the body weight was found to decrease by only ~0.5 kg (Nakayama *et al.*, 1981). Moreover, actual measurements of the total body fluid volume on the 12th day at 18.6 ATA showed no difference from that determined predive (Hong *et al.*, 1977). These observations can be explained only if the fecal and/or insensible water loss decreased correspondingly during hyperbaric exposure. Actual measurements of these variables showed that neither the fecal weight nor the fecal water content changed during the dive while the insensible water loss decreased by approximately 500 ml/day under high pressure (Hong *et al.*, 1977; Nakayama *et al.*, 1981). It thus appears that the increased urine flow observed at high pressure is accompanied by a corresponding reduction in the insensible water loss, whereby an overall body fluid balance is maintained at high pressure.

There are at least two reasons for the decrease of the insensible water loss at pressure. The first factor is the high chamber temperatures which would increase the water vapor pressure (at given relative humidity) of the environment into which the water vapor would diffuse according to the water vapor pressure gradient. Since the mean skin temperature is maintained at the comparable level at all pressures, the higher thermoneutral chamber temperature at pressure (see above) would tend to decrease the skin-to-environment water vapor pressure gradient even if the relative humidity is kept at the same level at high pressure. The second factor is the reciprocal relationship between gas diffusivity and pressure given by the Chapman-Enskog equation (Reid and Sherwood, 1966).

Based on these observations, we proposed that the primary mechanism of diuresis observed during the steady-state phase of hyperbaric exposure is the suppression of the insensible water loss. Such suppression of the insensible water loss during hyperbaric exposure would lead to an accumulation of free water, which would in turn decrease the plasma osmolality and inhibit the release of antidiuretic hormone (ADH). In fact, the plasma level of ADH has been shown to decrease significantly during exposure to 31 ATA (Fig. 2). Similarly, urinary excretion of ADH has

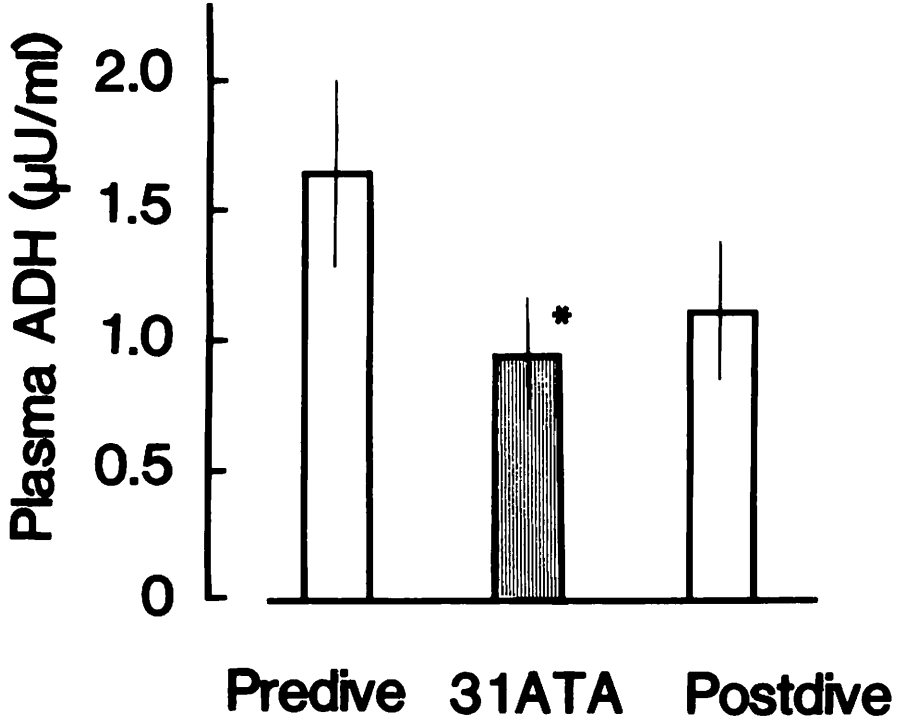

Fig. 2. Plasma antidiuretic hormone (ADH) concentration during predive, dive (at 31 ATA) and postdive days. Vertical lines on the top of the histogram bars represent ± 1SE. * indicates significant difference ($p<0.05$) compared to the respective predive control. Adapted from Claybaugh *et al.*, (1987).

been shown to decrease in many saturation dives (Hong and Claybaugh, 1989).

Although the suppression of the insensible water loss appears to be primarily responsible for the hyperbaric diuresis observed during a prolonged, steady-state phase of exposure to high pressure, it may not account for the diuresis observed during the early phase of hyperbaric exposure. For one thing, the diuresis develops too early during compression. When urine was collected on the compression day every other hour to determine the time course of the development of hperbaric diuresis in a 18.6 ATA dive (Hong *et al.*, 1977), it was found that the urine flow increased markedly 6 hr after the start of compression (at about 10 ATA). In other words, the diuresis seems to develop too soon to be accounted for by the suppression of the insensible water loss. Moreover, as stated above, this early hyperbaric diuresis was accompanied by increased excretion of

osmotic substances as well as by indirect evidence for dehydration (e.g., increases in the hematocrit and plasma protein concentration). In addition, the body weight decreases during the first several days of hyperbaric exposure after which it either becomes stabilized or slowly returns to the predive level. The time course of changes in body weight, plasma protein concentration, hematocrit and the plasma volume (calculated from changes in hematocrit values using Van Beaumont's formula) is illustrated in Fig. 3. Moreover, this early hyperbaric diuresis is not always accompanied by a reduction of the urinary ADH excretion but is sometimes associated with an increase in urinary ADH (Hong *et al.*, 1977). These characteristics of the early hyperbaric diuresis are clearly different from those of the steady-state hyperbaric diuresis (see above), suggesting that another mechanism not related to the suppression of the insensible water loss may be involved in the development of the early hyperbaric diuresis. However, this mechanism is totally unknown at present.

The hyperbaric diuresis is often associated with natriuresis, especially when the environmental pressure is above 10 ATA. However, this natriuresis is usually observed in the face of increased plasma renin and aldosterone levels as well as the urinary excretion of aldosterone (Claybaugh *et al.*, 1984; Claybaugh *et al.*, 1987; Hong *et al.*, 1977). Preliminary studies on atrial natriuretic factor (ANF) also indicate that there is no correlation between the plasma ANF level and natriuresis during hyperbaric exposure (unpublished data of Sagawa *et al.*). On the other hand, evidence has been accumulating that high hydrostatic pressure *per se* may inhibit the active Na transport across an epithelium (Hong *et al.*, 1984).

As stated above, the urinary excretion of K and P_i increases under high pressure (Hong *et al.*, 1977; Shiraki *et al.*, 1989). Although the mechanism for the above phenomena is not understood, the kaliuresis could be attributed to the increased plasma aldosterone level (see above). The plasma parathyroid hormone (PTH) level was determined in a 31 ATA dive in order to elucidate the mechanism(s) for the phosphaturia; however, the PTH level remained unchanged during hyperbaric exposure despite the persistent phosphaturia (Claybaugh *et al.*, 1987).

When the Japanese divers were exposed to a saturation pressure above 25 ATA, a marked increase in overnight urine flow was observed by JAMSTEC investigators (personal communication). This unexpected phenomenon was confirmed in subsequent dives conducted at 31 ATA, in which comprehensive studies were undertaken to elucidate the underlying mechanism (Nakayama *et al.*, 1981; Shiraki *et al.*, 1987).

Several parameters of renal function at 31 ATA are compared between the daytime (0700-2200 h) and the nighttime (2200-0700 h) and the results are shown in Fig. 4. These studies indicate that, although both

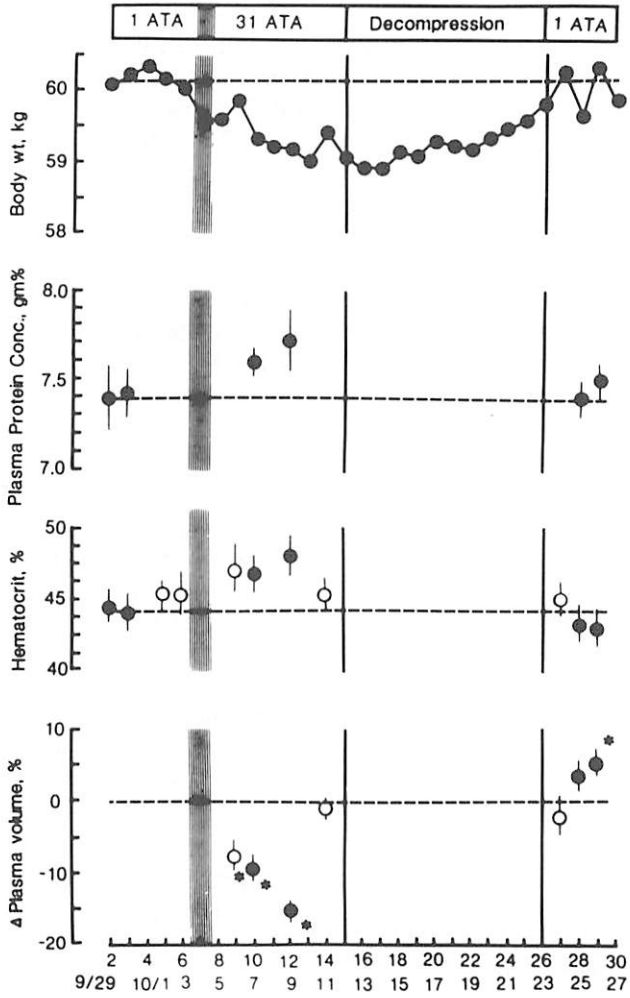

Fig. 3. Body weight, plasma protein concentration, hematocrit, and percent changes in plasma volume during the course of a 31 ATA dive. Body weight measurements and blood samples were carried out at 0700-0730 h. Solid circles represent the mean of all 4 subjects. Shaded area indicates the compression phase. Open circles represent the mean of 3 subjects. Vertical bars indicate ± SE. Plasma volume was calculated from changes in hematocrit values using Van Beaumont's formual (Beaumont, 1972). * indicates significant decrease ($p<0.05$) from the predive 1 ATA level. The abscissa shows both dive days (upper) and calendar days (bottom). From Shiraki *et al.* (1987) with permission.

diurnal (daytime) and nocturnal (nighttime) urine flows increased significantly during exposure to 31 ATA, the relative magnitude of the increase was much greater for nocturnal (150%) than for diurnal (50%). However, the endogenous creatinine excretion remained the same throughout the dive in both periods, indicating that the glomerular filtration rate is unchanged at pressure during both day and night.

Urine osmolality decreases to a comparable level at pressure in both periods, but the amounts of total osmotic substances excreted increases significantly only during the night. Overall, the diurnal excretion of K, P_i and urea increases while that of Na and Cl tends to decrease at 31 ATA, resulting in no net change in the excretion of total osmotic substances. Similarly, the nocturnal excretion of K and urea increases significantly at 31 ATA; however, in contrast to the diurnal pattern, the nocturnal excretion of both Na and Cl does not decrease but rather tends to increase while that of P_i and Ca remains the same at pressure. Moreover, the smaller relative increase in diurnal urine flow at pressure is entirely due to the corresponding reduction in the negative free water clearance while nocturnal diuresis at pressure is accompanied by both an increase in the osmolal clearance (accounting for 80-90% of the nocturnal increase in urine flow) and a slight decrease in the negative free water clearance (Fig. 4). In other words, hyperbaric diuresis is basically a water diuresis during the day and an osmotic diuresis at night. Increases in the excretion of Na, K, Cl and urea at night accounted for approximately 85% of the increase in the excretion of osmotic substances at 31 ATA.

In order to explore the endocrine mechanisms underlying the above described hyperbaric nocturia, Claybaugh *et al.* (1987) determined the diurnal and nocturnal excretions of ADH and aldosterone during the course of the Seadragon VI dive. They found that the urinary excretion of ADH decreased significantly at 31 ATA, but more importantly, the degree of inhibition was not different between day and night. As expected, the urinary excretion of aldosterone increased at 31 ATA but the degree of increase was again not different between day and night. Therefore, neither ADH nor aldosterone seems to play any role in the development of hyperbaric nocturia. Obviously, the circadian rhythm for certain physiological functions is influenced by high pressure. Most likely, the central nervous system controls such alteration of the circadian functions.

C. Cardiovascular Function

As observed in all previous saturation dives, we also observed a hyperbaric bradycardia in early cooperative dives at a relatively modest pressure

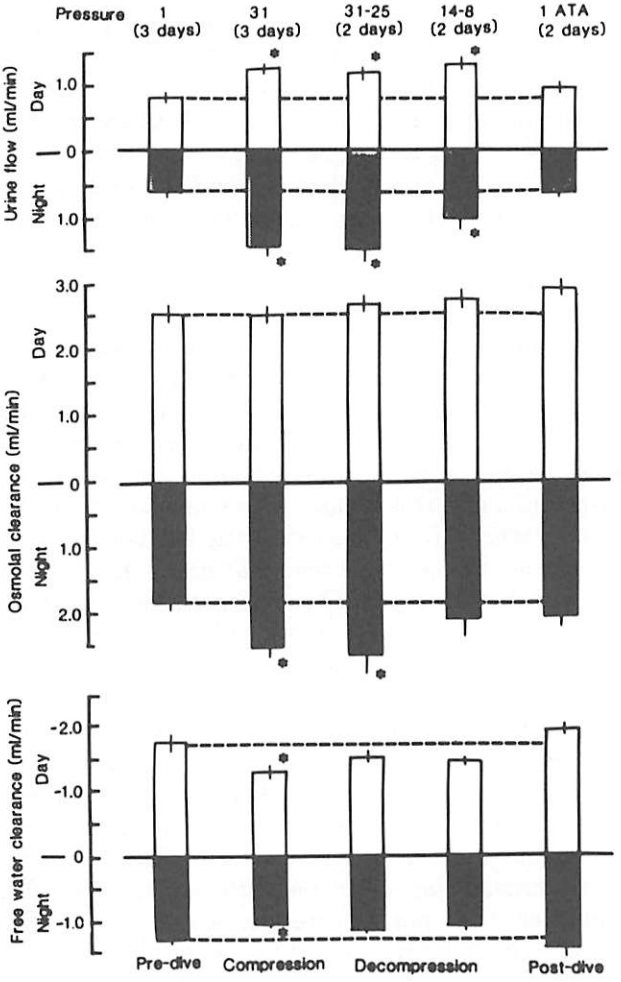

Fig. 4. Diurnal (daytime) and nocturnal (nighttime) urine flow and osmolal and negative free water clearances during various dive periods. Each bar represents the mean (± SE) of 12 (for 3 d) or 8 (for 2 d) measurements in 4 divers. Since blood samples were not taken during decompression, clearance values for early (31-25 ATA) and late (14-8 ATA) decompression periods were estimated by using the respective plasma values for 31 and postdive 1 ATA periods respectively. * $p<0.05$ as compared to the corresponding predive 1 ATA value. From Shiraki *et al.* (1987) with permission.

of 7 ATA (Matsuda *et al.*, 1975. We also observed that the degree of bradycardia was maximal during the first three days at 7 ATA, after which the bradycardia gradually disappeared during the rest of the hyperbaric period. Such a time dependence of the hyperbaric bradycardia was also confirmed in subsequent dives at 18.6 ATA (Smith *et al.*, 1977) and 31 ATA (Ohta *et al.*, 1981). In one of the latter dives, the bradycardia was already evident when the heart rate was measured during a 90 min compression stop at 5.5 ATA, exhibited maximal bradycardia when the pressure reached the ultimate level of 18.6 ATA, and then disappeared within 3 days under high pressure; during the postdive 1 ATA period, the heart rate increased significantly above the predive control level. A virtually identical pattern of the time-dependence of hyperbaric bradycadia (and its recovery) was observed during a 31 ATA dive (Ohta *et al.*, 1981). Another interesting observation is that lowering the ambient temperature during steady-state hyperbaric period did not cause or potentiate the bradycardia when it increased blood pressure and oxygen consumption (Matsuda *et al.*, 1975; Smith *et al.*, 1977).

In order to study the behavior of the cardiac output while the heart rate undergoes time-dependent variations, the stroke volume was determined by a means of impedance cardiography (Smith *et al.*, 1977). Overall, there was an inverse relationship between the heart rate and the stroke volume such that the cardiac output remained unchanged even at the peak of hyperbaric bradycardia. The use of impedance cardiography also provided another piece of information about the thoracic conductance changes during hyperbaric exposure. With the onset of compression, the thoracic conductive volume (which reflects the intrathoracic blood volume) increased linearly until the pressure was increased to 12.3 ATA when the urine flow increased markedly, suggesting that the early hyperbaric diuresis may be related to the increase in the thoracic blood volume. The reason for the increase in the thoracic conductive volume during the early hyperbaric period is not clear, although it could be attributed to the increased negative intrathoracic pressure observed during inspiration of a denser gas mixture (Smith *et al.*, 1977).

As stated earlier, there is evidence to indicate that a modest dehydration develops during the early phase of compression. In addition, the divers are confined to a limited space, often with minimal activities. Therefore, it is not unreasonable to suspect that a state of cardiovascular deconditioning may develop during saturation diving. Accordingly, a cardiovascular index of deconditioning was assessed, in a recent dive at 31 ATA, from the measurements of blood pressure and heart rate before and during 15 min of a 90° body tilt (Arita *et al.*, 1987). The results indicated that a state of cardiovascular deconditioning is already evident within

24 h of exposure to 31 ATA. In fact, one diver fainted during the tilt at 31 ATA while no such episode occurred before or after the hyperbaric exposure. The fact that cardiovascular deconditioning occurs within 24 h of hyperbaric exposure strongly suggests that the initial phase of cardiovascular deconditioning is not related to physical confinement but to the factor(s) directly or indirectly associated with the high pressure *per se*.

In the above described 90° body tilt studies, the changes in plasma renin and ADH levels were also determined (Matsui *et al.*, 1987). The results were very interesting in that hyperbaria enhanced renin but eliminated ADH responses to head-up tilt. During the 1 ATA control period, the 90°body tilt induced marked increases in both plasma renin and ADH. The failure of the ADH system to respond to the 90° body tilt at high pressure suggests that the baroreceptor sensitivity is perhaps inhibited by high pressure. On the other hand, the baroreceptor sensitivity is not inhibited by the enhanced renin response but the ADH system may be under the influence of strong inhibitory forces such as the reduction of plasma osmolality and/or the increased intrathoracic blood volume (see above). Regardless of the mechanisms underlying these interesting phenomena, it is important to find out if and how these differential endocrine responses to the 90° body tilt at 31 ATA are related to the above described cardiovascular deconditioning.

D. Pulmonary Function

The vital capacity (VC) and its subdivisions were determined by spirometry during a 18.6 ATA dive (Smith *et al.*, 1977), and the results are shown in Table 4. In nonsmokers, the VC decreased by ~300 ml while it increased in smokers by ~400 ml during the first week at pressure before tending to fall with time. Compared to predive, the expiratory reserve volume (ERV) was increased ~600 ml while the inspiratory capacity (IC) fell by ~400 ml at depth. Most interestingly, the residual volume (RV) increased (by 530 ml) in all divers as a result of dive and remained increased in 4 (out of 5) subjects even 1 year later. Similar studies conducted at 31 ATA more recently gave qualitatively comparable results (Table 4), with the exception of the RV which remained unchanged (Ohta *et al.*, 1981). Typically, these lung volume changes observed at pressure are seen when subjects are exposed to an increased airways resistance (Campbell, 1968). Since the relationship between increased gas density and increased airway resistance is firmly established (Maio and Farhi, 1967), the lung volume changes observed during hyperbaric exposure may be expected.

TABLE 4.

Lung volume changes (ml,BTPS) during saturation diving

Pressure (ATA)	ΔVC	ΔIC	ΔERV	ΔRV	Reference
18.6	+250	−375	+629	0.53*	Smith *et al.*, 1977
31	+150	−280	+530	0	Ohta *et al.*, 1981

*Postdive value

Studies on other respiratory functions at pressure showed expected decreases in forced expiratory volume, maximal voluntary ventilation and maximal expiratory flow rate in a pressure dependent manner over pressure range of 1-31 ATA (Ohta *et al.*, 1981). However, the air trapping index, which was derived from the difference between VC and forced vital capacity and expressed at % of VC, was within normal limits throughout the dive. Interestingly, the peak expiratory flow showed a tendency to recover during a 2 week exposure to 31 ATA while no such tendencies were apparent in maximal voluntary ventilation and forced expiratory volume.

The ventilatory response to CO_2 at 31 ATA was significantly depressed to 83% of the response at 1 ATA at an alveolar P_{CO_2} of 50 torr and to 79% at an alveolar P_{CO_2} of 60 torr (Fig. 5). Although $P_{0.1}$ at 31 ATA was slightly higher than 1 ATA at each level of alveolar P_{CO_2}, there were considerable variations among the divers, and the mean value at 31 ATA was not significantly different from that at 1 ATA. However, it is not clear whether the $P_{0.1}$ value determined at high pressure also solely reflects central inspiratory activity (CIA). Since it is possible that there may be a change in the relation between CIA and inspiratory muscle shortening, the interpretation of the $P_{0.1}$ data should be done with caution.

Maximal inspiratory pressures increased gradually but significantly during a 2-week exposure to 31 ATA while maximal expiratory pressures remained essentially unchanged (Ohta *et al.*, 1981). The mechanism behind the increased maximal inspiratory pressure at depth is obscure. Training is an unlikely explanation because the postdive value was not different from the predive value. It is possible that the different compressibility of the gas in the lungs at 31 ATA and 1 ATA may have resulted in differences in chest volume and, therefore, in the length and power exerted by the inspiratory muscles.

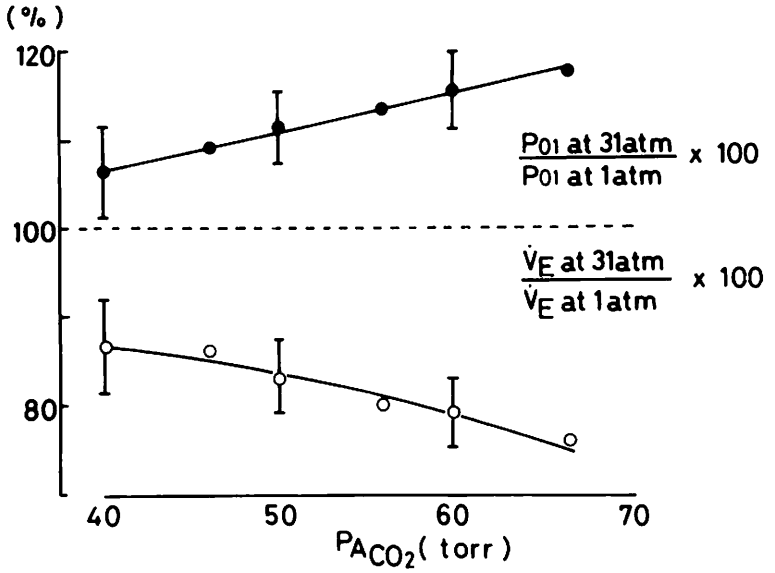

Fig. 5. $P_{0.1}$ and ventilatory responses to CO_2 at various alveolar CO_2 pressures ($PACO_2$). Values at 31 ATA expressed as percent of those at 1 ATA. Vertical bars represent ±1 SE. From Ohta *et al.* (1981) with permission.

E. Maximal Aerobic Power and Exercise Capacity

Maximal work capacity, maximal aerobic power and maximal exercise endurance were determined before, during and after exposure to 18.6 ATA (Dressendorfer *et al.*, 1977) and 31 ATA (Ohta *et al.*, 1981), and the results are summarized in Table 5. In the 18.6 ATA dive, it may be noted that both the maximal aerobic power and the maximal exercise endurance time increased significantly at depth a long as the P_{O_2} of the environmental gas was kept at a slightly hyperoxic level of 0.3 ATA. However, when the level of P_{O_2} of the breathing gas was artificially lowered to 0.2 ATA at depth, both the maximal aerobic capacity and the maximal exercise endurance time decreased to the corresponding predive level. These results indicate that the divers are able to maintain their maximal aerobic capacity at 18.6 ATA despite the ~30% reduction in the maximal voluntary ventilation. In other words, the ventilatory capacity does not seem to be a major factor limiting the maximal exercise capacity. The maximal ventilation during maximal exercise was only 68% of maximal voluntary ventilation at 1 ATA while the corresponding value increased to 85% at 18.6 ATA.

At 31 ATA, the maximal voluntary ventilation decreased by ~45% as compared to 1 ATA. Moreover, both maximal exercise capacity and maximal

TABLE 5.

Maximal exercise capacity ($\dot{W}$), maximal aerobic power ($\dot{V}O_2max$) and maximal exercise endurance time (ET)

Pressure (ATA)	PIO_2** (ATA)	$\dot{W}$ (W)	$\dot{V}O_2max$ (l/min;STPD)	ET (min)	Reference
1 (predive)	0.2	230	3.10	4.19	
18.6	0.3	232	3.20*	6.22*	Dressendorfer *et al.*, 1977
18.6	0.2	230	3.10	4.58	
1 (postdive)	0.2	230	3.10	—	
1 (predive)	0.2	240	3.11	—	
31	0.4	205*	2.71*	—	Ohta *et al.*, 1981
1 (postdive)	0.2	230	2.89*	—	

* significantly different from the corresponding predive 1 ATA value.

** O_2 pressure of the breathing gas

aerobic power decreased significantly at 31 ATA despite the fact that the Po_2 of the chamber gas was raised to 0.4 ATA at depth. This means that the exercise capacity at 31 ATA seems to be limited by the ventilatory capacity. In fact, in this 31 ATA dive, the maximal ventilation during maximal exercise were equivalent to 74% of the respective value of the maximal voluntary ventilation at both 1 and 31 ATA. However, there may be other additional factors limiting the exercise capacity and aerobic power. As indicated in Table 5, both the maximal exercise capacity and the maximal aerobic power did not fully recover during the postdive control period. This suggests that there may be a time-dependent loss of exercise capacity, most probably due to the confinement in a limited space with minimal activities. In fact, the divers were not allowed to engage in regular daily exercise in the 31 ATA dive while the divers in the 18.6 ATA dive were encouraged to exercise regularly using a bicycle ergometer installed inside the hyperbaric chamber.

As discussed above, the resting heart rate decreases during the first few days under high pressure, after which it returns to the predive level. Although the heart rate increases linearly during exercise at depth, the heart rate (HR) at a comparable level of exercise was significantly lower at pressure than at 1 ATA (Dressendorfer *et al.*, 1977; Ohta *et al.*, 1981). In other words, the O_2 pulse ($\dot{V}o_2$/HR) was consistently higher at pressure as compared to that at 1 ATA. On the other hand, the ventilatory equivalent

($\dot{V}_E/\dot{V}O_2$) significantly decreased while the cardiac output was well maintained during maximal exercise at depth.

F. Responses to Water Immersion

A simple head-out immersion induces profound changes in cardiovascular, respiratory, renal and thermoregulatory functions even at 1 ATA. Since actual dives in the sea involve both water immersion and hyperbaric exposure, it is important to study the effects of water immersion under high pressure. Therefore, we studied the effects of immersion in water of 15°C at 11.5 ATA (Matsuda *et al.*, 1978) and in water of 34-35° at 31 ATA (Matsuda *et al.*, 1981). In these studies, the divers were resting during head-out immersion and no physical exercise was allowed.

In the 11 ATA dive (Matsuda *et al.*, 1978), cardiorespiratory, thermal and renal responses to a 30-min head-out immersion in 15°C water were studied at 1 ATA air and 11 ATA He-O_2 environments in divers wearing dry suits. Cardiorespiratory responses to immersion (reductions in heart rate, ERV, VC, and thoracic impedance; and increases in stroke volume, cardiac output, and IC) were comparable at both 1 and 11 ATA. However, the thermal response to immersion (a reduction in mean skin temperature and increase in skin heat flux and suit conductance) were significantly greater at 11 ATA as compared to those at 1 ATA. The rate of urinary excretion of norepinephrine increased significantly during and after immersion at 11 ATA but not at 1 ATA. Moreover, the immersion diuresis was greater and lasted longer at 11 ATA than at 1 ATA although there was no difference in the endogenous creatinine clearance. As expected, this immersion diuresis ws accompanied by a significant natriuresis and the decreased urinary excretion of both aldosterone and ADH at 1 ATA. At 11 ATA, the rate of urinary excretion of these hormones before immersion was lower compared to that at 1 ATA and did not change significantly during immersion despite the presence of diuresis and natriuresis (Fig. 6). These results indicate that immersion in a hyperbaric He-O_2 environment presents a greater cold stress than that at 1 ATA air, and also that the immersion diuresis and natriuresis at high pressure may be modulated by a factor or factors other than inhibition of aldosterone and ADH.

In the 31 ATA dive (Matsuda *et al.*, 1981), cardiovascular and renal responses to a 2-hr immersion in thermoneutral water (34-35°C) were studied in the resting subjects wearing only shorts. Both rectal temperature and O_2 consumption remained unchanged before, during and after immersion at both 1 and 31 ATA, indicating that the thermoneutral temperature of water is not altered at high pressure. It was also noted that

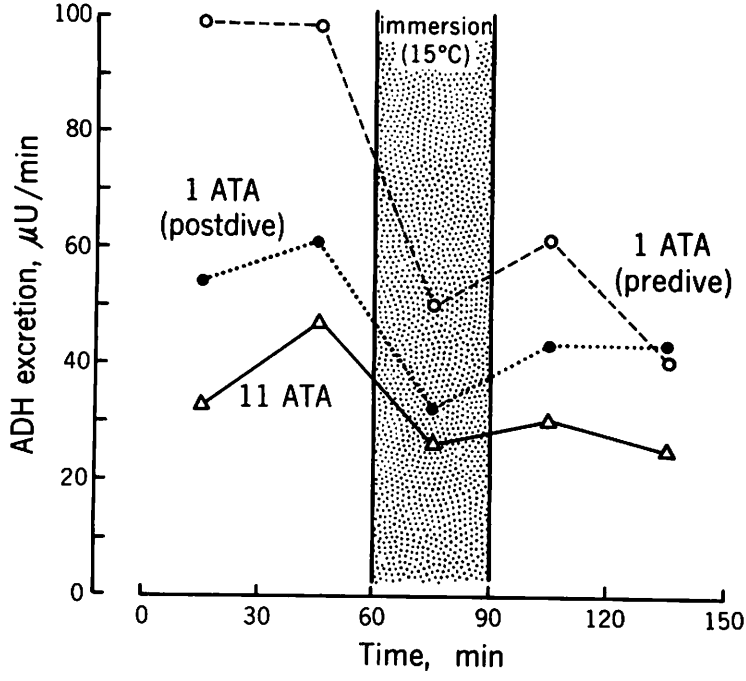

Fig. 6. Urinary excretion of antidiuretic hormone (ADH) before, during (shaded area) and after 30 min head-out immersion in 15°C water at 1 and 11 ATA. Qualitatively similar trend was observed for the urinary excretion of aldosterone. Adapted from Matsuda *et al.* (1978).

the mechanical effects of immersion on the static lung volume (reduction in ERV and VC and an increase in IC) are not altered by pressure. Although qualitatively similar changes in cardiac and renal functions were observed during immersion at both pressures, there were significant, quantitative differences in the response among three experiments carried out at 1 ATA predive, 31 ATA and 1 ATA postdive. These differences were particularly noteworthy for the magnitude of the immersion-induced increases in stroke volume (and cardiac output) and urine flow. For instance, the magnitude of the immersion-induced increase in stroke volume was 65 ml at 1 ATA predive as compared to 41 at 31 ATA and 31 ml at 1 ATA postdive. In other words, there was a progressive reduction in the magnitude of immersion-induced increase in stroke volume as the

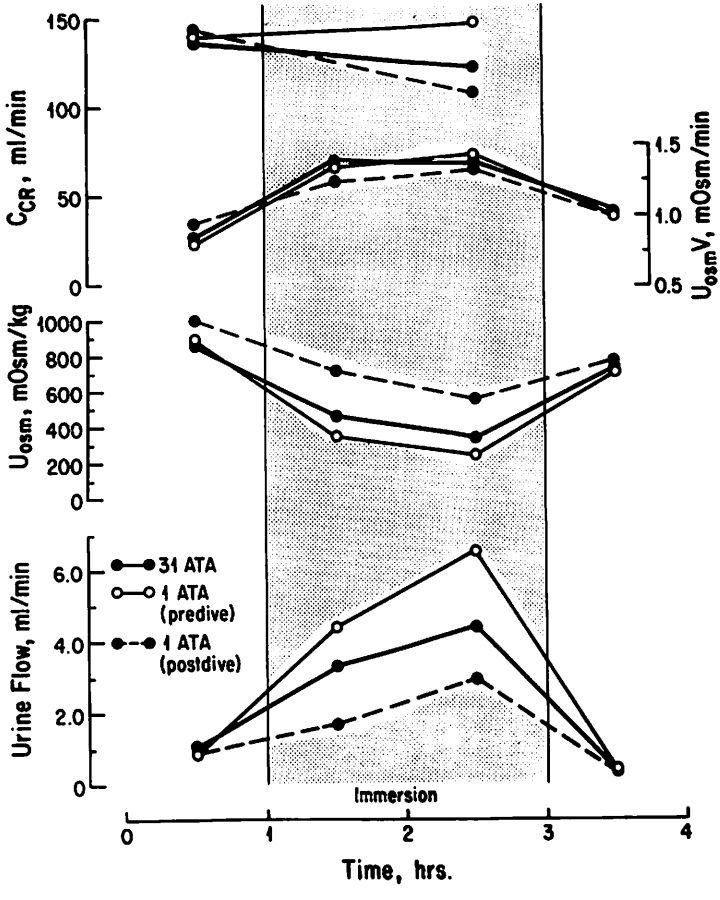

Fig. 7. Urine flow, urine osmolality (U_{osm}), urinary excretion of osmolal particles ($U_{osm}V$), and endogenous creatinine clearance (C_{cr}) before, during (shaded area), and after 2 hr head-out immersion in 34-35°C water. Adapted from Matsuda *et al.* (1981).

dive progressed. Identical trends were observed for the degree of immersion-induced diuresis but not for the immersion-induced natriuresis (Fig. 7). Thus, the immersion diuresis was the greatest during predive 1 ATA and decreased to an insignificant level during the postdive ATA period. Such a time-dependent attenuation of the immersion diuresis is most

likely related to the corresponding time-dependent changes in the stroke volume response to immersion. As stated above, both the maximal work capacity and maximal aerobic power decreased progressively during the long 31 ATA dive period. Therefore, it is tempting to speculate that time-dependent attenuation of immersion-induced stroke volume and renal responses may be related to the progressive decline in physical fitness. But, again, it is not clear to us how they could be related to each other. At least in this study, the creatinine clearance during immersion decreased progressively as the dive progressed, which could explain the immersion diuresis data. Although urinary excretions of both ADH and aldosterone did not show any significant reduction during immersion either before, during or after exposure to 31 ATA, an overall negative correlation between the urine flow and the rate of ADH excretion was observed. Moreover, the plasma level of aldosterone decreased significantly during immersion at both 1 and 31 ATA. These results suggest that both ADH and aldosterone may play some role in the development of renal responses to head-out immersion. The urinary excretion of prostaglandin E_2 (PGE_2) increased during immersion at both 1 and 31 ATA, a finding consistent with a view that the immersion diuresis is, at least in part, due to an increased release of PGE_2 (Epstein, 1978). However, there was no difference in the PGE_2 excretion between 1 and 31 ATA either before or during immersion.

IV. SUMMARY

During 1973-1978, six saturation diving experiments have been carried out under the U.S.-Japan Cooperative Diving Research Program supported by UJNR. All of these dives have dealt with He, and the effects of a prolonged hyperbaric exposure on various physiological functions have been studied. The results obtained from these studies may be summarized as follows:

1. The divers are able to maintain their energy balance during a long period of exposure to pressure up to 31 ATA.
2. Comfort temperatures for prolonged stay in hyperbaric He has been defined.
3. The mechanisms of hyperbaric diuresis has been partly elucidated.
4. A significant natriuresis is often observed during hyperbaric exposure, but the underlying mechanism is not clearly understood.
5. Hyperbaric nocturia is observed at pressure above 25 ATA, but the underlying mechanism is not understood.

6. Hyperbaric bradycardia is observed in all dives, but it is transient and disappears within a few days under high pressure.
7. Hyperbaric bradycardia is accompanied by an increase in the stroke volume and consequently, the cardiac output remained unchanged.
8. There is indirect evidence suggesting that a state of cardiovascular deconditioning exists at 31 ATA.
9. Hyperbaric enhances renin but eliminates ADH response to a 90° tilt.
10. There are changes in the vital capacity and its subdivision upon hyperbaric exposure.
11. The ventilatory response to CO_2 is significantly depressed at 31 ATA.
12. Both maximal aerobic power and maximal workload are well maintained at 18.6 ATA but decreased significantly at 31 ATA.
13. A head-out immersion in 15°C water resulted in a greater diuresis and cold stress at 11 ATA than at 1 ATA.
14. The stroke volume and renal responses to a head-out immersion in 30-35°C are attenuated at 31 ATA as compared to those at 1 ATA.

ACKNOWLEDGEMENT

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8

Thermal Regulation in Dry and Wet Hyperbaric Environments

Sueko Sagawa and Keizo Shiraki

I. INTRODUCTION

When a man is confined in a high pressure He-O_2 atmosphere he is far more affected by the environmental temperature than a man living in air at normal atmosphere. Similarly, water immersion places a much more severe thermal load on him than when in air of the same temperature. These are primarily due to the high thermal conductivity, specific heat

and density of that environment. Because of the great cooling effect of the environment, his thermoregulatory mechanisms are believed to be incapable of preventing a decrease in internal body temperature during a prolonged exposure to low temperature. However, it is possible for humans to possess a physiological adjustment to keep their body heat balance in extreme thermal environments. If this is also the case in a hyperbaric environment, the effective adjustment of the body will be achieved mostly by an appropriate redistribution of blood flow and readjustment in countercurrent heat exchange in the heat exchange organs. Therefore, careful observations of the heat exchange mechanisms in thé tissues are required to delineate the thermal regulation in hyperbaric environments.

This review paper is constructed on the basis of two different sets of observations: 1) the effect of human thermoregulation in high pressure gaseous environments and 2) thermal balance and physiological responses of man during simulated dives in water of various depths. Firstly, besides determining a correlation of permissible temperature and pressure of gaseous environments, various circulatory functions during superimposed heat loading have been described. Secondly, thermoregulatory mechanisms in wet-suited divers have been described in connection with the depth, including underwater exercise at various water temperatures. Is a man capable of preventing the increase in heat drain by altering his physiological adjustment as the environmental pressure increases? To answer this important question, the lower critical water temperature has been determined at various pressures because at this particular temperature insulation of the tissues becomes maximum as a result of maximum vasoconstriction. Measurement of tissue insulation in different parts of the body is helpful to delineate the problem. The effect of thermal balance during exercise at various water temperatures has been determined.

These observations indicate that humans in dry and wet hyperbaric environments are capable of adjusting thermal homeostasis, to a certain extent, by means of changing the ratio of blood flow distribution between the proximal and distal parts of the body.

II. THERMODYNAMICS — A BASIC CONCEPT

In normal humans, fluctuation of the core body temperature is very small in the face of large alterations in environmental temperature. On the other hand skin temperature has great variability. Under most conditions body temperature represents a balance between heat production and heat dissipation in the body. At a steady state in general, heat exchange between the body and the ambient environment can be expressed

by the following equation:

$$M - E \pm C \pm R = S$$

where **M**, is the rate at which heat is produced by metabolism; **E**, the rate of heat lost by the evaporation of water; **C**, the rate of heat loss (or gain) by convection-conduction; and **R**, the rate of heat loss (or gain) by radiation. In the many instances of temporary non-steady state, the right side of the equation, defined as heat storage (S) is not zero. For example, when metabolism exceeds the heat loss by evaporation, convection, and radiation during vigorous exercise, the heat storage becomes positive. On the other hand, it gives a negative value when, on exposure to cold, heat loss is great and the compensatory increase in metabolism is somewhat delayed.

Heat loss in man is effected mainly through the skin and partly through the respiratory tract. Heat is lost through the skin for the most part by radiation, convection, and evaporation. The relative amounts of heat loss from the body through the three avenues vary with conditions. When a man is seated in a room of moderate temperature, radiation and convection account for about 77% and evaporation, including other miscellaneous avenues for the rest of the total heat loss (DuBois, 1936).

The range of ambient temperature between 28 and 31°C (Erikson *et al.*, 1956) can be considered the zone of vasomotor regulation of body temperature in an unclothed man, which is termed as thermoneutrality. In this zone, heat loss may be altered by changing the cutaneous vascular tone, in the main, of the limbs. The thermal equilibrium may be maintained without either sweating or increasing metabolism. Namely, the blood flow of the skin can adjust the flow of heat from the core to the periphery. An expression of the delivery of heat from the core to surface is called tissue conductance, and the reciprocal of conductance is defined as tissue insulation. The lowest end of the zone of vasomotor regulation is called "the critical temperature". Below this temperature, the core temperature cannot be maintained without increasing metabolic heat production, i.e., shivering. Convection increases because of the body movements during shivering, leading to an increase in total heat loss and hence conductance.

At the neutral temperature heat loss and heat production are approximately the same and skin vessels are somewhat dilated. Below this zone peripheral vessels constrict, and above it they dilate progressively and vaporization suddenly increases because of sweating. In normal atmospheric pressure (1 ATA), the range of this temperature shifts somewhat lower (between 20 and 30°C) in a lightly dressed and mildly active man.

III. THERMAL BALANCE IN WATER

That the human body cools faster in water than in air of the same temperature is well recognized. The main reasons for this are that the specific heat of water is 1,000 times, and thermoconductivity is 25 times greater than that of air. This direct loss of body heat in the water is a dominant thermal problem of divers and, in fact, dive duration is primarily determined by this body heat loss (Kang *et al.*, 1963; Kang *et al.*, 1965).

A. Heat Transfer Coefficient of Water and Critical Water Temperature

The primary avenue of heat transfer from the body surface to the surrounding water is convection and conduction. The combined heat transfer coefficient for convection and conduction varies from 38 kcal/(m^2·h·°C) in still water to an average of 55 kcal/(m^2·h·°C) in stirred water. Shivering in still water raises the heat transfer coefficient from 38 to 43 kcal/(m^2·h·°C) (Boutelier *et al.*, 1971). For the combined heat transfer coefficient, the conductive component is about 9 kcal/(m^2·h·°C) regardless of the degree of stirring, while the convective heat transfer coefficient increases from 81 kcal/(m^2·h·°C) in still water to 344 kcal/(m^2·h·°C) at a swimming speed of 0.5 m/sec (Rapp, 1971). These values are 100 to 200 times higher than those in 1 ATA air (1 to 2 kcal/(m^2·h·°C). Despite such a marked difference in the convective heat transfer coefficient between air and water, heat loss in water has been estimated to be only about two to five times that in air at the same temperature, indicating that the heat loss in water is largely limited by the body (core-to-skin) tissue insulation and not by the skin-to-core heat transfer coefficient.

The range of neutral temperature for a resting unprotected man immersed in water is between 33 and 35°C, and varies inversely with the subcutaneous fat thickness of the subject (Craig and Dvorak, 1966; Smith and Hanna, 1975). Moreover, the critical water temperature (T_{cw}), i.e., the lowest end of the zone of vasomotor regulation at which maximal peripheral vasoconstriction develops, is between 29 and 33°C, depending inversely upon subcutaneous fat thickness (Rennie, 1965) (Fig. 1). Since the water temperature in which a diver is most often involved is much lower than this temperature range, it is obvious that the diver is exposed to a considerable cold stress.

