HYDROGEN AS A DIVING GAS

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BACKGROUND AND PROBLEM STATEMENT

It is a pleasure to welcome you to the Institute for Marine Biomedical Research of the University of North Carolina at Wilmington.

As many of you know, at this Institute part of our program for a long time has been research on the physiological and pharmacological problems of deep diving. Certainly what we shall discuss during the next few days will fall in that category. The Conference that we are about to embark upon was conceived five years ago in discussions between Claes Lundgren and me, at a time when both of us felt that the time might be ripe to resume much larger scale human experimentation with hydrogen than had been carried on for a number of years. We went to the Undersea Medical Society, with this proposal, and the Undersea Medical Society in turn went to the National Oceanic and Atmospheric Administration (NOAA) in the hope of securing funds, but at that time was turned down. The project was revived last year with funding from NOAA and I was approached to organize it. In the meantime, the courageous French and Swedish hydrogen diving experiments either had taken place or had been planned and were about to take place, and it seemed to me that the scope of the Conference as originally envisioned no longer met the requirements of what was then in order. Since NOAA could not provide the extra funding needed, I went to the French Navy, the French National Research Council, the Swedish National Defence Research Institute, and the Swedish National Research Council to see whether one could find support for some of the visitors whom I felt it would be essential to invite. These organizations did in fact come to our aid, and it is thus thanks to all of these agencies together with NOAA and UMS that this Conference has been put together.

We shall be talking to two communities, that of pharmacologists and biologists on the one hand, and the industrial and diving community on the other. The material we have before us seems to me a classic example of basic research carried successfully to the transition from research to development and application. With regard to the scientific group, we shall try to address what bearing the data have on theories of anesthesia and on both the qualitative and quantitative aspects of the interaction of anesthetic agents with high pressure. With regard to the diving community, we obviously shall try to consider what bearing the biological data has on the ability of man to perform work effectively in deep water and to do so safely. We will also have to talk about the special problems of handling, storage, and operational use of a gas that for a long time was remembered primarily because it helped to burn up the zeppelin *Hindenburg*. Finally, I hope that in our last session we will be able to talk about the meaning of all these data tot he future of diving. After all, those of you who have been concerned with diving are well aware that other technologies are growing apace to compete with diving by man exposed to the medium, and that implies that any major advances in the technology and the biology of diving are certain to shape the competitive relations between the different approaches to work underwater.

These are the concepts that we have tried to build into the program. I hope that as we go through our discussions,we have an interesting time, and

that the agencies who have come to our aid to put this Conference together will agree at the end that the effort was worthwhile.

It seems appropriate to begin our discussion by looking briefly at the historical background that brought the field to the point where the large-scale human experiments we shall presently hear about became ethically and practically feasible. This first section will comprise three communications: a note on the role of animal research in this field by Dr. Naquet and me, an inquiry into the possible toxic effects of hydrogen by Dr. Fife, which also has marked historic overtones, and appropriately, a report by Dr. Örnhagen on animal research concerning H_2 in Sweden.

The bibliography is extensive and we have decided to place it at the end of this volume as an appendix that is relevant to all of our discussions, and to proceed here directly to the papers and the discussion.

Ralph W. Brauer, Ph.D.
Chairman

SECTION I
Historical Aspects

CONTRIBUTIONS OF ANIMAL EXPERIMENTATION TO THE ESTABLISHMENT OF APPROPRIATE CONDITIONS FOR ETHICAL USE OF HYDROGEN AS A COMPONENT OF DEEP DIVING ATMOSPHERES

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Since 1789 a total of 39 papers has been published dealing more or less directly with problems pertinent to the possible use of hydrogen as a component of diving atmospheres. If one divides these papers into those based on the results of animal experimentation on the one hand, and all other categories, including studies using human subjects and theoretical ones, on the other, and then plots the resulting two distributions as functions of time (Fig. 1), some most interesting patterns emerge. First, the data reveal the very early onset of interest in H_2 dating back to Lavoisier (1). Second, they show the brief surge of interest following the work of Behnke, Hildebrand, and others establishing inert gas narcosis as such and resulting in the human trials of Case and Haldane (2) and in those of Arne Zetterström. (4-6). They reveal the prolonged gap of interest in H_2 following the tragic death of that young Swedish engineer. And finally they reveal that most recent and by far the most intense burst of interest in the use of H_2, beginning in about 1965 with experiments comparing narcotic effectiveness of He and H_2 (7). Fig. 1 shows clearly that this latest surge of interest in H_2 was introduced and led by animal experimentation which reached its peak level during the 5 yr between 1970 and 1975, thereafter to decrease progressively with each succeeding 5-yr span. Simultaneously, other types of experimentation dealing with H_2, increasingly involving preparations for and actual conduct of diving experiments involving human subjects (31-33, 35), progressed at an ever-increasing pace. It is thus difficult to escape the conclusion that here is an instance where animal experimentation furnished the basic data upon which others found it possible to initiate work directly aimed at testing the feasibility of exposing human subjects to this gas and gathering the benefits that might result from its unique properties.

It is in order then to inquire what contributions animal experimentation made to permit this development. If one examines the subjects touched upon by the 17 papers reporting animal experiments concerning H_2, these are found to address seven categories (Table 1); animal experimentation has failed so far to address three remaining categories of biological data of operational

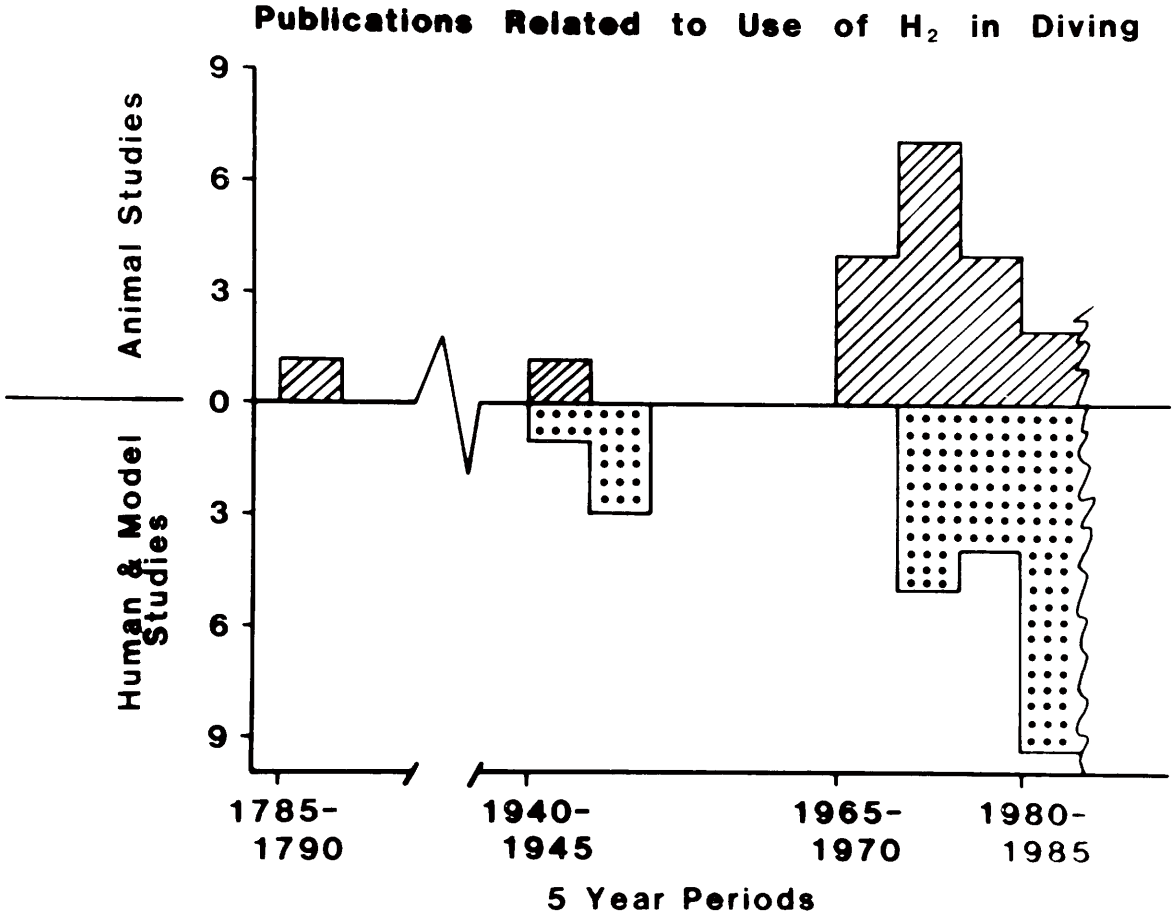

Fig. 1. Distribution of publications related to the use of hydrogen in diving over successive 5-yr periods, and partitions of the total effort between animal experimentation and all other types of investigation.

interest. Primary contributions of animal research in this field, therefore, seem to have been aimed at the problem of the safety of exposing man to H_2; at assessment of the narcotic potency of this gas; at its interaction with the high pressure neurologic syndrome (HPNS); and at providing some guidelines toward development of decompression schedules and toward assessment of the importance of countercurrent diffusion problems in transfers between H_2 and He atmospheres. Let us briefly summarize the specific contributions made by animal experimentation to each of these topics.