B. Quantity of Heat Loss

According to the ama study in Japan and Korea (Kang *et al.*, 1983; Shiraki *et al.*, 1986), the diving ama lose approximately 1,000 kcal/day while diving, and it is estimated that the ama have developed certain

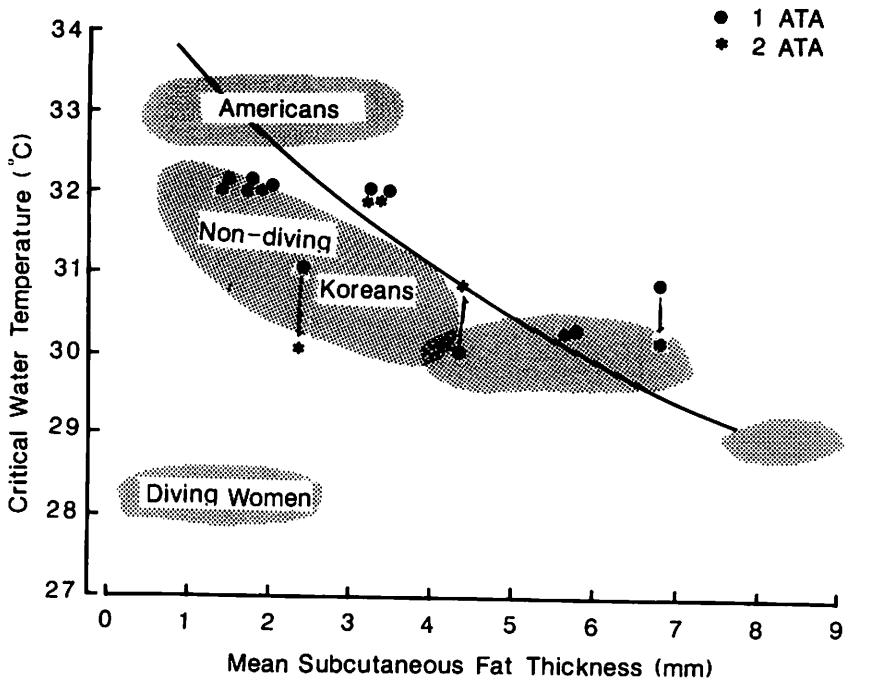

Fig. 1. Relationship between critical water temperature and mean subcutaneous fat thickness in U.S. men and women, nondiving Korean men and women, and Korean diving women. Individual data of unprotected subjects at 1 and 2 atmospheres absolute (ATA) are plotted in the figure (data from Park *et al.*, 1988). Areas encompass range of values. Note the low critical water temperature for diving women relative to their subcutaneous fat thickness. (Modified from Rennie, 1965).

physiological adaptations to cold. A laboratory experiment suggests subjects can voluntarily tolerate a loss of 200 to 300 kcal of body heat in one h or so (Craig and Dvorak, 1976; Webb, 1976; Webb, 1978).

C. Protection by Wet Suits

The range of neutral water temperature for a resting subject is 33 to 35°C. When cold water stress is moderate (T_w above 25°C), however, it is possible to maintain reasonable thermal equilibrium by increasing heat production by exercise (Sagawa *et al.*, 1988). A man can maintain his normal body temperature in water of 32°C when he is engaged in continuous underwater work that doubles oxygen consumption (2-met exercise), and a 3-met exercise keeps body temperature normal in water temperature of 26°C (Craig, 1971; Sagawa *et al.*, 1988; see also the following section).

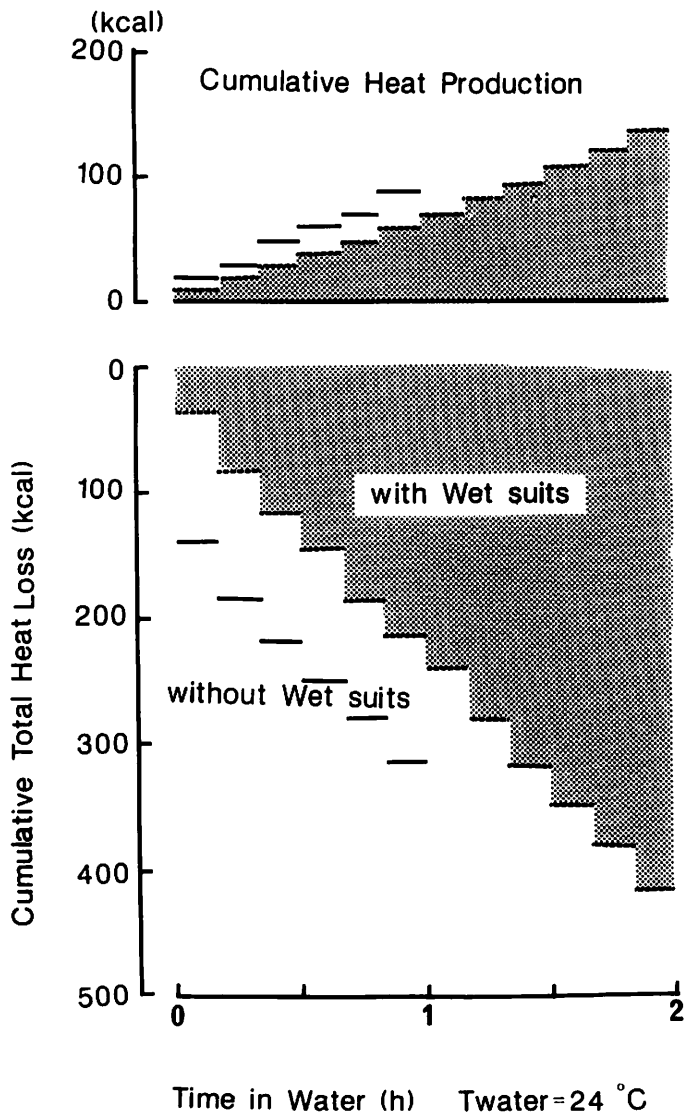

Fig. 2. Cumulative heat production and heat loss during immersion in water of 24°C with and without protective wet suits. (Adopted from Craig and Dvorak, 1976).

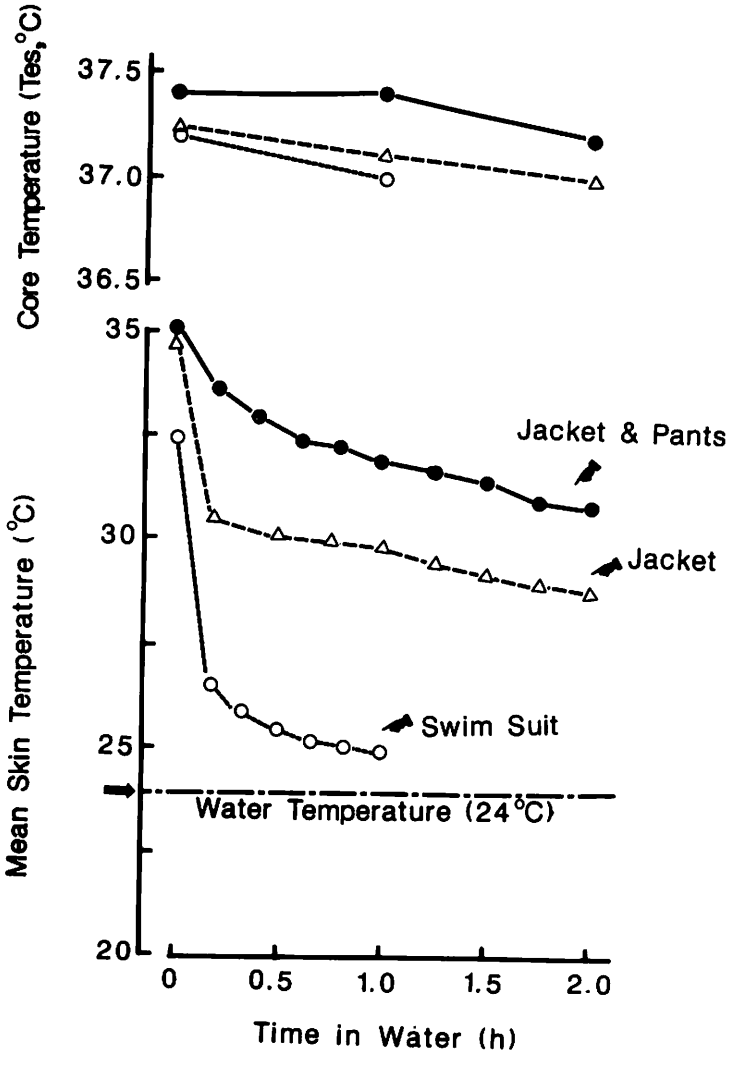

Fig. 3. Changes in esophageal (T_{es} and mean skin temperatures during immersion in water of 24°C with and without protective wet suits. (Adopted from Craig and Dvorak, 1976.)

However, as water temperature decreases further (below 24°C), heat loss becomes so great that it becomes virtually impossible to maintain thermal balance without wearing a protective wet suit. Fig. 2 provides the results of a typical experiment. Without wet suit, the subject generated 90 kcal during 1-h immersion while losing 315 kcal, and the subject developed visible shivering. On the contrary, with the full wet suits the rate of both heat production and heat loss decreases by about 30% by the end of 1.5 h; both the cumulative heat production and total heat loss are comparable with that observed in the subject at the end of 1 h without the suit. The most obvious difference with and without the protection of the suit is noted in the skin temperature (Fig.3). Without protection, skin temperature decreases rapidly. With the neoprene jacket only skin temperature (T_{sk}) remained considerably above the water temperature. Fig. 3 also provides changes in core temperature (esophageal temperature) of the subject during immersion with and without the protective suits. In all three cases, core temperature decreases by the same amount, 0.2°C. However, in the case with the full suits the reduction does not occur until the second h. With the jacket alone the rate of fall in core temperature is about half of that observed without protection. In both experiments the subject with the suit feels comfortable until the end of the 2-h immersion (Craig and Dvorak, 1976).

IV. SHOULD A MAN EXERCISE IN COLD WATER TO RETARD THE FALL IN BODY TEMPERATURE?

A. Work Intensity

Many factors have been reported to influence the rate at which individuals cool when they are immersed in cold water. These factors include subcutaneous fat thickness, surface area-to-mass ratio and exercise (Burton and Edholm, 1955; Craig and Dvorak, 1968; Keatinge, 1960; Pug and Edholm, 1955). The role of exercise, however, remains controversial. Several papers (Cannon and Keatinge, 1960; Keatinge, 1961; Hayward and Keatinge, 1981) have reported that the performance of exercise accelerates the rate of fall of core temperature when compared to the rate seen during resting in cold water. Keatinge (1969), reported that this is the case for water temperatures below 25°C (Fig. 4). The results of other authors (Costill *et al.*, 1967; Craig and Dvorak, 1968; McAdle *et al.*, 1984; Nadel *et al.*, 1974) suggest that the intensity of the exercise performed also influences core temperature during cold water immersion. These authors have reported that the performance of exercise during immersion in water at temperatures between 17 and 24°C reduces the rate of fall of

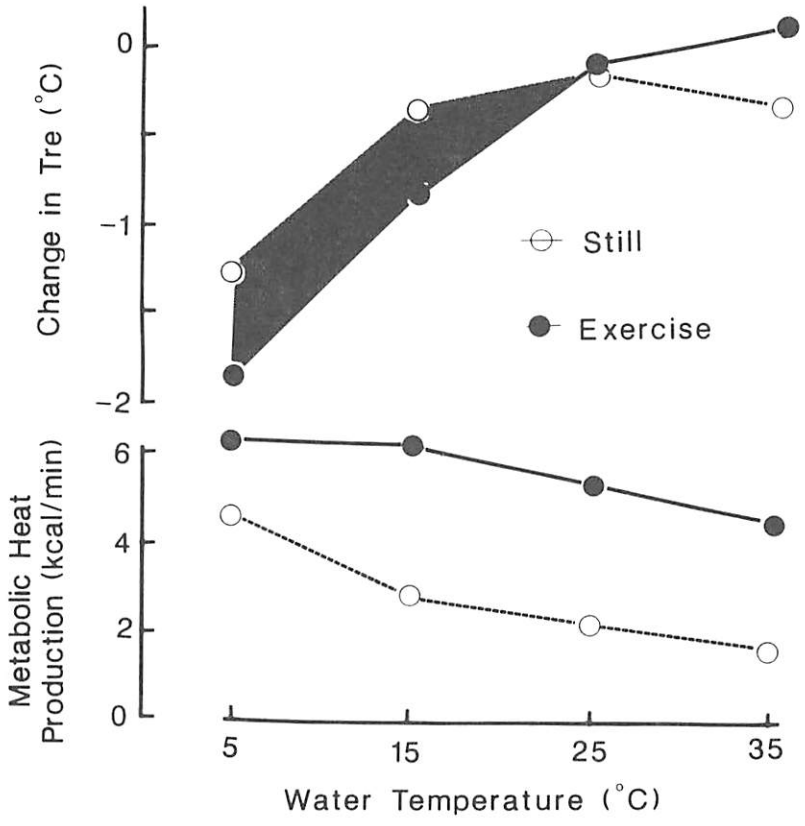

Fig. 4. Effect of exercise on body temperature and heat production in water at different temperatures (adopted from Keatinge, 1969).

core temperature when compared to control static immersion. In all of the above studies the exercise employed has been whole-body in nature, consisting of either swimming or rowing movements. Toner *et al.* (1984) and Toner *et al.* (1985) have reported that leg-exercise is more effective than rest for maintaining esophageal temperature in water as low as 18°C.

This crucial water temperature may be determined by several factors such as exercise intensity and type, fat thickness, and duration of immersion. Therefore, from the physiological point of view it is important to establish a relationship between water temperature and work intensity to keep the body temperature unchanged in water. Sagawa *et al.* (1988) have carried out an experiment in healthy male subjects to give a series

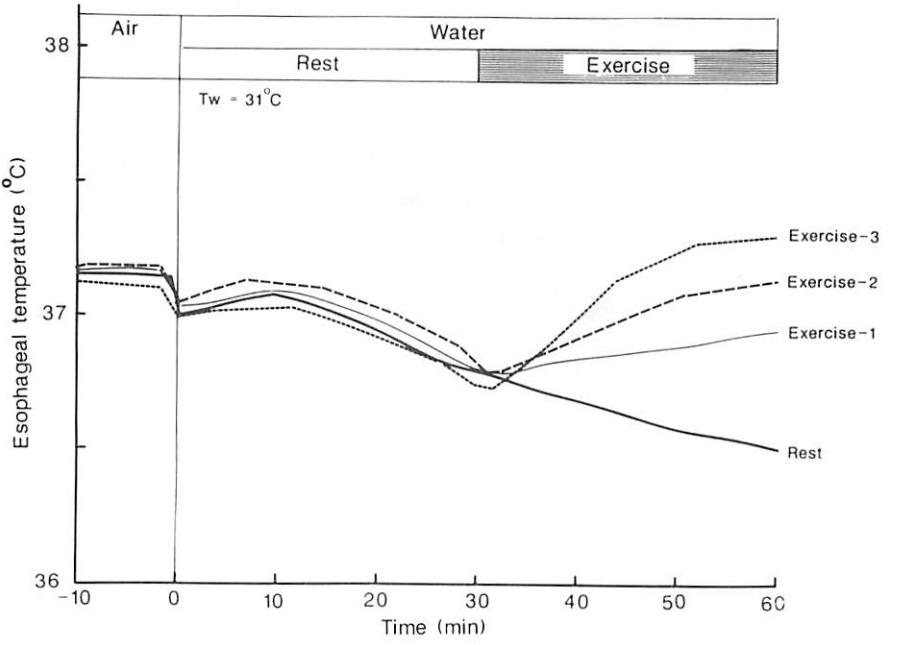

Fig. 5. Time course of average changes in esophageal emperature at different work levels in water of critical temperature (31°C). Exercise-1, -2, and -3, mean intensity of exercise at 1, 2, and 3 met, respectively. (Data obtained from Sagawa *et al.*, 1988).

of graded leg exercises (from 2 to 4 met) for 30 min followed by a 30-min rest in water of different temperatures. They have conducted a series of experiments at water temperature of 1) 2°C below critical water temperature (29°C); 2) critical water temperature (31°C); 3) thermoneutrality (34°C) and 4) 2°C above thermoneutrality (36°C). Fig. 5 shows a typical effect of leg exercise on the core temperature (esophageal temperature) at critical water temperature. During in-water rest, esophogeal temperature gradually decreases with time, however, exercise raises esophageal temperature to a higher level than the resting value and the rise in temperature is in proportion to the work intensity.

The time course of the cumulative heat storage in water is shown in Fig. 6. At rest, cumulative heat storage is nearly nil at thermoneutrality, increases at above-thermoneutrality, and decreases at below-thermoneutrality. However, leg exercise shifts the cumulative heat storage upward at each water temperature. This indicates that the heat which is generated during the underwater exercise exceeds the heat loss in water. This particular experiment has showed that the leg exercise is more effective

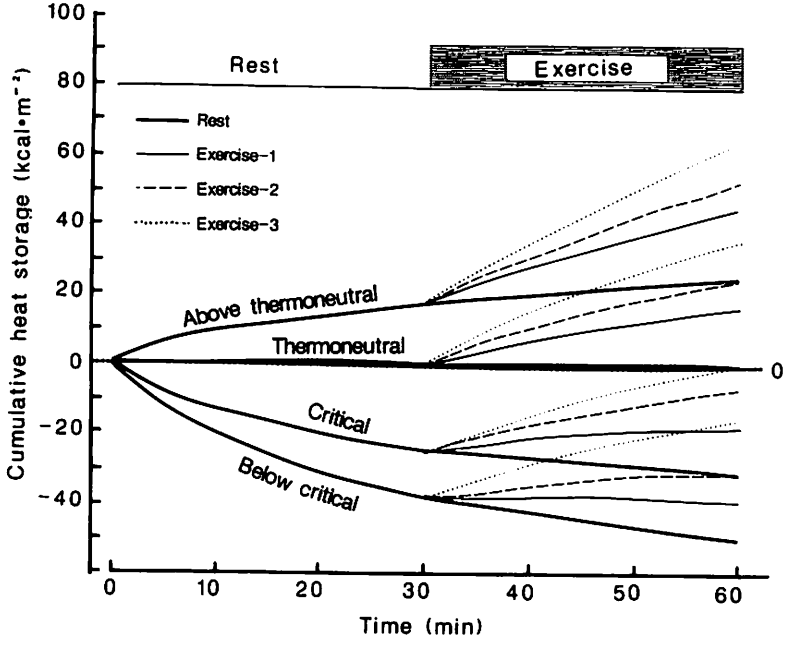

Fig. 6. Average time course of cumulative heat storage during rest and exercise in water of various temperatures. (Adopted from Sagawa *et al.*, 1988).

for maintaining core temperature than rest, however, intensity of the exercise should be proportionally high as the water temperature becomes low. In practice, a work intensity more than 200k cal/m²/h (about 4 met) can not be continued for a long period of time in water; therefore the lowest T_w in which man can maintain his body temperature by generating heat is around 25°C, in agreement with another report (Keatinge, 1960).

Thus, T_w of 25°C may be the lowest water temperature in which an average unprotected man can continue exercising without lowering his core temperature (crucial water temperature). Below the crucial water temperature, body temperature will continue to decrease even if exercise is continued. However, the unprotected male ama of Japan lower their core body temperature in water of 27°C during diving with a metabolic heat production of 200 kcal·m^{-2}·h^{-1} for 1 hr (Shiraki *et al.*, 1986). This

water temperature of 27°C is higher than the estimated threshold water temperature of 25°C. This disagreement may be attributable to the fact that during harvest dives in the ocean the ama swim preferentially by use of the legs and arms. This type of exercise may accelerate body heat loss, lowering body temperature as reported by others (Toner *et al.*, 1984). Therefore, the type of the exercise in water is no doubt an important factor modifying heat drain from the body (see the following section).

The finding that the core temperature falls at a faster rate during static immersion conflicts with earlier works (Cannon and Keatinge, 1960; Keatinge, 1961; Hayward and Keatinge, 1981), in which, however, the subject has been working with a fixed work intensity, whole-body in nature, usually involving swimming or rowing movements. These authors have concluded that exercise has an adverse effect on thermoregulation through an increased whole-body conductance, caused by the larger muscle blood flows associated with exercise. Their summary is that the increase in heat production due to whole-body exercise is less than the increase in body heat loss, except when body insulation is much greater than normal.

Classically, authors (Craig and Dvorak, 1968; Pugh and Edholm, 1985) have reported an intimate relationship between the fall in core temperature and the skinfold thickness of subjects during immersion. Recently, Veicsteinas *et al.* (1982) have suggested that in cold water vasoconstricted muscle acts in series with fat and skin to provide tissue insulation. Rennie (1987) has stated that the insulation of resting subjects in cold water is made up of 75% vasoconstricted muscle and 25% subcutaneous fat and skin. During swimming or heavy shivering the "variable" resistance of muscle vasoconstriction will be lost due to an increased blood perfusion to exercising muscle, leaving only the "fixed" resistance of the subcutaneous fat and skin. If the conclusions of Rennie (1987) are correct, then during static cold water immersions one might expect the fall in core temperature of subjects to be more closely related to body weight (or muscle mass) than subcutaneous fat thickness. During dynamic cold water immersion, when the variable insulation of muscle is lost, the fall in core temperature should be more closely related to subcutaneous fat thickness than to body weight (Golden and Tipton, 1987).

B. Type of Exercise

The results of the leg-exercise study suggest that the type of exercise performed is an important factor to influence body temperature, because the "leg-only" exercise resulted in smaller falls in core temperature when compared to an equivalent static immersion (Golden and Tipton, 1987).

Consideration of the results of the leg-exercise (Golden and Tipton, 1987; Sagawa *et al.*, 1988) and the arm-exercise (Toner *et al.*, 1985) suggests that the arm is an important source of heat loss during whole-body exercise in cold water. Assuming that the leg component of whole-body exercise increases heat gain more than heat loss, then as whole-body exercise results in negative heat balance, heat loss from the arm component must exceed the gain obtained from the legs.

The majority of recognized swimming strokes require a higher level of work from the arms than the legs; even at similar levels of work, the arms, because of their smaller muscle mass, will receive relatively higher blood flows than the legs. This will result in a delivery, by mass flow, of more heat to the arms. The ability of the arms to retain heat is less than that of the legs; the arms have approximately twice the surface area-to-mass ratio of the legs (Burton and Edholm, 1955) and the conductive pathway from the core to the surface of the limbs is shorter in the arms than in the legs.

In summary of this section, there are several factors that help to determine whether the performance of exercise during cold water immersion will accelerate or retard the fall in core temperature. These factors include the water temperature, water agitation, fitness and fatness of the individual, type of clothing worn (if any), and the intensity at which exercise is performed. In addition it is strongly suggested that the type of exercise performed may also be an important factor. Many of these factors interact; leg exercise, for example, may only help maintain core temperature when it is performed at a high intensity. The number of possible interactions between the factors noted above make it very difficult to give general advice concerning whether or not individuals should exercise following accidental immersion in cold water.

V. REGIONAL HEAT LOSS DURING EXERCISE IN WATER

The critical temperature in water is considerably higher than in air. Since the maximal tissue insulation is obtained at this critical temperature (Rennie, 1987) an appreciable vasoconstriction of the limbs and the skin may be induced at the relatively higher temperature in water. Sagawa *et al.* (1988) have measured the regional insulation of different parts of the body during underwater exercise at various water temperatures. They have confirmed that the overall body insulation during rest is highest in water of critical temperature and decreases in water of both colder and warmer than critical temperature, because insulation of the tissue decreases due to shivering in water of colder than critical temperature, and also decreases in warmer water due to decrease in vasoconstriction.

It is generally agreed that tissue insulation significantly decreases during underwater exercise (Park *et al.*, 1984; Rennie, 1987). As regards the regional difference in tissue insulation, Sagawa *et al.* (1988) have concluded that during immersion in water cooler than the critical temperature, insulation of the trunk is less than that of the limbs probably due to a longer conduction path way in the limbs, countercurrent heat exchange, and a predominant shivering in the trunk; during immersion in water temperature of neutral (34°C) or warmer (36°C), however, insulation of the limbs decreases more than the trunk, suggesting that an attenuated countercurrent heat exchange causes a reduction in insulation in the limbs. This finding of Sagawa *et al.* (1988) is of prime importance, because the result indicates that leg exercise facilitates heat loss from the limbs when the water temperature is lower than thermoneutrality due to a release of vasoconstrictor tone in the skin vessels rather than active vasodilation of these regions, and exercise in warmer water than thermoneutrality, on the contrary, causes vasodilation in the trunk to facilitate heat drain into the water. In support of the above conclusion, a higher increase in heat loss in the limbs (H_{limb}) than that of the trunk (H_{trunk}) has been observed during exercise as depicted by a higher H_{limb}/H_{trunk} ratio in water cooler than thermoneutrality. Interestingly, exercise in water cooler than thermoneutrality does not increase heat loss in the trunk as the exercise intensity increases. If this observation is the case for all dynamic immersion, exercise-generated heat will be preserved more efficiently in the trunk than the limbs. In an extreme situation, insulation in the trunk may be at maximum even during muscular exercise in cold water, while insulation in the limbs is changing. Sagawa *et al.* (1988) have concluded that in cool water, insulation of the limbs is high during rest but it decreases as the intensity of leg-exercise increases, although insulation of the trunk changes little. This finding, therefore, has suggested that an effective protection from heat drain during exercise in water is attained by preventing heat loss especially from the limbs.

VI. THERMAL BALANCE IN DRY HYPERBARIC ENVIRONMENT

As the fractional concentration of nitrogen in the chamber, added to prevent high-pressure nervous syndrome (Bennett, 1976) is much lower than that of helium, the thermal problems have exclusively dealt with the helium-oxygen environment. In normal air environments, a lightly clothed man moving around is comfortable at temperatures between 20 and 30°C. However, when the gas environment changes from air to 80% He and 20% O_2 at 1 ATA, the comfort temperature range changes to between 23 and

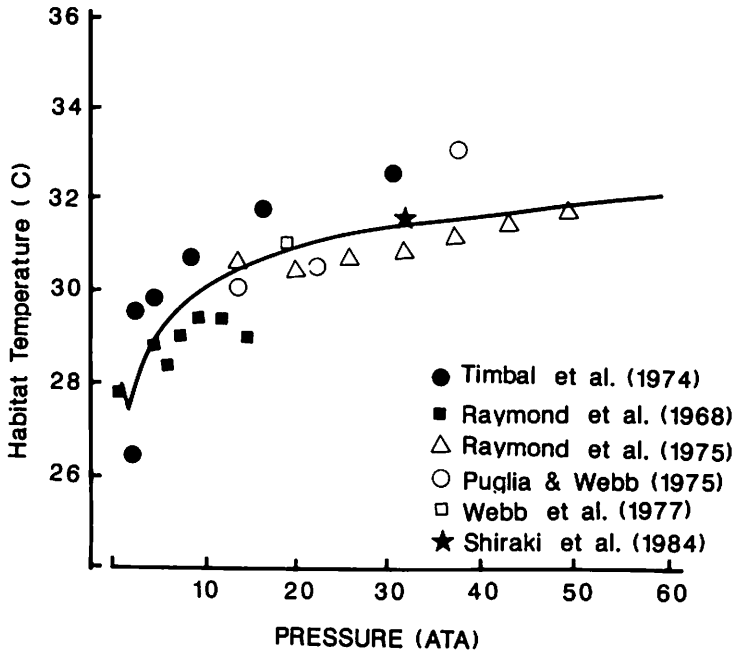

Fig. 7. Comfort temperatures for a prolonged stay in hyperbaric helium-oxygen. (Modified from Webb *et al.*, 1977).

30°C. The change in comfort temperature range is attributable to the increased convective heat loss in the helium-oxygen environment. In helium-oxygen saturation dives, the fractional concentration of helium increases with pressure, while that of oxygen decreases to maintain a constant Po_2 at 0.3-0.4 ATA. Thus, the chamber gas at 31 ATA, for example, contains 96% helium and 1.3% oxygen. This environment increases density, specific heat, and thermal conductivity more than viscosity, resulting in a remarkable increase in convective heat loss from the body surface (Webb, 1970).

Another unique aspect of heat transfer in the hyperbaric environment is the change in the evaporative heat loss. The coefficient for water vapor diffusion decreases as an inverse function of pressure regardless of the gas composition (Paganelli and Kurata, 1977). The heat transfer property in hyperbaric helium-oxygen environments indicates that convective heat loss increases while evaporative heat loss decreases progressively as ambient pressure increases. However, the magnitude of the increase in

convection is far greater than that of the decrease in evaporative heat loss, resulting in an elevation of the comfort temperature as the ambient pressure increases (Raymond *et al.*, 1975) (Fig. 7). Moreover, the comfort temperature range becomes very small, as in the case of immersion in water. In most of the helium-oxygen saturation dives carried out in the early days, the chamber temperature was kept at a level lower than the comfort temperature as shown in Fig. 7, resulting in a marked increase in heat loss (mostly convective). When the chamber temperature has been raised as pressure increased to keep the diver comfortable, a thermal homeostasis has been observed at 31 ATA He-O_2 environment (Nakayama *et al.*, 1980; Raymond *et al.*, 1975; Shiraki *et al.*, 1982; Shiraki *et al.*, 1984). The thermal gradient between the skin surface and the surrounding gas becomes progressively smaller as pressure increases, and this situation could be comparable to that of the subject immersed in water. In a He-O_2 environment, the heat loss by convection increases markedly, while that by evaporation and radiation decreases as the ambient pressure increases. The reduction in evaporative heat loss at high pressure can be attributed to a reduced diffusion capacity of vapor (Paganelli and Furata, 1977). The reduction in radiative heat loss can be attributed to the decreased thermal gradient between skin and ambient temperature. It is important to note in Fig. 8 that the respiratory convective heat loss increases from 1 W at 1 ATA air to nearly 20 W at 49.5 ATA. According to a study conducted by the U.S. Navy, a diver engaged in heavy exercise with an oxygen consumption of 1 l/min (STPD) breathing cold gas (7°C) at 3 ATA lost 681 W through the respiratory system, which represents 6.5% of his metabolic heat production (Hoke *et al.*, 1976). At 31 ATA, about 95% of this respiratory heat loss was due to convection, and the rest, evaporation for humidifying the inspired gas. At 1 ATA air, however, the convective component accounts for about 10% of the respiratory heat loss (Moore *et al.*, 1976).

VII. THERMAL BALANCE IN WET HYPERBARIC ENVIRONMENT

A. Suit Insulation

The insulation provided by a neoprene wet-suit is based upon its trapped air (Beckman, 1967). Volume of this trapped air and thus the suit insulation will be inversely proportional to hydrostatic pressure. The apparent suit insulation is reduced by approximately 45% at 2 ATA and 52% at 2.5 ATA as compared with 1 ATA value (Park *et al.*, 1988). When the relation is extended to a high pressure, the suit insulation at 31 ATA, for instance, would be almost nil (Shiraki *et al.*, 1989). Fortunately,

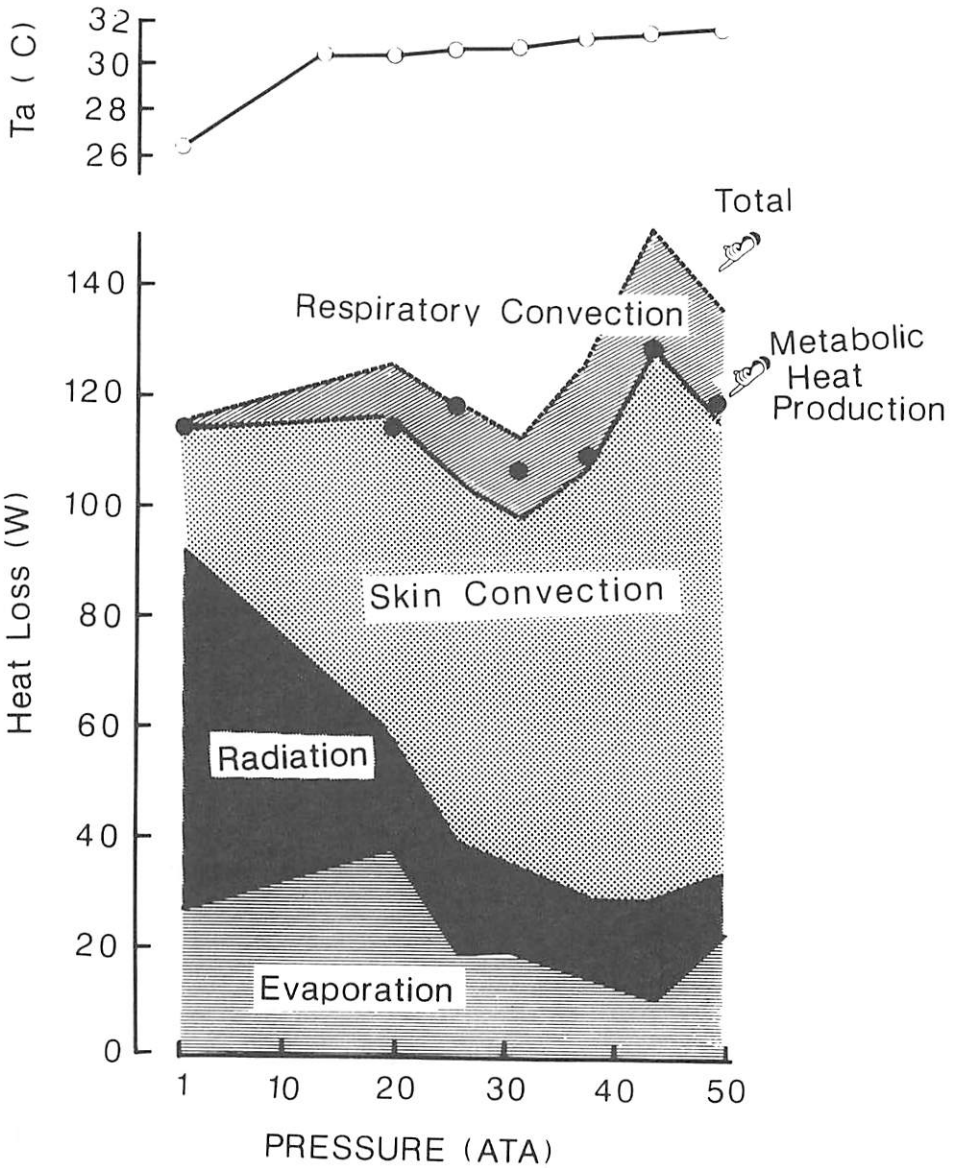

Fig. 8. Ambient temperature and heat loss through various avenues as a function of ambient pressure. (Adopted from Raymond, *et al.*, 1975.)

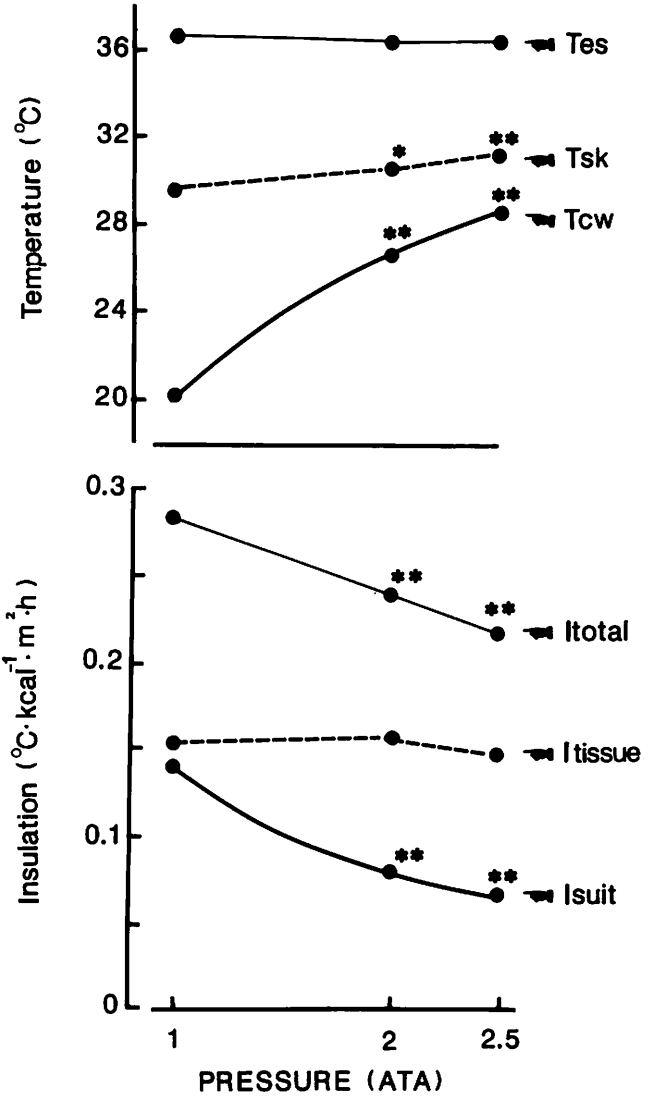

Fig. 9. Relationship between pressure and critical water (T_{cw}), esophogeal (T_{es}), and mean skin (T_{sk}) temperature during immersion at 1, 2, and 2.5 ATA (top) and mean wet-suit insulation (I_{suit}), total peripheral insulation (I_{total}), and mean body insulation (I_{tissue}) during water immersion in T_{cw} at 1, 2, and 2.5 ATA (bottom). *P<0.05, and **P<0.001 compared with corresponding value at 1 ATA (adopted from Park *et al.*, 1988).

however, this is not the case in saturation dives, because the wet suits regain their original thickness in 24 h by refoaming in the neoprene with the environmental gas ($He\text{-}O_2$). Thus, the diver is able to perform an excursion dive in water of 25°C without encountering major thermal problems at 31 ATA (personal communication from the Japan Marine Science and Technology Center, Yokosuka, Japan. Data is from a 31 ATA saturation dive, project code named New Seatopia carried out in 1985). In a non-saturation dive, such as scuba dive, the suit insulation decreases curvilinearly as the diver goes deeper, and the diver loses a tremendous amount of heat even if the water temperature of the sea is not extremely low (Park *et al*, 1988). For open sea dives where all divers, in practice, wear any sort of protective suits to minimize body heat loss, it is important to consider thermal problems connected with the wet environment and high pressure. It can be said that the optimal thermal protective garment for underwater workers is one which: 1) provides an adequate insulative layer which is unaffected by depth, 2) is not significantly compromised by water flow, and 3) can be provided with an insulative gas layer which has an insulative value equivalent to that of air at 1 ATA. For instance a four-layer 1/4 inch unicellular neoprene foam wet-suit at 1 ATA gives enough protection to maintain body heat in 5°C water for 5 hours. This suit provides 2.65 CLO ($0.48\ °C \cdot kcal^{-1} \cdot m^2 \cdot h$) of insulation to the subject, which is adequate thermal protection for the body. However, the suit is so bulky and ponderous as to effectively immobilize the subject (Beckman, 1967). It would be an ideal suit that provides insulation equal to that provided by the 1 inch thick unicellular neoprene foam but without limiting mobility. Such utopia might possibly be approached by the concept of a rigid pressure suit as conceived for the lunar landing garment of astronauts and proposed for adaptation to deep sea water (Beckman, 1967). In this concept a rigid but maneuverable outer garment would permit man to stay dry and work in 1 ATA air while diving in ambient pressures of many atmospheres.

Another potentially critical problem associated with wet saturation dives is respiratory heat loss. The respiratory heat loss of a diver in cold water at depth can lead to a severe negative heat balance. This problem can be eliminated only by heating and breathing gas (Piantadosi, 1981).

B. Changes in Critical Water Temperature in Various Pressures

It is well established fact that insulation of the tissue is maximum in water of critical temperature, however still it is not known whether this is the case in a hyperbaric environment. Accordingly, it is of prime importance to know how the critical water temperature changes in relation

with depth. Once we know the relation of critical water temperature with depth, we can observe whether the magnitude of maximum vasoconstriction is the same as that on the surface. Iwamoto *et al.* (1988) have observed the effect of pressure on tissue insulation and have concluded that high pressure (2 ATA) neither alters cutaneous vasomotor responses nor changes critical water temperature compared with normal atmospheric pressure. Park *et al.* (1988) have observed changes in the critical water temperature in subjects wearing wet suits at 2 and 2.5 ATA in comparison with 1 ATA. They have found that the average critical water temperature of wet-suited subjects is 22.3, 26.5, and 28.5°C at 1, 2, and 2.5 ATA, respectively. The reduction in wet suit insulation at pressure is exactly compensated for by increasing water temperature, such that suit heat loss changes similarly, resulting in a similar degree of skin cooling; consequently vasomotor control for internal heat transfer is of an equivalent degree at all pressures. The data clearly indicate that the increase in T_{cw} of wet-suited subjects at high pressure is a simple consequence of changes in suit insulation, and does not involve alterations in physiological mechanisms controlling body heat conservation.

The skin temperature in the most distal extremity (hand and foot) is significantly higher at pressures than at the surface (24.9, 27.3 and 28.6°C for 1, 2 and 2.5 ATA, respectively, at the end of 3-h immersion). However, in other regions the skin temperature does not significantly vary with the pressure. Whether this indicates that in a wet-suited individual the skin temperature of distal extremities does not play an important role in the determination of threshold skin temperature for the shivering response is not certain.

VIII. REGIONAL HEAT LOSS AND INSULATION AT VARIOUS DEPTHS DURING REST IN WATER

A systematic evaluation of regional heat loss and its contribution to overall body heat exchanges in subjects wearing wet suits in various water depths and temperatures is of prime importance. A precise knowledge of regional heat flow is important not only for thermal economy of wet-suit divers during cold water operations but also for usefulness in the design of a protective device.

Shiraki *et al.* (1988) have measured regional heat exchange during a 3-hour exercise in 9 wet-suited subjects immersed in water of critical temperature at 1, 2 and 2.5 ATA. They made a direct measurement of changes in regional heat loss from the skin (H_{tissue}) and suit surface (H_{suit}) concomitantly with core body and skin temperatures. From these data heat loss due to water convection under the suit ($H_{conv} = H_{tissue} - H_{suit}$) and

thermal insulation of the tissue and wet suit have been estimated. The critical water temperature increased as the pressure increased. The average critical water temperature is 22.3 ± 0.2°C (SE) at 1 ATA, 26.5 ±0.3°C at 2 ATA and 28.5 ±0.3°C at 2.5 ATA (Fig. 9, top figure).

In all cases, a large amount of heat loss has occurred from the whole body during the initial 30-40 min of immersion; the chest contributes a major amount of the loss. During the later immersion period, heat flux from the trunk remains unchanged from the initial, but that from the extremities declines progressively.

The suit insulation decreases reciprocally as the pressure increases, but tissue insulation remains unchanged among the pressures tested. The convection under the wet suits accounted for 11.5%, 3.6% and 5.5% of the total heat loss at 1, 2, and 2.5 ATA respectively. The heat loss through this avenue is entirely accounted for by that from the chest in all pressures.

The tissue insulation of the trunk increases slightly during the initial 20 - 40 min of immersion, then remains unchanged, whereas that of the limbs increases progressively over the entire course of immersion (Fig. 10). This indicates that in the limbs in the wet-suited diver the maximum vasoconstriction is not attained within 3 hours in water of critical temperature. In this respect, the immersion with wet-suits is different from the unprotected immersion. These data have clearly shown that the capacity to increase tissue insulation is much greater in the extremities than in the trunk in agreement with other observations in cold exposure (Cannon and Keatinge, 1960). Perhaps, for this reason the heat flux can be extensively reduced in the extremities, but not in the trunk, during a prolonged immersion. Ferretti *et al.* (1988) have observed in naked subjects immersed at critical temperature that tissue heat loss in the limbs levels off after approximately 1 h, suggesting that I_{tissue} reaches a certain maximum level within 1 h.

Because of a small surface area and an extremely high tissue insulation of the hands and feet, the heat loss through these portions is relatively small (Table 1). Thus protection with gloves and boots may have no practical value insofar as body heat conservation is concerned during cold water immersion.