Table 1

Summary of papers dealing with H_2 exposures

Thirty-six papers dealing with H_2 exposures; of these 16 involved animal experiments, of which:

9	focused on safety, possible pathologic effects
6	focused on anesthetic potency
5	focused on HPNS activity
3	contained data regarding decompression
2	miscellaneous (cancer)
1	thermal effects
1	countercurrent diffusion problems
0	respiration
0	long-term exposures and residual effects
0	voice

Concern with safety is perhaps the earliest scientific motivation that led to animal experimentation. As early as 1789, Seguin and Lavoisier exposed guinea pigs to H_2-O_2 mixtures and found that the animals could survive such atmospheres safely and that their O_2 consumption rates in this medium seemed to be very much the same as in N_2-O_2 mixtures (1). The Russian investigator, Lazarev, was probably the first to subject any animal to elevated pressures of H_2. His experiments were cut short by World War II and he was only able to report on a single mouse (!) which, however, furnished some interesting and provocative observations, the full significance of which was not realized until many years later (3). He reported that his pioneer mouse survived the exposure to H_2-O_2 mixtures safely, though "a bit benumbed." Resumption of work with H_2 in 1965 swiftly added to the list of animals and species that had safely survived H_2 exposures of up to 24 h at pressures up to 70 ATA (7,8). A warning note was soon interjected by a series of experiments in which animals failed to survive what appeared to be much more conservative H_2 exposures (9,14). It was probably these latter experiments that discouraged resumption of human experimentation on a large scale until the possible implications of these ominous-sounding experiments had been evaluated. This was accomplished in part by extensive and careful investigation of dogs exposed to H_2 partial pressures up to 70 ATA, decompressed, and followed by careful pathological workup (16,22). These experiments reconfirmed that the animals routinely survived the H_2 exposures and that they did so without showing any recognizable pathologic changes. The

definitive evidence in the sequence of studies bearing on this matter was careful recapitulation of the supposedly incriminating experiments, using the same species and replicating as far as possible the original conditions, only to encounter once again 100% survival of uninjured animals (29). With this piece of work, the scientific community at large apparently accepted the conclusion that experiments impugning the safety of H_2 had been definitively refuted, and resumption of experiments involving human exposures followed almost at once.

However, at this point animal experiments have left three aspects of the subject uncovered: Since no one has been able to replicate the experiments resulting in bradycardia and death of the animals during the relatively short exposures of (9) and (14), the uneasy possibility remains that some unknown factor causing bradycardia and death may lurk unrecognized in H_2 exposures. The tentative conclusion is that we must look for the cause in unrecognized impurities in the H_2 used in those particular experiments, but this remains to be tested and confirmed. Second, to date the longest period of animal exposure has not exceeded 24 h. Although human exposures to H_2-containing atmospheres of more than 1 wk in duration have been conducted successfully, it remains a desirable goal of animal experimentation to test the safety with which exposures can be extended to periods comparable to those currently in use in industrial saturation dives and to probe for criteria optimizing the tenuous balance between narcotic effects and antagonism to HPNS effects in $He-H_2-O_2$ atmospheres. Finally, looming in the background as a result of the striking success of recent human deep-diving experiments utilizing H_2 is the possibility that these results will encourage penetrations to depths not hitherto attained, and that at these depths pressure effects or H_2 effects not previously encountered might assume an importance which they have not displayed in any of the diving situations hitherto tested [cf. (31)].

With regard to *anesthesia*, the earliest results of animal experiments (3) were obtained before the recognition of pressure effects on the CNS. The first few years of the post-1965 thrust of animal experimentation were dominated by attempts to unravel these relationships and for the first time provided a precise estimate of the relative intrinsic anesthetic potency of H_2 as displayed in two species (7,10). It is pleasing to note that the estimate thus derived has now been confirmed to a most satisfying degree of precision in the first deep human dive designed with these animal results in mind (32), indicating that for purposes of estimating narcotic potencies the mouse is a remarkably good man. What the animal experiments failed to predict was the possibility that the quality of H_2 narcosis may differ significantly from that of N_2 narcosis, a possibility raised by observations during both the French (32) and Swedish (33) H_2 dives in 1983 and 1984, respectively. While this leaves room for further animal experimentation in this area, it seems likely that in practice the burden of further development here will be carried largely by more extensive human experimentation that is clearly in the offing.

INTERACTION WITH HPNS

Concurrent with the first description of HPNS as such on the basis of animal experiments were indications that, like other inert gas narcotics, H_2 is capable of antagonizing development of at least some of the symptoms of HPNS (7). While this conclusion was presently developed into quantitative proof of the anti-HPNS effectiveness of H_2 in mice (17), experiments with primates were not unanimous on this conclusion (12,13,15,19).

Using baboons (*Papio papio*) implanted with different electrodes permitting records of EEG, electromyogram (EMG), and electro-oculogram (EOG), Rostain et al. (19) confirmed these data and concluded that HPNS differs depending on the compression method, depth, and mixture used. For example, they demonstrated that the introduction of 6-8% N_2, in a mixture of H_2-O_2, does not prevent the apparition of epileptic seizures between 600 and 700 m if the compression stays fast and the curve nonexponential. On the contrary, the progressive introduction of 5.5% N_2 into the mixture, with an exponential compression profile with stage of 40 min every 100 m, enables baboons to be taken to a depth of 800 m with no epileptic seizures and with a reduced HPNS. This technique of compression was utilized in man, using different mixtures, O_2-He, He-O_2-N_2, and minimal HPNS was observed (36).

At this time very few experiments have been done with O_2-H_2 mixture in baboons using the same technique permitting the registration of EEG, EMG, and EOG. The only one found in the literature (13) corresponds to six dives from 300 to 700 m realized with fast linear compression, and with the same percentage of H_2, 99%, starting from 200 m. Tremor appeared in all baboons at 450 m. EEG modifications tended to show a discrete slowing of the rhythm and a tendency of the paroxysmal activity to disappear around 460 m. Nevertheless, between 650 and 700 m epileptic fits appeared.

Thus, the final conclusion that could be passed from animal experimentation to those planning human trials was that there was good reason to expect some anti-HPNS effect of H_2, but that the magnitude of this effect in man could not readily be predicted because of important species differences in this respect. It is perhaps in order to note that part of the difficulty here arose from the statistical character of both the narcotic/anti-HPNS effects and the HPNS symptoms themselves which made some of the published data difficult to interpret [cf. (31)]. Evaluation of the human results and of the extent to which they bear out these predictions will form an important part of this symposium [cf. (37)].

A new factor that has been recognized only over the last 2-3 yr, concurrently with the human experiments, is the effect of acclimation to inert gas narcosis [even at high pressure (38)]. This raises the possibility that as a result of such acclimation, subjects having undergone prolonged H_2 exposures might prove to be hypersensitive to the CNS effects of high pressure, making transfer from H_2-containing to H_2-free heliox atmospheres potentially hazardous. Here again the human experiment Hydra V seems to have furnished indications bearing out the predictions based on animal experiments, a matter that also will become clearer later during these discussions.

DECOMPRESSION AND COUNTERDIFFUSION PROBLEMS

Experience gained during the course of animal experimentation during the 1960s and early 1970s indicated that, as one might have expected from the physical properties of the gases, safe decompressions after H_2 exposures require longer periods and slower decompression parameters than were found safe after comparable He exposures in the same species (15,16,19). While these conclusions undoubtedly entered into the considerations upon which decompression tables for the human experiments were developed, it seems likely that in practice those developing the new tables paid more attention to the available physical and solubility data than to the semiquantitative data available from any of the animal experiments.

Countercurrent diffusion phenomena and the resulting isobaric bends phenomena were first described in the course of human experiments and most of their subsequent analysis likewise have relied more on human than on animal experimentation (34). Thus, when transfers from H_2 mixtures to He were carried out during Hydra V, the occurrence and severity of isobaric bends phenomena that might result could not be predicted with any confidence.

THERMAL EFFECTS

Only one communication has dealt with the thermal effect of substituting H_2 for He in mice. This showed that significantly higher temperatures are required to maintain body temperatures at predetermined, supposedly "normal" levels in H_2 than in He at high pressure. So far as we know the human experiments conducted to date have failed to give any indications of significant differences between pure He and the He-H_2 atmospheres in this respect.

It is perhaps not surprising that the important work on the beneficial effects of substituting H_2 for He from the point of view of *breathing resistance* should have been carried out exclusively in man where highly sophisticated techniques for making such measurements are well standardized [cf. (23,32,35)]. There are no animal experiments dealing with the *hydrogen voice* and here again it is to be expected that progress will rely largely on human experimentation.

Recapitulating this brief overview it appears that animal experimentation made its major contribution to this field (a) by establishing that H_2 can be breathed safely at pressures well beyond those likely to be encountered in the foreseeable future in diving practice; (b) by correctly assessing and forecasting the narcotic effects of H_2; and (c) by correctly demonstrating and forecasting the beneficial effects of H_2 with regard to key symptoms of HPNS and pointing out the hazards of transferring men from He-H_2-O_2 to He-O_2 at great depths. These three contributions made it possible from both ethical and practical points of view to plan and to undertake diving experiments in which men were to breathe He-H_2 under pressure, defining beforehand the key limitations as well as some of the key benefits to be expected from utilization of this gas. Animal experimentation contributed to a negligible extent to assessment of the remaining important benefit that derives from the use of this gas in deep diving, i.e., the great improvement in the ease of breathing He-H_2-O_2 atmospheres at

high pressure relative to heliox or He-N_2-O_2. Animal experiments made minor contributions to recognition of decompression and thermal problems to be expected. Contributions still to be sought from animal experimentation are likely to focus primarily on the evaluation of possible hazards due to long-term exposures and perhaps to very deep exposures, and to a lesser extent on clarification of the somewhat peculiar characteristics that appear to distinguish N_2 narcosis from H_2 narcosis.

We believe it is fair to conclude from this brief survey that in the case of the development of H_2 as a potential component of deep diving atmospheres, animal experimentation has played a most important role; without such experimentation conduct of the human experiments that are now taking place would have been far more risky and indeed in all probability would have been precluded on ethical grounds. It seems to us that the time distribution of publications in the field, as shown in Fig. 1, nicely illustrates the healthy sequence of events in this case in which animal experiments preceded and set the ground for the application of this gas to deep diving technology, an application which, as we hope the present conference will demonstrate, holds great promise of extending both the range of depths over which useful diving intervention is feasible and the period of time over which this technology is likely to survive the competition of other approaches to accomplishing useful work in deep water.

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THE TOXIC EFFECTS OF HYDROGEN-OXYGEN BREATHING MIXTURES

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The potentially toxic effects of molecular hydrogen on the body were first studied by Lavoisier in 1789 (1). He placed guinea pigs in a bell jar containing a mixture of hydrogen and oxygen in which the initial concentration of oxygen was "in nearly the same proportion in volume which exists between life-giving air and nitrogen gas in the atmosphere." The animals apparently survived 8 to 10 h. Although at the time it was felt that they succumbed to ammonia, it is probable that they died from CO_2 poisoning, since it now is well known that under similar experimental conditions animals will survive longer if CO_2 is absorbed.

One hundred and forty-eight years elapsed before an H_2-O_2 breathing mixture again was examined, this time by Case and Haldane (2). These workers breathed a mixture of H_2, N_2, and O_2 in a hyperbaric chamber at an ambient pressure of 10 atmospheres for up to 6 min without any adverse reaction.

In 1944, Arne Zetterström of the Swedish Navy conducted four open ocean dives on H_2-O_2 breathing mixtures (3). His first two dives were to a depth of 5 and 8 ATA breathing a three-gas mixture containing 72% H_2:24% N_2:4% O_2. He then conducted two additional dives to depths of 12 and 17 ATA breathing a two-gas mixture containing 96% H_2 and 4% O_2. On the 17 ata dive (160 m) he lost his life when one of the two winch operators raising his stage hauled him directly to the surface without observing decompression stops; since upon reaching the surface he still was breathing 4% O_2 he succumbed to hypoxia and probably air embolism (personal communication, H. Bjurstedt, 1976).

Interest in the use of H_2 for diving again lay dormant until 1965, when Brauer and coworkers (4) began to study the possible effects of H_2 on various mammals. Their work, principally on mice and monkeys, suggested that H_2 might have a less convulsive effect than He at the same pressures (5,6), but the full scope of biological effects was not precisely determined. This work did, however, lead to the conclusion that molecular H_2 is not toxic and is less convulsant than He. Thus, up to this point there was no evidence to suggest that molecular H_2 was harmful to the body, although certain individuals continued to confuse molecular H_2 with ionic H_2, suggesting that H_2 gas might alter body pH.

As a result of these favorable results from short exposures with small animals and the successes of Zetterström, in 1967 Brauer and his co-workers (5) at COMEX in Marseille attempted to carry out a human dive to 300 m, at which depth they planned to shift to a hydrox breathing mixture. Because of the appearance of the high pressure nervous syndrome (HPNS) they were forced to abort the dive before changing to hydrox. Again, however, there was no

implication of H_2 as being toxic to the body.

By 1967 interest in the use of hydrox for deep diving increased in the United States. In addition to the work of Brauer, Edel (7), supported by a commercial diving company, began to study the possible use of H_2 as a replacement for He. The diving company financed several early man dives, beginning with hydrox exposures of 10 min at a simulated depth of 7 ATA. Independently, Fife, supported by Texas A&M University Fund for Organized Research and the U.S. Navy, also began to develop the capability to work with H_2 using dogs. In 1968, Fife and Edel joined efforts to conduct several extended deep saturation dives on two dogs, first at a depth of 10 ATA and then at 31 ATA. Work also continued with man dives to gradually increase H_2 exposure at a depth of 7 ATA. This series ended in 1969 with exposures of up to 2 h duration. One of us (W.P.F.) was exposed to a 1.5 h, 7 ATA hydrox dive followed 8 d later by a 2-h dive to the same depth. No ill effects were noted from the H_2, although in some of the shorter dives several of the divers experienced mild decompression sickness.

In 1969 there appeared the first indication that the use of hydrox might be detrimental. This work was carried out by Michaud et al. (8), who exposed five rabbits to 29 ATA in a chamber submerged in the ocean. These animals began to present ECG abnormalities after about 2 h, and by 7 h all were dead. This was followed by studies by Fructus et al. and their coworkers who compressed baboons to depths ranging from 31 to 68 ATA. We have received conflicting reports on this study. One is that, of the eight baboons used, all demonstrated abnormal EEGs and four died. Several of them revealed brain abscesses. However, we also have received reports that all of the animals survived and lived for a number of years.

It was our personal feeling that the deaths of the rabbits (and possibly baboons) were not due to H_2, but probably due to toxic contamination in the breathing gas. We also speculated on the possibility that these animals may have suffered hypothermia, which will be discussed later. In any event, both Edel and Fife continued to carry out human dives without seeing any evidence that H_2 was toxic. The work by Örnhagen, Lundgren, and Muren in 1978 (personal communication, 1980) tended to support the safety of hydrox. These workers subjected 12 rabbits to 30 ATA for periods of from 24 to 48 h. All animals survived with no evidence of organ damage.

Fife then began a two-pronged attack on the problem. One series of studies was on dogs, working at a simulated depth of 31 ATA for periods ranging from 24 to 107 h of hydrox exposure. The other thrust was a series of dives on humans. These human subjects ranged from 23 to 58 yr of age and involved the development of decompression tables for up to 45 min bottom time at a depth of 10 ATA. No ill effects were observed on any of the human divers. Again, this suggested that hydrox was not significantly toxic to the body.