IX. HEAT LOSS DURING EXERCISE IN WATER OF VARIOUS PRESSURES IN PROTECTED DIVERS

It has been reported that exercise greatly reduces insulation of the wet suit in cold water (Wolff *et al.*, 1985), or water at critical temperature (Yeon *et al.*, 1985). This phenomenon has been attributed to convective

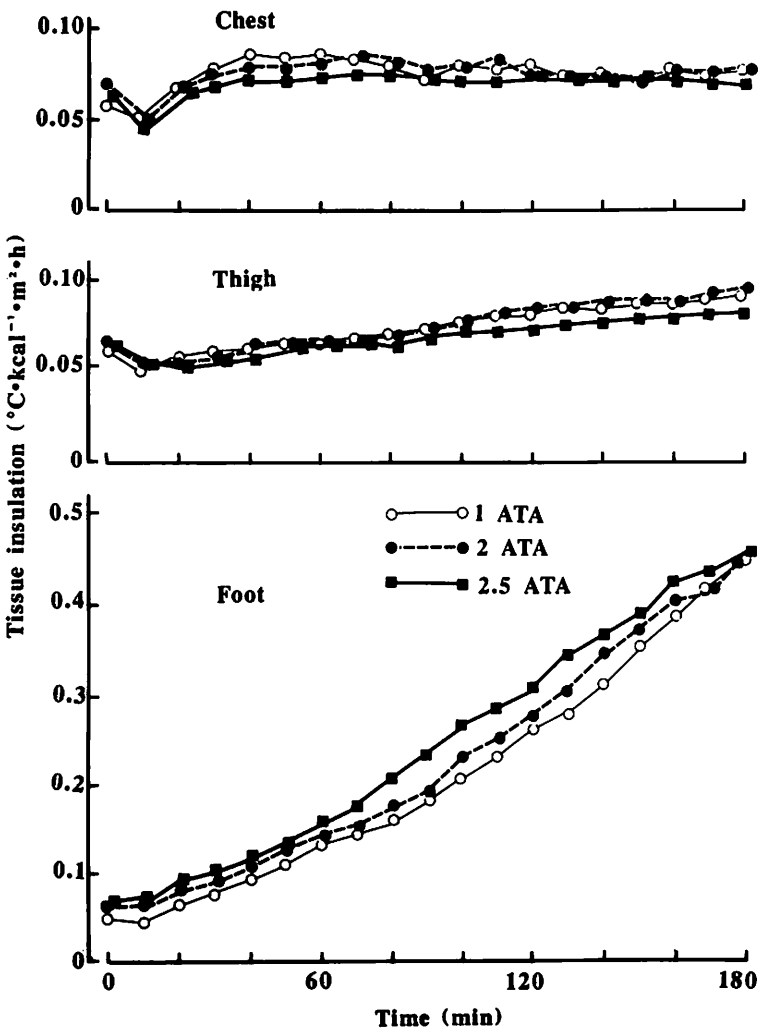

Fig. 10. Changes in tissue insulation in various parts of the body during static immersion at critical temperature.

TABLE 1.

Regional Tissue Heat Flow During Static Immersion at Different Pressures at Critical Water Temperature

Regions	1 ATA	2 ATA	2.5 ATA
Whole Body	98.6±5.0	85.8±2.7	81.8±4.0
Chest	21.1±2.5	15.8±1.0	16.1±1.9
Back	17.5±1.0	18.7±1.0	17.7±1.0
Forearm	5.8±0.3	4.7±0.3	4.8±0.3
Hand	10.4±1.2	6.6±0.4	5.9±0.3
Thigh	25.5±1.5	23.8±1.0	23.0±1.5
Calf	13.7±0.7	12.3±1.0	11.6±0.6
Foot	4.6±0.5	3.8±0.5	2.8±0.3

Values are means ± SE in kcal/h of average values of last 15 min of immersion at critical temperature. ATA, atmospheres absolute. Heat flow was calculated by multiplying regional heat flow measured by individual surface area of corresponding part of body.

heat flow underneath the wet suits (Wolff *et al.*, 1985) and/or an increased effective surface area of the suits (Yeon *et al.*, 1985). However there is divergent evidence that wet suit insulation which is measured by a direct measurement of heat flow from the skin and suits changes little during leg exercise in water of critical temperature (Table 2). The disagreement may be attributed to an erroneous overestimation (Wolff *et al.*, 1985) of convective heat dissipation from the water layer underneath the suits. Or in the earlier report (Yeon *et al.*, 1985) insulation has been calculated without accounting for the convection by the movement of the water layer between the skin and wet suits, and the suit insulation has been underestimated during exercise. Although the suit insulation is independent of the work, the heat dissipation through the suits increases in proportion to the exercise intensity because the gradient of the surface temperature between the skin and wet suits becomes greater as the exercise intensity increases. The heat flow through the skin increases as the intensity of work increases in water of critical temperature and tissue insulation decreases in contrast with increase in wet suit insulation. This fact may suggest that the increment of heat dissipation is solely due to the conduction caused by an increase in temperature gradient between exercising muscle tissue and the skin surface, since blood flow in the skin is not an influence during exercise of which intensity is less than 3 met

TABLE 2.

Wet Suit Insulation During Underwater Exercise in Different Pressures at Critical Water Temperature

	Rest			2 met exercise			3 met exercise		
Region	1 ATA	2 ATA	2.5 ATA	1 ATA	2 ATA	2.5 ATA	1 ATA	2 ATA	2.5 ATA
Whole Body	0.141 ± 0.005	0.081 ± 0.001	0.069 ± 0.002	0.133* ± 0.002	0.074* ± 0.002	0.062* ± 0.002	0.135* ± 0.003	0.072* ± 0.002	0.060* ± 0.001
Chest	0.228 ± 0.032	0.114 ± 0.005	0.114 ± 0.015	0.252 ± 0.022	0.128 ± 0.011	0.109 ± 0.016	0.231 ± 0.023	0.134 ± 0.017	0.125 ± 0.021
Back	0.213 ± 0.004	0.117 ± 0.005	0.091 ± 0.002	0.193* ± 0.005	0.111 ± 0.004	0.093 ± 0.003	0.194* ± 0.005	0.111 ± 0.003	0.092 ± 0.006
Forearm	0.110 ± 0.003	0.065 ± 0.002	0.049 ± 0.003	0.099 ± 0.003	0.057 ± 0.003	0.044 ± 0.003	0.106 ± 0.006	0.056* ± 0.003	0.050 ± 0.003
Hand	0.121 ± 0.005	0.076 ± 0.003	0.066 0.006	0.120 ± 0.004	0.061 ± 0.003	0.054 ± 0.002	0.120 ± 0.003	0.068* ± 0.001	0.056 ± 0.003
Thigh	0.108 ± 0.006	0.061 ± 0.003	0.057 ± 0.002	0.110 ± 0.005	0.059 ± 0.004	0.047 ± 0.003	0.107 ± 0.003	0.058 ± 0.006	0.049 ± 0.003
Calf	0.100 ± 0.003	0.052 ± 0.002	0.041 ± 0.002	0.097 ± 0.003	0.058* ± 0.002	0.043 ± 0.002	0.110 ± 0.006	0.054 ± 0.003	0.043 ± 0.003
Foot	0.133 ± 0.011	0.098 ± 0.016	0.076 ± 0.011	....	0.081 ± 0.061	0.107 ± 0.239	....	0.070 ± 0.145	....

Values are means ± SE in $°C \cdot kcal^{-1} \cdot m^2 \cdot h$ of average values of last 15 min of immersion at critical temperature. ATA, atmospheres absolute. *$P<0.05$ vs 1 ATA.

(Rennie, 1987). It is not practical to consider a prolonged underwater exercise with work intensity of higher than 5 met (Sagawa *et al.*, 1988), we may, therefore, assume that a wet-suited diver exposed to the water of critical or below critical temperature virtually attains the maximum vasoconstriction. The diver is at his maximum vasoconstriction when he dives deep in the sea, where water temperature is mostly lower than the critical temperature which corresponds to the depth (Park *et al.*, 1988). An increased heat generation in the working muscles without decrease in suit insulation during underwater exercise will retard the rate of the fall in core body temperature in the protected diver working in a cold and deep sea. Accordingly it is suggested that dynamic immersion for wet-suited divers is advantageous to maintain the body temperature at depth compared with static immersion as is the case in unprotected divers (Sagawa *et al.*, 1988). In other words, wet suits function as if the thickness of the fat layer increased in the diver. It is of prime importance, therefore, to establish a relationship between the intensity of the work and the core body temperature in the wet-suited diver in connection with the depth of the dive.

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9

Saturation Diving in the National Oceanic and Atmospheric Administration Office of Undersea Research

William S. Busch

I. INTRODUCTION

At the request of the Administrator of the National Oceanic and Atmospheric Administration (NOAA), a distinguished panel was established in September 1985 to examine the needs of the nation in the field of undersea research and to review and make recommendations on NOAA's role in this area. The panel identified NOAA as the agency responsible for:

> Fundamental research and applied research and development driven by a mission to support the nation's civilian needs and interest in ocean exploration, industrial and economic development, conservation of coastal and oceanic resources, and knowledge to support effective management of the nation's oceanic affairs (Jennings, *et al.*, 1986).

As such, the panel recommended that a directed undersea research and development program be implemented that would provide research scientists with access to specialized tasks and technologies essential to maintain intellectual leadership in the oceans.

NOAA's Office of Undersea Research (OUR) has historically provided researchers in the marine science community with an ensemble of undersea facilities and capabilities in support of their research activities. In doing so, OUR acts as a focal point for undersea research working closely with other governmental agencies, academia, industry, private research organizations and international scientific bodies. Its geographic coverage is not limited to the coastal Unites States but includes all areas of interest in the world's oceans and great lakes, offering research opportunities in a variety of unique marine environments and ecosystems.

The systems and facilities provided by OUR cover a broad scope of technical capabilities ranging from simple self-contained underwater breathing apparatus (SCUBA) to very sophisticated deep diving submersibles and saturation habitat systems. Detailed discussions of these capabilities are provided in OUR's most recent annual report (NOAA, 1988).

When possible, OUR supports scientific activities and ensures that each of its programs are driven by scientific needs that are identified by NOAA and the scientific community. Specific areas emphasized by NOAA include:

- Global Oceanic Processes
- Pathways and Fate of Materials in the Ocean
- Coastal Oceanic and Estuarine Processes
- Ocean Lithosphere and Mineral Resources
- Biological Productivity and Living Resources
- Ocean Services

While responding to NOAA's requirements for providing diving research support related to both at-sea field operations and scientific missions, OUR also takes direction provided by the 1978 Outer Continental Shelf Land Act Amendments, Secion 21 (e). The Act charges NOAA with the responsibility for conducting research in underwater diving techniques and the development of equipment for protection of human safety and improvement of diver performance. Such studies include, but are not limited to, decompression and excursion table development and improvement and all aspects of diver physiological restraints and protective gear for exposure to hostile environments.

Continuing needs expressed by undersea scientists include: to increase their allowable bottom time, to maximize their working depths, and to enhance their *in-situ* experimental capabilities. To address these needs, OUR supports numerous activities in diving related research and technology development. A recent major accomplishment was the development and implementation of the manned undersea saturation habitat, AQUARIUS, along with the calculation of new NITROX diving tables. These new tables and the enhanced habitat design will allow scientists the ability to conduct marine research while saturated at depths greater than the 50 ft seawater (fsw) restriction for air saturation.

II. HISTORICAL PERSPECTIVE

Since its inception in 1971, NOAA's Undersea Research Program has had a history of conducting scientific research using saturation techniques. It has also sponsored both fundamental hyperbaric research and the development of diving related technology to enhance saturation diving techniques. In fact, many NOAA personnel and NOAA sponsored scientists were involved in early saturation development and feasibility programs such as TEKTITE I and II, SEALAB, and AEGIR. The purpose of the programs was to prove the concept and demonstrate the usefulness of these saturation diving techniques to the marine scientific community.

In 1971, NOAA began the Bahamas Banks Research Program using the HYDROLAB saturation habitat built by Perry Submarine Builders, Inc. It lasted for four years with more than 300 scientists participating. The Puerto Rico National Underwater Laboratory (PRINUL) Program, which used the La Chalupa habitat, began in 1972 and continued through 1974. More than 42 scientists conducted over 1,700 dives and demonstrated the advantages of a mobile sea floor habitat.

To become further involved in fundamental saturation research, NOAA joined forces with Japan under the auspices of the United States and Japan Cooperative Program in the Natural Resources (UJNR) and developed the SEADRAGON series of saturation research dives. Decompression tables, breathing gas mixtures, and cardiovascular problems were only some of the many hyperbaric physiological areas investigated. These efforts are still ongoing with a total of seven separate dive missions having been conducted.

1975 also found NOAA involved in two other projects using saturation diving, Project SCORE (Scientific Cooperative Operational Research Expedition) and the FISSHH (First International Saturation Study of Hearing and Hydroacoustics) project. SCORE used the HYDROLAB facility in the Bahamas off the coast of Freeport. Sixteen scientists participated in

this project conducting four saturation missions. FISSHH used the German owned HEGOLAND habitat and was truly an international project. Poland shipped the German habitat to a location off the U.S. New England coast and the program was led by U.S. scientists with researchers from the U.S., Germany, Poland, and the Soviet Union participating in the four month study (Miller and Koblick, 1984).

The concept and design for an autonomous deep diving submersible, OCEANLAB, that would have world-wide ranging capability and support saturated diving to 300 m, was started by NOAA in 1977. However at the completion of the preliminary design and cost trade off analyses in 1979, the project was cancelled.

Concurrent to the OCEANLAB design effort NOAA purchased the HYDROLAB. After being refurbished, it was moved to a new location one half mile off the Northern coast of St. Croix, U.S. Virgin Islands, as shown in Fig. 1 and placed into operation in 1978 by Farleigh Dickenson University's West Indies Laboratory. During the period 1978 to 1985, HYDROLAB was the only undersea habitat in operation in the free world that was totally dedicated to marine science. During that period, more than 55,000 accident-free hours of saturation by scientists were logged with 11,000 hours of excursions. A total of 85 scientific missions were completed with more than 330 scientists participating from 94 U.S. institutions and 14 foreign organizations (Busch, 1987).

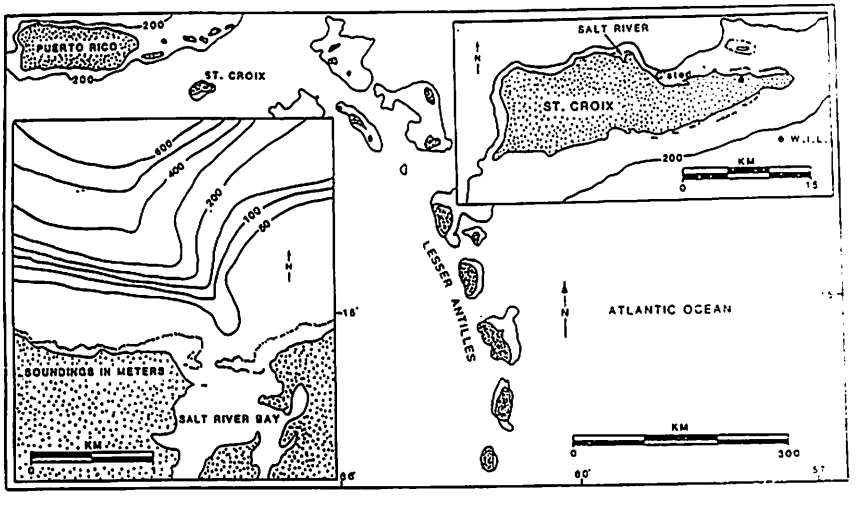


Fig. 1. Map showing the location of Salt River Submarine Canyon.

III. STATE-OF-THE-ART HABITAT

While the HYDROLAB was very successful and provided researchers with new opportunities in unique locations, it was limited to a depth of 50 fsw, could only accommodate four scientists, and had minimal onboard analysis and experimentation capabilities. To meet the increased need of the scientists to be able to go deeper for longer periods of time and to be able to move to different locations, NOAA developed the next generation of saturation habitats, the AQUARIUS.

Based on experience gained from past programs, results from hyperbaric research, safety requirements, and enhanced user requirements, a number of new concepts were incorporated into the design of this system. First and foremost was the requirement for ensuring maximum safety of both aquanauts and support staff during all phases of a mission, including while the scientists were in the habitat, while excursioning, during decompression, and when on the surface both before and after the mission. Using state of the art computer and remote sensing technology, all critical life support, environmental, and operational parameters are monitored continuously as shown in Fig. 2. In addition to the computer links which relay the status of the life support system parameters, such as O_2 and CO_2 levels and compartment temperature and pressure to the shore base, video cameras continuously survey the activities of the aquanauts and a visual status of the onboard control panels.

To support the concept of a broad ranging and multi-ecosystem science program, the new facility had to be readily movable. This would allow for periodic relocation to new research sites as dictated by scientific pressure. The habitat was therefore designed to be mounted on a baseplate which would be installed on different types of seafloors and under varying water conditions. For transporting the habitat and for supporting remotely located operations, a Mobile Support Barge (MSB) is used. It also provides a platform for a topside command and control base station, and a dry-dock capability as required for periodic maintenance of the facility.

To enhance the research opportunities available to the scientist beneath the sea, the AQUARIUS provides many experimental capabilities normally found in land based marine field laboratories. Both wet and dry laboratory features are provided such as hot and cold fresh water, aquaria, refrigerated and freezer space for specimen storage, ample countertop and work surfaces, and the ability to support special instruments and equipment unique to the respective experiment. A major feature of the system is the onboard PC computer system and its real-time data link to the shore providing the scientists with access, via telephone links, to their computers and data bases back home. The onboard computer also

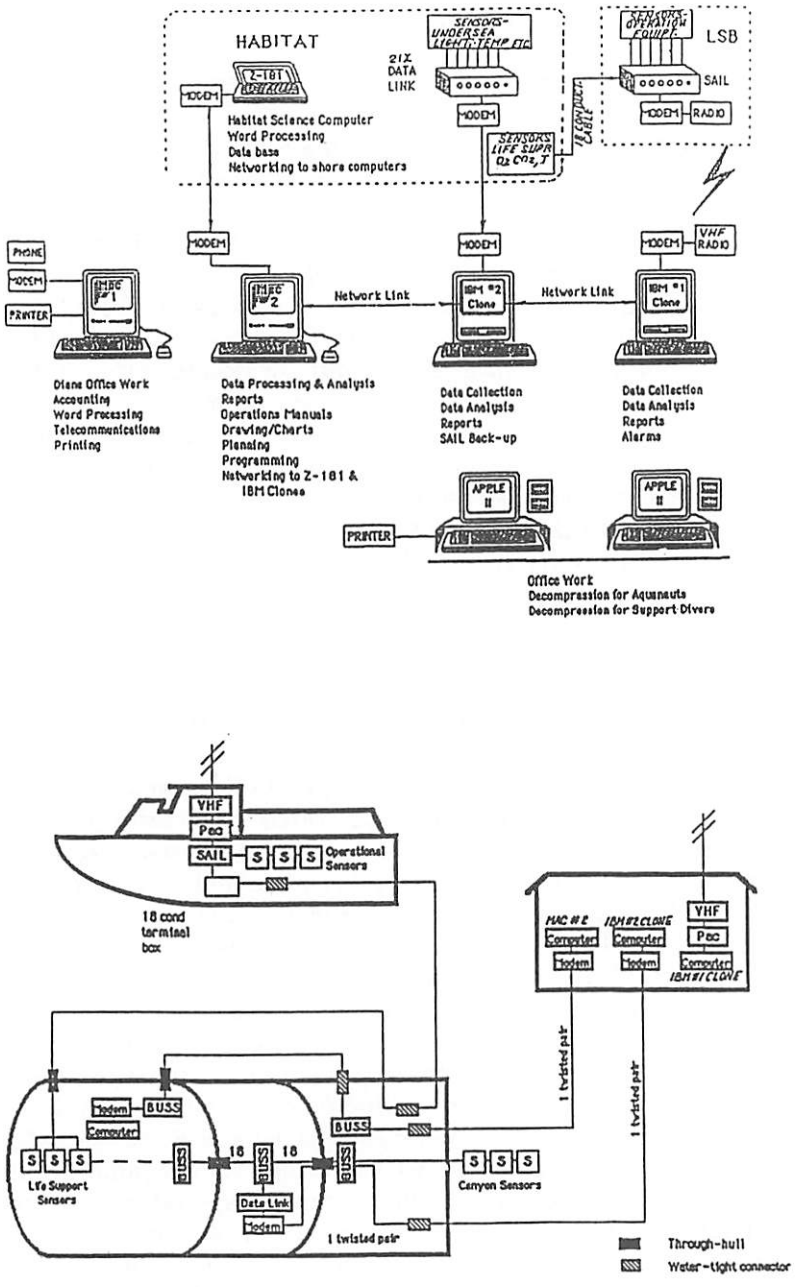


Fig. 2. Data Monitoring Systems and Computer Links.

allows for monitoring of experiments placed outside on the seafloor, the gathering of long term, *in situ*, and ambient environmental data, the monitoring and analysis of each aquanaut's daily dive profiles. Other experiments, if placed outside and in view of one of the many viewports that range in size from 8 inches to 23 inches in diameter, may be monitored directly from inside the habitat (NOAA's Undersea Research Center at FDU, 1988a).

While the HYDROLAB could only support four scientists for a maximum of 10 days, the AQUARIUS is capable of supporting five scientists and one operations staff person for up to 30 days. However, it is envisioned that the average mission length will be 10 days. A staff member is included in every mission. He or she is responsible for the operation of the habitat thereby freeing the researchers to concentrate primarily on the research. In addition, when the saturation portion of the mission is completed, the lengthy decompression phase is controlled from the surface by staff personnel.

Another major enhancement in the habitat's capability is the increased saturation storage depth. Since the HYDROLAB could only use air, the maximum saturation depth was approximately 50 feet seawater (fsw). At depths greater than 50 fsw, ordinary air can not be used because of oxygen toxicity. Instead, a specialized breathing gas mixture known as NITROX is used which has an increased amount of nitrogen thereby decreasing the amount of oxygen. New decompression tables and treatment procedures had to be developed for using NITROX in this saturation mode (Hamilton *et al.*, 1988). In addition, the HYDROLAB could not be brought to the surface while under pressure because of its one-way pressure design. The AQUARIUS, however, was built with a two-way pressure capability so that it could be pressurized on the surface or be at one ATA on the seafloor. It also has the capability of going to 230 fsw internally to allow for conducting appropriate hyperbaric medical treatments if required while at the maximum saturation depth of 120 fsw.

Since its first mission at the beginning of this year, AQUARIUS has been extremely effective in providing the scientists with many new undersea research capabilities. It is anticipated that 8 to 10 missions will be conducted each year.

IV. FACILITIES, SYSTEMS, AND EQUIPMENT

The overall system, as shown in Fig. 3, consists of the actual habitat, its surface life support barge (LSB), a submerged baseplate, the mobile suport barge (MSB), and the shore-based control center. While the performance specifications for the habitat are provided in Fig. 4, detailed

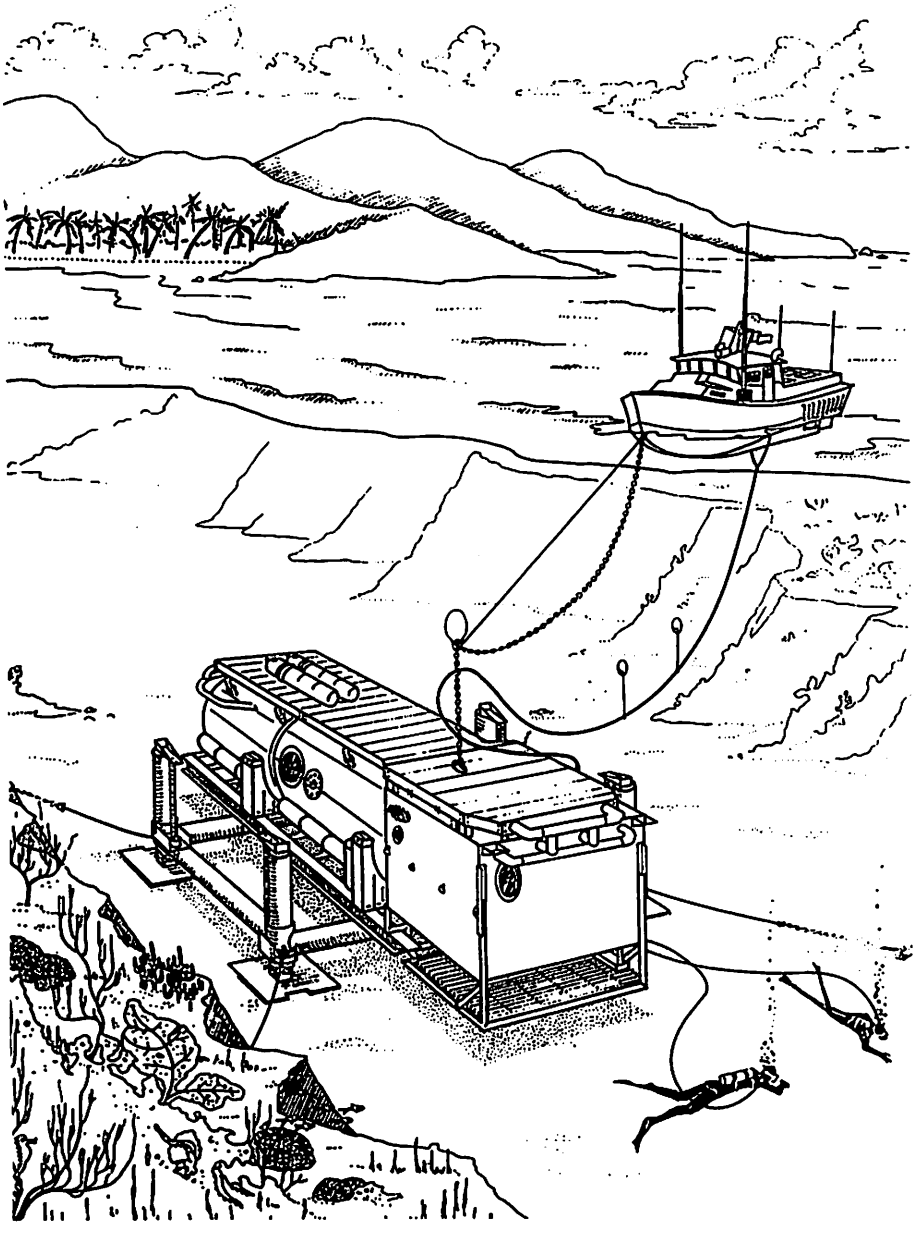


Fig. 3. Overall System Configuration.

General Data

Overall Envelop and Dimensions:		
Length:	43 ft	
Breadth:	20 ft	
Height:	16.5 ft	
Internal Lengths and Volumes:		
Main Lock (ML)	21.5 ft	1400 ft.^{3}
Entrance Lock (EL)	8.5 ft	500 ft.^{3}
Wet Porch (WP)	8.0 ft	700 ft.^{3}
Internal Diameter		
Wet Porch:		
Length:	8 ft	
Breadth:	12 ft	
Height:	7 ft	

Weights:

Dry in Air:	
Habitat	163,790 lbs.
Ballast and Trim:	11,000
	174,790
Displaced:	164,960
Buoyancy:	
WP Blown Dry:	44,000
WP Flooded (with 6" bubble)	7,000
Surface Buoyancy — 3.0 ft Freeboard: (ballast tank blown)	11,410
Payload (mission weight including personnel, provisions, and equipment)	5,000
Baseplate:	232,000

Personnel Accommodations:

5 Scientists, 1 Staff Technician

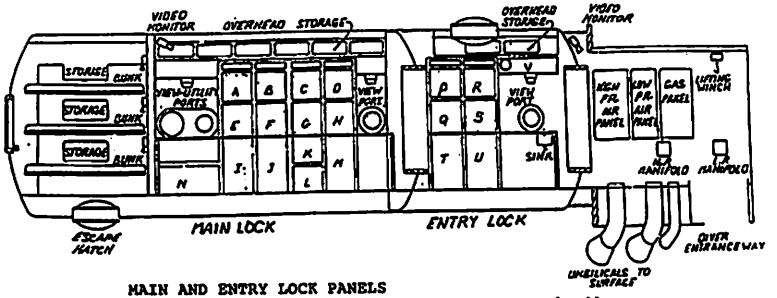
Mission Duration:

Average:	10 days
Maximum:	30 days

Hyperbaric Capability:

Maximum External Depth:	120 fsw (54 psi)
Maximum Internal Depth:	232 fsw (103 psi)
Emergency Life Support:	72 hours for 6 persons + 1 decompression from maximum depth

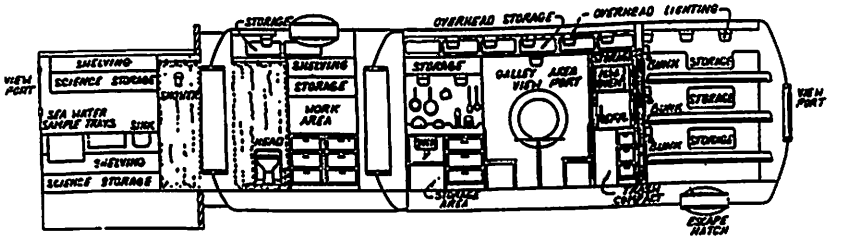
Fig. 4. Specifications of NOAA's Aquarius Habitat.



MAIN AND ENTRY LOCK PANELS

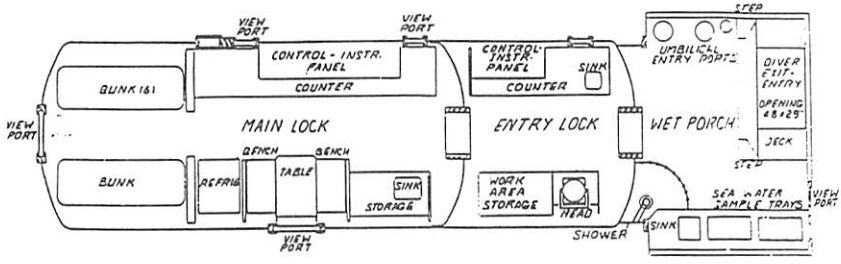
A	Caison gage	K	DC Power supply #1
B	Bibs supply	L	DC Power supply #2
C	DC Power distribution	M	AC Circuit breaker
D	Auxiliary AC/DC Panel	N	Blowdown muffler
E	Communications	O	Shelf
F	Atmosphere makeup	P	AC/DC Power distribution
G	AC Power distribution	Q	Communication
H	Video monitor and VCR	R	Bibs mask supply
I	Compartment Exhaust	S	Atmosphere makeup
J	Compartment pressurization	T	Compartment exhaust
		U	Compartment pressurization
		V	Caison gage

HABITAT LAYOUT - STARBOARD ELEVATION



HABITAT LAYOUT — PORT ELEVATION

Fig. 4. Specifications of NOAA's Aquarius Habitat (Cont.)



HABITAT LAYOUT — PLAN VIEW

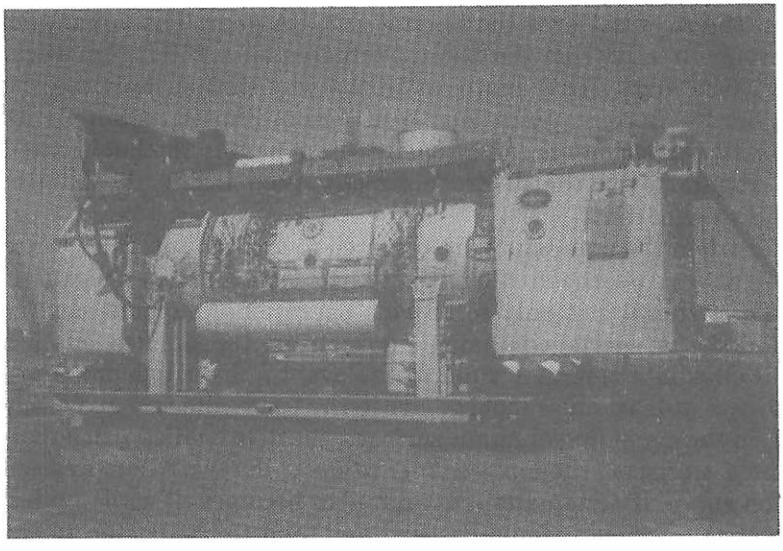


Fig. 4. Specifications of NOAA's Aquarius Habitat (Cont.)

descriptions and discussions of their respective operations are found in the references (Smith and Rounds, 1988; Kalvaitis *et al.*, 1987).

In addition to these major components, two other systems were added to support the aquanauts while in the water. The GAZEBO is an open bell structure placed on the seafloor adjacent to the habitat. A fresh air bubble is maintained inside with hard wire communications to the habitat and shore. This provides the aquanauts with a place where they can enter, remove their mask, relax, hold conversations, and talk to those in the habitat or on shore. It can also be used for an in-water emergency or as a refuge in the event the habitat had to be evacuated. To preclude having to carry the tanks into the habitat, a rack is provided on the GAZEBO for storing the tanks and the aquanauts go to and from the habitat by holding their breath. However, an umbilical hose with a regulator is available in the event of a problem.

To increase the aquanauts' horizontal excursion capability a remote way-station is placed, if possible, in an area close to the scientist's working area. It is normally placed at the same depth as and within a 30 m radius of the habitat. Similar to the GAZEBO, the way station is an open bell. It also provides the scientist with two tethered umbilicals allowing use of full-face masks. The umbilical is neutrally buoyant allowing the researcher freedom to do his or her work. It also provides the hard wire communications to the habitat, to other divers on the umbilicals, and to the surface support boat overhead. To transit to and from the way-station the scientist uses the habitat SCUBA gear. The aquanauts may also work directly from the habitat tethered on a 150 ft. umbilical using a full face mask. This again, as in the way-station, provides the diver with hard wire communications as well as unlimited air supply. In this way, *in-situ* experiments can be easily set up next to the habitat and monitored regularly by the diver or directly from inside the habitat through the view ports.

Except for when the aquanauts are tethered to the habitat, the surface dive boat is always overhead whenever the scientists are in the water. The purpose of this is not only to provide operational support such as fresh air tank drops, special equipment, and retrieval of samples, but also to provide immediate emergency aid in the event a diver has problems. There is always at least one support diver in the boat suited up and ready to respond. In the event an aquanaut surfaces, the dive boat can, in a matter of minutes, transport the injured diver to one of the two recompression chambers on shore. If an aquanaut is injured or becomes ill while underwater, the staff physician would descend and tend to the person in the habitat. If warranted because of the seriousness of the injury, the mission could be terminated and the entire team decompressed back to the surface.

V. TYPICAL DIVE SCENARIO

The scientists that will be saturating are required to arrive at the shore base at least three days prior to the start of the mission. This allows for medical checks, briefings on safety, emergency, and operational procedures, verification of diving experience and capabilities, underwater tours of the canyon and the facilities available,. and other pre-dive activities. Many scientists choose to arrive even earlier; up to one week ahead of time. They may conduct pre-mission activities such as surveying their research site, gathering "ground-truth" data by surface diving, setting up experimental apparatus, establishing their surface analysis and support capabilities, or preparing specimens and materials to be used in their research.

Likewise, at the completion of the mission, the scientists are required to remain on site for at least two additional days for debriefings and to ensure that no side effects have occurred. Some remain for as long as a week to work up their data, to obtain supporting data from the surface, and to prepare preliminary reports.

It is important to emphasize that throughout the entire process from the original solicitation for research proposals to the completion of the mission, close interaction is required between the project staff and the researchers. In this way the researcher knows precisely what facilities are available, what can and cannot be done, and what research opportunities are available. Also, the project staff learns what science is being proposed and what capabilities will be needed. The staff is very experienced and willing to work closely with researchers in developing their research projects and satisfying their needs. This close communication also ensures that everything is ready when the team appears on site.

Typically a research mission lasts ten days, with five scientists being saturated. If needed, topside scientists may also assist in gathering and analyzing data and samples in support of those in the habitat.

The normal dive scenario of the AQUARIUS allows scientists the maximum amount of time in the water for performing their research, conducting numerous daily excursions, and working around the clock. The habitat is currently located at the head of the Salt River Marine Canyon as shown in the artist's conception, Fig. 5. It is at a depth of 61 fsw, with a hatch depth of 50 fsw. The canyon has a gentle sloping floor with two parallel walls that provide the marine scientist unique ecosystems having a diversity of fauna and flora.

As true of all NOAA's undersea research programs, diving operations at the AQUARIUS must conform to NOAA's diving regulations (NOAA, 1983). As such, the maximum allowable depth for the divers is 130 fsw

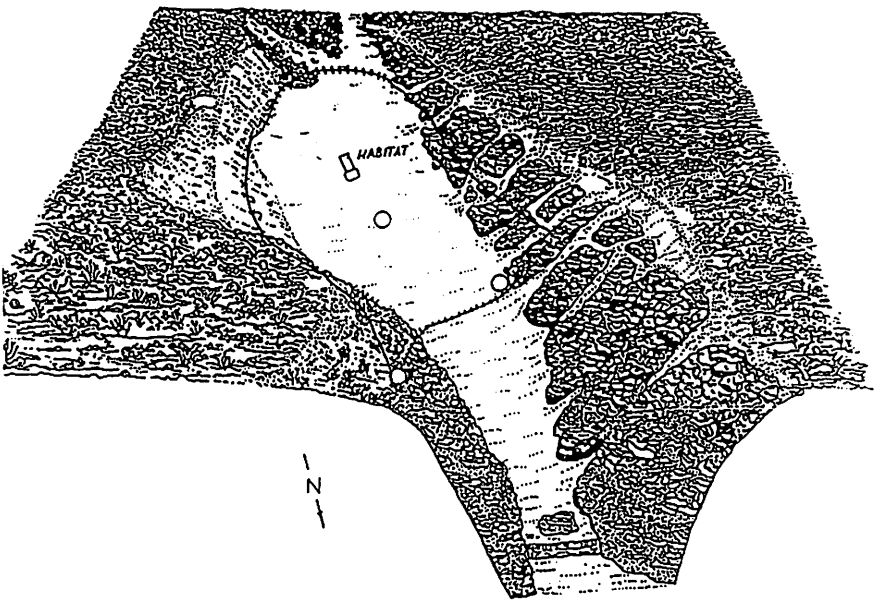


Fig. 5. Artist's conception of Salt River Submarine Canyon (O Way Station, ++++ Excursion Boundary).

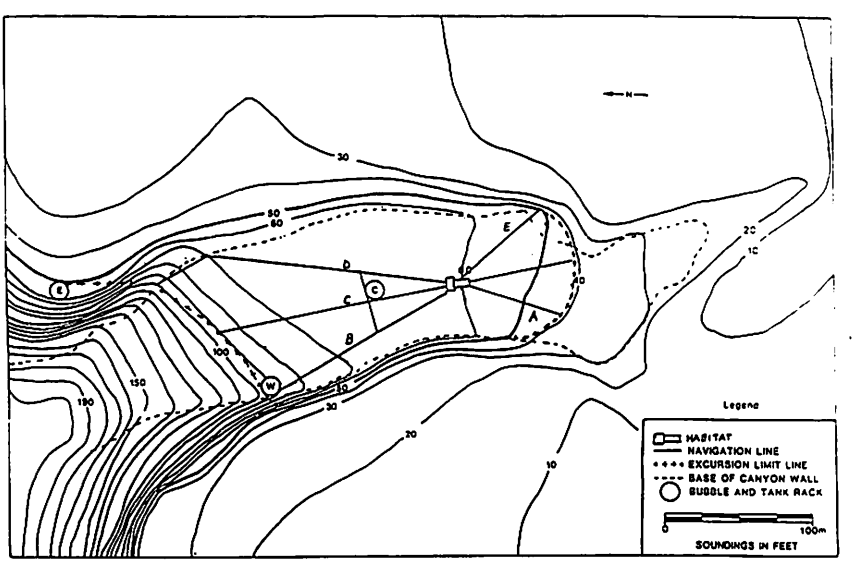


Fig. 6. Topographical canyon map and navigation grid system.

with all dive profiles being restricted to no decompression limits. Under certain conditions with special case-by-case approval, the depth limit may be extended to 150 fsw. Because of being saturated, the upward depth limit is 45 fsw. Horizontal excursions are limited to 350 m which represents 20 minutes of swimming time for the average aquanaut. However, with the maximum depth extended to 150 fsw, the seafloor contours and topography often limit the actual excursion distance. Fig. 6 is a topological map of the canyon showing the depth contours and the horizontal excursions limits. A horizontal grid system also indicated in the figure, provides the divers a visual means of locating the habitat and the way stations. It consists of polyproplyene line anchored on the sea floor with arrows that are placed every 10 ft and show the direction to the habitat. (NOAA's Undersea Research Center at FDU, 1988b).

With the habitat at a storage depth of 50 fsw, the aquanauts are allowed 9 hr of daily bottom time without decompression for depths less than 100 fsw. The first excursion can last up to 6 hr with a subsequent minimum surface interval (in the habitat) of 4 hr This also allows for another excursion of up to 3 hr per day. Note, however that for an excursion to 150 fsw, only 42 min would be allowed. After the required surface interval, a subsequent excursion on the same day woud be limited to only 21 min. Obviously, the allowable working time at 150 fsw is greatly reduced compared to depths less than 100 fsw. However, experience has shown that, at this research site, more than 90% of the research is accomplished at depths less than 95 fsw. Since most species of corals exist only at depths where light penetrates, many scientists using the AQUARIUS are not interested in going deeper.

A minimum of 12 hr surface interval in the habitat is required prior to the diver being allowed to repeat the above maximum excursion times. In addition, to provide a safety margin, the no decompression time limits for all excursions are decreased by 5 min during actual dive operations. Unlimited bottom time is allowed at depths with ± 3 fsw of the saturation depth. In this range, the scientists who are working with tethered umbilicals from either the habitat or way station can remain in the water as long as required for their research.

The aquanauts are free to go anywhere in the canyon within the required excursion, depth, and time limits. All dives are conducted with a "buddy" and no one is allowed in the water by themselves. At least one hour prior to leaving the habitat, they must inform the shore base of their dive profile plan, what they will be doing and any special support they may require. One person must always remain in the habitat. Upon their return, the shore base must be notified.

The goal of the project staff is to ensure that the aquanauts are free to conduct their research and not be encumbered with operational and "habitat-keeping" activities. The shore base constantly monitors the habitat's and the aquanauts' activities on a 24 hr basis. The on-board staff member takes care of all operational needs and where possible, helps the scientists.

VI. FUTURE DIRECTIONS

In support of enhancing the diver's capability in the water for both saturated diving and diving from the surface, numerous efforts will be addressed in the future. They will include not only fundamental hyperbaric physiology but also technology development and operational procedure improvement. Accurate, reliable, and long term dive profile recorders are needed that can be interfaced directly with a computer, recording parameters such as depth, time, oxygen partial pressure, and ambient temperature. For safety, a three dimensional tracking system is needed for tracking individual divers from both the habitat and the surface support boat. From a physiological focus, work is needed in developing tables and procedures for multi-level diving, long term no decompression shallow water repetitive diving, and the use of mixed gas on excursions from saturation storage depths. In addition the need for a highly mobile shallow open-bell/habitat system has been identified by many scientists. This would require development of tables and procedures for bounce diving down to the submerged bell with a subsequent surface decompression in a deck decompression chamber. Additional studies are needed in the area of the effects of in water hazardous materials on divers, better accident management and on-site emergency response, and use of oxygen in decompression.

The AQUARIUS offers a unique opportunity for the study of some of these topics. Many of the efforts could be conducted in conjunction with other on-going science missions on a "piggy-back" basis. Because it supports up to 60 aquanauts per year, the program also offers the possibility of obtaining good statistical data.