Although many of these studies provided subjective evidence that hydrox was not toxic, there needed to be further objective evidence to assure that hydrox did not result in subtle physiological damage to the body. For that reason, Fife carried out an extended series of animal studies in dogs to

search for histological changes as well as changes in the blood picture.

The following blood enzyme parameters were examined:

1. Serum alkaline phosphatase (SAP);
2. Creatine phosphokinase (CPK);
3. Lactate dehydrogenase (LDH);
4. SGOT; and
5. STGPT.

In addition, the following blood components were studied:

1. Total serum calcium (TSC);
2. Cholesterol;
3. Urea nitrogen;
4. Total protein;
5. Glucose;
6. Serum phosphorus;
7. Hematocrit;
8. Red blood count; and
9. White blood count.

Table 1 reflects some of the blood enzyme changes with hydrox and with He (used as a control), while Table 2 presents blood chemistry data. Most of the differences shown were not statistically significant. Serum alkaline phosphatase, cholesterol, and serum protein were slightly increased while TSC was decreased in the postdive samples from both groups of dogs. The slight increase in cholesterol does not come as a surprise since we have previously found that nonspecific stress tends often to increase blood levels. Creatine phosphokinase and LDH were elevated in the postdive samples from dogs on He, but decreased in dogs exposed to hydrox. However, again these changes were not statistically significant. No consistent trend was detected in the other parameters measured.

TABLE 1
BLOOD ENZYMES

	Predive		Postheliox		Posthydrox	
	MEAN	SD	MEAN	SD	MEAN	SD
Alk. Phos. IU	25.36	21.64	28.00	23.08	30.00	8.21
SGOT IU	33.82	19.42	36.80	9.50	21.75	7.14
SGPT IU	39.30	25.99	28.60	2.70	35.67	25.54
CPK IU	267.00	195.17	376.50	85.58	92.67	59.05
LDH IU	319.36	288.58	427.20	234.89	324.10	477.59

TABLE 2

BLOOD CHEMISTRY

	Predive		Postheliox		Posthydrox	
	MEAN	SD	MEAN	SD	MEAN	SD
Cholesterol mg/dl	175.67	43.08	207.20	21.38	210.50	58.26
Total Protein mg/dl	6.90	1.38	7.60	1.23	7.52	1.80
Urea N mg/dl	13.92	4.54	12.14	2.17	13.63	3.77
Creatinine mg/dl	0.93	0.32	0.98	0.29	0.98	0.38
Ca mg/dl	10.53	0.72	9.98	1.41	9.31	1.18
P mg/dl	5.45	1.07	4.68	0.51	5.43	1.45
Glucose mg/dl	82.73	14.14	102.40	16.82	55.50	31.30
HCT	43.57	7.36	43.75	6.18	39.80	4.00

Increased SAP and decrease in TSC raise the possibility of a change in calcium homeostasis in dogs inhaling these gas mixtures. This possibility suggests the need for further investigation because of possible effects on neuromuscular irritability and homeostasis. The increase in CPK and LDH in dogs inhaling heliox may reflect increased muscular activity or subclinical intravascular hemolysis. However, such hemolysis was not observed grossly in the blood samples drawn. Increases in CPK and LDH were not seen in dogs exposed to hydrox. This further adds to the suggestion that hydrox is not damaging to the body.

Studies also were carried out to determine whether H_2 was toxic to the lungs and the liver. These studies involved pre- and postdive biopsies of both organs. The biopsy techniques were the same as those used on humans. Tissues of both organs were examined both by light and electron microscopy.

More than 300 micrographs were studied on 25 dogs. A critical evaluation of the lungs showed little that was remarkable. In some animals there appeared to be a slight increase in the amount of collagen but in all instances it was felt that the conditions that precipitated this were not related either to hydrox or heliox for two reasons: First, it appeared to be present in most predive specimens. Second, it was felt that there was insufficient time for collagen to develop during a dive even if an appropriate insult occurred. As a further indication that such an insult did not occur, attention is directed to the animals that had a second series of lung biopsies related to subsequent dives. No evidence was found that these

animals suffered any long-term or late-developing ultrastructural changes that could be attributed to a previous dive. In addition, type B cells appeared to be completely normal, as did the mitochondria, endothelium, and basement membranes. We found no evidence of basement membrane separation, degeneration, thickening, or edema. Liver histology appeared to be entirely normal for both hydrox and heliox dives.

In our studies 26 dogs took part in 31 dives. Of that number only four died as a result of the dives. Two died during a hydrox dive and two during a heliox dive. The hydrox dogs died within a few minutes of each other after 16 h of hydrox exposure. The heliox dogs died within 1 min of each other after 17 h of exposure at 31 ATA. A thorough study of these fatalities revealed that the same contaminated cylinder of O_2 was used to mix both the hydrox and the heliox used in these dives. A subsequent analysis of this O_2 revealed that it contained hydrocarbons, probably acetylene which was traced to the gas supplier. Again, there was no indication that the H_2 was the cause of either death.

Since molecular H_2 has a specific heat nearly twice that of He, it was found that animals at 31 ata tended to lose body heat. While this does not represent a toxic effect in the usual sense, it is important to control because it can represent a major loss of heat both through the respiratory tract as well as from the skin. To study this, we developed a temperature sensor/transmitter (9) which could be implanted in the abdomen of the animal and would transmit temperature by FM. Fig. 1 reflects the great influence that ambient temperature has on the core temperature of the animal when under such great pressure. It can be seen that at 31 ATA in a hydrox environment ambient temperature must be maintained at around 34^{o}C if the animal is to maintain a normal core temperature.

A study of the EEG was carried out at depth by means of an implanted EEG transmitter. This transmitter was self-contained and was potted in a mixture of bees wax and paraffin wax. Brain leads were implanted and the wires run under the skin to the transmitter located under the skin of the chest wall. Most animals showed a slightly changed EEG, but still within normal limits during compression. The most noticeable abnormalities occurred during hypoxic episodes at depth.

It is perhaps instructive to consider one of these hypoxic instances. Using the predive EEG as control the subject showed no apparent abnormal EEG activity for the first 22 h hydrox exposure, 12 h of which were at 31 ATA. At this time the animal gradually over 1 h developed opisthotonos, tachypnea, and apprehensiveness followed by convulsions. At that time, the O_2 level had dropped to 0.7% (0.6% is normoxic at 31 ATA). The O_2 level was quickly raised to 1.5% and within a few minutes the convulsions stopped. The animal recovered from all postural symptoms, although the EEG continued to show the loss of beta waves. During the subsequent stay at 31 ATA the EEG gradually returned toward normal. It did, however, reveal a loss of the superimposed beta band on the delta and theta waves. This activity is somewhat similar to that observed in humans suffering from HPNS (10). This animal continued to show an improved EEG until during decompression. When it reached 19 ata the inspired O_2 level again was inadvertently reduced and

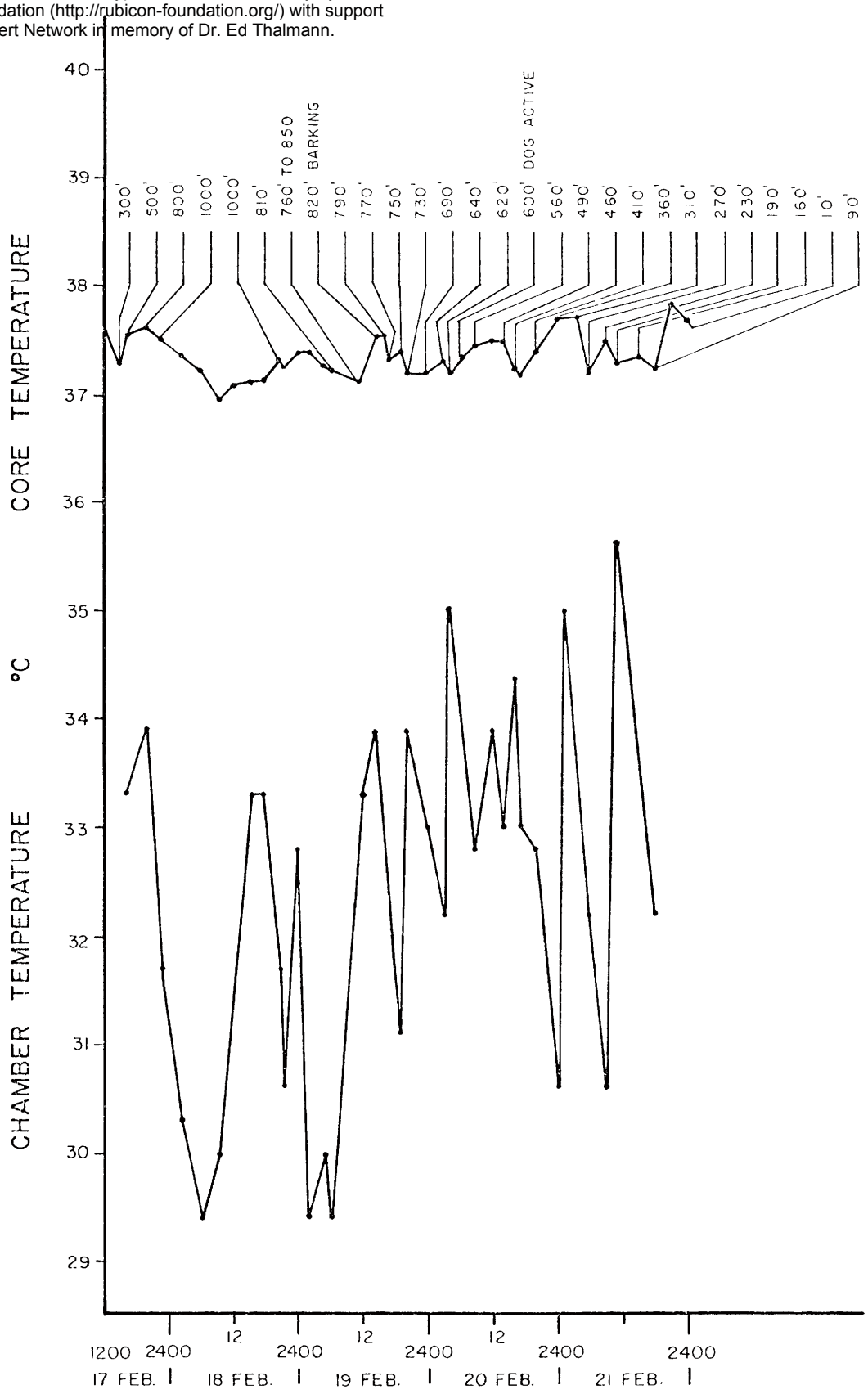

Fig. 1 *Comparison between body core temperature and chamber ambient temperature. The numbers above the core temperature represent chamber depth in feet of sea water.*

the EEG again became abnormal. When the O_2 level was raised, the EEG again reverted toward normal. It was found that if heliox were being used, the O_2 levels could be held at the normoxic level without causing EEG changes.

This observation raised again the possibility that molecular H_2 is not completely inert in the body. Perhaps it should not be considered to be toxic, but it may have an effect on certain enzyme systems, possibly those related to cytochrome oxidase.

A 6 yr study was carried out on the possible effects that frequent exposure to hydrox might have on fertility and fetal development. It would appear that hydrox has no adverse effects either on fertility or fetal development. Two female dogs were found to have been about 1 mo pregnant at the time of their 31 ATA dive. Both delivered a full litter of healthy pups. Further, nearly all female dogs became pregnant at least once after a hydrox dive. Two had three litters after four hydrox dives. It also appears that hydrox diving has little if any adverse effect on the life span of the subjects. Two of the animals kept after the dives lived to ages 15 and 17 yr, respectively. One, however, died of metastatic breast cancer, the other of metastatic epithelioma. Both were in good health until late in the course of the disease. At autopsy, none revealed any neurological abnormalities.

The large number of successful hydrox dives to a simulated depth of 31 ATA and the survival of some of these animals for a number of years in apparently normal health suggests that dissolved molecular H_2 even at a partial pressure of 22,853 mmHg (97% of 31 ATA) does not result in identifiable irreversible physiological damage. On the other hand, there are several indications that molecular H_2 may not be completely inert in the body, particularly at elevated partial pressures. Earlier work by Dole (11) indicated that at high partial pressures (500 Torr) molecular H_2 scavenged alkyl radicals in polyethylene. Although this pressure is far above that used in our studies with mammals, a pilot study by Fife (unpublished data) suggests that the scavenging effect of molecular H_2 may occur at pressures in the range of biological importance. In this study, Fife painted a carcinogen, methylcholanthrene, on the backs of 10 mice. Five of them were placed in a hyperbaric chamber and compressed to 10 ATA of 97% H_2: 3% O_2. Each 48 h they were again painted with methylcholanthrene. At the end of 2 wk, all of the control animals that received no H_2 showed open lesions. All of those that received hydrox treatment showed only a dark brown discoloration at the site of the methylcholanthrene, but no open lesions had developed in any of the treated animals. At the end of 2 wk, one of the experimental animals died. It was replaced by one of the controls which had open lesions. Within 5 d these lesions had disappeared, although they remained in all of the other control animals. She did not continue these observations to see if squamous cell carcinoma developed. This preliminary study suggests that molecular H_2 scavenged the high energy-free hydroxy radicals which are produced by methylcholanthrene and many other carcinogens.

In summary, in our view the overwhelming evidence indicates that H_2 is not toxic to the body at any pressures so far studied. However, there is a

possibility that molecular H_2 does carry out a scavenging activity both on some metabolic enzymes and probably on high energy free-hydroxy radicals. - This latter may serve as a protective device against the damage that such radicals can cause within a cell. In fact, it appears that molecular H_2 may serve as an adjunct to superoxide dismutase normally found in cells.

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DISCUSSION FOLLOWING BRAUER AND NAQUET, AND FIFE PRESENTATIONS

ÖRNHAGEN: You touched the topic of pH and pH changes. We are fairly well satisfied that there are no pH changes in the animals we have seen. But there is another possible effect: In food processing you can hydrate unsaturated fats by exposing them to H_2 and catalysts at some 200° C at very low pressures--1 or 2 bars. I wonder if any of you have heard of any possible catalytic effects of enzymes in the body activating H_2? If so, maybe there is a risk of hydration of unsaturated body fats.

FIFE: We didn't look at fatty acids but only at cholesterol. As you would expect, the cholesterol levels often went up, but we felt that this was a response to nonspecific stress and I don't think that that would bear at all on what you are talking about. On that I don't have any indication at all.

SMITH: The hydrogenation process is normally carried out at quite high pressure and also in the presence of very special catalysts. I don't know the details of the process but I suspect it's quite difficult to get it to go.

FIFE: There are a lot of enzymes in the body that could perhaps do this. I think that was your point, Hans. We really haven't looked at the enzymes, and what about the cytochrome A3 and some of the others?

BRAUER: I would suggest that much of what may be affected in the sense that you are talking about may not show up until much longer exposures than those we have seen so far. I think we will probably all agree that one of the early items in any future research program will have to be multiday or perhaps multiweek exposures to H_2. At that point the sort of question you are raising here seems to me totally in order. I must admit that I agree with Professor Smith that the likelihood of my mice, or your monkeys, or your people getting stiff because their fats are becoming saturated is really quite small. Less unlikely candidates for enzyme catalyzed hydrogenation effects might be lipids in functionally critical sites such as gangliosides, which are directly involved in CNS function.

MILLER: The rates at which the fatty acids in biological membranes are coupled with and incorporated into phospholipids and turned over and metabolized are very high. The body tends to control the degree of saturation in the membranes. Thus, even if there were partial hydrogenation of fatty acids in lipids, the body could be expected to react to this by breaking down the lipids concerned and providing a supply of unsaturated fatty acids to maintain the membrane properties.

ÖRNHAGEN: Would it be possible to use one of the tools for measuring membrane fluidity to look upon the state of the membrane?

MILLER: The only way to do that accurately is probably to use gas-liquid chromatography to analyze the fatty acids.

BRAUER: One of the things likely to get in the way of experiments like that

are acclimation phenomena. We shall talk a little bit later about this. They are quite marked, and they obviously could enter into any adjustments or displacements such as we are talking about here.

GIRY: I have some information to pass on to you, derived from work of Dr. Brue as of last week. There is no modification of the O_2 metabolism of red blood cells at 100 bar heliox or hydrox.