The AQUARIUS is truly a state-of-the-art scientific facility dedicated entirely to marine science. It provides researchers with the ability to translate their shore based marine laboratory capabilities directly into the sea where they can more effectively carry out their work. In many cases, without this habitat, this research would not be possible.

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10

Nitrox and Heliox Saturation Diving in China

Zhong Yuan Shi

I. INTRODUCTION

China has been developing her saturation diving technology since 1975. The experiments in this area have been mainly conducted by the Chinese Underwater Technology Institute (CUTI) and Underwater Engineering Company which are under the Chinese Ministry of Communications, and by the Chinese Navy Medical Research Institute. Also, some of the research institutes from the Chinese Science Academy and some universities also share contributions in this field. Since then, a series of experiments including air saturation diving, N_2-O_2 (Chen, 1985; Zhang *et al.*, 1984; Zhao *et al.*, 1982; Zhao and Shi, 1982), and He-O_2 (Shi and Zhao, 1981; Shi and Zhao, 1987) saturation diving have been carried out. In addition to these, the CUTI scientists also performed a 5000 m high altitude simulated diving experiment and a high altitude diving experiment which was conducted in a lake at 4420 m above sea level.

II. AIR SATURATION DIVES

As for the N_2-O_2 saturation diving experiments, we reached a maximum depth of 50 m with a maximum duration of one month (including decompression). The maximum depth of excursion was 75 m in a dry chamber (30 min) and the experimental excursion in open-sea was to a maximum depth of 64 m (217 min). The air saturation dives conducted are summarized in Table 1.

III. HELIOX SATURATION DIVES

For He-O_2 saturation diving, we have completed several experiments covering 302m, 200m and 165 m. In addition, we performed an 80 m saturation dive with a 100 m experimental excursion in open sea. In 1987, we conducted a 300 m saturation dive in a dry chamber with a 300 m excursion in a wet chamber at CUTI's facility (Table 2). That was a comprehensive underwater experiment with multiple objectives. Recently, we conducted a 25 m nitrox saturation dive; its air excursions were between 50 and 75 m. In the experiments mentioned above, we concentrated our studies on physiology, hyperbaric medicine and decompression theory, the influence of hyperbaric pressure and hypobaric pressure, and of hyperoxia and hypoxia on physiological changes as well as on the underwater working capability. Furthermore, researches were also made on diving equipment, underwater communication systems, underwater tools, high pressure systems, and a helium reclamation and purification system. There are reports available to describe the research work mentioned above. I will now focus this report on the 300 m He-N_2-O_2 saturation diving which was completed last year and the collaborative Chinese-American project on nitrox saturation excursion diving, held recently.

IV. 300 m TRIMIX (He-N2-O2) SATURATION DIVING

From May 23 to June 12, 1987, a He-N_2-O_2 saturation diving experiment to a depth of 300 m was conducted in the hyperbaric chamber system which is located at the Chinese Underwater Technology Institute, Shanghai, China. Some eight research projects were arranged in this experiment. These included:

1. Evaluation of China's first 300 m He-O_2 saturation diving chamber system and its auxiliary systems.
2. Fine tuning the automatic control system for chamber pressure and partial pressure of oxygen.

TABLE 1.

Air Saturation Diving, 1977-1979

No. of Exp.	Date	Number of Subjects	Depth (m)	Time of Exposure (day)	Decompression Time (hr:min)	Oxygen Time (hr:min)	Number of Bends	Method of Decompression
1	Nov. 23 — Dec. 4, 1977	6	20.0	10	43:31	6:26	0	stage
2	Dec. 19 — Dec. 29, 1977	6	30.5	7	70:45	7:30	0	stage
3	May 2 — May 13, 1978	7	30.5	8	72:38	7:00	0	stage
4	June 1 — June 12, 1978	7	30.5	9	70:50	7:00	0	stage
5	July 13 — July 23, 1978	3	30.5	6	67:13	6:40	0	stage
6	Aug. 5 — Aug. 18, 1978	7	36.5	9	79:03	9:33	0	stage
7	May 17 — June 16, 1979	7	36.5	26	95:54	10:25	0	linear
8	June 30 — July 11, 1979	6	50.0	5	171:30	12:30	1	linear
9	Dec. 3 — Dec. 13, 1979	5	36.5	6.5	89:47	10:47	0	stage

TABLE 2.

Helium-Oxygen and Helium-Nitrogen-Oxygen Saturation Dives

Name	120 m. $He/0_2$ Saturation Diving/165m Excursion	200 m. $He/0_2$ Saturation Training Dive	302 m. $He/0_2$ Saturation Dive Experiment	300 m. $He/N_2/0_2$ Saturation Diving Experiment
Year	1979	1982	1981	1987
Date	12/19-12/26	3/31-4/7	5/9-5/22	5/23-6/12
Number of Divers	3	4	3	4
Depth (m)	120	200	302	300
P_{o_2}(kpa)	31-40	38-42	35-40	35-40
P_{N_2}(kpa)	<112	80	120	350
P_{co_2}(pa)	<1000	<1000	<500	<500
Chamber Temperature (°C)	30-32	30 ± 2	30-32	29-32
Humidity (%)	46-72	60	40-80	50-80
Compression Time (hr:min)	4:20	9:00	29:50	9:40
Bottom Time (h)	44.80	53.00	43.50	166.00
Decompression Time (h)	79.50	107.25	239.00	305.00
P_{o_2} During Decompression (kpa)	44-51	60-63	47-51	51.0-51.5
Total Dive Time (day)	7	7	13	20
Excursion	Dry Chamber 165m	None	None	Wet Chamber 16 man-dives
Equipment	3x Company (Norway)	Comex (France)	3x Company (Norway)	Home Made

3. Testing the helmet and mask, water-heated diving suit, and hot water system for 300 m dive.
4. Evaluation of underwater telephone and tools.
5. Assessment of helium reclamation and purification system.
6. Conducting research on diving physiolgy and hyperbaric medicine at 300 m depth.

A. The Compression Process

Four healthy and experienced professional divers were involved in the experiment. They were all well trained and excellent in diving performance. Half a year before the experiment, they received a strict physical examination and technical training. Tests on physiological function covering nervous system, cardiovascular function, metabolism, visual, auditory and psychological function were performed one week before the experiment. Adjustments of the chamber system with accessories were completed in advance so as to make sure that there would be no unexpected changes for the subjects or the mechanical system. While compressing, the trimix gas mixture adopted for the experiment was Po_2 0.4 ATA, N_2 4.6 ATA and the balance He. Compression projects were designed to compress to 10 m with compressed air, then go on compressing to 90 m with pure helium and finally to compress to the scheduled depth with helium and nitrogen. A chromatograph was used to measure the nitrogen concentration during compression. Compression rate was 5 m/min to 180 m. During the 2-hour stop at 180 m, electroencephalogram, ECG, and tremorgram were recorded. No physiological abnormality was noted. Then, depth increased to 240 m at a rate of 3 m/min. According to the scheduled test requirements, divers had a 6-hour stop at 240 m, completed lunch, a nap, as well as a systematic physiological function test in succession; neither clear decrement of physiological function nor discomfort appeared. The 300 m terminal depth was reached by compressing at a rate of 1.5 m/min from 240 m. The total compression time was 9 hr and 40 min which included 1 hr and 40 min in compression and 8 hr of stops. No signs of high pressure nervous syndrome (HPNS) were found during the entire compression process.

B. Saturation

Divers were saturated at 300 m for 7 days and nights as planned, and completed a series of tests in both dry and wet conditions. Divers were tested for physiological function three times in the dry chamber on the 2nd, 5th and 8th day of saturation. Cerebral, cardiovascular, respiratory,

visual, auditory and psychological functions were examined. At night, records were made on some divers for somnolence, EEG, ECG, EMG and respiratory frequency. Also, urine collections were made and their content analyzed. No evidence of physiological abnormality was found. All the values were within the normal ranges. On the 3rd, 4th, 6th, and 7th day of the saturation exposure, 4 divers carried out excursion dives in the wet chamber for a total of 16 man-dives. The water depth in the wet chamber is 3 m. Divers tested the locally-manufactured TZ-300 helmet and MZ-300 mask and compared them to equivalent, imported products. We concluded that the domestic products performed similarly to the foreign products. This suggests that China's research and manufacturing level have kept abreast with the world at an advanced level.

Hot water diving suits were tested in the wet chamber in 16 man-time diving operations. As it is well known, both the diver's health and working efficiency are greatly influenced by the cold water condition of the open sea. Therefore, we made special efforts in developing the hot water diving suit. During this saturation dive, a test was conducted on this hot water diving suit. The lowest water temperature was 9°C. Divers' body surface and rectal temperatures were recorded. A comparison of diving suits was made between domestic and foreign products. No obvious differences were discovered.

Divers' aerobic capacity was studied by using a bicycle ergometer built by the staff of this Institute, both in dry and wet conditions. Only moderate workloads were required of the divers. While doing the physical loading test, researchers collected expiratory gas which were analyzed for O_2, and CO_2 concentrations and expiratory minute volume was measured. Records were made for some indices of cardiovascular function, in order to discover physiological differences between divers receiving the same physical loads at various depths. Observations were also made on cardiopulmonary functional reserves and recovery speed. The results showed their work ability at a moderate load was not changed at the 300 m depth compared to the surface control.

On the 7th day of saturation, divers tested four sets of underwater hydraulic tools, in both dry and wet chambers. The underwater tools tested were shock spanner, cutting saw, scraper, and sharpener. These tools were powered by a hydraulic power source of 140 ATA. The test showed that all these 4 sets of tools are acceptable in terms of design, operation, touch, as well as easy handling by the divers. The successful development of these 4 sets of hydraulic tools provides a reliable expectation for future operation in deep sea exploration.

The helium unscrambler (Sh-2) and a 381 m long communication cable which were newly built in China were tried in both the wet and dry

chambers at various depths throughout compression and decompression, and remained at 300 m for some time. From the dialogue test and intonation recording, we believe that this product also is of a quality comparable to imported ones of the same type.

C. Decompression

Development of decompression tables remains a key technical problem in the trimix saturation diving. Helium has a different physical characteristic from nitrogen. Solubility is greater for nitrogen than helium. Therefore, at the same partial pressure and temperature, the dissolved N_2 volume in tissues is larger for nitrogen compared to that of helium. On the other hand, the diffusion rate of N_2 is slower than that of helium, since diffusion rate is inversely proportional to the square root of molecular weight. For this reason, both saturation and desaturation rates of N_2 in the body are much slower as compared to helium. The presence of both N_2 and He presents a difficult problem for efficient decompression in the He-N_2-O_2 saturation dives.

In this dive, we formulated a 307 hr decompression profile based on existing tables and our own accumulated experience. Apart from this, we also adopted a continuous decompression method. During decompression, bubble detection by a doppler ultrasonic device was performed 3 times a day, morning, afternoon and evening. The experiment showed our decompression profile to be safe and reliable. No symptom of decompression sickness was noted.

D. The Hyperbaric Chamber System

The hyperbaric chamber system employed in this experiment is the first manufactured in China. This system meets the requirements of carrying out HeO_2 saturation diving at 300 m, diver training, physiology research, and hyperbaric oxygen treatment. It can also serve for the testing of diving equipment. The diving complex consists of two main chambers, a control room, and the auxiliary equipment. The chamber system consists of 2 dry chambers which are of the same configuration, and a wet chamber. The dry chamber is a space designed to accommodate four divers. The wet chamber is designed for simulating the underwater environment, which enables divers to perform excursions. The wet chamber is divided into upper and lower parts. The lower part can be filled with 3 m of water and the upper part has a space of 17 cubic meters.

E. Automatic Environmental Control System

Chamber pressure and Po_2 are controlled by an automatic system. This is China's first system of this kind to have been put into operation. The control system is fitted with domestic-produced pressure transducer and Po_2 sensors which send the real-time measurements of both chamber pressure and Po_2 to an A/D convertor and a computer. Pressure and Po_2 are maintained at a desired level by a software package to control a variety of valves in storage cylinders and the exhaust system. This machine and computer program arrangement allows us to control pressure and Po_2 at set values during compression, saturation, and decompression. This system produces excellent control and stability, and is a great improvement in controlling the hyperbaric environment, saving manpower and achieving a greater degree of accuracy.

F. Helium Reclamation and Purification System

Helium reclamation and purification is important to China since she lacks a helium resource. This system was manufactured completely in our Institute. At present, the machine is being used to recover the helium from the exhaust gases. The rate of recovery has reached 85% or higher. The membrane separation is used to obtain purified helium which complies with the national standard.

V. U.S.-CHINA COLLABORATIVE RESEARCH

A collaborative experiment which included the Chinese Underwater Technology Institute, NOAA's Office of Undersea Research, and Hamilton Research, Ltd. was conducted at CUTI's facility in Shanghai during October, 1988. The experimental objectives were to extend the validation of NOAA's new repetitive, excursion, surfacing techniques, and oxygen procedures for habitat diving (Hamilton *et al.*, 1988). This was designed to cover longer, deeper excursions, oxygen exposure management, a test of decompression algorithm for multiday repetitive excursions computed on a 'worst case' basis, and the saturation decompression after excursions. The objectives were successfully accomplished.

Four experienced divers were saturated at 25 msw for 5 days, during which time they did 15 air excursions to depths between 50 to 75 msw, for times up to 240 min. Decompressions from excursions were mostly no-stop, but 5 required stops ranging from 3 to 116 min. Saturation decompression began with the 'precursory' ascent following a brief return to 25 msw. Doppler bubble detections showed some bubbles following excursion,

Spencer score II and occasionally III, and during saturation decompression, especially after muscle flexing. However, no symptoms of decompression sickness were reported. Oxygen exposure reached its peak at 6 days at 3,103 Oxygen Toxicity Units, but no symptoms were reported. Vital capacity measurements, which showed some variation, did not reveal any changes. An unexpected change in pulmonary blood flow measured with impedance plethysmography showed changes in 3 of the 4 divers during periods of high decompression stress, which is typical of pulmonary hypertension. Additional physiological measurements showed anticipated responses (Hamilton *et al.*, 1989). While these experimental findings are important, perhaps the most significant result was the initiation of cooperation between scientists of these two countries.

So far, we have made some important progress in saturation diving experiments and have accumulatd a great deal of experience and data, which needless to say, are beneficial to the practical diving operations in the future. What's more, we have also secured some necessary diving equipment from both domestic producers and abroad, chiefly the U.S., France, and Norway. Some of these facilities have been affixed onto diving vessels and oil platforms and have been used well in training divers and simulated saturation diving experiments in the open sea. However, saturation diving technology has not been well applied to the practical diving operations in China at present, due to the as-yet limited ocean petroleum exploration and production. It is a very urgent goal for us to put our saturation diving technology into practice in China.

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11

Confidence in Decompression Safety

P.K. Weathersby

I. INTRODUCTION

Every decompression procedure carries some risk of the diver suffering decompression sickness (DCS). The object of this paper is to show how to estimate this DCS risk, and to establish how confident one should be about the estimate.

It appears that there are 3 ways to confidently obtain a safe decompression schedule. First, one could apply the physically and physiologically correct theory and predict an outcome. With the correct theory the prediction would be as reliable as the prediction of electrical current in a simple circuit after a known voltage is applied. Is such a correct theory available today? Clearly not. The theory would have to provide a quantitative framework for all relevant mechanisms, and we would also need the correct parameters, or "engineering data" to make full predictions. Decompression theories are based on the assumption (still unproven) that DCS results from bubbles of inert gas. The correct theory requires a mastery of the kinetics of inert gas exchange in people. Present theories cannot even confidently answer the question: does nitrogen or helium exchange faster? Indeed several theories have opposite answers to that question

that have yet to be critically addressed by a direct experiment (Homer and Weathersby, 1980). The correct theory also requires a mastery of bubble kinetics within a living human. Elsewhere in this book is Yount's exposition of such a bubble kinetic theory, but I am sure Yount would agree it is far from completely demonstrated to correspond to joint pain DCS in humans. The correct theory would also require answers to any interactions between gas kinetics and bubble kinetics, such as whether the presence of bubbles affect gas elimination rates, by how much and when? (Weathersby and Homer, 1981) Again, some interesting speculative answers are available, but a confident and precise answer is simply unavailable.

The second general means to establish a reliable and confident answer would be extensive direct testing. That is, even without knowing how to make correct predictions, we could obtain some decompression procedure and test it enough to build up a confidence in its performance. How much is enough? It is a general observation that such tests are not fully reproducible. This important "random" aspect of DCS must be dealt with statistically. When the same procedure is used with different people, or even with the same person on different occasions, the outcome is not constant: DCS may occur or it may not occur. Building confidence then consists of generating statistical confidence limits for the conditions of the test.

II. REPETITIVE TESTS

Consider the following possible test results on a proposed new schedule (Table 1). In this example, we assume that many subjects have repeated the same dive and decompression. We have reproduced all conditions carefully and thus assume that all outcomes are equally valid. Thus our statistical "model" is that there is a single underlying rate of incidence for this decompression schedule. The trial's purpose is to estimate the unknown % incidence of DCS, and the confidence limits about that incidence. The column %DCS is the raw incidence observed. Because of the known variability of DCS, we cannot be sure that this raw incidence is precisely the underlying incidence, and in fact it almost never is. The confidence limit entries in Table 1 are taken from tabulated 95% confidence limits on binomial distribution (Deim, 1962). Interpretation of the confidence limit is: with the trial result as given, we can assert that the actual underlying DCS incidence is within this range and be correct about 95% of the time. If we only need to be 90% or 80% certain, then correspondingly narrower confidence limits are available.

TABLE 1.

Uncertainty in Single Repeated Trial, No DCS

DCS Cases	Trials	% DCS	Confidence Limits, on % DCS
0	5	0.0	0.0 - 52.2
0	10	0.0	0.0 - 30.9
0	20	0.0	0.0 - 16.8
0	50	0.0	0.0 - 7.1
0	180	0.0	0.0 - 2.0
0	400	0.0	0.0 - 0.9

Entries in Table 1 show the uncertainty expected for trials that do not result in DCS. As the trial size increases, the uncertainty decreases. If the trial was only 5 safe dives, the incidence might be as high as 52% DCS; if it extended to 50 safe dives, we could be confident that the schedule would not produce over 7% incidence in the long run. About 180 dives free of DCS would be required to feel confident that the schedule in question is actually safer than 2% DCS, and nearly 400 repeated safe dives would be needed to convince us that the schedule is safer than 1%. Clearly, tables accepted after only 5 or 10 safe dives do not provide any real assurance of actual safety.

Seldom has it happened that a long trial had no cases of DCS. More commonly, one or more cases occur, and the question becomes: are these cases "proof" that the procedure is seriously unsafe, or were we unfortunate in having the rare DCS case occur despite a generally low expected DCS incidence? Table 2 shows the results of several hypothetical trials that actually did result in DCS. In each case the raw results are 2% DCS, and the confidence range again shrinks with the effort of more dives. With a total trial size of 250 dives we would be confident that the actual incidence was under 5%; over 1000 dives would be needed to ascertain that our observed 2% was actually no higher than 3%.

TABLE 2.

Uncertainty in Single Repeated Trial, Some DCS

DCS Cases	Trials	% DCS	95% Confidence Limits, on % DCS
1	50	2.0	0.1 - 10.7
2	100	2.0	0.2 - 7.0
5	250	2.0	0.6 - 4.6
20	1000	2.0	1.2 - 3.1

Seldom do we have the resources to conduct 100 or more trials on each procedure we expect to validate. For testing each schedule, the process of sequential design can generate some efficiency if the trial is set to test that schedule until a given acceptance or rejection rule has been satisfied (Hays *et al.*, 1986; Homer and Weathersby, 1980). Nevertheless, the same "ballpark" is present: 20-50 dives can reassure us that the procedure is better than 10%; several hundred are required to assert confidently that the schedule is better than 2%.

Is this degree of testing a realistic possibility? The only answer seems to be no. If we needed to examine a decompression schedule from saturation at 400 fsw to "prove" that the incidence of DCS was under 2%, Table 1 shows that with the best of luck, a sequence of 180 man-dive tests are required. With a spacious chamber allowing 6 men to dive together, and allowing 2 weeks for chamber set-up, saturation, and decompression for a single run, some 60 weeks intensive chamber use would be needed, at a cost well over $1,000,000.

III. PROBABILISTIC MODELS

The third general approach to gaining confidence employs aspects of both theory and statistically guided testing. Let us start with a specific example of saturation excursion diving. In Table 3 of Homer and Weathersby (1985) are the known list of such dives as of 1982. Some 310 tests are listed, but with limited replication provided, certainly less than the hundreds per condition shown earlier to allow real confidence in safety. Many tests are "almost" replicated, say steps to 154 fsw from various saturated depths with 3-13 exposures each. Can the results on one test be used to provide information on another schedule which is similar but not identical? The answer is yes, but it requires a statistical modeling approach. Substantial progress with that approach has been made in recent years (Hays *et al.*, 1986, Parsons *et al.*, 1988; Tikiusis *et al.*, 1988; Vann, 1987; Weathersby *et al.*, 1984, Weathersby *et al.*, 1985; Weathersby *et al.*, 1987).

The model must predict the probability of the outcome of any known exposure, such as the 310 exposures just mentioned. Thus we must express the probability of decompression sickness, p(DCS), as a function of the important features of the dive.

$$p(DCS) = f(\text{dive}) \qquad [1]$$

And since many dives are safe, we also provide the probability of a safe outcome:

$$p(\text{no DCS}) = 1.0 - p(DCS) \qquad [2]$$

TABLE 3.

Predicted p(DCS) for Air Saturation Decompression NOAA Table 12-10

Air Depth (fsw)	Decompression Time (min)	p(DCS), % 95% Confidence Limit
25	741	0.4 - 2
30	855	1.4 - 4
35	885	3 - 7
40	915	5 - 11
45	945	8 - 16
50	975	12 - 22

To be able to compare to data we need a measure of how well the predictions fare. This is provided by the likelihood function, L, which takes the prediction of each individual outcome and multiplies them as independent probabilities to achieve the overall probability of likelihood of the entire set of known exposures.

$$L = p(\text{outcome 1})\, p(\text{outcome 2}) \ldots p(\text{last outcome}) \quad [3]$$

The objective then is to adjust any parameters in the predictive model until L is maximized, that is until we achieve a maximum likelihood or ML. (Because the individual probabilities are much less than one, L and ML are commonly expressed by their natural logarithms). As a trivial exercise, one can demonstrate that the simplest of all models,

$$p(DCS) = K \text{ (i.e. does not depend on dive profile)} \quad [4]$$

can be applied to the data of Table 2 with the expected answer. For example take 1 case of DCS out of 50 trials. L is composed of 1xK and 48x(1.0 − K) which has a maximum at K = 0.02.

In general, this function in Eqn [1] accepts descriptions of the dive depths, times, and gas mixtures. Although not yet attempted, measures of individual susceptibility such as those discussed by Ward *et al.*, 1987 elsewhere at this Symposium, could also be included in the formulation of p(DCS). The functionality is supplied by any theory or empirical formula capable of generating the probability prediction. For the example data of helium one-step decompression (Weathersby *et al.*, 1984), the exposure time (i.e. saturation — defined as 40+ hr at depth), and gas mixture (on the assumption that only inspired He needs to be considered), were kept constant. Therefore the remaining variables needed to describe the decompression are helium partial pressure before the excursion (labelled P_1) and depth afterward (P_2). We will now step through an empirical

process. (A detailed example is in the Appendix). First, a simple measure of the decompression stress, R, is the magnitude of the decompression step itself:

$$R = P_1 - P_2 \qquad [5]$$

This stress needs a dose-response formulation to predict probability. The Hill equation can be applied for that purpose:

$$p(DCS) = \frac{R}{R + R_{50}} \qquad [6]$$

The parameter R_{50} is the decompression stress required to cause DCS in 50% of the divers who receive such a stress. Note that the model says that any stress (pressure reduction more than zero) has a finite probability of DCS that eventually approaches a p(DCS) of 1.0 (i.e. 100% incidence) as the pressure reduction gets very great.

Use of the 310 helium one-step decompression (Weathersby *et al.*, 1984) data with the model described by Eqn [6] and [2] is direct. One tabulates all 310 trial values of R with their known outcomes, and tries different values of R_{50} until a ML is achieved. Different uses of the marginal cases is discussed in Weathersby *et al.* (1984) and Weathersby *et al.* (1987); for the results described here each marginal was considered 1/2 case of DCS. With that use of the data, we find that the best value of R_{50} is 843 fsw.

A decompression of over 800 fsw to produce 50% DCS is disturbing in that most people would expect a much greater incidence from such a severe decompression. Indeed with that R_{50}, we predict that a 200 fsw decompression step would lead to a 19% incidence of DCS — probably too low an estimate. More insight into the problem is provided by using the "Null" model of Eqn [4] ($K = 0.069$) that denies any effect of depth which actually gives a ML almost identical to the ML from the Hill model.

This unsatisfactory result leads us to the next refinement in modeling. Many people have suggested that the "safe" amount of step decompression is larger at deeper depths. We can explore that quantitatively by allowing our 50% DCS parameter to vary with depth:

$$R_{50} = a + b P_2 \qquad [7]$$

When the ML is obtained with this model, we find that $a = 181$ fsw and $b = 2.55$, with an improvement in L by a factor of over 1000. This large an improvement in Likelihood is almost certainly not due to the chance improvement in L when an additional parameter is used in the model. The formal test of such a statement is a Likelihood Ratio test (Kendall and Stuart, 1979). The predictions of this improved model also agree with

our expectations: for a diver breathing about 0.4 ATA O_2 in helium, a 200 fsw decompression step from 200 fsw to the surface runs a 41% chance of DCS; while the same size step from 1000 to 800 fsw has the lower predicted p(DCS) of 7.5%.

We can expand the model further by adding a term in $P_2{*}P_2$ to Eqn [7] to see whether the depth dependence of DCS risk is curved rather than linear, as suggested by some theoretical models such as Yount's, described in Yount (1979) and Yount and Hoffman (1986), and elsewhere in the Symposium. We find that such a nonlinear functionality is not justified by the 310 helium-saturation dives (Weathersby *et al.*, 1984).

IV. CONFIDENCE LIMITS

Another important component of prediction is the amount of uncertainty in the predictions themselves. This uncertainty arises from 2 sources: statistical uncertainty in the model parameters due to limitations in data and imperfect fits, and uncertainty from choice of the "wrong" model that forces bad predictions, especially into types of dives not well represented in the available data. At this time, this source of uncertainty can only be addressed by comparing predictions of different models which have similar success at fitting the known data.

There is a formal means of dealing with the first statistical uncertainty, called propogation of errors (Ku, 1966). (Like other statistical tools applied to decompression modeling, conclusions drawn from the calculations should be viewed with some caution, as the underlying mathematical assumptions apply to our situation only approximately.) The formula states that for any function, f, based on a set of estimated parameters B, the standard error of the calculated value of f is:

$$SE(f) = \left[\sum_{B_i}^{\text{All Parameters}} \sum_{B_j} \frac{\partial f}{\partial B_i} \cdot \frac{\partial f}{\partial B_j} \operatorname{Cov} B_i B_j \right]^{1/2} \qquad [8]$$

where the double sum extends over all estimated parameters, and the covariance entries are obtained from fitting models to the data. For approximate 95% confidence limits on f, twice the SE is added to and subtracted from the value of f itself. (In some cases, like when f is a low value of p(DCS), it is preferable to apply the propagation of errors on the log of f to avoid a lower limit less than 0% DCS). For the predictions just discussed, the function f is the p(DCS) from Eqn [1,5,6,7]. Parameters and covariance matrix are from fitting the 310 helium dives to that model (Weathersby *et al.*, 1984), see Appendix. When Eqn [8] is used, the p(DCS)

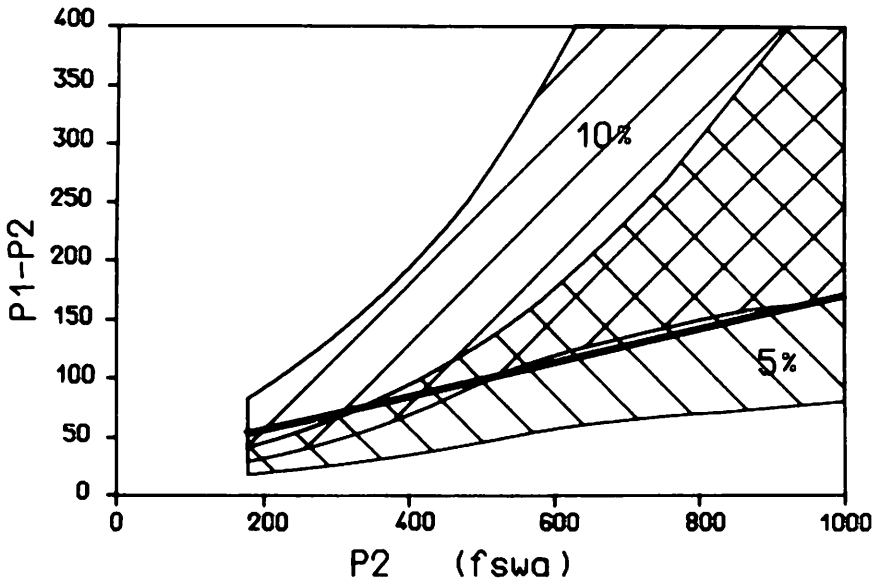

Fig. 1. Human single-step decompression on helium. Amount of pressure reduction (R = $P_1 - P_2$ is plotted against final pressure (P_2) in feet of seawater (fsw). The two hatched areas are approximate 1 SE bands on conditions of 5% DCS and 10% DCS as estimated by methods described in the text. Solid line is 1980 allowable U.S. Navy limit assuming inspired O_2 of 0.4 ATA. From Weathersby *et al.* (1984).

for the 200 fsw to surface step is found to lie between 12 and 71%, and the 1000 to 800 fsw step to have a DCS chance of 1 to 14% (both 95% confidence limits from 2 S.E. bands around the prediction). These rather wide margins indicate that the step from 1000 fsw is safer than the shallower step, but reminds us that the uncertainty from use of "only" 310 dives makes individual predictions not very precise; this is the same message as from Table 2.

A graphical picture of confidence limit results is in Fig. 1. The quadratic extension of Eqn [7] (Weathersby *et al.*, 1984) was applied to the 310 dives and predictions made of 5% DCS and 10% DCS conditions of P_1 and P_2. Propagation of errors around the estimates provided 1 S.E. bands shown by the cross-hatching in the Fig. 1. A rather severe overlap is obvious, demonstrating that 5% and 10% predictions cannot be reliably separated. Superimposed on the 5 and 10% bands is a solid line from the then-allowable U.S. Navy limit on unlimited duration upward excursion diving from helium saturation. The uncertainty bands are large, but it appears that the allowed limits are more conservative in the deeper regions. Such an operational decision as where to add additional margins of safety can be aided by an analysis such as this.

V. MANY COMPLEX DIVES

The principles mentioned above can be applied to large numbers of decompression procedures that span a significant range in depth, time, and breathing gas. Ultimately it will be possible to develop a single model capable of reliably predicting p(DCS) for all conditions of interest. To date, however, our focus has been on describing air or N_2-O_2 dives of variable duration. HeO_2 saturation decompression or short excursion dives from saturation has not been examined.

For the statistical analysis of such a complex set of exposures, a model is needed that deals with both depth and time in a systematic manner. We applied a set of models that were formulated with an integrated "decompression risk" through and following any dive:

$$p(DCS) = 1.0 - \exp(-\int r\, dt) \qquad [9]$$

In Eqn [9], the term r is a measure of instantaneous risk of DCS, which is integrated over the decompression and for some hours after the dive. The integral expression has proven superior to a classical "maximum supersaturation" view in describing different types of dives (Parsons *et al.*, 1988; Vann, 1987). The risk can arise from several different parallel compartments (designated A, B, C, etc.):

$$r = rA + rB + rC = \ldots \qquad [10]$$

The instantaneous risk within each compartment is proportional to a relative supersaturation:

$$rA = aA\,(PtN_2A - Pamb)/Pamb \qquad [11]$$

Here aA is the proportionality constant, PtN_2A is the calculated tissue nitrogen pressure, and Pamb is current ambient pressure. Normalization by Pamb was found to be a reasonable approximation to the depth-dependent tolerance of supersaturation described above (Weathersby *et al.*, 1984). PtN_2 is calculated by assuming single exponential gas exchange kinetics (1 traditional "tissue") whose time constant was estimated from the data. Alternatively the tissue tension can be calculated by a multiexponential residence time function (Weathersby *et al.*, 1979) which has a closer approximation to measured inert gas exchange kinetics in mammals. In all these models, inspired oxygen is ignored in keeping with most decompression calculations and a recent direct study of oxygen's effect (Weathersby *et al.*, 1987). A family of 10 risk models with different gas exchange terms within the framework of Eqn [10-11] was developed for different data sets (Hays *et al.*, 1986; Weathersby *et al.*, 1985).

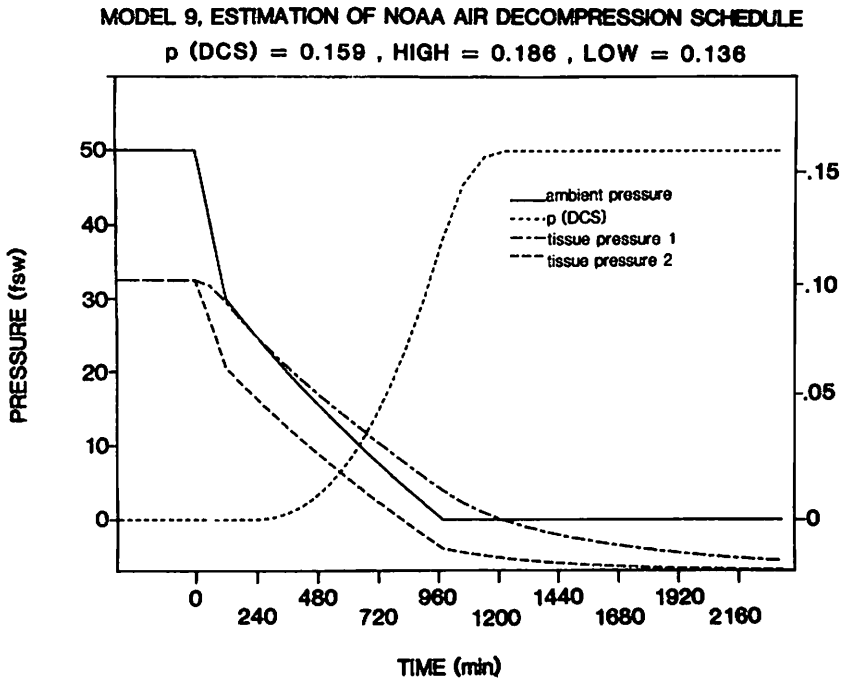

Fig. 2. Evaluation of DCS risk on saturation decompression from 50 fsw breathing air. From Hays *et al.* (1984).

A total of 1992 air and N_2-O_2 dives have been systematically examined with these models (Hayes *et al.*, 1985). Included were 279 saturation exposures. Data for these dives cannot be accurately represented simply as pairs of pre- and post-saturation pressures. Instead a series of pressure-time-gas composition nodes describe the history of each dive. We use up to about 75 of these nodes currently. Substantial effort is expended in verifying data and resolving inconsistencies. In most cases it is necessary to consult original logs or investigators. The degree of data accuracy required depends on the model used. For example, some of the nitrogen kinetic parameters used in Eqn [11] change substantially if a large decompression step is entered as requiring 2 vs 3 minutes. For models like Yount's that feature a "bubble crushing" aspect of compression (Yount, 1979), the initial descent rates will be critical, even though they are poorly recorded for most dives.

Several models with 7-9 parameters well described the 1992 known exposures (Hays *et al.*, 1986). One of these (designated Model 9 in the

report) will be used to illustrate the analyses. Fig. 2 is a plot of a saturation dive profile specified by the NOAA Diving Manual (Miller *et al.*, 1979), in this case decompression from 50 foot air saturation. The solid line shows the course of the 975 min decompression. The dashed and dash-dotted lines are computed values of tissue nitrogen tension which track downward from the prior saturated value. For the model used here, 2 multiexponential "tissues" were used in Eqn [10]. One curve responds rapidly compared to the decompression and never encounters a supersaturated condition ($r < 0$ throughout). The slower responding "tissue" develops a supersaturation when it exceeds ambient pressure from about 240 min into the decompression until about 4 hours after return to surface (0 fswg). During that time, the risk integral, Eqn [9], accumulates and finally produces a total predicted p(DCS) of 16%.

Uncertainty in this calculation was calculated with the propagation of errors using all 8 parameters and their covariance matrix. The resulting 95% confidence limits are in Table 3 for several NOAA air saturation procedures. The 50 fswg saturation has a predicted range of 12 to 22% DCS, around the 16% best estimate presented above. Other procedures from shallower depths appear to be progressively safer. The confidence limits are still not very precise, despite the nearly 2,000 dives used as a basis for the predictions. In most cases there is a 50% uncertainty about the best estimate. Are these estimates accurate? To our knowledge, there are no exposures to 50 fsw following this schedule exactly. In many year use of a habitat placed by NOAA at 42 fsw, several hours of oxygen are added to this decompression with an overall DCS rate of about 2% (Shane, 1987).

TABLE 3.

Predicted p(DCS) for Air Saturation Decompression NOAA Table 12-10

Air Depth (fsw)	Decompression Time (min)	p(DCS), % 95% Confidence Limit
25	741	0.4 - 2
30	855	1.4 - 4
35	855	3 - 7
40	915	5 - 11
45	945	8 - 16
50	975	12 - 22

VI. CONCLUSIONS

Once we have accepted that DCS is a random event for each individual exposure, probabilistic models are a necessity. The goal would have the model embody the "correct" physiology, physics, and pathology; but that goal is far from being achieved. In the meantime, "partly correct" models are extremely useful. As more becomes known about DCS mechanisms, model elements can be replaced in a modular fashion to make the model "more correct". At each step, the model should be fit to the best data set available. The fitting obtains best estimates for parameters that are not already known from external considerations. It also provides a single metric — the value of the likelihood function itself — which allows a comparison among models.

ACKNOWLEDGEMENTS

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APPENDIX: PROPAGATION OF ERRORS ON p(DCS)

Consider the uncertainty in the estimate of p(DCS) for a single step excursion using a model described in the text:

$$f = p(DCS) = \frac{R}{R + R_{50}} \qquad [A1]$$

using the risk definition of:

$$R = P_1 - P_2 \qquad [A2]$$

and the linear form of R_{50}:

$$R_{50} = a + b\,P_2 \qquad [A3]$$

which with the substitutions becomes:

$$f = \frac{P_1 - P_2}{P_1 - P_2 + a + b\,P_2} \qquad [A4]$$

To calculate confidence limits on the prediction, need the propagation of errors formula:

$$SE(f) = \left[\sum_{B_i}^{\text{All Parameters}} \sum_{B_j} \frac{\partial f}{\partial B_i} \cdot \frac{\partial f}{\partial B_j} \text{Cov } B_i B_j \right]^{1/2} \quad [8]$$

The expansion of [A5] to get the variance (SE*SE) for this 2 parameters model is:

$$\text{Var}(f) = \left(\frac{\partial f}{\partial a}\right)_2 \text{Var}(a) + \left(\frac{\partial f}{\partial b}\right)_2 \text{Var}(b) + 2 \frac{\partial f}{\partial a} \frac{\partial f}{\partial b} \text{Cov}(ab) \quad [A6]$$

The partial derivatives of f with respect to a and b are straightforward:

$$\frac{\partial f}{\partial a} = \frac{-(P_1 - P_2)}{(P_1 - P_2 + A + BP_2)} x2 = \frac{-p(DCS)^2}{(P_1 - P_2)} \quad [A7]$$

$$\frac{\partial f}{\partial b} = \frac{-(P_1 - P_2)P_2}{(P_1 - P_2 + a + bP_2)} x2 = \frac{-p(DCS)^2 P_2}{(P_1 - P_2)} \quad [A8]$$

In Weathersby *et al.* (1984) the helium step decompression dives and models were presented. Actually the data were slightly different since alveolar rather than inspired gas tensions were used. The numerical outcome is essentially unchanged. The following parameters and covariance entries were obtained for the above model:

a = 181 ± 196.5	Var(a) = 38,603
b = 2.551 ± 1.466	Var(b) = 2.1482
	Cov(ab) = −229.39

For a numerical example, take a diver saturated at 1000 fswg breathing 0.394 ATA of O_2 in helium. He makes a rapid decompression to 800 fswg.

$P_1 = 1000 - (.394)33 + 33$	= 1020 fswa
$P_2 = 800 + 33$	= 833 fswa
$R = P_1 - P_2 = 1020 - 833$	= 187 fsw
$R_{50} = 181 + (2.551)833$	= 2306 fsw
p(DCS) = 187/(187 + 2306)	= 0.0750
$\partial f/\partial a = -(.075)(.075)/187$	= −0.00003008
$\partial f/\partial b = -(.075)(.075)(833)/187$	= −0.02506
Var(p(DCS))	= .001083
SE (p(DCS))	= .033

Thus the 95% confidence limits are 0.75 ± 2(0.33) or .009 to .141

12

The Physics of Bubble Formation: Implications for Improvement of Decompression Tables

David E. Yount

I. INTRODUCTION

Thirteen years ago at the first International Symposium on Man in the Sea, I presented two papers on behalf of the Tiny Bubble Group, the first dealing with the physics of bubble formation (Yount, 1975) and the second dealing with the improvement of decompression tables (Yount *et al.*, 1975). Not quite satisfied that we had solved all of the problems of diving medicine on our first attempt, my colleagues and I have been working on these same two topics ever since.

Today we return to the scene of the crime. Accordingly, this paper will be partly recapitulation, partly summary, and partly status report. If we were artists, we might call it a retrospective, that is, an exhibition showing the work of an artist or, in this case, a group of artists over a span of years. Whereas our debut 13 years ago was essentially empirical, we now have a theoretical model for bubble formation, and we have actually used this model to calculate a comprehensive and realistic set of diving tables.

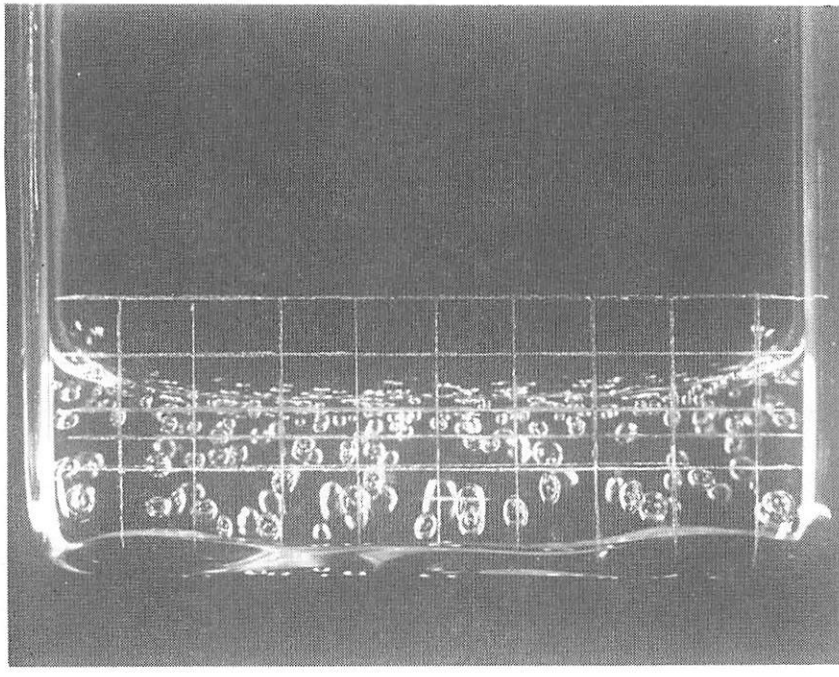

Fig. 1. Photograph of a gelatin sample taken a few minutes after decompression.