LUNDGREN: A remark regarding the flammability of H_2-O_2 mixtures. Dr. Fife mentioned in passing that one of the tests to which they put their mix was to attempt to ignite it by sparks, a thing that could readily be done in experimental settings. To make such a procedure meaningful it is important to know that the amount of energy put into that spark is of great importance for the result. This was brought out in work by Dr. Holmstedt[1] at the University of Lund in Sweden. He showed very clearly that some of the proportions of H_2 to O_2 in mixtures that have been claimed by others to be nonexplosive were so only because appropriate means of igniting them were not used. A clean bill of health can only be given a H_2-O_2 mixture after testing it with adequate means of ignition.

GIRY: May we come back to the Michaud experiment. I went through the protocols of that work and investigated with people who ran the experiments. Alas, the chemist who did the gas analyses died 3 yr ago and there is no recall. But the man who provided the gas is still alive and has assured me that there has been no variation in the composition of the H_2 processed since well before the time these dives were performed. I went back through the protocols and it is my opinion, shared by a number of other people, that these rabbits which were experimented on in an underwater pressure chamber died of cold. With heat losses potentiated by the high heat conductivity of H_2 at a partial pressure of 30 bars, and with a temperature regulated at 20°C in a system in which there was no recorder, it seems most likely that these animals died of cold.

ÖRNHAGEN: I recall that in these animals EEGs and ECGs were continuously recorded. As far as I know nothing was mentioned about artifacts such as you ought to find as a result of tremendous shivering. If an animal is freezing to death you expect, at the beginning of the temperature drop, much noise in both the EEG and the ECG. Why wasn't that mentioned in connection with these recordings? Moreover, as I shall mention in a separate presentation a bit later, we dropped the ambient temperatures of some of our experiments to around 29°C for some hours without any other effect than shivering.

GIRY: When you conduct high pressure work in which the central nervous system is affected, let's say through inert gas narcosis, you may modify greatly the degree of body restlessness by any kind of shivering. Furthermore, it is well known that when you are intoxicated, shivering tends to be

[1]Holmstedt GS. The upper limit of flammability of hydrogen in air, oxygen, and oxygen-inert mixtures at elevated pressures. Combustion Flame 1971; 17:295-301.

suppressed. In my opinion death in this case was modified by the narcosis that H_2 also creates, as well as probably by hypoxia.

BRAUER: Musacchia and others have shown that if you insist on inducing hypothermia, doing so in high pressure heliox environments, or even in a He environment at quite modest pressures, often allows you to bring it about without evoking very pronounced temperature defence, including shivering, provided you go about it carefully. May I come back to your slide, Bill, showing the drop of body temperature in your dogs. Perhaps it is in order to caution you that if you put animals in a temperature gradient (as we are doing currently to determine preferred temperatures) you will find that deep body temperatures of mammals tend to be slightly lower at elevated pressures in heliox than at 1 ATA, provided the animals can choose where they want to be. I think there is some good theoretical reason why this should be so. Therefore, the custom that has grown up in the community of heat one's animal chamber until the rectal temperature of one's subject is 37°C or a bit higher may not be a physiologically sound one.

SWEDISH ANIMAL EXPERIMENTS USING HYDROGEN-OXYGEN MIXTURES AT PRESSURES UP TO 6.0 MPa

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In Sweden, the interest in the use of hydrogen as a breathing gas for diving was initiated by Arne Zetterström. However, the tragic outcome of his last dive in 1945, although not due to the diving gas, resulted in a termination of hydrox research in Sweden for the next two decades (1-3). Experimentation was resumed in the late sixties starting with investigations of the explosion limits (4). At that time plans were also laid for animal experiments but facilities were not available until 1979. The aim with the animal exposures was to further investigate the possibility of using hydrogen-oxygen as a breathing medium in diving before human experiments were made.

THE CHAMBER SYSTEM

The chamber system had an internal volume of 450 liter and had a maximum working pressure of 25 MPa. It was supplied by a double mixmaker capable of mixing 0.5 m^3/min of N_2-O_2 (nitrox) and H_2-O_2 (hydrox) at pressures up to 10 MPa. The mixmaker was based on the principle of injection of O_2 at high velocity perpendicularly into a high velocity H_2 or N_2 flow. The system had an external life support system using soda lime, silica gel, and activated charcoal. The scrubbing capacity was approximately 1.5 liter CO_2/h at a P_{CO_2} of 0.5 kPa. To compensate for metabolism and to increase P_{O_2} during decompression, O_2 was added into the scrubber circuit through a stainless steel capillary given a high velocity at small flows.

A thermistor-controlled water heating system could hold the chamber temperature at desired levels during periods of stable pressure. During fast compression temperature increases of 1-2^{o}C were observed.

Drinking water was pumped into the chamber and the overflow was used to flush excrements and urine into a sewer bowl to be evacuated two or three times a day. The chamber pressure, temperature, humidity, O_2, and CO_2 concentrations were continuously recorded. The N_2 and H_2 contents were followed by spot samples on the gas chromatograph, and impurities of carbon monoxide (CO), methane (CH_3), hydrogen sulfide (H_2S), and ammonia (NH_3) were checked by Drager tubes every 12 h.

The chamber system was used for rabbits, rats, and mice. All animals had free access to standard food pellets and water. The rabbits were individually caged and were fitted with bipolar ECG leads and subcutaneous temperature probes. The rats and mice were unmonitored. The rats were kept in groups while the mice were kept individually for urine sampling.

The first part of the compression was made with pure N_2 to lower the O_2

concentration of the chamber atmosphere. At 0.7 MPa (P_{O_2} = 0.03) a 97:3 hydrox mixture was flushed into the chamber at stable pressure. The H_2 was of standard industrial quality and had been produced by electrolysis of water. When the N_2 concentration was below 5%, the outlet valve was closed and compression was continued with 97:3 hydrox at a rate of 50 kPa/min. At a P_{O_2} of 50 kPa (total pressure 1.7 MPa) the O_2 addition was stopped and the compression continued with pure H_2 to a maximum of 6.0 MPa. The total compression time to 3.0 MPa including a shift of gas from nitrox to hydrox was 2 h. The bottom times in different exposures ranged from 24 to 155 h.

The decompression profiles displayed in Fig. 1 were originally tested for rabbits (decompression from 3.0 MPa) and then adjusted for pressures up to 6.0 MPa, and for smaller animals, rats, and mice according to their higher metabolism.

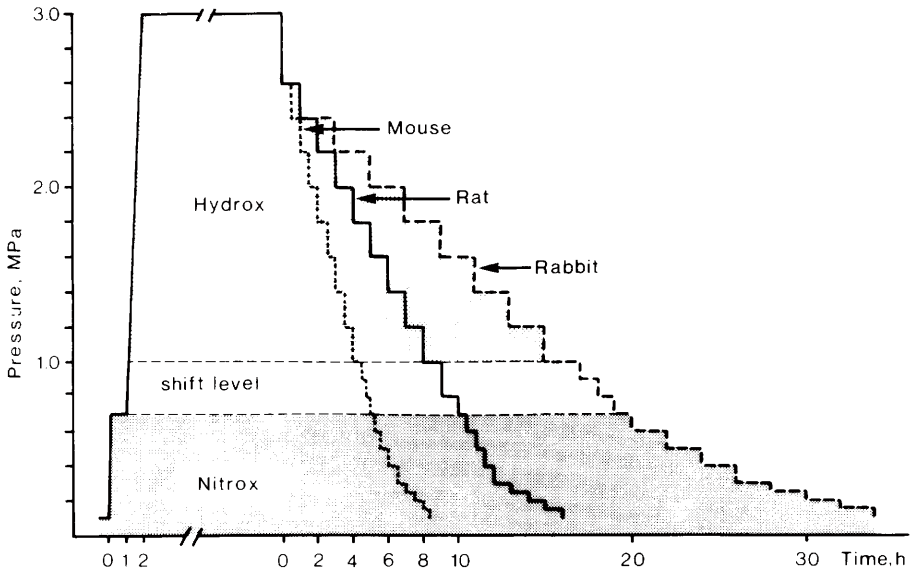

Fig.1 *Compression-decompression profiles used in most of the animal experiments with hydrox. The pressure level at which the switch to and from hydrox was done is indicated.*

The profile had an initial step to 2.6 MPa. It was thereafter linear to the shift point at 0.7-0.8 MPa and then curved to the surface. The total decompression time for rabbits was 34 h, for rats 15 h, and for mice 8 h. Using this profile we saw no decompression symptoms and no symptoms indicating counterdiffusion problems during the shift of gas.

RABBITS

A total of 21 compressions have been made using 32 rabbits. No adverse reactions like coarse tremor or convulsion were seen during the compression or bottom phase. A total of three rabbits died at pressure. One death was due to strangulation in monitoring leads, and two were due to decompression sickness during use of a shorter table than the one described above. None of the deaths could be attributed to the hydrox exposure. None of the

exposed and decompressed rabbits died during the postdive observation period (1 yr) and two rabbits have given birth to normal litters, one of which happened after four exposures to hydrox at 3.0 MPa.

Blood samples were drawn from six rabbits before and after hydrox exposures. No significant changes were observed in electrolytes, blood enzymes, or hematological parameters (Fig. 2).

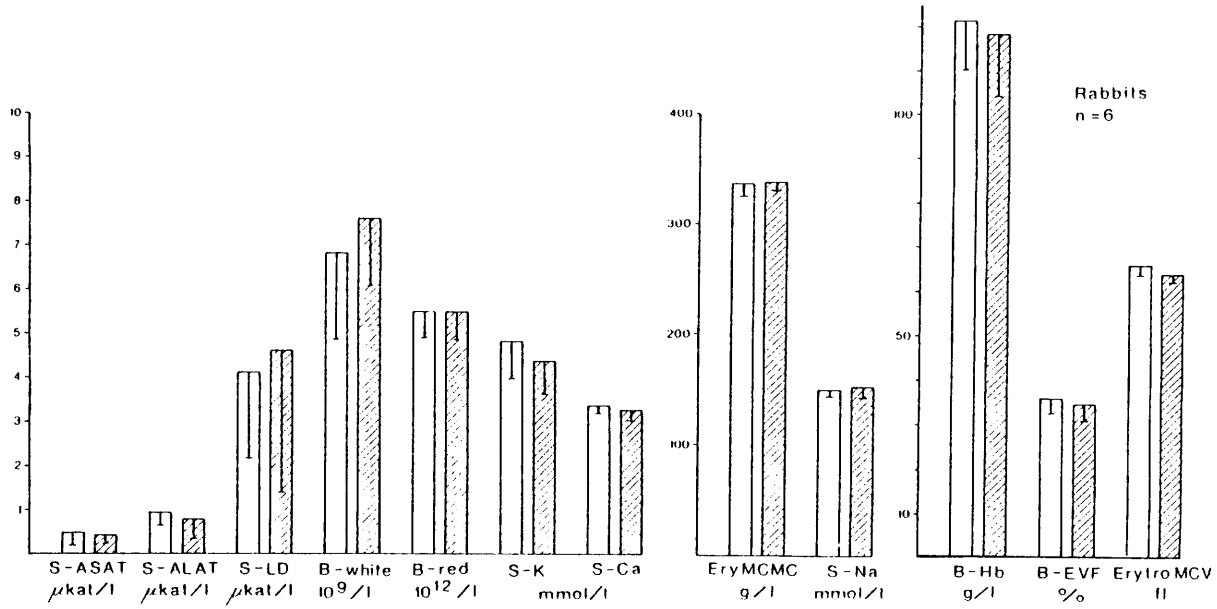

Fig. 2 Mean and SD of pre- and postdive blood samples from six rabbits exposed to 3.0 MPa hydrox for 24 h.

Continuous monitoring of heart rate and subcutaneous temperature showed no significant deviation from normal values as can be seen in Fig. 3.

Oxygen consumption and carbon dioxide production measured as changes in P_{O_2} and P_{CO_2} in the chamber atmosphere were found to be 0.95 and 0.79 l/kg x h, respectively on spot checks. This is in the upper normal range (5), which is probably due to the increased thermal stress seen in hyperbaric atmospheres. In certain exposures the chamber temperature was purposely lowered to 30°C to test a hypothesis that rabbits could not survive at this temperature in hydrox at 3.0 MPa. Shivering and ruffled-up fur were the only abnormalities observed, and all animals subjected to this procedure survived.

We have no proven explanation for the difference in results presented here and the results previously reported by French scientists (6,7). Apart from species differences there may also have been variations in susceptibility between different strains of animals. One may also speculate about differences in gas purity. Gaseous H_2 can be manufactured in various ways, not only through electrolysis of water, but also through cracking of H_2 containing molecules or from purification of overflow gas from iron works. Such overflow gas may contain arsine (AsH_3) as a contaminant, in very small

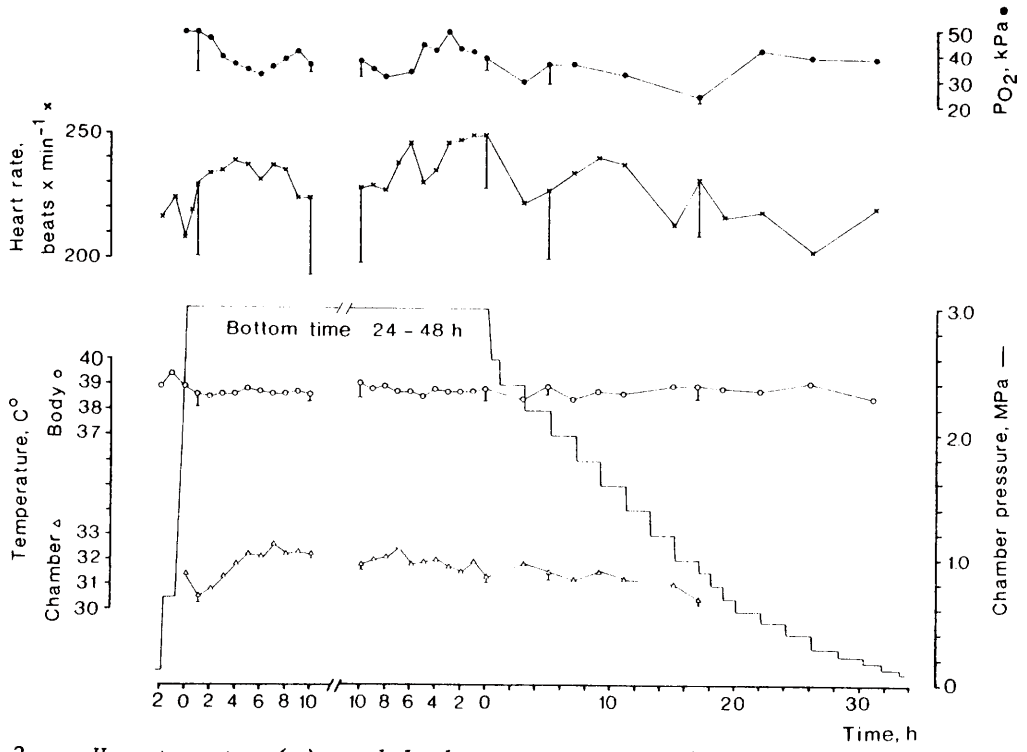

Fig. 3 *Heart rate (x) and body temperature (o) of 14 rabbits in five hydrox exposures to 3.0 MPa. Chamber pressure (-), chamber temperature (Δ), and P_{O_2} (·) are also shown. The symbols indicate mean values and the bars show one SD.*

amounts but enough to reach toxic levels at high pressure and continuous exposure.

RATS

Three compressions of a total of 30 rats have been made with bottom times up to 155 h. After decompression, the rats were killed and tissue samples from heart, liver, testes, and intestines were taken for histological analysis. No systematic findings indicating any effect caused by H_2 were found.

MICE

Two compressions of 12 mice were intended for a study of urine metabolites from fast-growing tissue during H_2 exposure. Due to difficulties in separating feces and urine at pressure, no reliable data were obtained. All animals survived the 24-h exposure at 3.0 MPa and decompression without visible signs of discomfort or pathological reactions.

CONCLUSIONS

Our findings in rats and mice are consistent with other reports regarding H_2 exposures of small rodents (8-10) in that no deleterious effects were observed. We were not able to confirm earlier findings of deleterious effects of hydrox breathing in rabbits at 3.0 MPa during periods of 24-48 h. We had no indications of any toxic effects of H_2 at the pressures and exposure times tested.

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DISCUSSION FOLLOWING ÖRNHAGEN PRESENTAION

BRAUER: What time of year did you conduct your experiments?