In the beginning, there was gelatin, first introduced independently by Strauss in Hawaii and by LeMessurier in Australia some 15 years ago. In the Hawaii experiments, the gelatin is supersaturated with gas by subjecting samples to various pressure schedules in a small pressure chamber. A typical result is shown in Fig. 1 (Yount and Strauss, 1976). The raw data consist of the bubble counts N and their corresponding pressure schedules.

Fig. 2, taken from one of those early Man-in-the-Sea papers (Yount *et al.*, 1975), is a plot of the maximum "safe" supersaturation p^*_{ss} in gelatin versus the initial crushing pressure $p_m - p_o$. Here we are referring to a rectangular pressure schedule in which there is an initial compression equal to p_{crush}, followed by saturation at the maximum pressure p_m, which is followed by a rapid decompression to some final pressure p_f. Graphs of this type of schedule are shown inset in some of the later figures.

Safe supersaturation in this early experiment was defined to be one bubble per 0.4 ml gelatin sample. The combinations of p^*_{ss} and p_{crush} that

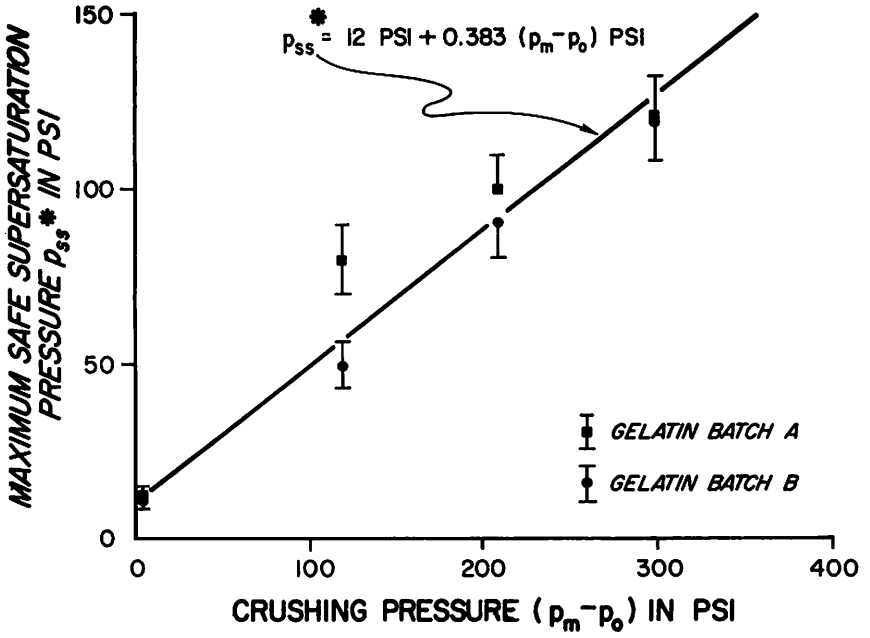

Fig. 2. Plot of the maximum safe supersaturation pressure p^*_{ss} versus the crushing pressure $p_m - p_o$. Safe in this early experiment was defined to be one bubble per 0.4 ml gelatin sample.

yielded one bubble per gelatin sample seemed to lie on a straight line that could be described by the equation

$$p^*_{ss} = 12 \text{ psi} + 0.383(p_m - p_o) \text{ psi} \quad (1)$$

Whereas this particular relationship was designed to produce exactly one bubble per sample in two similar batches of Knox gelatin, called Batch A and Batch B, we could have found other linear equations that would produce, for example, 10 bubbles per sample or 100 bubbles per sample or virtually any number we like.

It is also possible to produce 0 bubbles per sample and to calculate decompression schedules for gelatin that are optimal in the sense that they generate no bubbles and reach atmospheric pressure in the shortest possible time. If the sample is truly saturated prior to decompression, the optimum decompression profile is a straight line, as shown in Fig. 3 (Yount *et al.*, (1975). The standard U.S. Navy table for depth of 100 fsw

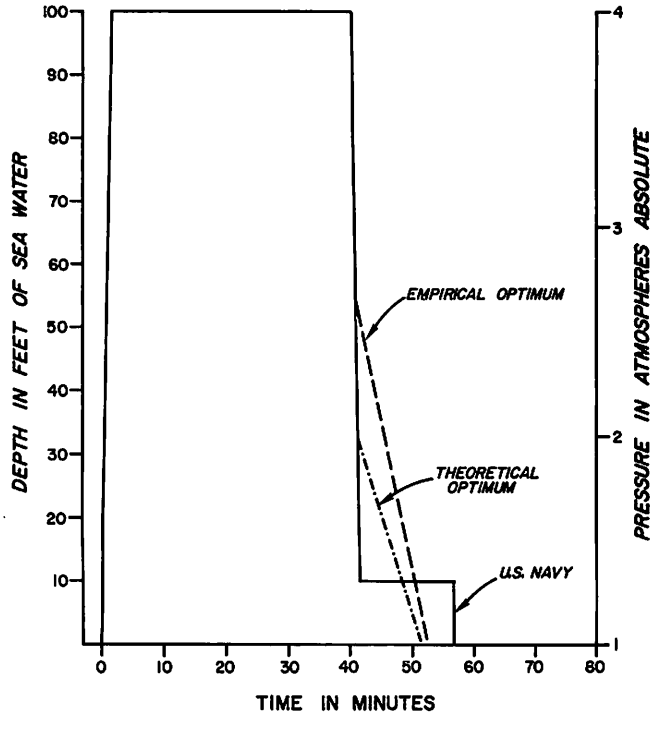

Fig. 3. Comparison of empirical optimum, theoretical optimum, and U.S. Navy decompression schedules for a 40-min dive to a water depth of 100 ft. The U.S. Navy table required 17 min to surface and yielded (12.9 ± 1.0) bubbles per sample; the empirical optimum schedule required 12 min and yielded (0.42 ± 0.19) bubbles per sample; and the theoretical optimum schedule required 11 min and yielded (0.00 ± 0.17) bubbles per sample.

fsw and a bottom time of 40 min required 17 min to surface and produced (12.9 ± 1.0) bubbles per sample. The optimum schedule found empirically by Dick Strauss required 12 min and yielded (0.00 ± 0.17) bubbles per sample.

Some months before the first Man-in-the-Sea Symposium, Ed Beckman, then at Texas A&M University, challenged me with this question: Based on what we now know about the physics of bubble formation, what would be the ideal way to decompress humans? I protested that we weren't ready for that, but he insisted that we give it our best shot. Guided by our gelatin studies, we chose a straight line as our decompression criterion, and we then adjusted the slope and the intercept to match the available decompression data on humans. With this one equation and with one set of tissue half-times, we were able to calculate reasonable schedules for two very disparate dives, the first to 200 fsw for 30 min and the second to 100 fsw for 14 days.

The ease with which we had covered this wide range of exposures suggested that we were on the verge of a breakthrough. Our discovery, if I may call it that, was that decompression sickness in divers is determined more by the physics of bubble formation than by any other factor. Since that initial thrust, we have continued to pursue two closely related goals: first, to improve our understanding of the physics of bubble formation and second, to develop a global theory of decompression sickness. By global, I mean a theory that describes the full range of diving experience with a small number of equations and parameter values.

II. BUBBLE NUCLEATION

Bubble nucleation refers to that process by which a gas or vapor phase is initially formed within a liquid. This can happen spontaneously through the random motion of gas or water molecules. The holes that result spontaneously from homogenous or *de novo* nucleation are of extremely short duration and rarely have radii larger than 10 Angstroms. For this reason, the theoretical threshold for homogenous nucleation in water is more than 1000 atm, much too high to account for bubble formation in divers.

Like divers, ordinary samples of sea water, tap water, or even distilled water form detectable bubbles when subjected to tensile, ultrasonic, or supersaturation pressures as small as 1 atm. It follows that bubble formation is not ordinarily homogenous; rather there must be some defect or inhomogeneity in the liquid which gets the process started.

It is well known that bubble formation thresholds can be significantly raised by degassing or by a preliminary application of static pressure. These are specific tests for stable gas nuclei. In other words, those defects or inhomogeneities which initiate bubble formation in aqueous media are gas-filled objects that persist for long periods of time.

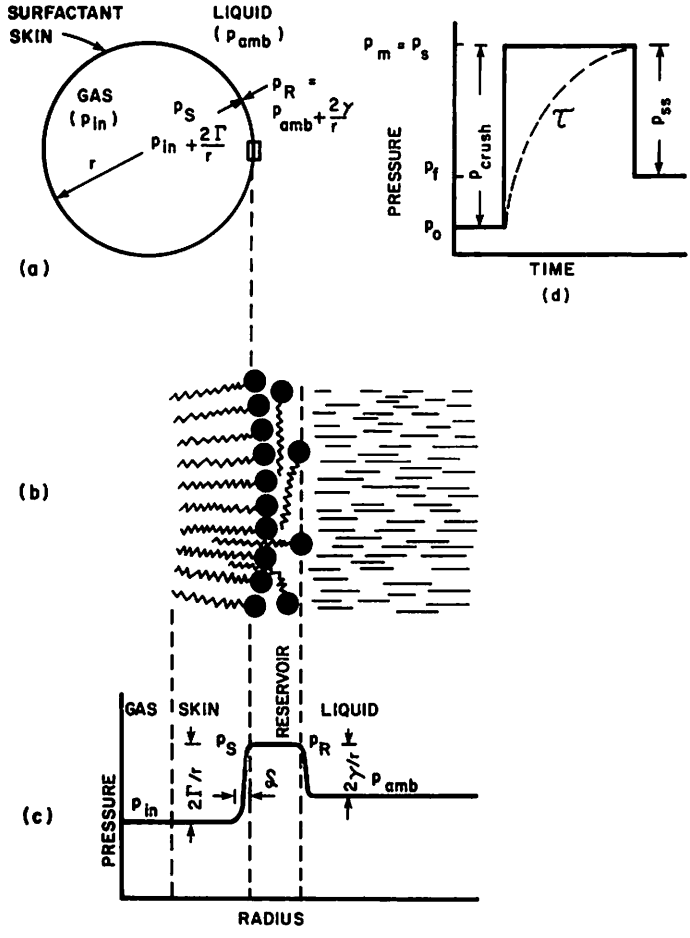

Fig. 4. Outline of the varying-permeability model. According to the VP model, bubble formation is initiated by stable microbubbles that are normally present in aqueous media unless steps have been taken to remove them. The stability of these microbubbles is due to elastic skins or membranes consisting of surface-active molecules. VP skins are ordinarily permeable to gas, and collapse is prevented by their compression strength, rather than by their impermeability. VP skins can become effectively impermeable to gas when they are subjected to large compressions, typically exceeding 8 atm (Yount, 1982).

The existence of stable gas nuclei is paradoxical. Gas bubbles larger than 1 micron in radius should float to the surface of a standing liquid, whereas smaller ones should dissolve rapidly due to surface tension. The main accomplishment of the Tiny Bubble Group has been to resolve this paradox by developing and experimentally verifying a new model for stable gas nuclei, which is illustrated in Fig. 4 (Yount, 1982).

According to the new model, called the varying-permeability model, the VP model, or just VPM, cavitation nuclei are simply stable microbubbles. The stability of these microbubbles is due to elastic skins or membranes consisting of surface-active molecules. Ordinarily VP skins are permeable to gas, and collapse is prevented by their compression strength, rather than by their impermeability. In the permeable regime, therefore, VP nuclei resemble spherical colanders more than spherical balloons. However, VP skins can become effectively impermeable to gas when they are subjected to large compressions, typically exceeding 8 atm. In the impermeable regime, therefore, the pores of the colander have closed, and the behavior is indeed that of a spherical balloon, albeit with a skin that is remarkably stiff.

By tracking the changes in nuclear radius that are caused by increases or decreases in ambient pressure, the VP model has provided precise quantitative descriptions of several bubble counting experiments carried out in supersaturated gelatin. This is illustrated in Fig. 5 (Yount *et al.*, 1979). In the permeable region below about 8 atm, we obtain a family of straight lines. When the skin becomes impermeable, the pressure inside increases during a further compression in a manner described by Boyle's law. This makes the nucleus more resistant to further crushing, causing the slope to decrease with increasing pressure. Essentially, there are three parameters in the VP model: the compression strength of the skin γ_c, which gives the slope, the initial radius r_o^{min}, which gives the intercept, and p*, which is the onset pressure for impermeability.

This brings us to the ordering hypothesis, which says that nuclei are neither created nor destroyed by the pressure schedule, and the initial ordering according to size is preserved. That is, if nucleus "A" is larger than nucleus "B" at the beginning of a pressure schedule, then both nuclei are still present at the end of the schedule, and nucleus "A" is still larger than nucleus "B".

It follows from the ordering hypothesis that each bubble count is determined by the properties and behavior of that one "critical" nucleus which is right at the bubble-formation threshold. All nuclei that are larger than the critical nucleus will form bubbles, and all nuclei that are smaller will not. Furthermore, a family of pressure schedules which yields the same bubble count N is characterized by the same critical nucleus and hence

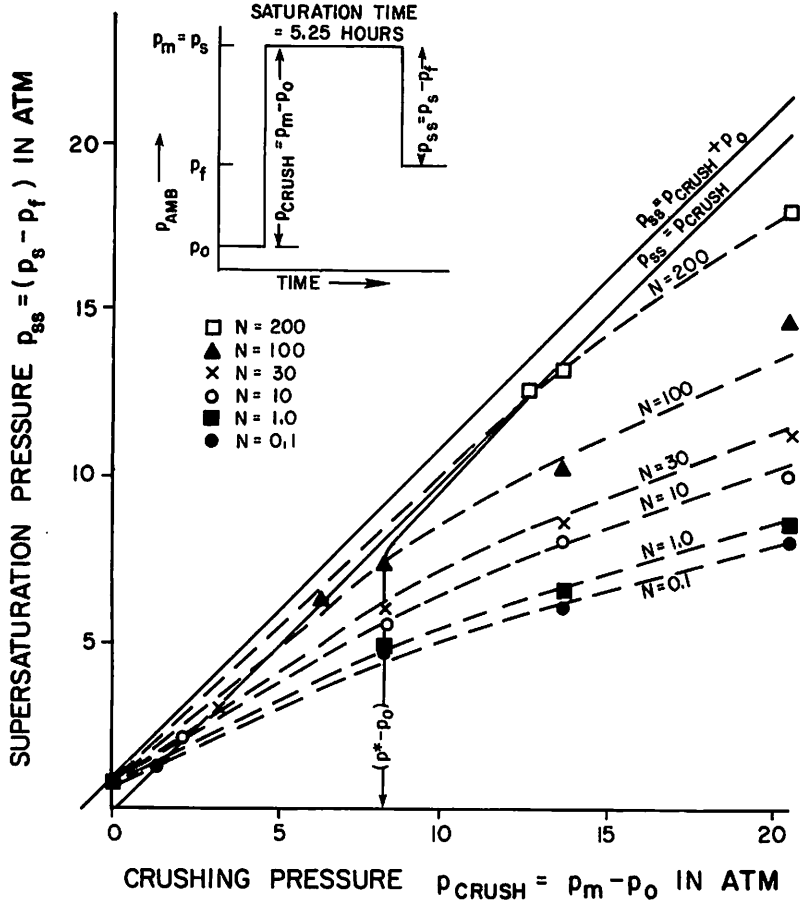

Fig. 5. Plot of p_{ss} versus p_{crush} for various numbers of bubbles per sample N. In the permeable region below $p^* - p_o$, the lines are straight. In the impermeable region above $p^* - p_o$, the slopes decrease with increasing crushing pressure in a manner determined by Boyle's law (Yount *et al.*, 1979).

by the same critical radius r_o^{min}, the same crumbling compression γ_c, and the same onset of impermeability p^*.

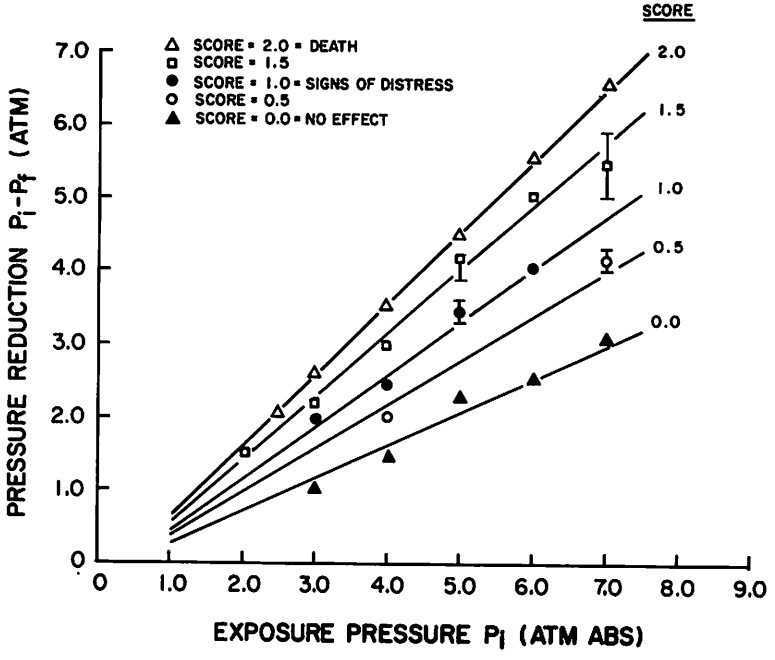

Fig. 6. Limits of pressure reduction $P_i - P_f$ versus exposure pressure P_i for various dive scores in fingerling salmon. The data points were obtained from D'Aoust *et al.* (1980), and the solid lines were calculated with the VP model (Yount, 1981).

The ordering hypothesis was applied to the gelatin data in Fig. 5 (Yount *et al.*, 1979) by finding combinations of p_{ss} and p_{crush} that give a fixed bubble count, N = 0.1, 1.0, 10, 30, 100, and 200 per 0.4 ml sample, averaged over many samples. For each value of N, a set of VPM parameter values was determined. The point at $p_{crush} = 0$ was found by evacuating samples originally at atmospheric pressure to negative gauge pressures until bubbles were seen.

The VP model has also been used to trace levels of incidence for decompression sickness in a variety of animal species including salmon, rats, and humans. In these applications, one additional assumption was made, namely, that lines of constant morbidity, such as 50% incidence of decompression sickness, are also lines of constant bubble number.

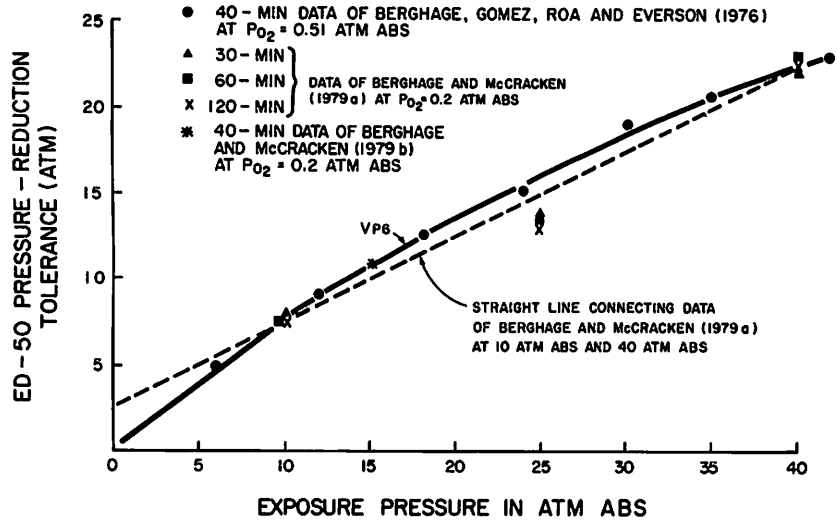

Fig. 7. Compilation of pressure-reduction tolerances versus exposure pressure for albino rats. ED-50 corresponds to an effective dose such that 50% of the rats tested showed signs of decompression sickness. The data were taken by Berghate *et al.* (1976), Berghage and McCracken (1979a and 1979b), and the solid line was calculated with the VP model (Yount, 1979; Yount and Lally, 1980).

The data for salmon, shown in Fig. 6 (DÁoust *et al.*, 1980; Yount, 1981), lie entirely in the permeable region; hence the VP model yields a family of straight lines, and we need at most two parameters for each line. Actually, we can do much better than this since there is a VPM equation which relates the slopes (γ_c) of these straight lines to their intercepts (r_o^{min}). Using this equation, we have generated five straight lines with only six parameter values instead of the ten which would ordinarily be required. This provides an *in vivo* test of the VP model with a standard error of $\sigma = \pm 0.23$ atm on the individual points.

The data on rats, extending from 6 to 42 atm, are shown in Fig. 7 (Berghage *et al.*, 1976; Berghage and McCraken, 1979a; Berghage and McCraken, 1979b; Yount, 1979; Yount and Lally, 1980). These data test another prediction of the VP model, namely, that there should be an impermeable region *in vivo*, just as there is *in vitro*. Recall that p* tells where the skin becomes impermeable to gas, but the way the lines bend over is determined by Boyle's law.

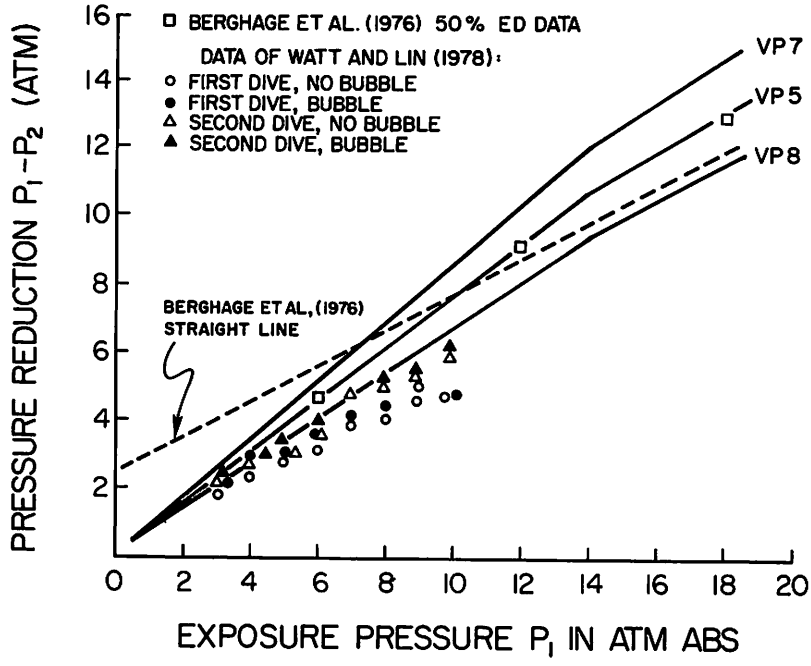

Fig. 8. Doppler bubble-threshold experiment carried out by Watt and Lin (1979). The squares are the ED-50 data points plotted earlier in Fig. 7. (Berghage *et al.*, (1976). The solid lines labeled VP5, VP7, and VP8 were calculated from the VP model for a range of effective doses centered at 50% (Yount, 1979). The single-bubble results lie just below these data points indicating that the onset of bubble formation in rats is a precursor to the onset of decompression sickness.

Fig. 8, obtained by Watt and Lin (1979), demonstrates that the onset of bubble formation in rats is indeed a precursor to the onset of decompression sickness. The data on humans show similar trends, but they are statistically very poor and erratic.

Direct experimental evidence that microbubble nuclei actually exist is given in Fig. 9 (Yount *et al.*, 1984). The medium is agarose gelatin. Moving clockwise from upper left are phase-contrast, Nomarsky, dark-field, and transmission-electron micrographs. The largest nuclei in each case have radii on the order of 1 micron.

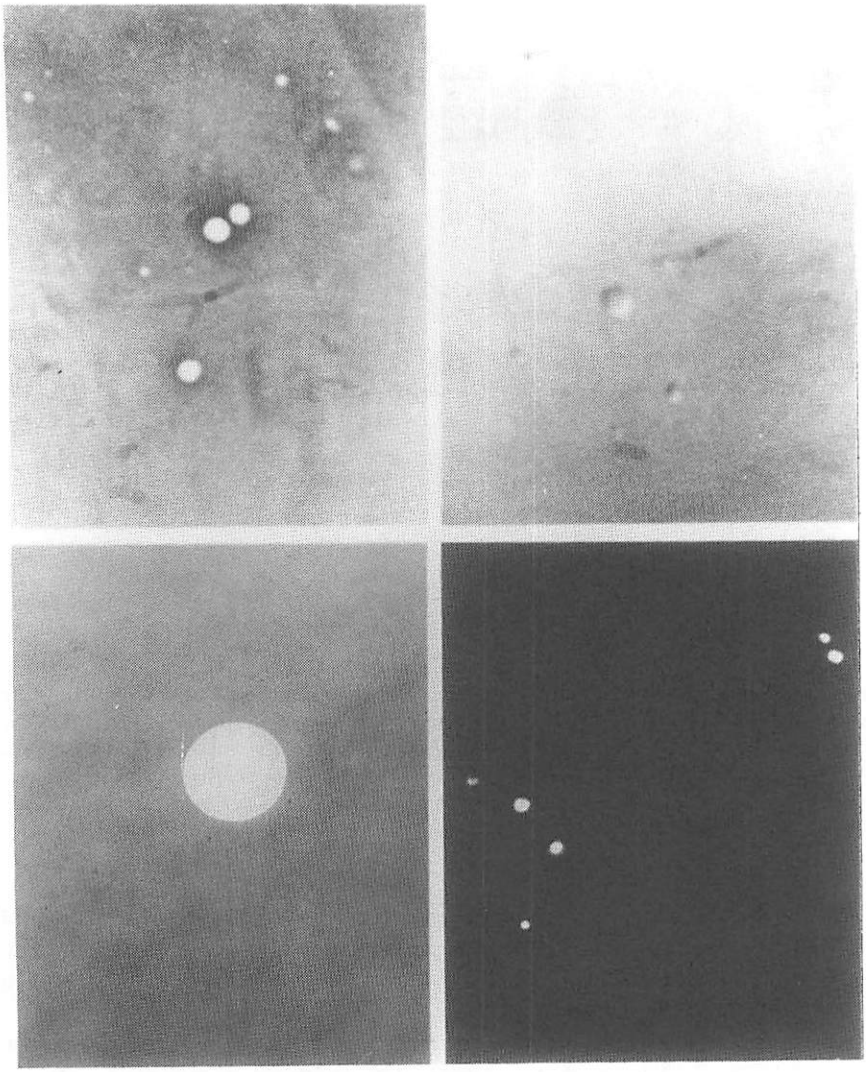

Fig. 9. Photomontage of candidate nuclei found in agarose gelatin. Moving clockwise from upper left are phase contrast, Nomarsky, dark-field, and transmission electron micrographs. The largest nuclei in each case have radii on the order of 1 micron (Yount *et al.*, 1984).

The structures identified as nuclei with phase-contrast and Nomarsky optics resemble ordinary gas bubbles. In the Nomarsky micrograph, the shadowing of the nuclei is opposite that of the surrounding gelatin, implying that nuclei are spherical cavities, rather than solid or liquid inclusions. Nuclei seen with dark-field illumination often have halos and are reminiscent of planetary systems, such as the moons of Jupiter. Large nuclei detected with the transmission-electron microscope usually appear as circular or ellipsoidal holes with clean edges. In all cases, the size distributions and shapes are similar, and there are very few background constituents. Under these circumstances, it is reasonable to assume that the same kind of object is being observed by all of the microscope techniques and in distilled water as well as in Knox and agarose gelatin.

Evidence that the objects identified as "stable gas nuclei" were both stable and gas-filled was obtained by using an inverted phase-contrast microscope which permitted liquid samples resting on a thin glass plate just above the field lens to remain undisturbed and in focus when subjected to a partial vacuum (Yount *et al.*, 1984). A small glass vacuum chamber surrounding the sample was connected to a much larger "buffer vacuum chamber" and then to a vacuum pump. With this setup, pressures in the range from 0.2 to 1.0 atm abs could be applied to the samples within a few seconds.

The main result of the vacuum-on, vacuum-off experiment (Yount *et al.*, 1984) was that nuclear radii increased when the pressure decreased and decreased when the pressure increased. Nuclei could be cycled repeatedly through various pressure schedules and still survive. In this way, it was demonstrated not only that nuclei are gas filled, but also that nuclei of different radii can be stable at the same pressure and that a given nucleus can achieve stability at many different pressures and radii.

Stable microbubbles appear to be commonplace in micrographs of plant or animal tissues. This can be verified by scanning through *The Journal of Cell Biology*. Nuclei, like ordinary gas bubbles, also have a tendency to accrete solid debris (Yount *et al.*, 1984; Yount *et al.*, 1979), which helps to account for Mulhern's observation of neutrally buoyant or negatively buoyant, stable microbubbles in seawater (Mulhearn, 1981). Abrahams and Buiocchi (1988) have observed that stable microbubbles can serve as nucleation sites for ZnS and/or (Zn, Cd)S precipitates.

Finally, mention should be made of the remarkable experiment of Johnson and Cooke (1980) who injected air bubbles into seawater and observed that although some bubbles dissolved completely, others stopped decreasing in size abruptly and remained as microbubbles apparently stabilized by films. Originally, the radial size distribution ranged up to 7 microns and peaked around 2 microns. During the first 4 hr, there

was little change. After 22 hr, although there was little reduction in the number, the microbubbles were generally smaller, and the radial distribution resembled a decaying exponential. The exponential size distribution is a signature for VP nuclei (Young, 1979) and has been derived from statistical mechanical considerations (Yount, 1982).

III. CALCULATING DIVING TABLES

As discussed in the introduction, our first attempt to calculate diving tables began with a straight line derived from bubble counting experiments in supersaturated gelatin (Yount *et al.*, 1975). The underlying assumption was that lines of constant bubble number are also lines of constant decompression stress. With the advent of the VP model (Yount, 1979), the empirical straight line was replaced by the VPM equations covering both the permeable and impermeable regions, and calculations were made for the salmon (Yount, 1981), rats, and humans (Yount, 1979). This approach works well for long exposures, but it breaks down when the exposure time is allowed to vary widely.

Fig. 10 illustrates what goes wrong (Yount and Hoffman, 1986). In this graph are shown the U.S. Navy (USN, 1970) and Royal Naval Physiological Laboratory (RPNL, 1968) "no-stop" decompressions along with various "practical observations," i.e., combinations of depth and bottom time which yielded no symptoms or only the mildest symptoms in actual dives (Leitch and Barnard, 1982). On this same graph, a line that produces a constant bubble number in the VP model is too flat. A much better description can be obtained by allowing more bubbles to form on the shorter dives than on the longer dives. This, in turn, suggests that total bubble volume, rather than bubble number, is the critical parameter.

Following this reasoning, the constant-bubble-number assumption was replaced by a "dynamic-critical-volume hypothesis" (Yount and Hoffman, 1986). As in earlier applications of the critical-volume criterion (Hennessy and Hempleman, 1977), it was assumed that signs or symptoms will appear whenever the total volume accumulated in the gas phase exceeds some designated critical value. The "dynamic" element of this new formulation is that gas is continuously entering and leaving the gas phase (Yount and Hoffman, 1986). Thus the accumulated volume is calculated as a function of time by integrating over the product of the bubble number and the degree of supersaturation, subtracting off the free gas that is being dissipated continuously by the lung.

Gas uptake and elimination are assumed to be exponential, as in conventional tables, and the tissue half-times range from 1 to 720 min (Yount and Hoffman, 1986). The treatment of oxygen is also conventional,

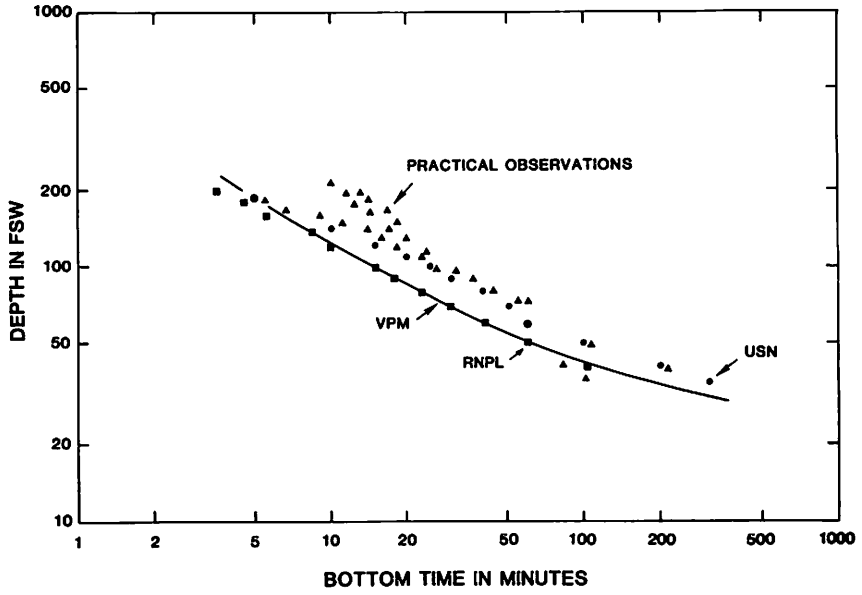

Fig. 10. Comparison of VPM (Yount and Hoffmann, 1986), USN (1970), and RNPL (1968) no-stop decompressions with various practical observations, i.e., combinations of depth and bottom time which yielded no symptoms or only the mildest symptoms. The VPM curve follows very closely the RNPL points at depths up to 140 fsw and passes through the USN point at 5 min, 190 fsw. Over the entire range, it serves as a safe, tight, and therefore useful lower bound.

i.e., to a first aproximation only the inert gases need to be taken into account. For oxygen partial pressures above 1800 Torr (2.4 atm), the quantity of oxygen *dissolved* in the arterial blood exceeds the amount that the body can use, and the hemoglobin is saturated with oxygen in both the veins and the arteries (Yount and Lally, 1980). As more oxygen is added,, the partial pressure of oxygen in the venous blood begins to rise, thereby adding to the "inert" gas partial pressure (Yount and Lally, 1980).

The VPM (Yount and Hoffman, 1986) and USN (1970) profiles for an "exceptional exposure" involving greater than normal risk are compared in Fig. 11. In both cases, the descent and ascent rates are 60 fsw/min, and the 3.33 min required to reach 200 fsw is counted as part of the 60-min "bottom time." The total decompression times are similar, the important difference being the deeper "first stop" of the VPM schedule, 130 fsw

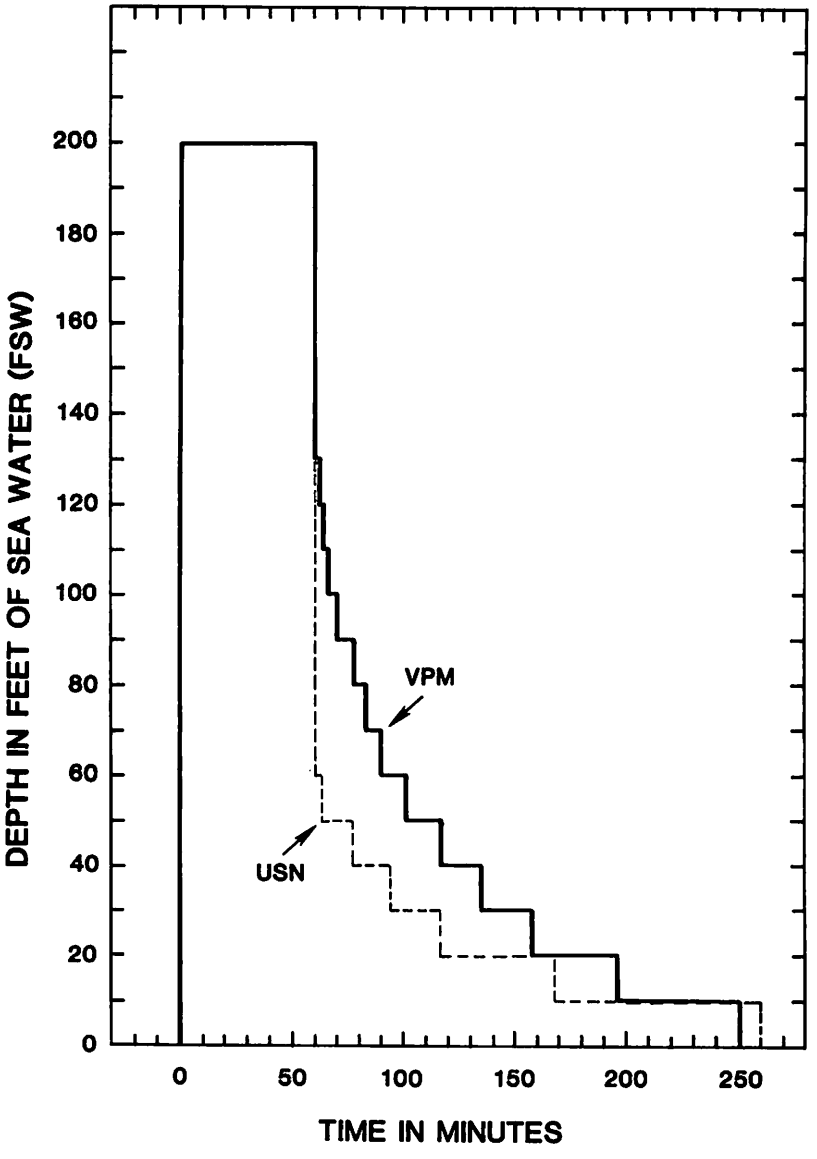

Fig. 11. Total ascent times versus bottom times at 100 fsw for VPM (Yount and Hoffman, 1986), USN (1970), RNPL (1968) and TEKTITE (Beckman and Smith, 1972) decompression tables. By connecting the no-stop decompressions in the lower left with saturation diving in the upper right, this figure illustrates how a global model with one set of parameter values can describe a wide range of diving experience.

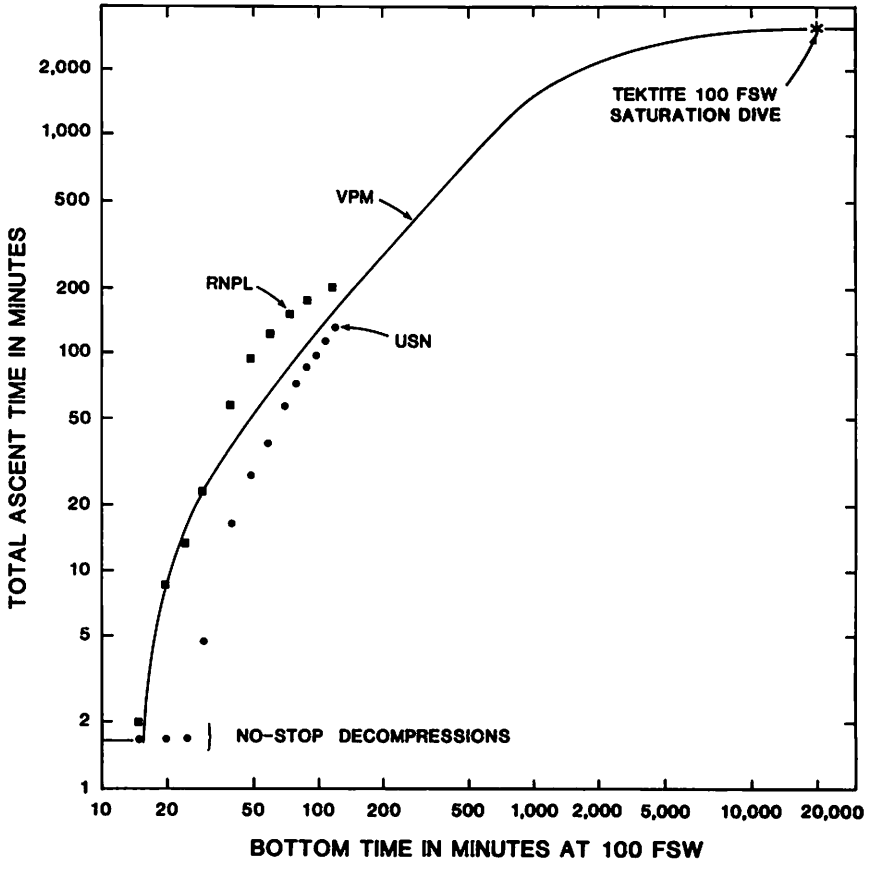

Fig. 12. Total ascent times versus bottom times at 100 fsw for VPM (Yount and Hoffmann, 1986), USN (1970), RNPL (1968), and TEKTITE (Beckman and Smith, 1972) decompression tables. By connecting the no-stop decompressions in the lower left with saturation diving in the upper right, this figure illustrates how a global model with one set of parameter values can describe a wide range of diving experience.

versus 60 fsw for USN. This is a persistent feature of the literally hundreds of comparisons that have been made of VPM tables with a variety of conventional tables now in use. The calculations indicate that the longer "first pull" of these conventional tables results in a larger supersaturation, a larger bubble number, and ultimately in a larger total volume of released gas.

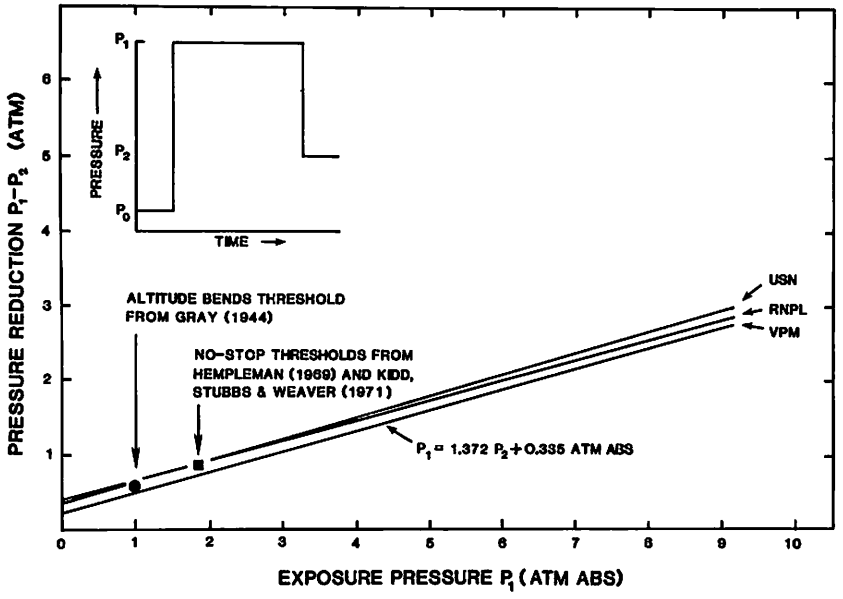

Fig. 13. Allowed pressure reduction $P_1 - P_2$ versus exposure pressure for USN (1970), RNPL (1968) and VPM (Yount and Hoffmann, 1986) air diving tables. In the limit of a nucleation-dominated regime, e.g., for dives of long duration, lines of constant critical volume are also lines of constant bubble number.

The global idea that it ought to be possible to describe the full range of diving experience with one model and one set of parameter values is illustrated in Fig. 12 (Young and Hoffman, 1986), which connects the no-stop decompressions in Fig. 10 with the 14-day, 100-fsw TEKTITE saturation dive (Beckman and Smith, 1972). The later has been used by humans without incident.

Fig. 12 also incorporates and exploits another idea, which is the principle of leverage. Whereas the USN and RNPL points at or near the 50-min bottom time vary widely because they are based on a relatively small number of "local" observations, the VPM dive to 100 fsw for 50 min is tightly constrained by the extensive data that exist at either end of this graph. In fact, the entire VPM curve for 100 fsw is tightly constrained by other data, such as those plotted in Fig. 10.

The assumption of constant bubble number was abandoned because it didn't work in certain cases and therefore could not form the basis of a global theory. What about those special cases where constant bubble number did work: does the dynamic-critical-volume hypothesis also give

reasonable predictions? The answer is yes because in those special cases, constant volume and constant bubble number are equivalent hypotheses.

The correspondence between bubble volume and bubble number is demonstrated in Fig. 13, which is a plot of the allowed pressure reduction $P_1 - P_2$ versus exposure pressure P_1 for a series of dives of long duration. Again, VPM (Yount and Hoffman, 1986), USN (1970), and RNPL (1968) are shown. The three straight lines are nearly parallel, and VPM is 0.1 to 0.2 atm lower than USN and RNPL. The fact that these lines are similar to the isopleths of constant bubble number in Figs. 2 and 6 verifies the above-mentioned correspondence for this rudimentary case.

The "no-stop threshold" in Fig. 13, $P_1 = 1.87$ atm abs, $P_1 - P_2 = 0.87$ atm, was obtained by averaging values obtained by Hemplemen (1984) and by Kidd *et al.*, 1971. The VPM result, $P_1 = 1.71$ atm abs, $P_1 - P_2 = 0.71$ atm, is 0.16 atm lower than the experimental average and is therefore "safe." The "altitude bends threshold" plotted in Fig. 13, $P_1 = 1.00$ atm abs, $P_1 - P_2 = 0.60$ atm, was measured by Gray (1944). The VPM limit of $P_1 = 100$ atm abs, $P_1 - P_2 = 0.52$ atm is again slightly lower, this time by 0.08 atm.

In contrast, the lines for USN and RNPL are both slightly higher than the experimental no-stop and altitude-bends thresholds plotted in Fig. 13, and in this sense they are not "safe." This illustrates the type of problem one encounters in attempting to extrapolate conventional tables based upon local trial-and-error rather than a global theory. Because of such problems, altitude bends and decompression sickness are usually investigated separately, as if they were different subjects.

Very little has been said about the physiological processes which presumably underlie any global model. For example, no distinction was made between "fatty, loose tissue" and "watery, tight tissue" (Hennessy and Hempleman, 1977), nor was it stated explicitly where the bubbles form or how they grow, multiply, or are transported. Finally, nothing was said about such factors as solubility, diffusion versus perfusion, tissue deformation pressure, or tissue-specific differences in surface tension. Following the principle of Ockhams razor, these ideas were omitted because there is no evidence that such a proliferation of free parameters is necessary when the VP model is used.

One by-product of this investigation is an improved understanding of practical decompression tables now in use. It is evident, for example, that profuse bubble formation is permitted by such tables, particularly during dives of short duration. Meanwhile, the number of primary bubbles, i.e., bubbles that form directly from nuclei rather than from other bubbles, is allowed to vary widely. The common assumption that the volume of released gas is critical seems still to be viable providing allowance is made for the body's ability to dissipate free gas at a useful rate.

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The Role of Complement Activation in Decompression Sickness

C.A. Ward, D. McCullough, D. Yee, D. Stanga and W.D. Fraser

I. INTRODUCTION

The Complement hypothesis has been introduced recently (Ward *et al.*, 1985; Ward *et al.*, 1987a; Ward *et al.*, 1987b; Ward, 1989) as an etiology for decompression sickness (DCS). This hypothesis claims that the complement proteins of blood plama mediate the reponse of the body to the presence of circulatory bubbles, that at least the short-term symptoms (i.e. those that follow within a few hours of the pressure profile) are produced by the "activation" of this system of approximately 20 serum proteins and that the variation in susceptibility both between individuals

and of one individual as a result of him/her repeatedly experiencing a pressure profile (i.e. Acclimatization) or as a result of him/her stopping their exposure to pressure profiles (i.e. De-acclimatization) results from the *sensitivity* of the individual's complement system to activation by bubbles at the time of the pressure profile. Before considering the methods by which this hypothesis may be applied, we first consider the mechanism by which the complement system is activated.

II. COMPLEMENT ACTIVATION — THE PATHWAYS

There are two pathways by which these sequentially activated proteins of the complement system can be stimulated to produce the membrane attack complex. One is the classical pathway. The activation of this pathway is typically initiated by an antigen-antibody reaction that allows the complement component Clq to bind the antigen-antibody complex. The second step on this pathway is the activation C2 and C4 and this activation results in the fragment of C4a, an anaphylatoxin, entering the fluid phase. The third step is the activation of C3 and results in a second anaphylatoxin, C3a, entering the fluid phase. The remainder of the activation of the classical pathway involves the same complement components as those that are members of the other pathway, the alternative pathway.

The activation of this latter pathway is initiated by the activation of C3, see Fig. 1. The exact mechanism by which this activation takes place is still the subject of research (Götze, 1988). The present evidence indicates that an internal thiolester bond of C3 is subject to spontaneous hydrolysis *in vivo*. This gives rise to C3(H_2O) molecule that in a Mg^{++} dependent reaction interacts with factors B and D (molecular weights 93k, 24k single peptide chains, mean serum concentration 210 and 2 μg/ml respectively) to produce C3(H_2O)-Bb (Götze, 1988). The latter component is the first convertase of the alternative pathway and reacts with C3 to produce C3b and C3a molecules.

It should be noted that to this point the reactions discussed take place spontaneously *in vivo;* thus a small number of C3b molecules are thought to be present at any time within plasma. If an activating surface (such as an air bubble) is introduced, these C3b molecules can be adsorbed and initiate the activation of the remainder of the alternative pathway, thereby producing more C3a in the fluid phase and activating the next complement component C5 to produce fluid in the phase C5a, another anaphylatoxin, and ultimately the membrane attack complex.

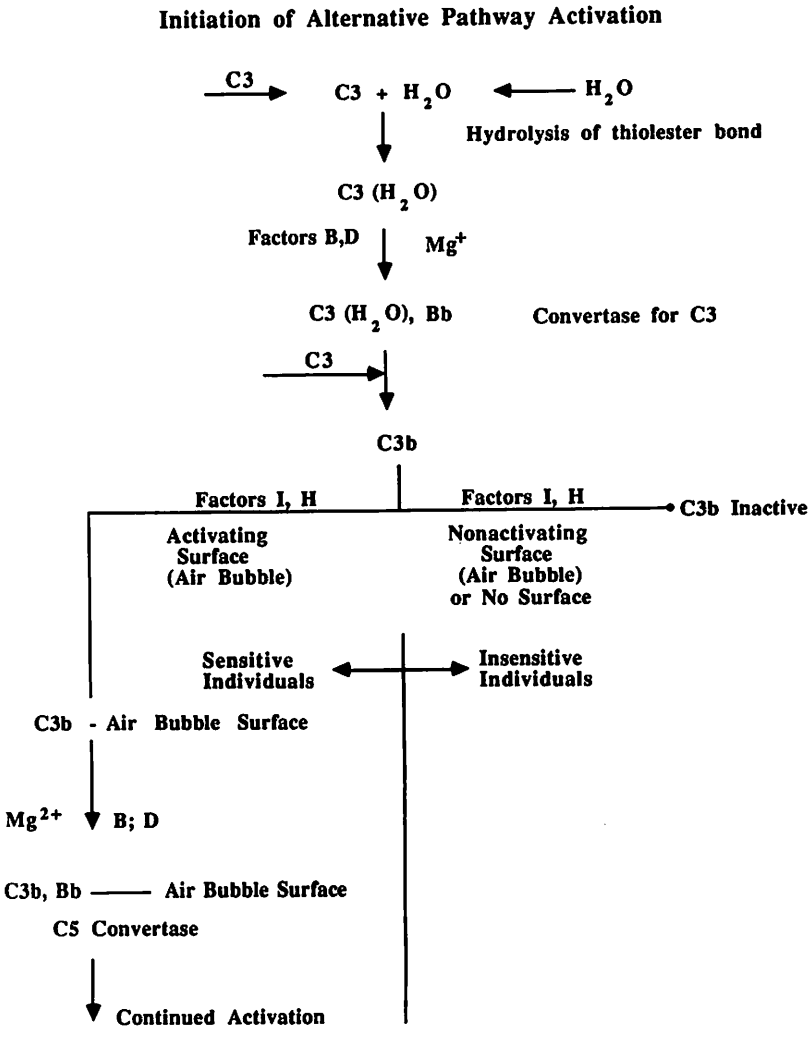

Fig. 1. Schematic of the initiation of complement activation by the alternative pathway.

If a non-activating surface is introduced or if no surface at all is introduced, then the C3b that is produced spontaneously is inactivated by factors H and I (molecular weights of 150K and 88K, single and double peptide chains, serum concentrations of 480 and 35 μg/ml respectively) (Götze, 1988).

Two differences in the mechanism of activation along the possible activation pathways should be emphasized. First, if the activation is along the classical pathway, then the initiating event is antibody-antigen dependent. Whereas when the activation is along the alternative pathway, the initiating event involves C3 and is followed by the activation of C5; thus C4 is not involved. This allows the pathways of activation to be identified because the fragment of C4a is produced when activation is along the classical pathway but not necessarily when the activation is along the alternative pathway. Secondly, the importance of C3 and factor B for activation of the alternative pathway is clear because their product is responsible for producing C3b and the latter is the unit that recognizes the foreign surface.

III. IS SENSITIVITY TO COMPLEMENT ACTIVATION GENETIC?

It is known that both C3 and factor B are genetically polymorphic, but the biological consequences of this polymorphism are not completely known at the moment (Alper and Propp, 1968; Ward *et al.*, 1986). There are two principal variants of C3 (C3F and C3S) and at least 26 rare variants. Factor B similarly has two principal variants (F and S) and at least 16 variants. It has been found that a large number of the C3 variants are similar in their efficiency in producing lysis of sheep erythrocytes (Colten and Alper, 1972). However, certain variants of C3 have been reported to have different binding capacities for mononuclear cells *in-vitro* (Alvilommi, 1974). The variants of C3 in the different populations have been assessed. For example, in the white American population the allele C3F has a frequency of 0.77, and C3S a frequency of 0.22 and the rare variants a frequency of 0.01 (Alper and Propp, 1968).

Below we review the evidence indicating a variation in the sensitivity of both human subjects and rabbits to complement activation when either type of plasma is incubated with air bubbles. We can not at this time relate the observed variation in sensitivity to complement activation by air bubbles to genetic variation in C3 or factor B. However, it does provide a possible explanation and it would mean that there are biological consequences of the genetic polymorphisms because we also find that both those individuals and those rabbits that are more sensitive to complement activation are also more susceptible to decompression sickness

(Ward *et al.*, 1986; Ward *et al.*, 1987a; Ward *et al.*, 1987b; Ward *et al.*, 1989).

IV. COMPLEMENT ACTIVATION IN HUMAN PLASMA

A. Incubation with Air Bubbles

As described in Ward *et al.* (1987a), blood samples (15 ml) were collected from each of sixteen healthy, male individuals by venipuncture into polypropylene syringes containing heparin (10 IU/ml blood). After being transferred into polypropylene tubes and centrifuged at 2,000 G for 15 min at 4°C, the clear plasma was separated and stored at −70°C until incubated with different stimulants.

In preparation for incubation, a plasma sample was thawed in a room temperature water bath. It was then centrifuged at 2,000 G for 15 min at 4°C. One portion, 1.5 ml, of the supernatant was placed in a 1.65 ml tube, capped and the remaining volume filled with small bubbles by vigorously shaking. This tube was then placed in a device that rotated it end over end on each cycle, and thumped the tube sharply so that the bubbles remained present throughout the incubation period.

Another portion of the supernatant filled a 1.65 ml polypropylene tube. It was carefully sealed and also placed in the rotating device, but it was not thumped. The rotating device, loaded with the plasma samples, was then placed in a heat bath, and incubated at 37°C with the samples under rotation for a period of 30 min.

B. Measurement

Afterwards, each was removed from the rotating device and centrifuged again (at 2,000 G and 4°C for 10 min). The supernatant from each sample was put into a polypropylene tube, and then placed in an ice bath until each could be assayed for the fluid phase metabolites of complement activation C3a des-Arg, C4a des-Arg and C5a des-Arg using commercially available kits. Complement activation occurring during the incubation would produce C3a, C4a, and C5a if the activation pathway were along the classical pathway or C3a and C5a if it were along the alternative pathway. These analphylatoxins would be quickly converted to their des-Arg versions in equimolar concentrations. Thus we assume the assay would give measures of C3a, C4a and C5a respectively.

The results of the assays are summarized in Tables 1 and 2 and in Figs. 2, 3, and 4.

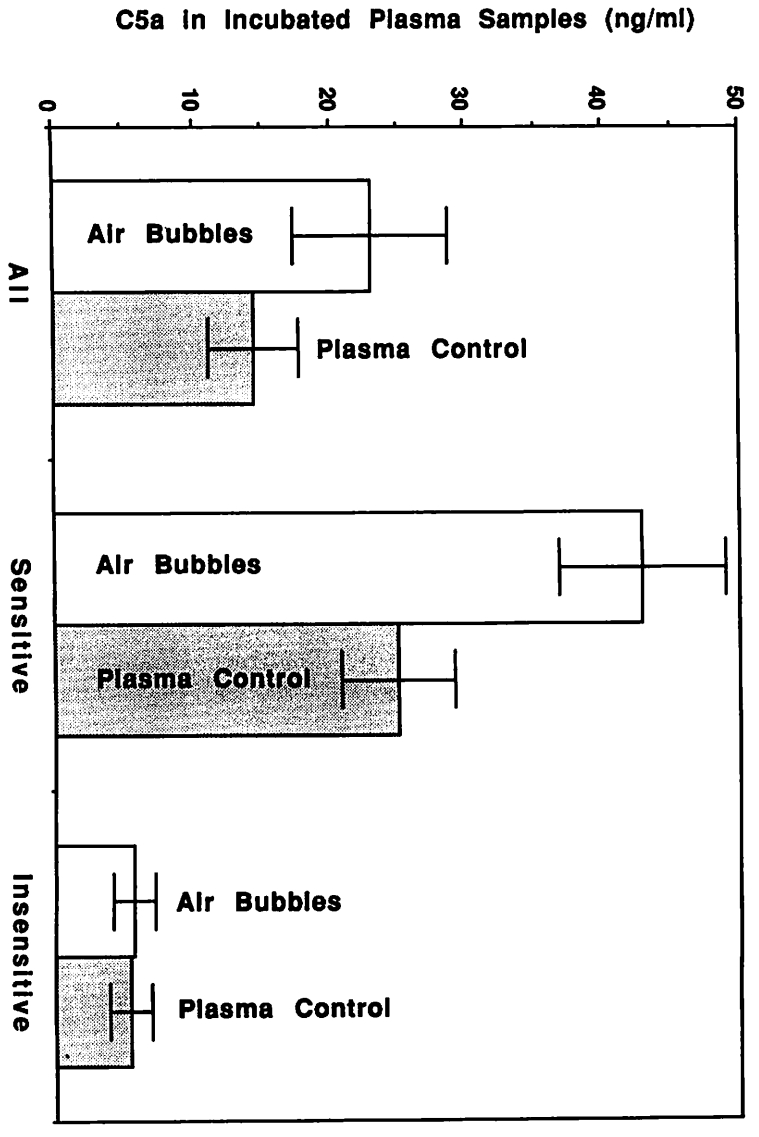

Fig. 2. Production of the anaphylatoxin C5a in the plasma samples of the total, the Sensitive, and the Insensitive groups of individuals resulting from incubating their respective plasma samples with air bubbles and as controls (Avg ± SE).

C. Individual Variations in Sensitivity

If there is complete complement activation by either pathway, there will be production of C5a. If one examines the amount of C5a being produced, by incubating the plasma samples with air bubbles then, as may be seen from Tables 1 and 2, one finds an extraordinary variation from one individual to another. It ranges from 2 to 64 ng/ml plasma. Thus there is a clear difference in sensitivity to complement activation by air bubbles within this group of individuals. Accordingly, the individuals were divided into two groups. One group was called Sensitive and members of it were distinguished from the Insensitive individuals by the amount of C5a that was found in their plasma samples. The members of the Sensitive group were those whose plasma samples incubated with air bubbles were found to contain 25 ng/ml or more of C5a. The measurements of C5a for the Sensitive and Insensitive groups are summarized in Fig. 2.

When the measurements of C5a for the total group are considered, one finds that the difference between the plasma samples incubated with air bubbles and those incubated as controls are significantly different (paired t-test, $p<0.03$). This difference results completely from the sensitive group of individuals. For them, the C5a concentration in the plasma samples incubated with air bubbles was significantly greater than that in their control samples ($p<0.01$, paired t-test). By contrast, for the Insensitive individuals, there is no significant difference between the plasma samples incubated with air bubbles and those incubated as controls.

Another difference should also be noted between the Sensitive and Insensitive groups. If one compares the C5a concentrations in either of the control samples or in the plasma samples incubated with air bubbles, one finds in both cases that the C5a concentration is greater in the plasma samples of the Sensitive individuals (t-test, $p<0.01$).

To determine the pathway of the observed complement activation, it is necessary to consider the measured concentration of C4a in the plasma samples of the Sensitive individuals. The results are summarized in Fig. 3. One finds that there is no stastically significant difference between the plasma samples of the Sensitive individuals that were incubated with air bubbles and those that were incubated as controls. The indications from this would be that the complement activation of the plasma samples of the Sensitive individuals incubated with air bubbles was along the alternative pathway. Thus the first step in the activation of this pathway involves the interaction of C3 and factor B with the air bubble (see Fig. 1).

The measured concentrations of C3a in the plasma samples of the two groups of individuals are summarized in Fig. 4, along with those for the

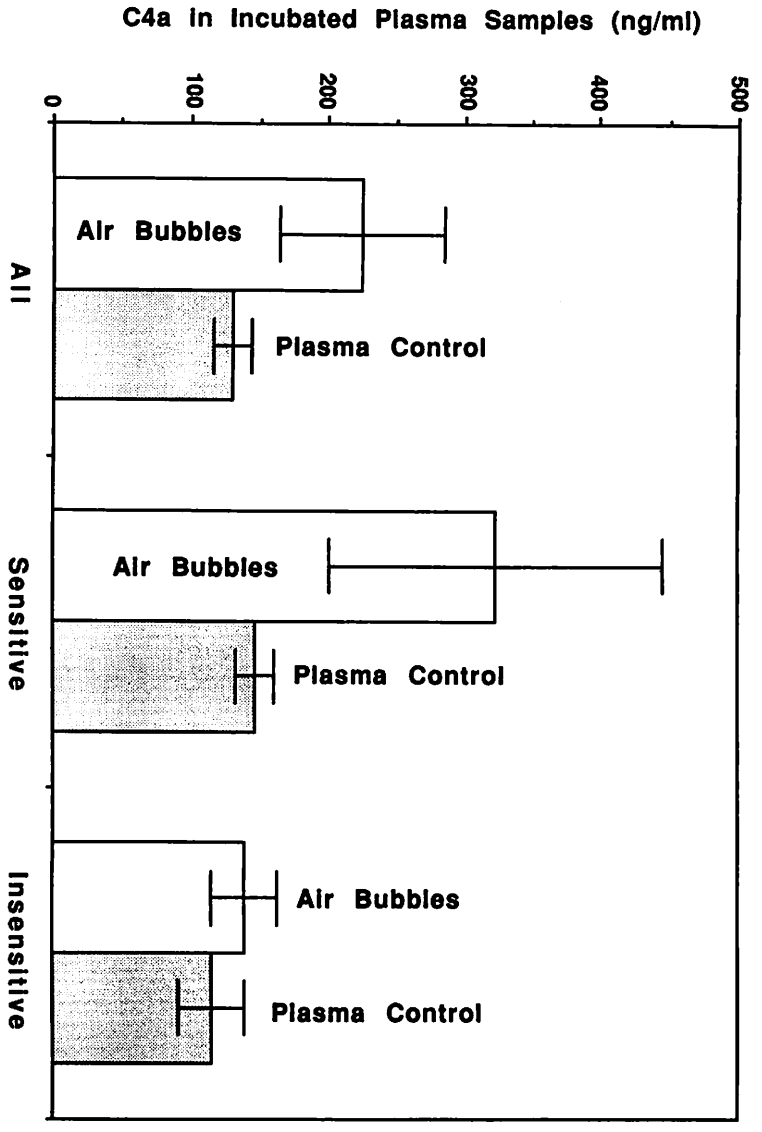

Fig. 3. Production of the anaphylatoxin C4a in the plasma samples of the total, the Sensitive, and the Insensitive groups of individuals resulting from incubating their respective plasma samples with air bubbles and as controls (Avg ± SE).

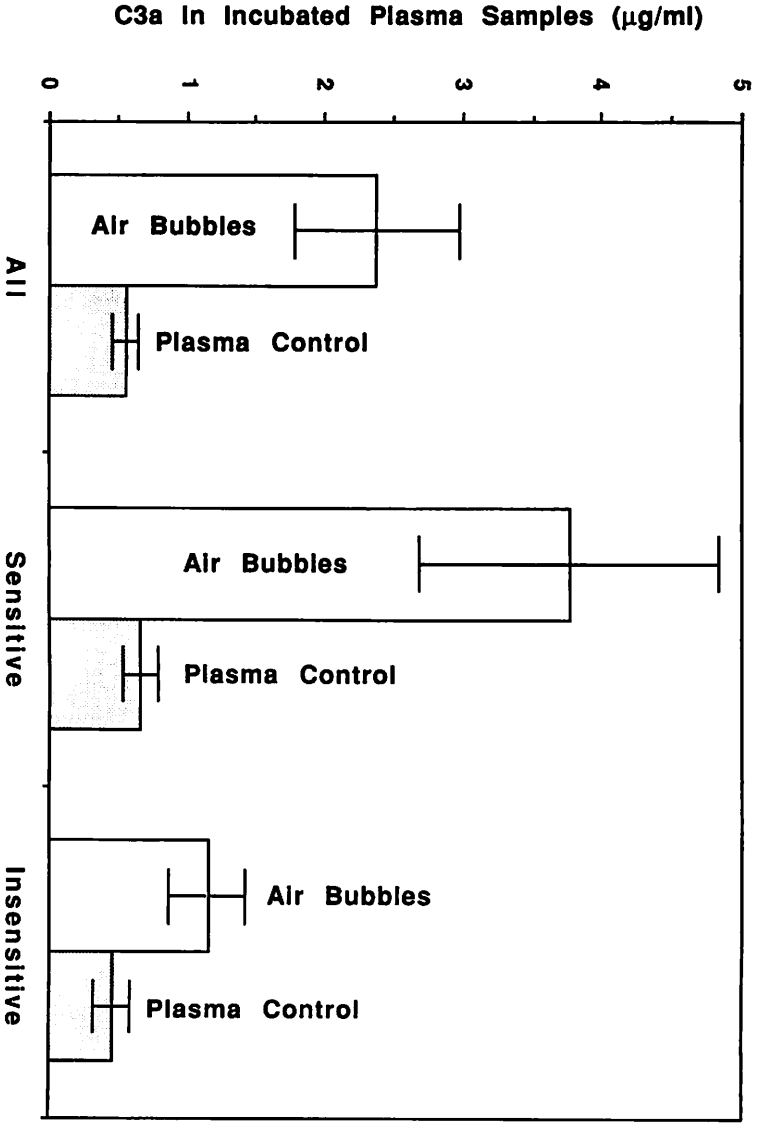

Fig. 4. Production of the anaphylatoxin C3a in the plasma samples of the total, the Sensitive, and the Insensitive groups of individuals resulting from incubating their respective plasma samples with air bubbles and as controls (Avg ± SE).

total group. As may be seen there, for the Sensitive group of individuals the plasma incubated with air bubbles was found to contain a significantly greater concentration of C3a than the plasma samples of this group incubated as controls ($p<0.01$, paired t-test). By contrast, there is no statistically significant difference between the plasma samples that were incubated as controls ($p>0.05$, paired t-test).

The individuals in the two groups may be compared in another manner by comparing the concentration of C3a in their control samples and in their plasma samples incubated with air bubbles. One finds that there is no statistically significant difference in the C3a concentrations in the control samples ($p>0.05$, t-test); however, one finds that there is a statistically greater amount of C3a in the plasma samples of the Sensitive individuals incubated with air bubbles than in those of the Insensitive individuals ($p<0.03$, t-test).

D. Sensitive and Insensitive Individuals

Since one group of individuals was identified that had native complement systems that were not activated as a result of incubating their plasma with air bubbles, they were ideal for examining for the susceptibility to DCS and such a study was conducted with these individuals (Ward *et al.*, 1987b). According to the complement hypothesis, the Insensitive individuals would be expected to be less susceptible to DCS than the Sensitive individuals.

The pressure profile to which each individual was subjected while breathing air is indicated in Tables 1 and 2. The depth is given in meters sea water (msw) and the time spent at that depth in minutes. The decompression procedure was according to the Defence and Civil Institute of Environmental Medicine 1983 decompression tables for standard air (Lauckner *et al.*, 1984). All of the pressure profiles were severe enough to produce bubbles that could be detected with Doppler monitoring. The bubble score at the precordial position was assigned as described in Nishi *et al.*, (1981) and is also listed in Tables 1 and 2 for each profile. In addition, the probability of DCS occurring on a particular profile, p(DCS) that had been assigned on the basis of the historical evidence and the maximum likelihood criterion (Weathersby *et al.*, 1984) are listed for each profile.

The criterion adopted to determine whether an individual experienced DCS was simply whether he complained of symptoms of DCS. If he did complain, then he was taken as having DCS. This is indicated in the last two columns of Tables 1 and 2.

TABLE 1.

Insensitive Individuals, Complement Activation Sensitivity, Pressure Profile, Bubble Score, and DCS Incidence

Individual No.	Complement Activation						Pressure Profiles	Bubble Score	p(DCS)	DCS?	
	C3a/ng/ml		C4a/ng/ml		C5a/ng/ml						
	Air Bubbles	Control	Air Bubbles	Control	Air Bubbles	Control	msw/min			Yes	No
3	1196	379	161	140	5.2	2.4	72/40	3.3	0.102		X
							36/50	2.0	0.042		X
							63/30	3.3	0.060		X
4	928	382	66.4	62	12.8	7.2	36/50	3.0	0.042		X
7	1493	1289	145	118	2.0	14.8	63/30	3.0	0.060		X
							72/40	4.0	0.102		X
8	330	271	94.4	52.4	2.0	1.6	63/30	3.3	0.060		X
							72/40	3.3	0.102		X
10	286	341	44.8	52.4	11.6	7.6	63/30	2.7	0.060		X
11	887	510	271	256	2.8	2.0	72/40	3.0	0.102		X
12	2589	67	184	143	5.6	4.8	54/30	3.0	0.036		X
							72/40	3.0	0.102		X
16	1536	484	138	95	3.2	2.8	36/50	3.0	0.042		X
							72/40	3.0	0.102		X
								Avg. 3.1	1.014	0 Yes	14 No

TABLE 2.

Sensitive Individuals, Complement Activation Sensitivity, Pressure Profile, Bubble Score, and DCS Incidence

Individual No.	Complement Activation						Pressure Profiles	Bubble Score	p(DCS)	DCS?	
	C3a/ng/ml		C4a/ng/ml		C5a/ng/ml						
	Air Bubbles	Control	Air Bubbles	Control	Air Bubbles	Control	msw/min			Yes	No
1	3996	461	134	83	36.2	28.4	45/40	3.0	0.048		X
							36/50	2.7	0.042		X
2	7494	958	196	169	66.0	30.0	45/40	2.7	0.048	X	
							36/50	4.0	0.042		X
6	7662	1041	294	156	63.8	39.6	45/40	3.0	0.048	X	
							45/40	2.0	0.048	X	
9	752	905	1044	115	36.2	6.0	45/40	1.0	0.048		X
							54/30	3.0	0.036		X
13	2038	430	224	168	30.6	19.7	45/40	3.7	0.048	X	
14	2834	514	244	182	42.4	29.8	45/40	3.3	0.048	X	
15	1678	398	129	155	25.8	22.0	45/40	2.7	0.048		X
								Avg. 2.8	0.504	5 Yes	6 No

E. Susceptibility to DCS

The pressure profiles to which the individuals were subjected were randomly chosen from five different possible ones. At the time of assigning the profiles, there was no knowledge by the subjects of their sensitivity to complement activation. They had only given a blood sample before beginning the series of profiles.

If one assumed that all individuals were equally susceptible to DCS, then based on both the average bubble score and p(DCS), the Insensitive individuals were by chance assigned the more stressful pressure profiles. Nonetheless, as may be seen from Table 1, this group did not experience any cases of DCS. Whereas, the Sensitive individuals, on the less stressful pressure profiles, experienced DCS on five of the eleven profiles to which they were subjected.

The Sensitive individuals are statistically more susceptible to DCS according to χ^2 contingency test (Sensitive: 5 DCS of 11; Insensitive 0 DCS of 14; $p<0.01$). However, it should be pointed out that each of the cases of DCS occurred when an individual was subjected to the 45 msw/40 min profile and the reason for this is not completely clear. Not all of the cases of DCS occurred on the same day; thus not all of the cases of DCS occurred on the same occasion. However, by chance none of the Insensitive individuals were assigned this particular pressure profile. The Insensitive individuals were, in fact, assigned the more strenuous pressure profiles, at least according to the p(DCS). They were assigned the 72 msw/40 min. profile on six occasions. It is more than twice as strenuous, according to its p(DCS), than the 45 msw/40 min profile. Yet none of the Insensitive individuals experienced DCS. Finally, it should be noted that the 45 msw/40 min profile is the most strenuous profile to which the Sensitive individuals were subjected, and they experienced DCS on five of the eight occasions on which they were subjected to the profile. Also by chance, they were subjected to this profile more than to any other. It was chosen for eight of eleven of their pressure profiles. Thus it is possible that the reason all the pressure profiles that resulted in a case of DCS were the 45 msw/40 min profile is because it happened to be the one chosen most often for the Sensitive individuals.

V. ACCLIMATIZATION AND DE-ACCLIMATIZATION

If on the basis of the evidence listed in the previous section, one accepts for the moment that the susceptibility of an individual to DCS depends on the sensitivity of his complement system to activation by air bubbles, then an explanation for the acclimatization and de-acclimatization can be

proposed. As discussed in an earlier section, when the complement system of an individual responds to the presence of an air bubble, it is the C3 molecule that is involved in starting the activation of the complement sequence. However, in the process, this molecule is fractured into components; one of them being C3a. Thus once a C3 molecule has been involved in the activation process, it can not be used again. A similar argument can be made for each of the other complement system molecules. Thus the process of activation depletes the concentration of the complement molecules, and their concentration does not return to normal until the body produces the required number of molecules. Thus when an individual experiences a pressure profile that produces bubbles in his/her circulatory system, if there is activation, one of the effects is depletion of the concentration of the complement molecules. If the next exposure to a pressure profile occurs before the body has restored the concentration of the complement proteins to the concentration they had before the previous pressure profile, their concentration will be steadily decreased until steady state concentrations are reached that is determined by the frequency of the pressure profiles and the degree of activation by the air bubbles on each profile. If the steady state concentrations of the complement proteins are sufficiently low, then the individual could experience very little complement activation in this steady state. Under this circumstance, the individual would be immune to DCS, according to the complement hypothesis.

This aspect of the complement hypothesis can be examined with animals becuase they can be pharmacologically decomplemented. Such a series of experiments has been conducted with rabbits.

The response of the complement system of rabbits to air bubbles has been found to be heterogeneous in the same fashion as that of the human complement system. A study has been performed in which plasma was collected from each of 21 white New Zealand rabbits and a portion incubated with air bubbles, a portion with zymosan (a substance known to strongly activate the complement system along the alternative pathway) and as a control, a portion without any stimulant added. The complement activation in each portion was assessed using a neutrophil aggregation test introduced by Craddock *et al.* (Craddock *et al.*, 1977a; Craddock *et al.*, 1977b; Hammerschmidt *et al.*, 1980). As with the human subjects, it was found that a group of rabbits could be identified for which there was no measurable complement activation that resulted from incubating their plasma with air bubbles, and another group of the rabbits for which there was significant complement activation.

For the rabbits, the sensitivity index was found to be the degree of complement activation in plasma incubated with zymosan as compared with

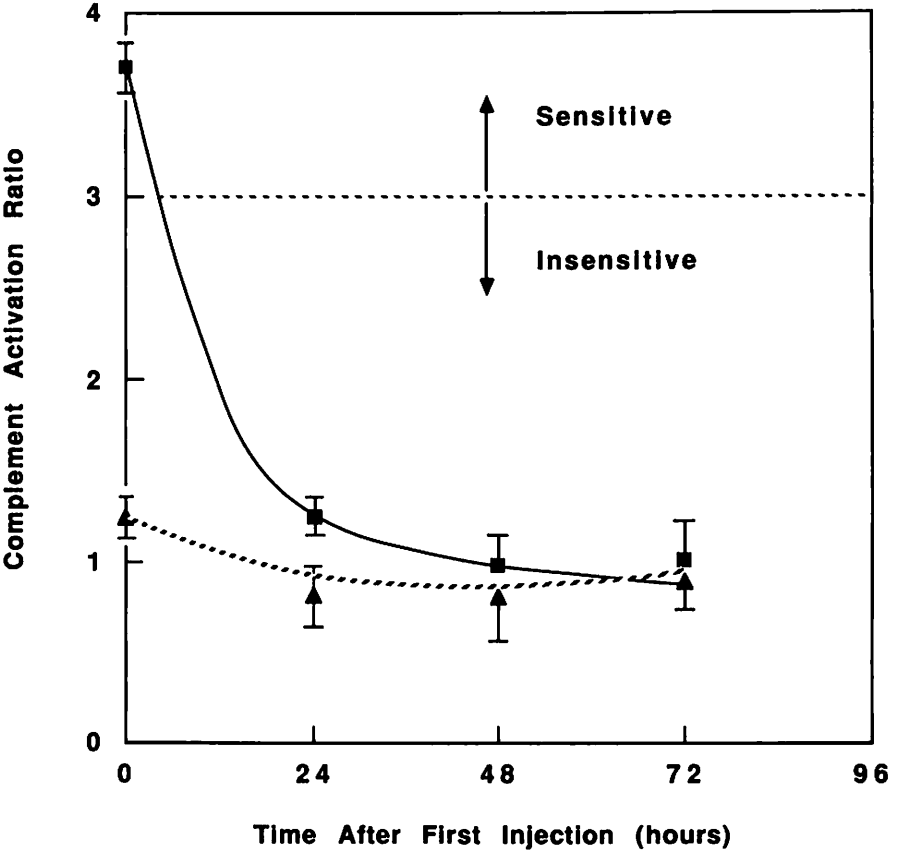

Fig. 5. Change in the sensitivity of rabbits as they undergo decomplementation. The solid line is the ratio of the autologous neutrophil aggregation produced by a portion of rabbit plasma incubated with zymosan to that produced by a control sample, and the dashed line is that produced from a portion of their plasma incubated with air bubbles to that produced by a control sample as a control (Avg. ± SE).

the plasma incubated as a control. Those rabbits for which the complement activation in their plasma sample incubated with zymosan was three times or more that of their control sample, were also found to have complement systems that were activated by air bubbles. These rabbits are referred to as Sensitive and the others as Insensitive.

By decomplementing a Sensitive rabbit, it can be converted into an Insensitive rabbit. The decomplementation procedure can be accomplished by injecting a factor derived from cobra venom (Ward *et al.*, 1985). In Fig. 5, the degree of complement activation is plotted for the group of

rabbits that were injected with the cobra venom factor on three successive days. The solid line is the average ratio of the degree of complement activation (neutrophil aggregation) in the plasma samples incubated with zymosan to that found in the plasma samples incubated as controls. Note that initially this group of rabbits was classified as Sensitive and that 24 hours after the first injection of cobra venom, a blood sample taken from each indicated that they had been converted to Insensitive rabbits. This is confirmed by the dashed line which is the ratio of the degree of complement activation in the plasma samples incubated with air bubbles to that in the control samples. Note that 24 hours after the first injection, this latter ratio is not statistically different from unity.

To determine whether decomplementing the rabbits prevents them from experiencing DCS, a series of experiments was performed in which all of the rabbits were subjected to the same pressure profile. The pressure profile involved subjecting a rabbit to a pressure of 2 ATA while it was breathing air. Each rabbit was held at this pressure for a period of 30 minutes and then returned to a pressure of 1 ATA. The gas was then switched to pure oxygen, and they were held at this condition for a period of five minutes. Finally, the pressure was reduced to 0.2 ATA while they were still breathing pure oxygen. The pressure chamber had been constructed so that a rabbit could be required to move on a treadmill while being observed and while at any pressure. To assess DCS, each rabbit was required to move intermittently on the treadmill while at 0.2 ATA and was observed for symptoms of DCS for a period of up to 30 minutes. The symptoms observed included dragging of a rear leg (or legs), gasping for breath, and becoming very excited before collapsing into unconsciousness.

Each rabbit was first subjected twice to the pressure profile. They were allowed to rest a minimum of three days between the profiles. This period of time had been found to be more than sufficient for their complement sensitivity to return to normal. Each of the five rabbits in the study were observed to have symptoms of DCS on both of these profiles. Rabbits that did not meet this criterion were not continued. Blood samples were taken after the second profile for later examination with the neutrophil aggregation test. Each of the rabbits was classified as Sensitive to complement activation according to this test.

Each of the rabbits was then decomplemented using the factor derived from the cobra venom. Twenty-four hours after their third injection, they were subjected to the same pressure profile for the third time. According to the results shown in Fig. 5, they should be Insensitive to complement activation at this time. None of the rabbits were observed to have symptoms of DCS on this third profile.

TABLE 3.

Examination of the Effect of Complement Activation Sensitivity on Susceptibility to DCS in Rabbits

Complement Activation	Pressure Profile			
Sensitivity (N = 5)	1st Occasion	2nd Occasion	3rd Occasion	4th Occasion
Sensitive	DCS? Yes	DCS? Yes		DCS? Yes
Insensitive			DCS? No	

Each rabbit was then given an additional three days of rest before being subjected to the same pressure profile for the fourth time. All of the rabbits were observed to have symptoms of DCS on this profile as they had on the first two occasions. A blood sample was taken after each rabbit had been subjected to the fourth pressure profile, and used to examine their sensitivity to complement activation at that time. Each was classified as Sensitive.

The results are summarized in Table 3. They indicate that if a rabbit was Sensitive to complement activation at the time they were subjected to the pressure profile, they were susceptible to DCS. Also, a rabbit can be made "Acclimatized" by decomplementing it, and it will lose "Acclimatization" when its complement proteins have returned to the state where they can be activated by air bubbles, i.e. when the rabbit is again sensitive.

VI. SUMMARY

The results reported above indicate that individuals who are sufficiently sensitive to complement activation by air bubbles also have a higher susceptibility to DCS. A test that can be used to identify those individuals who are susceptible to DCS has been described. Those individuals whose native complement system showed no activation when their plasma was incubated with air bubbles did not experience any cases of DCS when they were subjected to a number of different pressure profiles, each of which was severe enough to produce bubbles in their circulatory system that could be detected by Doppler monitoring.

The complement activation produced by air bubbles has been found to be along the alternative pathway. The first step in activating this pathway involves both the proteins C3 and factor B. Both of these proteins are known to be genetically polymorphic. Each molecule has two

principal variants and a number of rare variants. The genetic variation in these molecules provide a possible explanation for the variation in the susceptibility of individuals to DCS.

A mechanism has been proposed that gives an explanation for the phenomena of Acclimatization and De-acclimatization. When an air bubble enters the plasma of a sensitive individual, there is activation of the complement system. The activation process itself destroys a certain number of these proteins, thereby depleting their concentration. Their concentration is not returned to normal until the body has time to produce molecules for their replacement. Thus repeating a pressure profile more often than the rate at which the body could produce their replacements would result in the individual becoming decomplemented. De-acclimatization would simply follow when the individual stopped experiencing the pressure profiles.

To determine if this proposed mechanism of Acclimatization and of De-acclimatization is supported by observation, a series of experiments was conducted with rabbits. It was found that rabbits that were normally susceptible to DCS on a particular profile could be prevented from displaying these symptoms if they were pharmacologically decomplemented before being subjected to the profile. Thus they behaved as though they were "Acclimatized". Also, it was found that if an "Acclimatized" rabbit was simply allowed to rest in its cage for a period of time that was sufficient for its complement system to return to its normal sensitivity, then it was again susceptible to DCS on the same profile.

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14

Animal Models in Decompression

Edward H. Lanphier and Charles E. Lehner

Animals are employed in decompression studies for the same reasons that cause animals to be utilized in many other areas of medical research. We maintain that this can be a humane process that offers many advantages (Lehner *et al.*, 1987). A thorough review of the use of animals in decompression studies would be interesting and useful. That cannot be attempted here, but certain earlier investigations seem particularly worthy of mention.

I. HISTORICAL BACKGROUND

Among historical "landmarks," the earliest is surely Robert Boyle's 1670 report of a bubble in the eye of a viper decompressed with a vacuum pump. In *La Pression Barometrique*, published in 1878, Paul Bert reported decompression studies in a number of different species.

More familiar to most is the work of Boycott, Damant, and Haldane, reported in 1908. Those investigators used goats in studies that led to decompression tables for the Royal Navy. They commented upon their selection of species: "A few experiments were made with rabbits, guinea pigs, rats, and mice, but for regular use goats were selected chiefly because they were the largest animals which could be conveniently dealt with and which could be obtained in considerable numbers. The questions under consideration depend in a very fundamental way upon the rate of circulation in the animal under investigation."

Boycott, Damant, and Haldane (1908) believed that the susceptibility of an animal to decompression sickness (DCS) must depend primarily upon the rate at which its respiration and circulation removes the excess of dissolved nitrogen on decompression. They recognized the lesser DCS susceptibility of smaller animals and attributed this primarily to more rapid circulation.

II. COMPARATIVE STUDIES

Catchpole and Gersh (1947) reviewed the field and reported animal experiments in decompression conducted at the U.S. Naval Medical Research Institute during World War II.

In 1962, Kindwall reported a systematic study of comparative DCS susceptibility. He utilized rats, rabbits, guinea pigs, and cats exposed to high pressure for long periods and then rapidly decompressed. He found that these animals did not suffer from clinical "bends" except when decompressed almost explosively. Kindwall used Kleiber's formula for metabolic rate scaled in relation to body size (Kleiber, 1947) in attempting to determine how closely the circulatory rate might correlate with resistance to DCS. He concluded that his experiments ". . .would appear to cast some doubt on the theory that the shorter circulation time in small animals, *per se*, provides them with immunity to bends."

More recently, Lin and his associates (Lin, 1981; Lin, 1987; Lin *et al.*, 1984) have shown that the fundamental "bubble threshold" — the largest drop in pressure that will not produce bubbles — is essentially constant among species. This is evident experimentally only when species differences in gas uptake are ruled out by using saturation exposures, when

differences in gas elimination are minimized by very rapid decompression, and when minimal Doppler-detected venous bubbles are used as the end point. The importance of these factors points to their probable role in species differences in DCS susceptibility as ordinarily encountered.

Circulatory effects on rates of gas uptake and elimination clearly must be important. A less obvious factor is the likelihood that bubble formation, if it occurs more readily during decompression in one species than another, will further inhibit gas elimination (Thalmann, 1987) and thus magnify the effect of circulation time. Further magnification may occur with bubble formation if more-rapid gas elimination in one species minimizes the persistence and effects of bubbles. Body fat content must also be important (Catchpole and Gersh, 1947) at least in exposure to inert gases other than helium. Tolerance to gas bubbles in tissue may also differ among species (Flynn and Lambertsen, 1971) and could influence occurrence or clinical detection of DCS.

The conditions of comparison are probably also important. For example, rapid gas uptake in a brief exposure may tend to offset the protective effect of rapid gas elimination during decompression. Comparisons based upon saturation exposures may thus tend to magnify species differences. Trials with end points that involve major bubble formation may also emphasize differences. With at least this many interactive factors to consider, it would be surprising if theoretical analysis could fully explain or predict species differences.

The need for empirical determination of species differences under realistic conditions is evident. Kindwall's comparisons (Kindwall, 1962) have been mentioned. Flynn and Lambertsen (1971) studied a number of variables in mice and compared data for mouse, guinea pig, dog, goat, and man. They demonstrated a strong log-log relationship between body weight and ED50 nitrogen exposure pressure under saturation conditions.

Berghage, Davis, and Dyson (1979) took account of systematic data available for seven of at least 22 species known to have been used for decompression studies up to 1979. They tabulated decompression variables in relation to physiological variables for man, goat, guinea pig, rat, hamster, and mouse. Utilizing the observations of Flynn and Lambertsen (1971) they reproduced the log body weight/log ED50 plot, adding a point for rats. In addition, they determined intercorrelations among variables and estimated factors such as allowable pressure-reduction limits for different species exposed to different pressure levels.

Neither Flynn and Lambertsen (1971) nor Berghage *et al.* (1979) advocated attempts to extrapolate from small animals to divers. Rather, their aim was to permit estimation and extrapolation of basic decompression parameters among experimental animals.

III. SPECIFIC ISSUES

A number of specific problems and possibilities in decompression have been investigated in various animals. For example, Spencer and Clarke (1972) used sheep in developing the technique of Doppler bubble detection. Lin and his associates (Lin, 1981; Lin, 1987; Lin *et al.*, 1984) employed rats, cats, and dogs in determining the bubble thresholds already mentioned. Lehner and Lanphier and their associates have used sheep and pygmy goats to investigate the relationships between dive profile and DCS types (Lanphier *et al.*, 1984; Lehner *et al.*, 1985; Lehner and Lanphier, 1989) and also the latency of DCS (Lehner *et al.*, 1987). Lillo (1988) used rats in a study of the decompression effects of different gases. Lehner *et al.* (1987) have strongly advocated the use of large animals in preliminary testing of new decompression procedures.

IV. SPECIFIC TYPES OF DCS

A. Chokes

Animal experimentation has been especially useful in studies that would pose unacceptable risks in human subjects. For example, Bove *et al.* (1974) used dogs in experiments that involved both chokes and spinal cord injury. Atkins *et al.* (1988) employed sheep in a study of chokes, and Catron *et al.*, (1984) employed dogs in an investigation of pulmonary responses to acute decompression.

B. Spinal Cord DCS

Hallenbeck *et al.* (1975) used dogs in spinal DCS studies. Palmer *et al.* (1976) described pathological changes in the spinal cords of animals that had shown signs of central nervous system decompression sickness (CNS-DCS) following decompression. Palmer *et al.* (1987) subsequently provided comparable descriptions of the cords of divers who had died accidentally. Here, pathological findings were of particular significance since the divers concerned had no known clinical history of spinal DCS and no documented neurological abnormalities.

Hills and James (1982) and Francis *et al.*, (1988) used dogs in studies of the possible significance of autochtonous bubble formation within spinal cord tissue — as opposed to ischemic injury from arterial or venous obstruction by intravascular bubbles.

Adams *et al.* (1985) reported an advantageous sheep model of *dysbaric osteonecrosis*, another consequence of decompression that does not lend itself readily or ethically to experimentation in human subjects.

V. OBSERVATIONS AT THE UNIVERSITY OF WISCONSIN

We began using animals in decompression studies at the University of Wisconsin mainly because proposed experiments seemed likely to involve unacceptable risk to human subjects (Elliot and Kindwall, 1982). To minimize scaling factors (Berghage *et al.*, 1979; Flynn and Lambertsen, 1971; Schmidt-Nielsen, 1984), we were most interested in animals somewhere near humans in body size. Responses to decompression in domestic goats had been adequately reported (Boycott *et al.*, 1908; Davidson *et al.*, 1950), but we found little in the literature about sheep (Spencer and Clarke, 1972) and nothing about pygmy goats. We decided to investigate both species in the large chamber that we had acquired from The Ohio State University and installed in the University of Wisconsin Biotron.

A. Limb Bends

We began by determining "thresholds" in no-stop "ascents" from 24-h simulated dives in compressed air. We defined "threshold" as the lowest exposure pressure that produced a definite sign of decompression sickness in a given animal. The predominant sign in both goats and sheep was a limb-lifting, just as described and illustrated by Boycott, *et al.* (1908).

Boycott's famous photograph shows a goat holding up a foreleg and simultaneously being fed by a human hand. This is consistent with our strong impression that limb bends seldom bother the animals very much. They do not lose their interest in food and usually behave quite normally except for reluctance to bear full weight on the affected leg. In our animals, most cases of DCS resolve spontaneously in a relatively short time. If they do not, or if we suspect undue discomfort or disability, we use US Navy air treatment tables (1985), which are usually effective.

In most of our decompressions, we supplement careful observation with Doppler bubble detection (Spencer, 1976). Doppler grades have not appeared to have high predictive value in our studies, even in incipient chokes; and they do not correlate very well with individual DCS susceptibility (Lehner *et al.*, 1984).

Early studies indicated that most of our pygmy goats were slightly more susceptible to DCS than the domestic goats of Davidson *et al.*, (1950). Higher pressures were required to produce DCS in our sheep.

In Fig. 1, we have re-drawn the Flynn and Lambertsen (1971) — Berghage *et al.* (1979) graph of log ED50 vs log body mass, plotted our values on it, and calculated a new regression line. The ED50 pressure is on the line for domestic goats, slightly above for sheep, and slightly below for pygmy goats and humans.

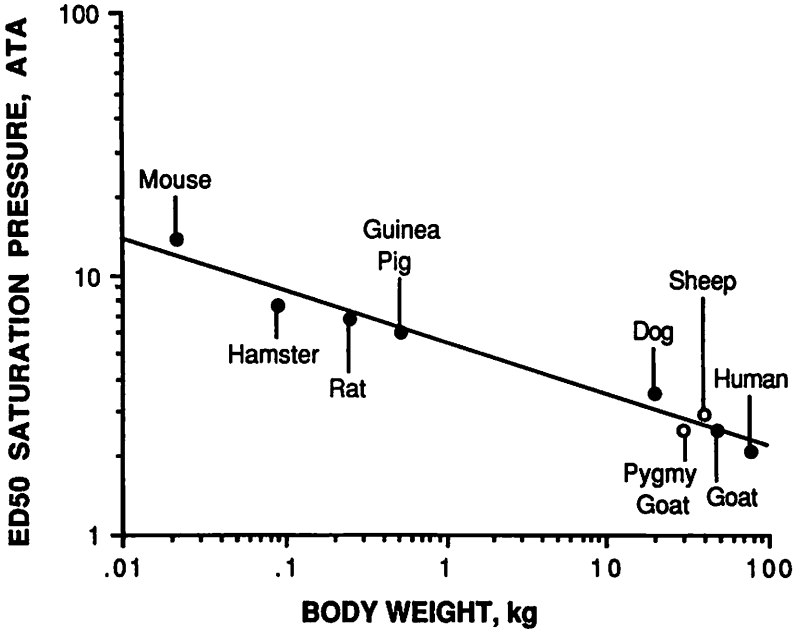

Fig. 1. Species tolerance of decompression after saturation exposure in terms of the effective dose (ED50) of pressure (ATA) as a function of body weight. Closed circles: data from Berghage *et al.*, 1979. Open circles: comparable threshold decompression responses of pygmy goats and mixed-breed sheep at the University of Wisconsin-Madison.

The great pitfall of basing anything on thresholds is that an animal that develops DCS at a given pressure may do so at quite a different pressure on another occasion, as illustrated in Fig. 2. For example, Pavlova developed DCS after a 4-h dive to less than 45 ft but then showed nothing in deeper dives until she reached nearly 60 ft weeks later.

When we realized how inconsistent "thresholds" could be, we shifted to a regression-modeling approach (Baker and Helder, 1985). This enables us to make use of all of the data and to estimate the exposure that would produce a certain percentage incidence. In Fig. 3, we have indicated the depths and times of the USN "no decompression" limits (USN, 1985) on a graph of estimated percent incidence as derived in sheep. The USN limits lie almost entirely between the lines for an estimated 1% and 5% DCS incidence in our sheep.

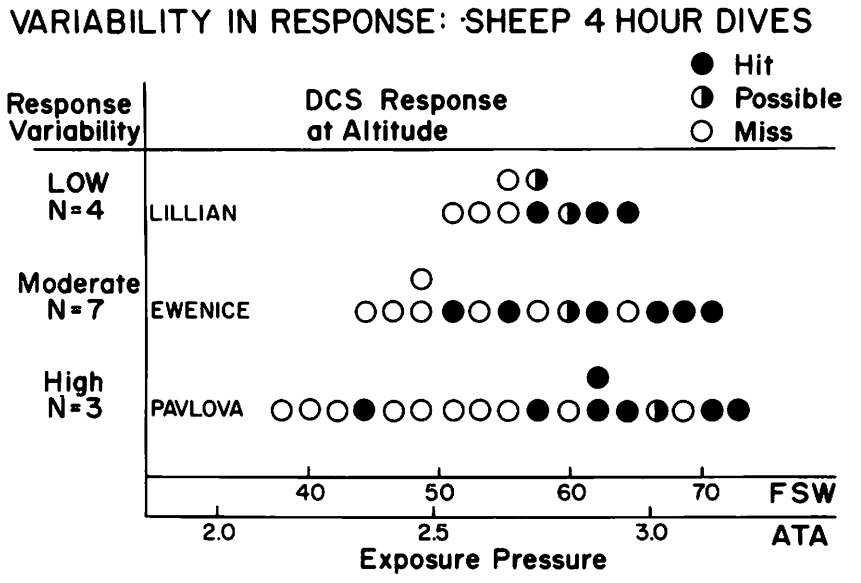

Fig. 2. Examples of variability in response to no-stop decompression following 4-h "dives" to different pressures during determination of thresholds.

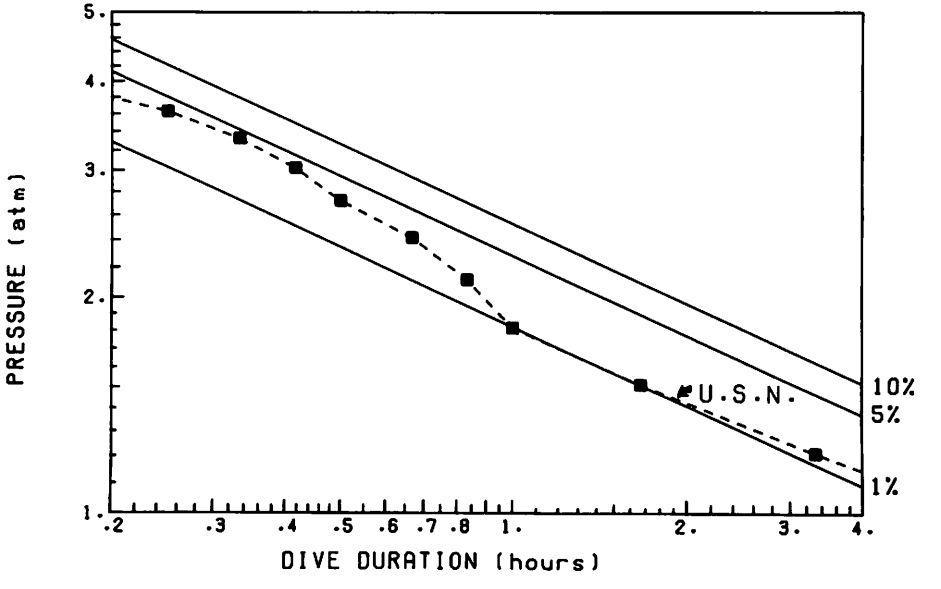

Fig.3. U.S. Navy "no-decompression" depth/time limits with lines for estimated percent incidence of DCS derived from experiments in sheep.

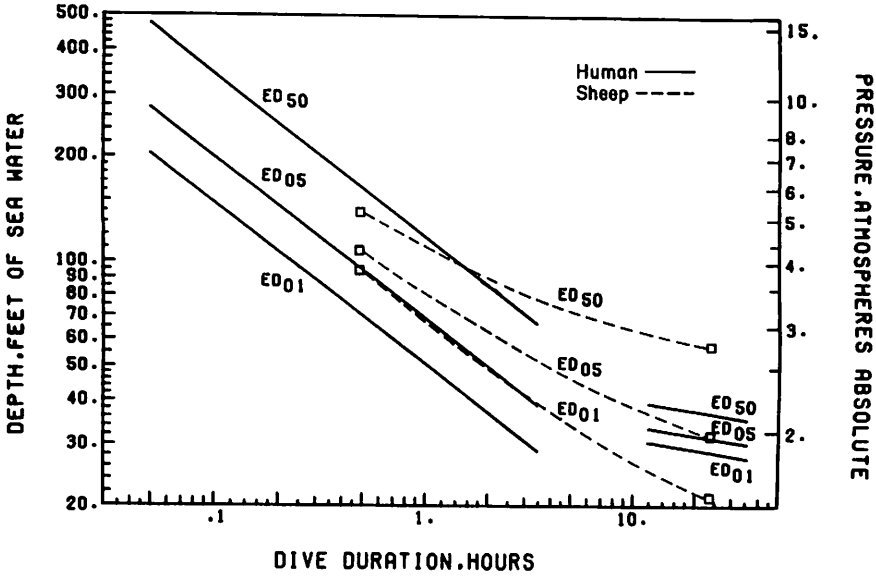

Fig. 4. Human and sheep responses to decompression from hyperbaric exposures to compressed air. Human responses were analyzed by a maximum likelihood regression fit (Baker and Helder, 1985) of the logistic-transformed, pooled responses with log pressure and log duration as independent variables. Sheep responses were similarly analyzed but without log duration as a variable. Point estimates of sheep DCS incidence were calculated from pooled responses. Human DCS incidence estimates (solid lines) cover the range of durations represented in the original data. (Shorter human duration data from Van Der Aue (1951), long-duration human values from Behnke, 1967.)

This approach is also useful for relating our data to experience in divers. In Fig. 4, we have plotted incidence estimates derived from human data reported by Van Der Aue *et al.* (1951) and Behnke (1967) to compare with our sheep findings. The agreement seems remarkably good. Limb bends predominated by a wide margin in 4-h dives as well as in decompression from 24-h "saturation" exposures.

B. Dysbaric Osteonecrosis

The 24-h study was complicated by a phenomenon that we called *late limping*, limb-lifting that recurred or began a day or more after decompression and persisted for more than 24 h. This seemed much too early to suggest dysbaric osteonecrosis according to the reported human timetable (Davidson, 1976), but the possibility that necrosis might develop more rapidly in animals led us to smuggle Louise Lamb, our prime

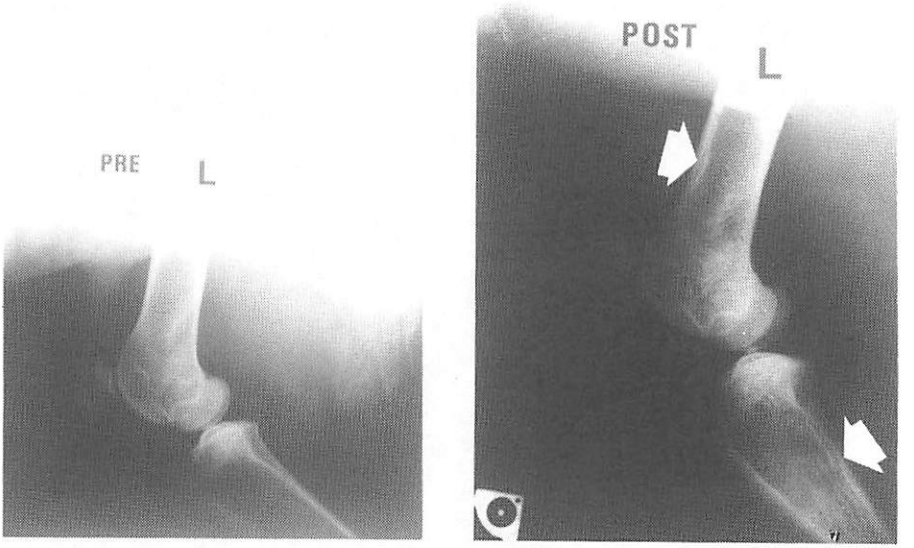

Fig. 5. Radiograms of left femur and tibia of sheep. Pre: Before exposure to increased pressure. Post: Following multiple exposures to 2.5-2.9 ATA, showing endosteal thickening (upper arrow) and linear opacities (lower arrow).

limper, into inpatient radiology in our new medical center. Our bone radiologist diagnosed bone necrosis compatible with dysbaric osteonecrosis (McCallum and Harrison, 1982) and a technetium bone scan showed "hot spots."

With this evidence, we suspected that the "late limpers" pointed to a practical animal model for bone necrosis. In later studies, we were able to produce bone necrosis routinely with repeated 24-h "dives" deep enough to produce frequent limb bends (Adams *et al.*, 1985). Widespread radiographic bone changes were found, as illustrated in Fig. 5.

Upon gross and microscopic evaluation, we found marrow necrosis even in bones that showed no definite radiographic abnormality. In the bone shown in Fig. 6, the diaphyseal marrow was necrotic. Endosteal deposition of new bone was a frequent finding, well-shown in Fig. 7. These changes appear consistent with classic descriptions of pathological findings in dysbaric osteonecrosis (Catto, 1976).

Microangiography (Rhinelander *et al.*, 1979), illustrated in Fig. 8, suggested that few if any original vessels persist in necrotic marrow and that ingrowth of new vessels from cortical bone precedes formation of new bone. If the period of greatest weakening in the repair process could be

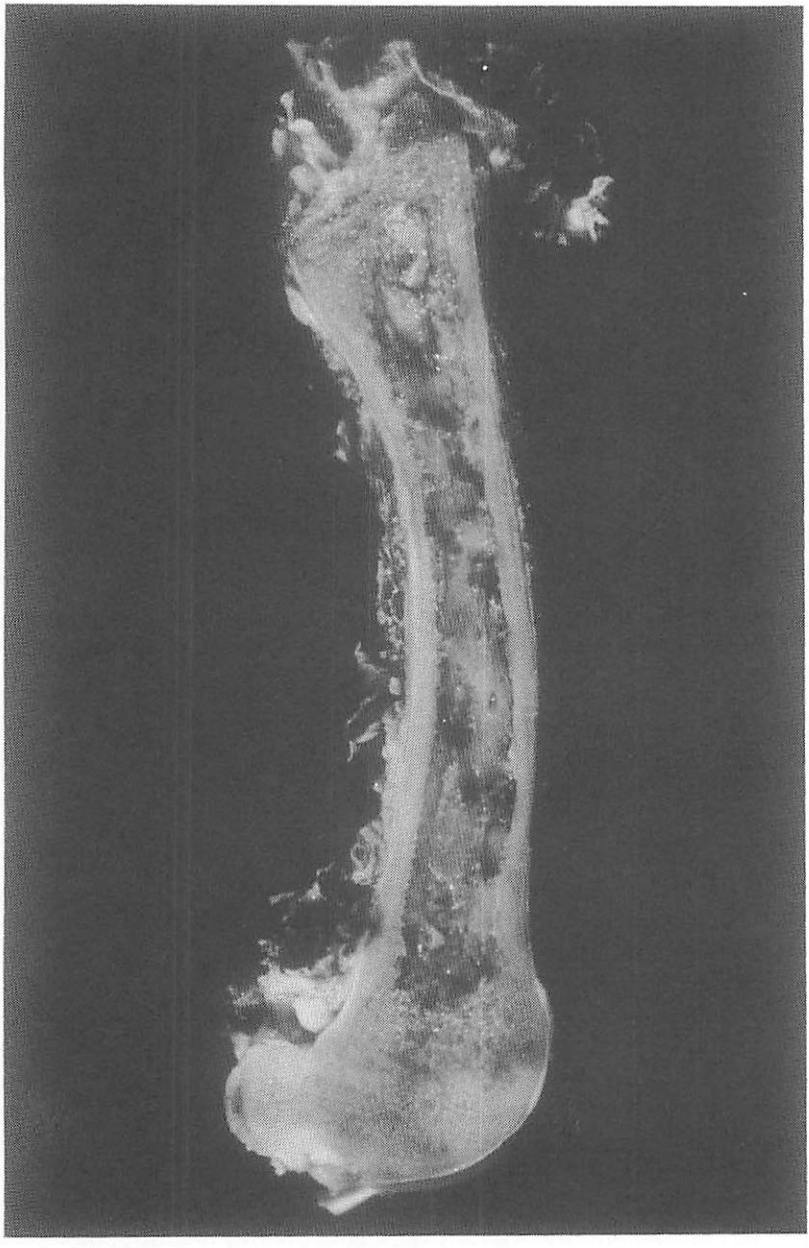

Fig. 6. Gross pathology of sheep long bone showing extensive medullary necrosis typical in dysbaric osteonecrosis.

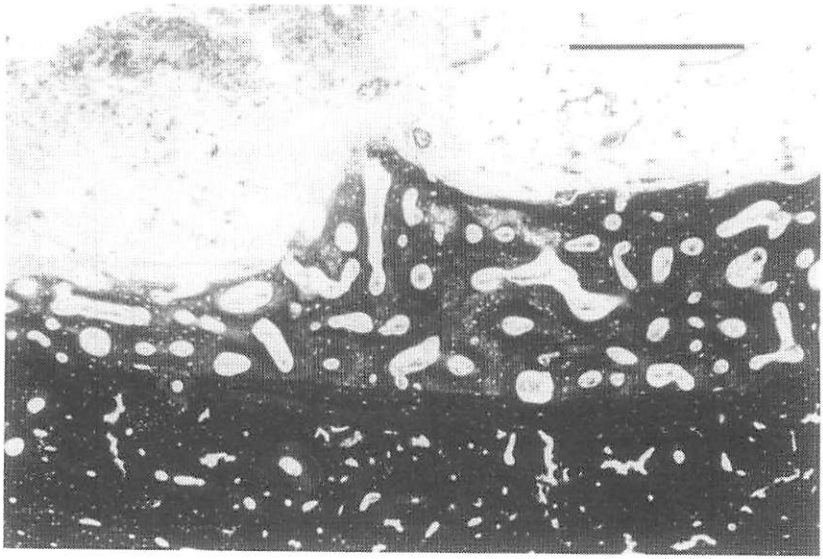

Fig. 7. Photomicrograph of affected diaphysis illustrating new bone formation with large lacunae adjacent to marrow (light areas). Endosteum (laminated) lies between new bone and cortical bone (darkest regions). [Scale = 1 mm.]

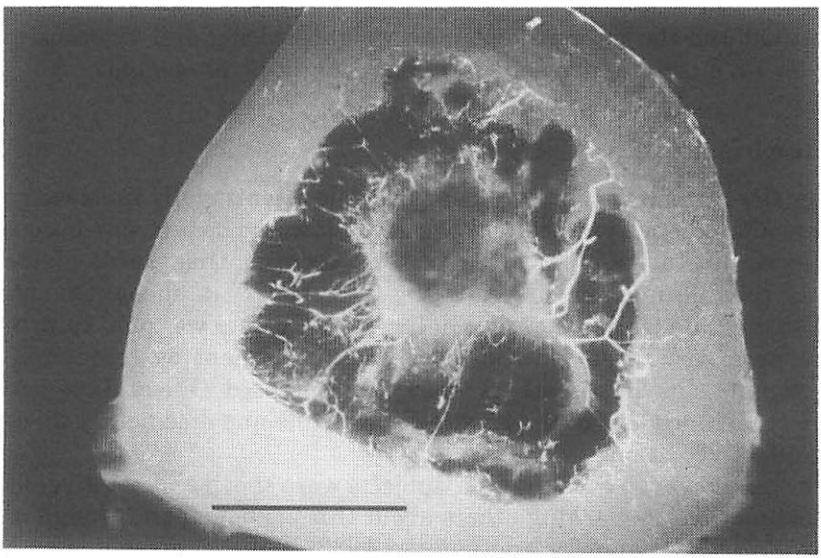

Fig. 8. Microangiograph (Rhinelander *et al.*, 1979) of section from sheep tibia indicating patent vasculature filled with Micropaque (R) barium sulfate (white), and ingrowth of vessels from cortical bone to a central medullary lesion. [Scale = 1 cm.]

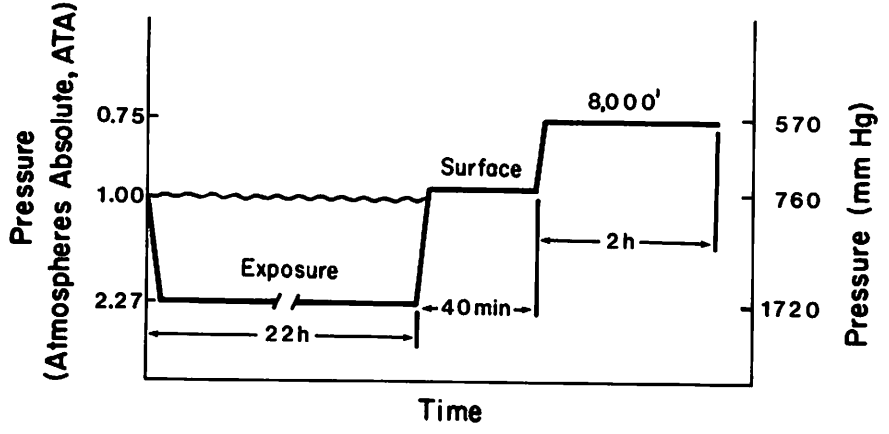

Fig. 9. Respiratory DCS study. Hyperbaric/hypobaric exposure protocol used to provoke respiratory decompression sickness in sheep (From Atkins, *et al.*, 1988).

identified and the patient kept from weight-bearing and vigorous exertion for its duration, permanent damage might be prevented.

C. Respiratory DCS

Our first attempt to produce bone necrosis intentionally involved exposure to altitude in a protocol that we thought would be both advantageous and safe. But instead of a model of bone necrosis, this profile yielded a highly reliable method for producing *"the chokes"* in sheep. One sheep died with white froth appearing in her mouth before we could return the chamber to ground level. The response to treatment by recompression was notably slow in two others which had collapsed. One of those had an acute recurrence late in the treatment schedule and died before we could take effective action.

We were never so glad that our subjects were sheep and not divers, and we lost no time in warning others about this phenomenon through a letter to *Pressure* (Lanphier and Lehner, 1982). We also presented a paper on this experience and subsequent observations in the 8th Underwater Physiology Symposium in 1983 (Lehner *et al.*, 1984). This animal model became the basis of a study of respiratory DCS (Atkins *et al.*, 1988).

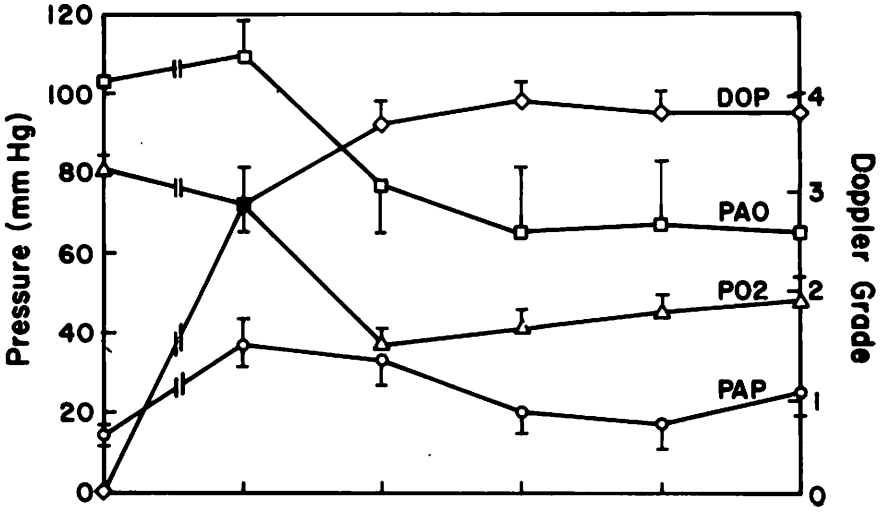

Fig. 10. Respiratory DCS Study. Physiological findings at each observation stage to 60 min of hypobaric exposure. Mean Doppler bubble grades (DOP), pulmonary arterial pressure (PAP), aortic blood pressure (PAO), and arterial Po_2. (From Atkins, *et al.*, 1988.)

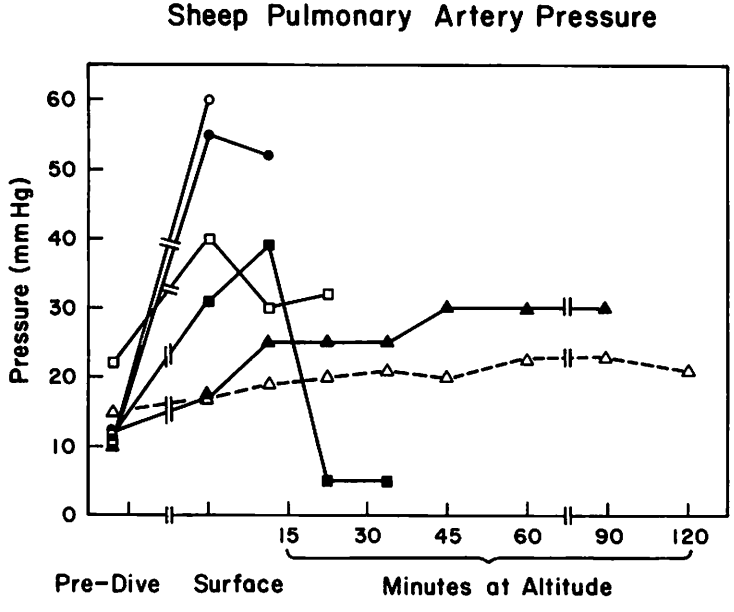

Fig. 11. Respiratory DCS Study. Individual mean pulmonary arterial pressures of 6 sheep. (From Atkins, *et al.*, 1988.)

The profile (Fig. 9) produced chokes in 17 of 18 animals. It involved 22 h at moderate simulated depth with direct ascent to surface. We observed the sheep at surface for about 40 min and then took them to 570 mm Hg — the pressure at about 8,000 ft of altitude — for 2 hours, or until the animals died or appeared moribund. (Note that 8,000 ft is an acceptable cabin altitude for commercial aircraft. We do not recommend flying home immediately after days of repetitive diving!)

As illustrated in Fig. 10, the precordial Doppler monitoring, represented by mean scores, showed large numbers of bubbles shortly after surfacing. Spencer's Grade 3 (Spencer, 1976) was reached at surface, and Grade 4 was approached at altitude. Overall, mean pulmonary artery pressure approximately doubled during this period. There was also a marked drop in aortic blood pressure and in arterial Po_2.

Individual pulmonary artery pressures in the six catheterized sheep are shown in Fig. 11. The end of each line shows when the animal died or was euthanized. None that reached or exceeded 30 mm Hg survived. One of these died at surface before altitude exposure. Only ten sheep remained after 1 hour at altitude. One animal whose pressure had not exceeded 30 mm Hg died after 90 min. Another, whose pressure remained close to 20 mm Hg, survived.

Altogether, nine animals survived. Most of these had shown definite signs of chokes but recovered. High body weight was the only detected risk factor likely to be important in diving.

D. Spinal Cord DCS

Pygmy goats appeared to be satisfactory substitutes for divers in most respects, but we had difficulty maintaining a healthy herd. Our final experiment with goats consisted of a series of 30-min dives. This series yielded a very unexpectedly high incidence of spinal cord injury (Lanphier *et al.*, 1984). Some of the animals died despite recompression, and one remained almost totally paralyzed after treatment. Relatively short, relatively deep dives in sheep produced very similar findings.

Up to this point, CNS-DCS had represented less than 10% of all of our DCS cases. In the short/deep dives, we were seeing about 50% of cases involving the spinal cord. This led us to look more closely at the relationship between dive profile and types of DCS. As shown in Fig. 12, we found that the short/deep dives produced a high incidence of CNS cases in our sheep, while 4-h dives and 24-h dives produced scarcely any. Limb bends were prevalent at all dive-durations, and chokes were common with both long dives and short exposures (Lanphier *et al.*, 1984; Lehner *et al.*, 1985).

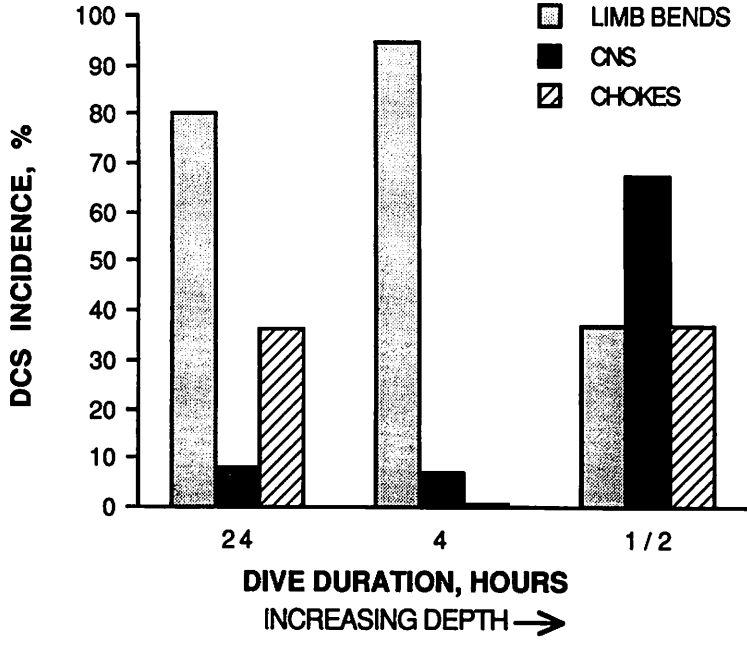

Fig. 12. Decompression sickness manifestations in sheep showing increased CNS involvement associated with shorter dives at greather depth. ($P<0.05$) (From Lehner, *et al.*, 1985.)

We also reviewed the literature and found that caisson and tunnel experience — with characteristically long, relatively low-pressure exposures — involved a low proportion of CNS cases. Diving experience — characterized by shorter and deeper exposures — showed a higher proportion (Lehner and Lanphier, 1989). In dives reported by Van Der Aue, *et al.* (1951), from observations in the 1940's, deeper dives provoked a higher proportion of CNS cases.

Fig. 13 is an estimation of the relative proportion of CNS-DCS vs limb bends cases, at the USN no-decompression limits, based on experience in our sheep. The predicted proportion of CNS cases drops rather sharply with longer dives and lesser depths. There also seems to be little doubt that the proportion of clinical CNS cases among scuba divers is now in the 50% bracket if not higher.

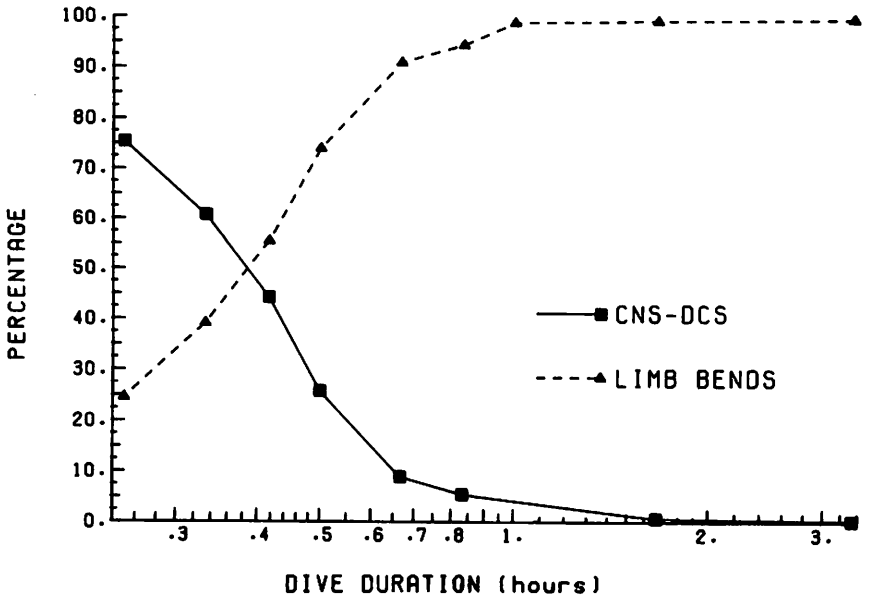

Fig. 13. Estimated percentages of CNS-DCS vs limb bends in sheep at the U.S. Navy no-stop limits for air dives. (From Lehner and Lanphier, 1989.)

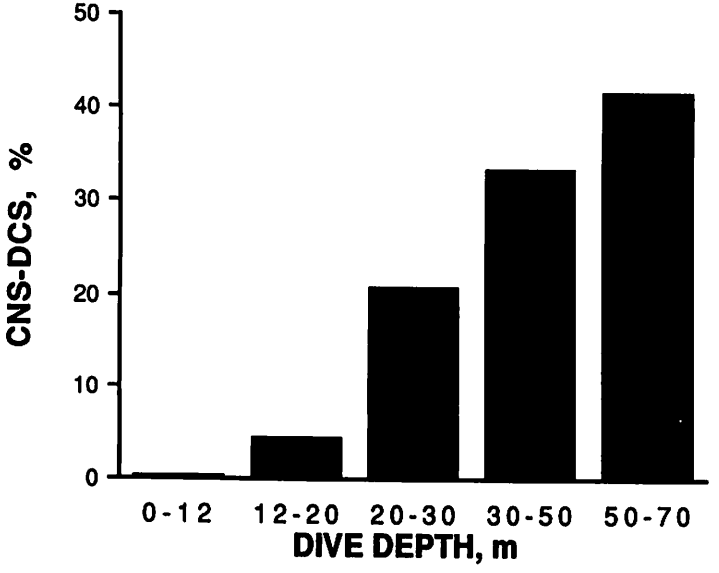

Fig. 14. Percentage of decompression sickness with neurological complications vs maximum dive depth in Israel as reported by Melamed and Ohry (1980).

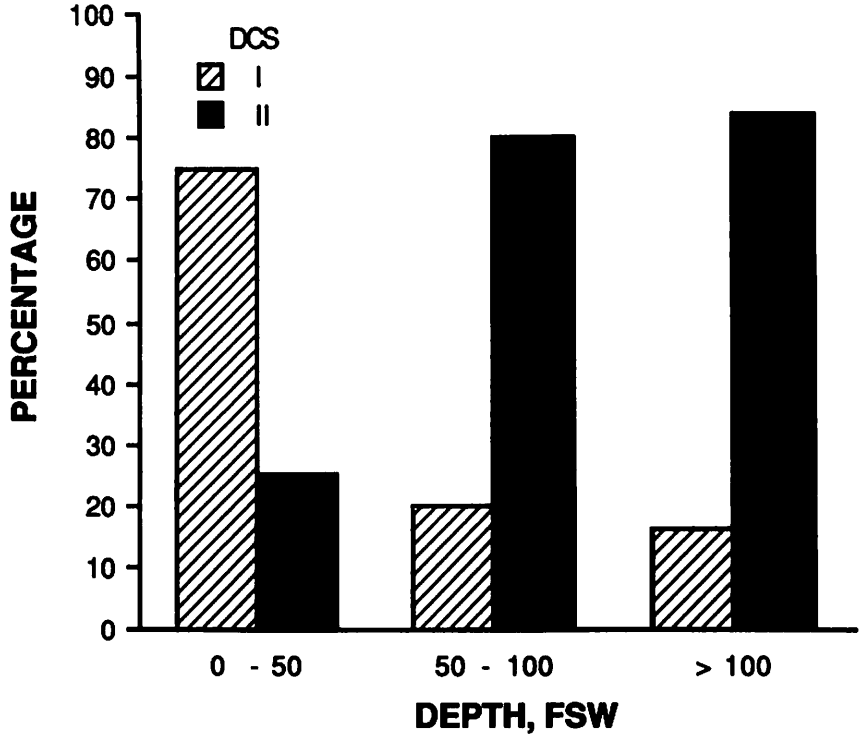

Fig. 15. Relative incidence of Type I and Type II among cases of DCS following dives to different depths as reported to the Divers Alert Network in 1983. (C. Wachholz, personal communication.)

Melamed and Ohry (1980) reported that the proportion of CNS cases in Israeli experience rose progressively with increasing depth. The right-hand column in Fig. 14 represents 50-70 m dives, and the proportion of CNS cases is close to 50%.

Reports from the Divers Alert Network (Dick and Massey, 1985; DAN, 1988) furnish similar values. DAN's analysis of 1983 reports included the depth of dive (Wachholz, C., personal communication), indicated in Fig. 15. Such figures mainly represent sports divers using scuba. Beyond 50 ft, Type II cases outnumber Type I by a large and increasing margin. Since the incidence of chokes is small, most of the Type II cases represents

CNS-DCS. The low incidence of Type II in shallower dives speaks against the argument that Type II is more likely to be reported to DAN. The incidence of CNS problems may be even higher than reported, considering the number of divers who would probably not recognize the significance of a numb foot or weakened limb (Clarke, 1980).

It took us some time to realize that we had come upon a very practical animal model of spinal DCS that does not require exposures greatly beyond the USN no-decompression limits. The pressures that produced CNS-DCS in 30-min dives were equivalent to depths from 119 to 139 fsw (36.3 to 42.4 msw). Ways of using this model are not hard to envision. One such way was demonstrated unintentionally.

VI. EXPERIMENT IN REHABILITATION

Jane was one of our favorite goats. She came out of a 30-min dive with nearly-total paralysis. She responded to treatment initially but had a recurrence that did not yield to recompression. She was conscious but could not even raise her head to drink.

Our veterinary neurologist found some vaguely encouraging signs, so we decided to try to keep Jane alive and see if any improvement would occur. Lacking veterinary intensive care facilities at the time, we installed Jane in a large box in EHL's study at home, held her head up to let her drink, changed her papers many times a day, and kept hay where she could reach it with little head movement. She improved, slowly but definitely.

In about two weeks, Jane was able to raise her head. In the 10th week, she pushed herself — on her belly — out of her box and into the next room. She was then moved outdoors and provided with a house with a door in both ends. In a few more weeks, Jane was able to remain standing for a few minutes if we set her on her feet. She continued to improve, and after weeks of being encouraged to take a few steps, she was able to walk. Eventually, she was able to run in an almost-normal fashion.

We thought this recovery was remarkable, and it sent us to older literature such as Sir Leonard Hill's *Caisson Sickness*, published in 1912 (Hill, 1912). There, we found reports of equally-remarkable recoveries, including a particularly striking case reported in 1905 (White and Bainebridge, 1905).

At about the same time, and Undersea Medical Society workshop on rehabilitation of paralyzed divers was being held. Early rumors suggested that the recovery potential of spinal DCS had been forgotten. Fortunately, the Proceedings (Miller and Permentier, 1985) indicated that most of the participants were aware of the potentially encouraging prognosis — important information in the management of affected divers.

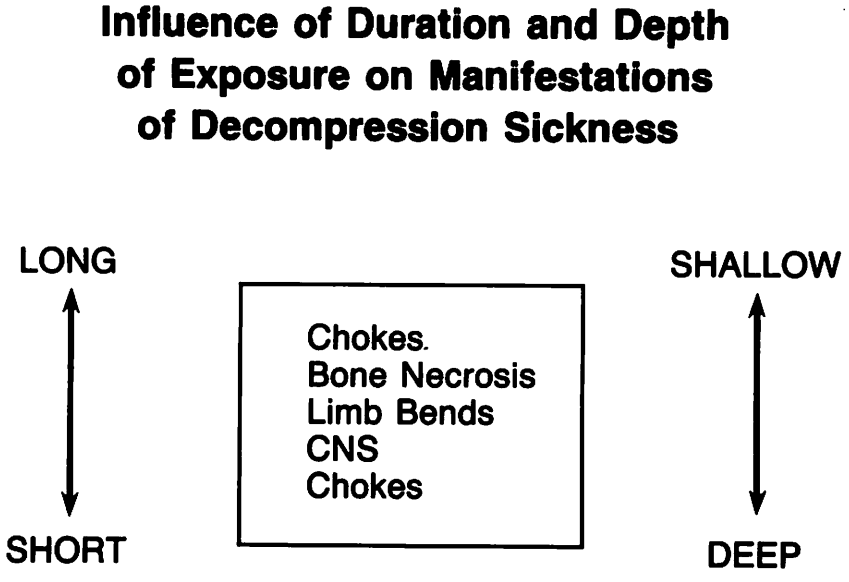

Fig. 16. Diagramatic representation of the relationship between depth/time of no-stop dives and associated forms of DCS (From Lanphier, *et al.*, 1984.)

We can thank Jane and serendipity for calling all this to our attention; and we hope sometime to go on from there — or that some other investigators will use our model to study prevention, pathogenesis, treatment, and rehabilitation in spinal cord DCS.

VII. CONCLUSION

The central finding of our observations is the influence of dive profile on the type of DCS (Lehner and Lanphier, 1989). We can summarize this with a diagramatic chart (Fig. 16). Limb bends are frequent in all types of exposures. Long, relatively low-pressure exposures favor limb bends, chokes, and bone necrosis. Short, relatively deep no-stop dives favor CNS-DCS, while chokes becomes important again in short/deep exposures. Largely by taking advantage of such findings, we now appear to have a practical animal model for each of the major forms of DCS. The salient features of our models are summarized in Table 1.

TABLE 1.

Summary of Animal Models (Sheep)

Limb bends:	Significant depth/time; inadequate decompression.
Bone necrosis:	Repeated long dives with frequent limb bends.
Respiratory DCS (chokes):	Long dive with excursion to altitude.
Spinal Cord DCS:	Short/deep no-stop dive.

In every instance except "limb bends," seemingly unexceptional procedures surprised us with serious consequences (Lehner *et al.*, 1987). This provides the strongest argument for careful use of animals, not only in basic studies but also in the earlier stages of testing decompression procedures. The use of animals such as sheep will probably never be a substitute for final testing in human subjects under realistic conditions, but optimal employment of suitable animals could greatly reduce the number of human trials required.

The most important use of the finding described here may be in defining and characterizing the relevant tissues affected in the different forms of DCS. For example, new decompression procedures should be made particularly safe from the standpoint of CNS-DCS and respiratory DCS, where the seriousness of potential injury is more crucial than the overall incidence of DCS (Lehner and Lanphier, 1989).

We hope that we and others can derive as much relevant information as humanely possible from these models, and from all animal studies in decompression.

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15

Doppler Evaluation of Decompression Tables

R.Y. Nishi

I. INTRODUCTION

The Doppler ultrasonic bubble detector, which enables the detection of moving gas bubbles in the circulatory system, is a valuable tool for the evaluation of decompression tables and profiles. Traditionally, the absence of clinical symptoms of decompression sickness (DCS) has been taken to be the ultimate indicator of safety. From a statistical point of view, however, proving the safety of dives using the binary outcome of DCS vs. no DCS with any reasonable degree of confidence would require

many more dives than are normally feasible (See also Weathersby in this book). Moreover, the diagnosis of DCS can be quite subjective. Gas bubbles in the circulatory system occur far more frequently than DCS and bubbles can be detected even in safe dives. The Doppler ultrasonic bubble detector provides far more information than DCS to assist in the assessment of the severity of dive profiles. In this paper, the technique of bubble monitoring and the classification of bubble signals will be described and the use of Doppler monitoring in bounce or non-saturation diving will be discussed. Only the application to manned diving will be considered.

The Doppler ultrasonic bubble detector is based on equipment originally developed for the measurement of blood flow. Bubbles are much stronger reflectors of ultrasound than the normal components of the blood, and therefore can be easily detected against the background signal from the blood. The Doppler ultrasonic flowmeter was first used for detecting circulating decompression gas emboli in the larger arteries and veins of sheep by Spencer and Campbell (1968). The first detection of bubbles in human divers, although unrecognized at the time, was in 1968 by Spencer and continuing work on human monitoring led to the development of the Spencer Precordial Transducer in 1970, an instrument specifically designed for decompression monitoring. A scheme for classifying the bubbles was developed by Spencer and Johanson (1974) and Spencer (1976).

The Doppler ultrasonic bubble detector was, at one time, believed to have potential as a personal decompression monitor where the individual could listen to his own bubbles and control his own decompression. It soon became evident that this was not practical because detectable bubbles in most non-saturation dives occurred after the surface was reached. It was only during severe dive profiles, in which a substantial amount of time was spent at the decompression stops (e.g., exceptional exposure dives), that bubbles were able to be detected at the decompression stops (Neuman *et al.*, 1976). In addition, the training required for identifying and classifying bubbles was too great to make it practical for the ordinary diver to be able to detect bubbles and control the decompression. Thus, Doppler is now recognized as being a tool primarily for post-dive analysis.

Since the early work of Spencer (1977), several other investigators have done extensive research in applying Doppler monitoring to a variety of decompression applications and in advancing the state of Doppler monitoring for manned decompression studies. For example, Masurel at the Centre dÉtudes et de Recherches Techniques Sous-Marines (CERTSM) and others in France used Doppler extensively for animal and human dives, both non-saturation and saturation (Masurel, 1987). In 1978, Kisman of the Defence and Civil Institute of Environmental Medicine

(DCIEM) and Masurel developed an alternative classification scheme for identifying and grading bubbles (Kisman *et al.*, 1978). From 1979 to 1985, DCIEM used Doppler for evaluating air decompression profiles (Nishi *et al.*, 1981) and applied the method to developing a new set of air decompression tables (Nishi, 1987). Doppler information was used to supplement the information obtained using the traditional method of DCS vs no DCS.

The main purpose in using Doppler, therefore, is to obtain comparative information, post-dive, to assist in determining whether or not a table or profile is safe or hazardous by determining the quantity and duration of bubbles resulting from that profile. The normal method for detecting venous gas emboli is to listen to the signal from the Doppler ultrasonic bubble monitor and to identify and classify the bubbles according to some classification scheme such as the Spencer code or the Kisman-Masurel (KM) code. Consistent and reliable bubble identification and grading require highly skilled and well-trained observers. The signal in the precordial region is extremely busy, with contributions from the blood flow, heart valves, and heart wall motion. Because human judgement is required, the interpretation of the signal can vary to some extent among observers; however, identification and classification of bubbles are still best done by human observers. Although there are some problems with subjectivity, human observers are more accurate overall for assessing bubbles in the precordial region than are automatic bubble detection systems.

II. DOPPLER MONITORING PROCEDURES

In order to provide a means for comparing results between different researchers and users of Doppler equipment, standardized procedures for monitoring dive subjects and identifying and classifying bubbles are required. Fortunately, the existing procedures and classification systems are similar enough that such comparisons can be made. The following describes a recommended standardized monitoring procedure. They are based on procedures used at DCIEM (Eatock and Nishi, 1986).

A. Doppler Hardware

The instrument used should be a simple continuous-wave (CW) Doppler ultrasonic device operating at 5 or 2.5 MHz developed specifically for detecting bubbles. CW Doppler instruments developed for clinical use tend to lack sensitivity and durability. The instruments should be readily available, relatively inexpensive, easy to use, provide a good signal, and

be reliable. Three CW precordial Doppler ultrasonic bubble detectors which are specifically designed for the hyperbaric environment are commercially available (Appendix A). These are manufactured by the Institute of Applied Physiology and Medicine (IAPM), Sodelec S.A., and Techno Scientific Inc. (TSI). Although the transducers are designed primarily for monitoring the precordial region (either the pulmonary artery or the right ventricle of the heart), other veins, such as the subclavian, the femoral, or the inferior vena cava can also be monitored to provide supplementary information. Monitoring is done by trained observers listening to the signals through headphones.

B. Monitoring Sites

Only moving intravascular bubbles can be found with the Doppler method. The primary site to be monitored should be the right ventricle (the precordial site) since an estimate of the rate of bubble production for the entire venous system can be obtained (assuming that the bubbles persist long enough to reach the heart). An alternative is the pulmonary artery. To supplement observations from the precordial site, the subclavian veins (both left and right shoulders) can be monitored. Bubble signals at these sites are unambiguous; however, they should not be used as an alternative to the precordial site because they do not cover the whole body.

C. Subject Position

The subject should be standing or lying down for the evaluation. Either position produces good results, so the choice can be dictated by convenience. The evaluations should be done for two conditions — one with the subject at rest, and the other after the subject has moved in some defined way. For the precordial evaluation, a standing subject would do a deep knee-bend — squatting down and standing up, in a smooth, continuous motion. For the subclavian site, the subject would clench his fist. The movement case is useful because it often produces a shower of bubbles that are easily identifiable.

D. Frequency of Monitoring

The objective in monitoring the diver is to obtain a history of the bubble evolution or production for each subject in the dive. Depending on the severity of the dive profile, bubbles are often not detected immediately after a diver surfaces, but start some time after. For some divers, delays of an

hour or more have been observed before bubbles were detected, but in most cases, bubbles tend to start earlier and peak about an hour after surfacing. Bubbles can persist for several hours after a severe dive. As it is not generally possible to monitor the divers continuously, the divers must be monitored periodically at some set time interval. For most non-saturation dives, monitoring should begin soon after the divers reach the surface and should be repeated at 30 to 40 min intervals for at least two hours. The exact time interval will depend on the number of divers being monitored and the profile being evaluated.

III. BUBBLE CLASSIFICATION METHODS

Identification and classification of bubbles should be according to the Kisman-Masurel (KM) method (Eatock and Nishi, 1986; Hjelle *et al.*, 1987; Kisman *et al.* 1978) or the Spencer method (Spencer and Johanson, 1974; Spencer, 1976). Both methods give similar results but it is believed that the KM method is easier to learn and use and gives a better representation of the bubble signal.

A. The Kisman-Masurel Code

The KM Code for classifying bubbles consists of three parameters which are used to describe the bubble signal (Tables 1, 2, and 3). By breaking down the bubble signal into these component parts, it is much easier to identify the bubbles and to classify them. The KM code can be used for both the rest and movement conditions. Each parameter is assigned a classification from 0 to 4. These parameters are combined to give a single bubble grade (Table 4) similar to that derived from the Spencer code but with a greater graduation.

The first parameter, frequency (f), represents the number of bubbles per cardiac period (Table 1). For code 4, the bubbles are so numerous that they cannot be individually distinguished.

TABLE 1.

Frequency Parameter

Code	Frequency (f) — bubbles per cardiac period
0	0
1	1 - 2
2	several 3 - 8
3	rolling drumbeat 9 - 40
4	continous sound

The second parameter differs for the two monitoring conditions — rest and movement (Table 2). For the rest condition, it represents the percentage (p) of cardiac periods having a specified bubble frequency (i.e., the first parameter from Table 1). For the movement condition, it represents the number of successive cardiac periods (d) having at least a specified bubble frequency following the movement. The first such period must occur within 10 heart beats following the movement.

TABLE 2.

Percentage/Duration Parameter

Code	Rest Percentage (p)	Movement Duration (d) Cardiac Periods
0	0	0
1	1 - 10	1 - 2
2	10 - 50	3 - 5
3	50 - 99	6 - 10
4	100	>10

The third parameter, shown in Table 3, is the amplitude of the bubble signal (A(b)) which is compared to the amplitude of the normal cardiac sounds (A(c)).

TABLE 3.

Amplitude Parameter

Code	Amplitude (A)			
0	no bubbles discernible			
1	barely perceptible,	A(b)	<<	A(c)
2	moderate amplitude,	A(b)	<	A(c)
3	loud,	A(b)	=	A(c)
4	maximal,	A(b)	>	A(c)

The three parameters are combined in the form 'fpA' for the rest case and 'fdA' for the movement case to give the KM code for each assessment. This KM code is reduced to a single bubble grade (bg) according to Table 4. It is recommended that bubble grades be represented as Roman numerals

rather than Arabic numerals to emphasize that these grades represent classifications and not numbers and that standard statistical analyses can not be used (Gatock and Nishi, 1987). It should be noted that some combinations of the KM code will never occur and some others are rarely seen. For example, 144 and 411 are physically impossible.

TABLE 4.

KM Codes vs. KM Bubble Grades

fpA/fdA	bg	fpA/fdA	bg	fpA/fdA	bg	fpA/fdA	bg
111	I−	211	I−	311	I	411	II−
112	I	212	I	312	II−	412	II
113	I	213	I+	313	II	413	II+
114	I	214	II−	314	II	414	III−
121	I+	221	II−	321	II	421	III−
122	II	222	II	322	II+	422	III
123	II	223	II+	323	III−	423	III
124	II	224	II+	324	III	424	III+
131	II	231	II	331	III−	431	III
132	II	232	III−	332	III	432	III+
133	III−	233	III	333	III	433	IV−
134	III−	234	III	334	III+	434	IV
141	II	241	III−	341	III	441	III+
142	III−	242	III	342	III+	442	IV
143	III	243	III	343	III+	443	IV
144	III	244	III+	344	IV−	444	IV

B. The Spencer Code

The Spencer code is used for precordial signals with the subject breathing quietly and otherwise motionless in a sitting or supine position. The bubbles are classified on a scale from 0 to 4 as shown in Table 5.

A comparison of the Spencer and the KM Codes shows that the two systems are similar, with the Spencer Code being a subset of the KM Code. Table 6 gives the equivalent KM Codes and bubble grades which correspond to the Spencer grades.

TABLE 5.

Spencer Scale for Grading Bubbles

Grade	Description
0	A complete lack of bubble signals.
I	An occasional bubble signal discernible with the cardiac motion signal with the great majority of cardiac periods free of bubbles.
II	Many, but less than half, of the cardiac periods contain bubble signals, singly or in groups.
III	All of the cardiac periods contain showers of single-bubble signals, but not dominating or overriding the cardiac motion signals.
IV	The maximum detectable bubble signal sounding continuously throughout systole and diastole of every cardiac period, and overriding the amplitude of the normal cardiac signals.

TABLE 6.

Correspondence between Spencer and KM Codes

Spencer Grade	KM Code (Bubble Grade)
I	111 (I−), 112 (I), 113 (I) 211 (I−), 212 (I), 213 (I+)
II	121 (I+), 221 (II−), 122 (II), 222 (II) 123 (II), 223 (II+)
III	242 (III), 342 (III+), 243 (III), 343 (III+)
IV	444 (IV)

The advantage of the KM Code is that it allows greater scope for classifying the bubble signal and allows for the movement condition. Although the KM code appears to be complex and more difficult than the Spencer code, it is believed that it is an easier system to learn because the classification is done in a systematic step by step manner. With experience, the breakdown into the three parameters can be done simultaneously. Proficiency in classifying bubbles according the KM code can be reached in considerably less time than with the Spencer code.

IV. BUBBLES AS INDICATORS OF DECOMPRESSION STRESS

Doppler-detected bubbles are not normally believed to be the cause of DCS, but their presence in the circulation may be indicative of bubbles elsewhere in the body. Large numbers of bubbles are not necessarily accompanied by DCS, nor do they directly lead to observable symptoms of DCS. However, incidents of DCS are generally accompanied by bubbles; hence,the risk of DCS does appear to be increased. Furthermore, there is some evidence that intravascular bubbles may cause subclinical damage that may have long-term effects; thus dives which produce many bubbles should be avoided (Eckenhoff, 1985).

A. Bounce or Sub-Saturation Diving

There have been several surveys of Doppler data which have shown a relationship between intravascular bubbles and DCS (Eatock, 1984; Vann *et al.*, 1982). Unfortunately, many of these have tended to combine data from a variety of sources such as air dives, helium-oxygen dives, and nitrox dives. A study of 2,483 subject-dives done at DCIEM since 1972 shows that the correspondence of DCS with bubbles depends on the breathing gas and whether or not oxygen was used during the decompression. Tables 7, 8, and 9 show the percentage of DCS events vs. bubble grades for these dives. All dives were done in a hyperbaric chamber with both dry and wet subjects.

Table 7 shows the results for 921 subject-dives on compressed air only. These dives were mostly taken from studies to determine safe diving limits using the DCIEM Kidd-Stubbs decompression computer model (Nishi *et al.*, 1981), to determine no-decompression limits for compressed air (Nishi *et al.*, 1982), and to develop a new set of air decompression tables (Nishi, 1987). The number of subjects observed with the given bubble grades at rest and after movement are shown, along with the number of subjects incurring DCS for each bubble grade. It can be seen that subjects having Grade II bubbles or greater have a higher risk of DCS. Three type II DCS were associated with Grade II bubbles at rest. Grade IV bubbles at rest are relatively rare; hence, the small number of subjects with this level. However, there is evidence to suggest that the risk of DCS will be extremely high with Grade IV bubbles. For example, Spencer and Johanson (1974) reported 2 out of 3 with DCS, and Neuman *et al.* (1976) reported 6 of 19 with DCS.

Table 8 shows the results for 701 compressed air dives with oxygen used during decompression and nitrox dives with a higher percentage of oxygen than compressed air. Most of these dives were conducted during

TABLE 7.

Correspondence between Precordial Bubbles and DCS for Compressed Air Dives

	At Rest					After Movement				
Bubble Grades	0	I	II	III	IV	0	I	II	III	IV
No. of Subjects (921)	666	84	79	90	2	599	86	64	147	25
No. with DCS (27)	2	0	4	20	1	1	1	3	17	5
Percent Incidence	0.3	0.0	5.1	22.2	50.0	0.2	1.2	4.7	11.6	20.0

the development of the DCIEM compressed air tables (Nishi, 1987) for in-water oxygen decompression where oxygen was breathed at 9 msw until the decompression requirements were completed and for surface decompression with oxygen where the subjects surfaced from the 9 msw stop and then recompressed to 12 msw on oxygen to complete the decompression requirements. The results are not as clear-cut as for those air dives where oxygen was not used during decompression. Five DCS cases occurred without any observable precordial bubbles at rest or after movement. However, it should be noted that in cases where no bubbles were observed precordially and DCS symptoms occurred in the shoulder or arm, bubbles were often observed in the subclavian vein on the same side as the symptoms. It is also possible that bubbles could have existed in other parts of the body. No Grade IV bubbles were observed in these dives. Of three Type II DCS, one was associated with no observable bubbles, one was associated with Grade II bubbles at rest, and the third had Grade III bubbles at rest.

TABLE 8.

Correspondence between Precordial Bubbles and DCS for Air with Oxygen Decompression and Nitrox Dives

	At Rest					After Movement				
Bubble Grades	0	I	II	III	IV	0	I	II	III	IV
No. of Subjects (701)	517	45	73	66	0	487	34	37	131	0
No. with DCS (14)	9	0	3	2	0	5	2	2	5	0
Percent Incidence	1.7	0.0	4.1	3.0	—	1.0	5.9	5.4	3.8	—

Table 9 shows the results for 861 helium-oxygen dives. These include breathing mixtures with 80% He and 84% He, and some dives with a semi-closed circuit breathing apparatus with a variable level of helium. Some dives in this set used the US Navy Partial Pressure Tables with oxygen decompression at 15 and 12 msw. Most were experimental dives from the current DCIEM program to develop a new set of helium tables as a replacement for the USN tables. Decompression from these dives include those using oxygen decompression at 9 msw, using air decompression from the first stop followed by oxygen decompression at 9 msw, using air decompression all the way to the surface, and using surface decompression with oxygen. The results show that the risk of DCS with Grade III bubbles is also much lower than for air.

TABLE 9.

Correspondence between Precordial Bubbles and DCS for Helium/Oxygen Dives

	At Rest					After Movement				
Bubble Grades	0	I	II	III	IV	0	I	II	III	IV
No. of Subjects (861)	565	42	89	162	3	522	20	47	205	67
No. with DCS (16)	5	0	1	9	1	5	0	0	7	4
Percent Incidence	0.9	0.0	1.1	5.6	33.3	1.0	0.0	0.0	3.4	6.0

A number of other sources exist for comparing the results of Doppler bubble detections with observed incidences of DCS. For example, the work done by Spencer and Johanson (1974) and Spencer (1976) on no-decompression dives provides some valuable comparisons (Table 10).

TABLE 10.

Bubbles vs. DCS for Compressed Air Dives Precordial Bubbles at Rest (from Spencer)

Bubble Grades	0	I	II	III	IV
No. of Subjects (124)	105	25	16	13	3
No. with DCS (11)	1	1	3	6	2
Percent Incidence	1	4	19	46	67

In these experiments, some subjects were put on surface oxygen or recompressed for oxygen therapy if bubble grades were too high or started soon after surfacing. The DCS cases in the table are for symptoms of pain only and do not include those divers without symptoms who were treated. Thus, it is uncertain whether these divers would also have incurred DCS if left untreated. However, the trend for greater risk of DCS with higher bubble grades can clearly be seen.

Powell and Johanson (1978) reported on the use of helium or neon as the breathing gas. They found a difference between the results for divers using no oxygen breathing during the final decompression stops and those using oxygen. In the first group, divers displaying Grade III or IV bubbles had a considerably greater probability of developing DCS than those with Grade I or II bubbles. Almost 2/3 of those with the higher bubble grades developed some form of DCS. In the second group, problems were not encountered in the divers until Grade IV bubbles were detected, and they concluded that divers with Grade III bubbles or less would be unlikely to encounter DCS. They postulated that the presence of elevated arterial oxygen tension allowed the tissues to tolerate a greater degree of embolization in the microcirculation.

Nashimoto and Gotoh (1977, 1978) studied 152 caisson workers and found that bubble signals were associated with 40 out of 49 workers with DCS (itches, bends and chokes). Bubble signals were heard in 48 of 103 workers without DCS. The results show that 79% of skin itches were associated with bubbles and all cases of bends and chokes were associated with bubbles.

TABLE 11.

Bubbles vs. DCS for Compressed Air (Caisson) Workers Precordial Bubbles at Rest (from Nashimoto and Gotoh)

Bubble Grades	0	I	II	III	IV
No. of Subjects (152)	64	35	30	22	1
Percent Itches (32)	14	29	40	5	0
Percent Bends (14)	0	11	10	32	0
Percent Chokes (2)	0	0	7	5	100

B. Saturation Diving

A considerable number of saturation dives have been monitored with the Doppler ultrasonic bubble detector, both during the final decompression

to the surface and following downward and upward excursions at depth. In saturation diving, however, the correlation between DCS and bubbles does not appear to be as strong as that for non-saturation dives. Table 12 shows a summary reported by Gardette (1979) and Gardette *et al.*, (1979) for articular or muscular pains and circulating bubbles.

TABLE 12.

Percentage of Articular and Muscular Pain vs. Precordial Bubble Grades for Saturation Dives (from Gardette)

	At Rest					After Movement				
Bubble Grades	0	I	II	III	IV	0	I	II	III	IV
No. of Subjects (162)	125	24	13	0	0	43	20	39	60	0
Percent Pain	12	29	31	—	—	5	10	23	22	—

These results showed a marked difference between bounce or no-saturation dives and saturation dives. Even with no observable precordial bubbles, there is a large risk of DCS. This apparent lack of correlation of DCS with bubbles has led some investigators to conclude that Doppler monitoring is of no use for saturation dives. However, it is evident that divers with bubbles, both at the Grade I and Grade II levels, are at higher risk than those without bubbles. Therefore, divers with such bubble scores should be kept under closer observation. Grade III bubbles at rest, although not reported by Gardette in his study, have been observed in other saturation dives. In one helium saturation dive in which DCIEM was associated, Grade III bubbles at rest resulted in Type II DCS. Others have observed that Type II DCS is often associated with large numbers of intravascular bubbles (Masurel *et al.*, 1976; Masurel *et al.*, 1977).

Masurel has recommended that corrective action be taken for helium saturation dives when high bubble levels are detected (Kisman and Masurel, 1983; Masurel, 1983). During the first part of the decompression (between 100 and 80% of the maximum depth), Grade 0 and I bubbles at rest are considered normal and require no action. With Grade II bubbles, the diver must be under close observation. For Grade III bubbles at rest, the possibility of vestibular or Type II DCS exists, and a decompression stop plus some compensation table is recommended. For Grade IV bubbles at rest, immediate recompression with a superoxygenated mixture is required because of the high probability of vestibular and Type II DCS. During the second part of the decompression (to the surface), Grade III bubbles at rest, if they persist, require the subject to breathe a superoxygenated

mixture. For Grade IV bubbles, a decompression stop or recompression together with a superoxygenated mixture is required. The action taken may be modified depending on the observations made on the other divers in the same dive. Masurel has used his observations of high bubble scores to interrupt the decompression from a saturation dive to reduce the risk of DCS (Masurel *et al.*, 1978).

The effect of slowing down the ascent rate during the decompression was also clearly illustrated during a saturation dive done at DCIEM to 360 msw (Eatock and Nishi, 1986). The initial decompression rate of 28.4 msw/24 hrs (1.58 msw/hr with a sleep stop between midnight and 0600) was changed to 18 msw/24 hrs (1.0 msw/hr with 6 hr sleep stop) at 100 msw, and then to 0.5 msw/hr for the last 10 msw. Forty hours after leaving 360 msw, occasional bubbles were detected in one of four subjects. Eventually, all subjects had some bubbles with movement, and two had numerous bubbles (Grade III with movement). The bubbles peaked as the depth approached 100 msw. After the decompression rate was decreased to 1 msw/hr the number of bubbles gradually diminished until on the second day after the decrease in rate, no bubbles could be detected. However, bubbles were observed again in one of the subjects as the 10 msw depth approached. Following the second decrease in decompression rate, no more bubbles were detected. This is in contrast to similar dives done at the Norwegian Underwater Technology Center (Hjelle *et al.*, 1987). The decompression rate from 350 msw was 27 msw/24 hrs until 14 msw. Eighteen subjects were involved. By the time 100 msw was reached, 7 of the subjects had Grade III bubbles after movement. By the last day of decompression, four divers had precordial Grade III bubbles at rest and 15 divers had Grade III following movement. No Grade IV bubbles were observed in any of the divers. Seven of the divers with Grade III following movement experienced intermittent discomfort and pains in the lower limbs during the last two days of decompression; one had intense, but transient knee pains. Bubbles persisted for 3 hours after surfacing in 12 subjects and in one subject for 15 hours.

It can be seen that reducing the rate of ascent as in the DCIEM dive would have been effective in reducing the number of subjects with Grade III bubbles and most probably in eventually eliminating all observable bubbles, and eliminating the discomfort and pains felt by the subjects near the surface. Thus, for saturation dives, the results of Doppler observations can be used in real-time to reduce the risk of DCS or eliminate symptoms of discomfort and pain.

V. DISCUSSION

All the data show that, in general, the incidence of DCS is higher for the higher bubble grades and that the incidence of DCS is low when few or no bubbles are detected. Thus, for the purpose of evaluating decompression profiles, we can say that dives which produce many bubbles in a majority of the divers can be considered to be stressful with a higher risk of DCS and should be avoided. Conversely, dives which produce few or no bubbles in the majority of the divers can be considered safe. In determining criteria for the use of Doppler results for evaluating experimental or existing dive profiles and tables, it is evident that different standards must be applied depending on the breathing gas being used. For compressed air dives, most of the subjects should have only Grade 0 or Grade I bubbles. On the other hand, for helium dives, most of the subjects could have Grades 0, I or II bubbles for an acceptable profile.

Thus, simple criteria for estimating the acceptability of a table could be easily established by trying to keep the number of divers exhibiting Grades II, III and IV bubbles at rest to some percentage of the total. For example, using the figures from Table 7 for compressed air only, the expected incidence of DCS for Grades II and III combined is approximately 14%. By designing the decompression profiles so that less than 35% of the subjects have Grades II and III bubbles and none have Grade IV, it is highly likely that the risk of DCS can be reduced to less than 5%. On the other hand, for recreational divers, where the risk of DCS desired is zero, then dives which produce Grades II, III and IV bubbles should be avoided. Spencer, in his study of direct decompression after compressed air exposures (Spencer and Johanson, 1974; Spencer, 1976), concluded that safe limits require zero occurrence of severe DCS symptoms but for practical reasons some incidence of bubbles had to be accepted. He proposed a 20% occurrence of bubbles and less than 5% occurrence of mild bends pain as a reasonable compromise.

There are two factors that complicate dive table evaluation with the Doppler bubble detector. First there is considerable variation in the response among different subjects (some individuals are bubble-prone and/or bends prone) and second, individual divers can respond differently to similar dive profiles at different times. Therefore, it is necessary to use some judgement in interpreting the results.

In two series of experimental dives on compressed air, it was found that dive subjects could be divided into three groups representing high, moderate, and low "bubblers" (Nishi *et al.*, 1981). It was also found that older divers were more susceptible to having bubbles and that the majority of those who suffered DCS were high "bubblers". During the current program for

for developing helium tables, several high "bubblers" were identified and these individuals were found to be more susceptible to DCS.

If Doppler monitoring is to be used for developing safe tables, it is important that a mix of high and low "bubblers" be used as subjects. Tables developed with low "bubblers" can be hazardous for high "bubblers". Conversely, tables developed with high "bubblers" may be too conservative. It is also important that divers who are high "bubblers" and who are also prone to DCS be restricted in their diving and not be allowed to dive severe dive profiles.

There are other factors that can affect the tendency of subjects to have large levels of bubbles. For example, fatigue before a dive has been found to have a tendency to produce bubbles (Masurel, 1976). Similarly, after a dive, fatigue is usually accompanied by high bubble levels. Other factors may be the state of hydration of the subjects, obesity, age, level of fitness, infections, whether the diver may be a smoker (Gatock and Nishi, 1987), etc.

There are two main advantages to using Doppler monitoring. Doppler monitoring provides far more data than observing the incidence of DCS. For example, in the 2,483 DCIEM dives, bubbles were observed in 30%, whereas DCS occurred in only 2.3%. Therefore, not as many dives are required to establish a safe table using bubble scores than are required if DCS is the only criterion. It is often possible to use bubble observations to compare the results of two dives, even in the absence of DCS. If no bubble results were available, it would have to be concluded that there were no observed differences between the dives. The Doppler results may show that one profile will generate many bubbles in most of the subjects whereas the other may generate only a few bubbles; thus a difference between the two profiles becomes evident. In addition, in the absence of DCS and bubble results, there may be no way to determine how close to DCS threshold these dives are. It is unlikely that an experimental dive program, for example, to determine a DCS threshold, would be approved today if a high incidence of DCS were considered likely. As decompression procedures become safer, decompression testing could involve profiles that produce few or no cases of DCS, hence making the bubble results more important. In fact, with Doppler bubble monitoring, we can speak of decompression stress rather than DCS as the end point for evaluating dives. It should be noted that one need not "bend" divers to know whether or not a dive is safe.

Bubble results are more objective than DCS results. Although there is some subjectivity in classifying bubbles, well-trained observers will generally be able to identify the presence of bubbles. Success in detecting bubbles depends on the vigilance of these highly trained observers, and

although bubbles can sometimes be hard to detect, the results cannot be hidden by the diver. Divers may not report symptoms of DCS or conversely may report symptoms, because of apprehension and uncertainty, which are not directly attributable to the decompression. The main disadvantage of Doppler ultrasonic bubble detection is that it is time-consuming and labor-intensive, and demands extreme concentration for the observer.

Although this study has concentrated primarily on precordial bubbles, it is important that the results of other body sites be considered as well. For example, if all bubble results are combined from the precordial and subclavian sites, the relations between DCS and bubbles would change slightly from those of Tables 7 to 9. The number of individuals with DCS and no observable bubbles would most certainly be reduced since subclavian bubbles were observed in many of these.

In cases where DCS occurred with no observable bubbles at rest or after movement, it should also be noted that not all bubbles can be detected with the Doppler ultrasonic bubble monitor. Bubbles must be sufficiently large so that the echoes from the bubbles can be heard above the background signal of the red blood cells and other moving particles and surfaces. It has been estimated that bubbles must be approximately 80 micrometers in diameter to be detectable in the precordial region. Thus, bubbles could exist but not be detectable. In the subclavian veins, smaller bubbles can be detected because of the reduced background noise. It should again be emphasized that intravascular bubbles are not believed to be the cause of DCS. However, their presence may indicate the existence of extravascular bubbles which can cause DCS. Other body sites should be checked if possible.

One finding that warrants further study appears to be that upper body symptoms are better correlated with subclavian bubbles and that lower body symptoms are better correlated with precordial bubbles. More studies will be made of the data in the DCIEM Doppler database (which includes all 2,483 subject-dives reported here, representing over 10,000 individual monitorings) and data from other investigators which are available in compatible form. It is important that all investigators using Doppler standardize on procedures and classification methods (whether KM Code or Spencer Code) so that there is a common basis for comparing results.

VI. SUMMARY

The Doppler ultrasonic bubble detector can have an important role in the process of decompression table evaluation since it can give comparative

information on the decompression stress of the dive even in the absence of DCS. As the risk of DCS increases with increasing levels of bubbles, it is possible to assign some risk factor to dive profiles by noting the number of divers with bubbles and the levels observed. Thus ultrasonic bubble detection can give far more information than the traditional DCS vs. no DCS approach with fewer dives, and, it is not necessary to bend divers to determine if a dive profile is safe.

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APPENDIX I

Suppliers of Doppler Ultrasonic Bubble Detectors

a) Techno Scientific Inc., 60 Caster Avenue
Woodbridge, Ontario, Canada L4L 4X2

b) Sodelec, 31, Traverse Prat,
Pointe-Rouge, 13008 Marseille, France

c) Institute of Applied Physiology and Medicine
701 16th Avenue, Seattle, Washington, USA 98122

16

The Future of Manned Diving

David H. Elliott

I. THE FUTURE OF MANNED DIVING

The first International Symposium on "Man in the Sea" began with several perspectives from different nations, continued with a full program of physiology and ended with three papers on the outcome to divers of decompression and diving accidents. We did not discuss the future of diving. Perhaps in 1975 we saw no need to doubt the continuing development of operational diving and the continuing success of physiological research into extending man's capabilities in the sea. Why, then, does this equally full and exciting meeting end with this review of the future of manned diving? Has something happened to change our optimism about the future of what we do? Certainly there has been a severe reduction in the availability of research funds in most of the participating nations. The navies have not extended their operational deep diving requirements and the oil industry has a recession. Certainly, also, we have moved from the pioneering days of harvesting relatively easy R&D information to where greater effort is necessary in order to achieve seemingly smaller gains.

At the same time, there have been other significant changes. There is the improved cost-effectiveness of remotely-controlled robots and so a reduction in the need for divers to perform particular tasks. There is also a concurrent increased awareness, voiced at the last Man in the Sea symposium in relation to diving accidents, that diving as an occupation might lead to subtle, but permanent changes in the central nervous system.

So there are indeed good reasons why a symposium of responsible scientists in this field should consider the future of manned diving. In this forum we should reflect the special concerns that are expressed about health and safety in manned diving but should also, I hope, conclude with me that the concerns about possible neurological damage in divers can be met with increased vigilance and co-ordinated epidemiology, that the difficulties in achieving research funding are reasons to justify more vigorously the many challenging research proposals before us, and that manned diving does indeed have a long and healthy future ahead.

Before we examine the reasons for this and, perhaps, identify some of the priorities, we must first define "manned diving". From my review I will exclude normobaric diving because submarines and one atmosphere diving suits present a relatively small degree of physiological hazard, and I will confine myself to the man in the sea who is exposed to its ambient pressure.

II. COSTS AND BENEFITS

Diving will always be a hazardous activity, the future for man as a diver will depend upon the balance between benefit and cost as it is perceived by whoever makes the decision to dive. This decision includes the diver but the decision process is not always confined to him. The term 'cost' is not just the financial cost but includes the consequences of possible diving accidents and illness. We should acknowledge that this balance is not the same for all types of diving.

For Sports Divers the benefits are clear, they are the personal benefits of pleasure and achievement. In professional scuba diving as performed, for instance, by salvage seekers, coral and shellfish harvesters, diving scientists and dive instructors, the same benefits are enhanced by cash. The financial costs to the scuba diver are relatively small, the hazards are personal, rather than imposed by a third party, and, once beyond the novice phase, the risks of diving usually seem too remote to be much of a personal consideration. That decompression sickness has doubled in recent years is not likely to affect the popularity of sports diving or its future.

In Commercial Diving the cost-benefit analysis does not follow the same path. The cost-effectiveness of the diver is judged by his employer against the cost-effectiveness of alternative underwater tools. The risk of accidental injury or decompression illness enters this analysis, but only as the financial cost of ensuring the diver's health and safety to some particular standard. Within the depth range of compressed air diving the relative cheapness of the diver ensures his future. This seems true of not

only inland and inshore but also of offshore diving. In the deeper depths of mixed gas diving, the greater costs of supporting the diver safely have meant that, for the oil and gas industry, a greater proportion of the diver's routine inspection and maintenance tasks are now done by remotely operated vehicles (ROV's). In spite of the great improvements in robots, there remain a number of underwater tasks that can only be done by the human hand. The majority of oil field engineers now appreciate the need for divers not only for repairs and welding but also when things go unexpectedly wrong. At least one major oil company maintains a policy to pursue no offshore development unless either the depth is accesible to divers in the case of some unforeseen emergency, or that they could accept the financial consequences of having no capability for manned intervention.

In Military Diving the balance is again quite different, the tasks may be classified but in peace and in war the need for divers will remain.

As therefore there is a future for divers, what is the future of diving?

For this we will abandon the classification of the diving by sports, commercial and military as many problems fall into several such categories. So, from the wealth of what has been presented at this symposium, this analysis will select some examples and, for the future of manned diving, propose a few priorities.

III. MIXED GAS DIVING

From my vantage point close to the North Sea I will first consider the future of deep mixed gas diving. In spite of the vision of the future expressed at the 1975 symposium and subsequently justified by the achievements of, for example, the Atlantis dive series by Duke University and the Hydra dive series by Comex at Marseilles, the development of commercial deep diving appears to have come to a standstill at less than half the depths that have been achieved in the laboratory and in experimental or demonstration dives at sea.

The primary limitation at present is partly the lack of need for deep diving. Current field developments are predominantly within the range of accepted diving practice and, until there is a rise in the value of oil and gas, will remain so. Thus this should be a temporary lull. The problem is that without continued funding, hyperbaric laboratories become idle and research teams are disbanded. The diversity of the oil industry fail to realize that R&D in deep diving takes years to complete and that the current lull provides the ideal opportunity to prepare for future field development in deep water.

Other limitations of manned deep diving occur at the interface between man and his equipment. Recent work in Europe has focused upon the acceptable performance characteristics of the ergonomics of tool design, underwater breathing apparatus, the provision of well-controlled supplementary body and breathing gas heating, the availability of a "come-home" bail-out bottle of sufficient duration to get the diver back into the bell and the improvement of verbal communications. Other considerations include the provision of emergency medical care for the sick or injured diver together with the requirement, by some authorities, to evacuate the diver by transfer-under-pressure ("Hyperbaric Ambulance"). The provision of a hyperbaric lifeboat (HRV) is a regulatory requirement that, in practice, can be met only "so far as is reasonably practicable". Among its many problems are those that are mechanical, such as rescue and retrieval and those that are physiological, such as thermal balance. Indeed the particular problem of compressing a saturation team that is close to arrival at surface, back down to join the working saturation team, still at their living depth, has led the Norwegian government in its current redraft of its diving regulations to limit deep diving in systems with only one HRV to 180m (c. 600 fsw).

Another limitation to deep diving may be the perception of long-term adverse sequelae. Currently before diving deeper than 350m (c. 1150 fsw) the diver in some countries is subjected to a vast array of special tests, many of which are neuro-psychometric, neuro-imaging and electro-physiological. But, as discussed last Sunday under the aegis of the Medical Research Council, there are few agreed formal procedures (as there were when bone X-rays for divers became common) and no internationally agreed diagnostic criteria (as were generated for osteonecrosis many years ago by the MRC Decompression Sickness Panel). There is also an urgent need for adequate controls from both air-diving and non-diving populations. One cannot predict what such studies will reveal but, by analogy, from the early headline "Bone Rot Disease Cripples Divers" the MRC Panel progressed in 1984 to confirming the 4% prevalence of radiological lesions in healthy divers in the 1981 report (Decompression Sickness Central Registry, 1981), with only 12 pathological fractures of a joint surface in nearly 7000 men. Only when the nature of alleged long-term CNS damage can be quantified in a similar manner is there a possibility that this emotive issue may be lifted from the future of deep manned diving.

IV. COMPRESSED AIR DIVING

Some years ago accident data from the North Sea confirmed the view that oxy-helium diving is generally much safer than compressed air diving.

In Commercial Diving the mixed gas diver is in a more predictable environment and his eventual decompression is relatively slow and under careful control. The commercial compressed air diver, on the other hand, is more exposed to the natural hazards of waves and current and his decompression is either in the water, with the associated difficulties of maintaining a constant depth, or, for reasons of safety, may use surface decompression procedures. Acute decompression sickness is perceived as a significant problem of air diving in the North Sea. In order to reduce the number of cases, Type II in particular, that were associated with deep and relatively prolonged air dives, the UK Department of Energy in 1986 limited the depth/duration exposure to approximately that of the 'limiting line' in the Royal Navy tables. This had been based upon a review of the logs of some 20,000 dives (Shields and Lee, 1986). However, the authors discussed several reasons why the available data could not validly be examined in very close detail. The consequence, however, was to define a limitation on the future of commercial compressed air diving based upon the inadequacies of our knowledge concerning decompression table validation in operational circumstances.

There is one further factor which is not scientific but anecdotal: that written-up dive logs inevitably contain a small percentage of errors, deviations from the selected table. An error may have occured at one of several points of the dive planning, procedure or in the written report itself. In contrast it has been said that the commercial dive log written up after a case of decompression sickness never contains an error. Whether or not this is true, there is no doubt that the actual profile of a dive rarely, if ever, is the "square wave" of depth and time as stated in the log and as used for the North Sea analysis. Rarely, if ever, does the diver follow the ascent rates and stoppages precisely.

In brief, therefore, the future of commercial air diving is itself secure but the future development of safe decompression procedures, particularly for deep, prolonged hard-working dives, requires much more work. In the development of an on-line depth recorder for the commercial divers, not only does the diving supervisor have an immediate visual display of what profile the diver has followed but a permanent record is made of all the important dive details (identity, environmental temperatures, oxygen breathing, and depth/time profile). This record not only demonstrates compliance with the selected decompression profile but also can be bulked with other dives to provide general data on the diving contractor's decompression safety performance and extended to include all commercial dives performed in the North Sea.

This provides an opportunity to analyze in detail a dive that resulted in decompression sickness. More importantly, perhaps, it also provides an

opportunity to improve and verify decompression tables and their calculation, a subject much discussed at several workshops most recently that of the Royal Norwegian Society of Arts and Sciences in June of this year. However it also provides yet another opportunity, that of following the diving history of the individual diver. To do so without good reason would, of course, not be cost-effective but tracking the record of the "bends-prone" individual or the history of a person who has developed juxta-articular bone necrosis or other long-term effect on health could be the source of some essential clues on causation.

The Sport Diver is altogether a different kind of compressed air diver. The future of sport diving seems secure but, at present, there do seem to be a few problems. These have become manifest as a change in the presentation and frequency of decompression sickness. Whereas 70 to 90% of compressed air decompression sickness used to present as joint pain, now the majority of presentations appear to be of a more serious nature. The reasons for this may or may not be the introduction of new decompression procedures by the divers, be they based on the correct or incorrect use of new tables or computers.

There is also the individual factor. Not all sport divers follow the wise rule of no-stop dives only though, even when they do, as shown by the figures from Divers Alert Network (DAN, 1988), problems may occur towards the end of a multi-day period of daily double dives. There are too many divers who believe that they know best. Perhaps by the process of natural selection a few experienced divers can dive, apparently safely, beyond the normally accepted limits of safe decompression. Sports divers tend to take their decompression liabilities to the limit, with an increasing number of serious cases of decompression sickness arising from deeper dives. We know from the work of Calder *et al.* what the sequelae might be (Palmer and Calder, 1987). Responsibility for the prevention of such accidents lies with the individual divers as well as with the diving organizations. The future of the sport relies upon it having a healthy image.

It has been 13 years since the first Man-In-The-Sea Symposium and even if it is another 13 years until the next one then I am confident that, in the year 2001, we will again be optimistic about the future of manned diving.

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