ZRNHAGEN: Early spring. We considered some of the possibilities why our rabbits survived while the French rabbits didn't. We had our animals caged outdoors before they were brought to the laboratory, and as you know rabbits can adapt very well to subfreezing temperatures. Therefore they might have

had better temperature compensation than those animals in southern France. This is of course only a speculation.

BRAUER: Some years ago I had a Canadian collaborator who had been interested in cold acclimation. He showed very convincingly that rats cold acclimatized by being kept outdoors during the Ottawa winter were far more cold resistant than even rats cold acclimated in a refrigerator to the same mean temperatures. So in your animals the acclimation effect could really be quite large in terms of metabolic scope, and of nonshivering thermogenesis and effective body insulation, even though any effect of denser pelage in the cold bunnies would probably have been annulled by the high hydrox diffusibility. It might be worth repeating some of these experiments with summer rabbits.

FIFE: Does anybody have a feel for what the quantity of heat is that can be carried off by H_2 under pressure vs. H_2 under 1 atm, or He for that matter? Are we talking about a major difference?

BRAUER: The rule of thumb there would be that by the time we are at these pressures it will be virtually exclusively convective heat loss, a large part of it respiratory. That will be directly in proportion to the heat capacity per unit volume times the temperature difference between exhaled and inhaled gas, and the first term of this in turn is nearly directly in proportion to the pressure. Thus, at 100 ata you are going to lose about 100 times more heat per breath than at 1 ata. Add to this that, as Brian showed yesterday, the molar heat capacity of H_2 is about 25% greater than that of He, and you would expect that thermal problems under H_2 at a low chamber temperature would really be quite severe. On the whole I think what we have heard here tends to support Dr. Giry's judgment that there is an excellent chance that the results of Michaud and colleagues' experiments do indeed represent a consequence of induced hypothermia rather than of any toxicity of the chamber atmosphere.

MILLER: Dr. Fife's experiments also suggest the possibility of contamination of a gas cylinder. Even though he put pure H_2 into it was there something else there in the beginning?

RAUER: But that was O_2.

MILLER: Yes, but was there an unexpected contaminant? I guess it will remain a puzzle until someone repeats the old experiments with the same results as Michaud and his people.

GIRY: Anyway I think that this is useless because now we have human saturation dives that are using this mixture and have found it to be nontoxic.

MILLER: Humans aren't rabbits.

SECTION II
Narcotic Effects

HYDROGEN: THEORETICAL CONSIDERATIONS

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The value of H_2 as a gas for use in diving is, and perhaps this hardly needs stating, entirely determined by its chemical and physical properties. Hydrogen was first prepared by Paracelsus in the 16th century by the action of sulfuric acid on iron. However, he failed to recognize that it was not air, and H_2 was not identified until the end of the 17th century when Robert Boyle observed it flammability, a property that sets well-defined constraints on its uses in diving. Hydrogen is a colorless, odorless gas which, at 273 K, is the lightest known. Chemically it is fairly inert, combining *at room temperature* only with fluorine or chlorine. At elevated temperatures it reacts with other halogens and, of course, O_2. Almost all these facts are relevant to the use of H_2 in diving.

EQUILIBRIUM GAS-PHASE PROPERTIES

The density of H_2 gas at 1 atm at 298 K is 0.0823 $g\text{-}L^{-1}$. The density increases approximately in proportion to the pressure at low pressures, but by 50 ATA deviations from this perfect gas behavior amount of 4%, the observed density being (unusually for common gases) less than that calculated on the basis of the perfect gas law. At 200 ATA the deviations reach some 15% (Table 1).

The low density of H_2 gas plays a crucial role in determining respiratory resistance. This is largely determined by the larger airways where Reynolds Numbers as high as 20,000 can be attained under conditions of heavy work. For the turbulent flow that exists under these conditions, the resistance is directly proportional to gas density. (This does not rule out a role for gas viscosity in contributing to respiratory limits.)

A further equilibrium property that is of importance in diving is the heat capacity at constant pressure. This to a large degree determines the heat loss that is associated with the respiration of cold gases. For H_2 the value at 1 atm and 298.15 K is 1.18 $J\ K^{-1}\ liter^{-1}$. This value is considerably higher than that for He which is about as high as that for N_2. The thermal problems in diving that occur with He are likely to be even more serious when H_2 is employed (Table 2).

TABLE 1
The density of hydrogen has in g·liter^{-1}

	T(K)		
P/atm	273.15	298.15	232.15
1	0.090	0.082	0.076
10	0.89	0.819	0.756
30	2.65	2.43	2.24
50	4.36	4.00	3.37
100	18.45	7.76	7.19
200	12.67	14.64	13.61

Source: Gas Encyclopedia, Elsevier, Amsterdam (1971).

TABLE 2

Properties of Common Gases

	Molecular Weight	C_p J K^{-1} liter^{-1}	η x 10^6 k gm^{-1} s^{-1}	K x 10^3 J K^{-1} m^{-1} s^{-1}
H_2	2.016	1.18	8.42	170
He	4.003	0.85	18.6	141
N_2	28.02	1.19	16.7	24.3
O_2	32.00	1.20	18.1	24.6
Ar	39.95	0.85	21.0	16.2

Cp = heat capacity at constant pressure at 298 K and 1 atm;
η = viscosity at 273 K;
K = thermal conductivity at 273 K

The heat capacity per liter increases approximately linearly with pressure, and the heat capacity per gram (at constant pressure) is almost constant, lying in the range of 14.2 - 14.5 J K^{-1} g^{-1} for temperatures between 273 and 323 K and pressures of up to 100 atm.

GAS TRANSPORT PROPERTIES

Though viscosity is not the determining factor in overall respiratory resistance, it is important in controlling flow in the narrow airways. To this extent it may influence the efficiency of respiration. The low viscosity of H_2 can only be beneficial in this respect (Table 2).

The thermal conductivity of H_2 is significantly higher than that of He and much greater than that of O_2 and N_2. This must add to the problems of thermal regulation that occur in diving.

DIFFUSION IN FLUIDS

A factor that plays a role in determining the development of the symptoms of decompression sickness is the rate of diffusion of gases when dissolved in a fluid. For most gases these diffusion coefficients are inversely related to the molecular cross section (which can be approximated by the two-thirds power of the critical volume.) However, in the case of the lighter gases, He and H_2, anomalously high values are observed due to quantum mechanical effects that can be related to a parameter, Λ, which represents the ratio of the de Broglie wavelength to the molecular diameter. The value of this parameter is *less* for H_2 than for He, and the diffusion coefficient of H_2 in organic liquids is less than that of He despite its lower molecular weight (Table 3). As diffusion plays a crucial role in bubble growth it is reassuring that H_2 is "more normal" than He and should produce no unexpected difficulties.

GAS SOLUBILITY

The solubility of a number of common gases including hydrogen is given in Table 4. Such solubilities play and important role in determining both the degree to which gases can cause decompression sickness and their narcotic potency.

The extent to which gases cause narcosis is related to their solubility in fatty substances. We can characterize the latter more precisely as solvents whose solubility parameter δ (defined $\delta = (-E/V)^{1/2}$, where E is the energy per mole of vaporization as a fluid and V its molar volume) lies in the range 9-10 $cal^{1/2}$ $cm^{-3/2}$. A suitable candidate for our discussion is benzene for which $\delta = 9.15$ $cal^{1/2}$ $cm^{-3/2}$ and for this extensive solubility data are available (Table 4). Simple calculations on this basis indicate that the partial pressure of H_2 required to induce narcosis would be some 65 atmospheres. However, at these pressures, the antagonistic effect of pressure must be taken into account. We have carried out calculations using the constant volume hypothesis which lead us to predict that the effective anesthetic pressure will be much higher. We can also approach this problem

TABLE 3

Diffusion coefficient of gases dissolved in liquids D cm_2 s^{-1} x 10^4

	Ω*	$(C_4F_9)_3N$[a]	CCl_4[b]
He	2.67	13.8	20.0
H_2	1.73	8.25	9.75
Ne	0.59	6.35	~ 6.3
Ar	0.10	3.8	3.63
N_2	~ 0	-	3.40
O_2	~ 0	-	3.82

[a]Powell RJ, Hildebrand HJ. J Chem Phys 1971; 55:9
[b]Nakanishi K, Voight EM, Hildebrand JH. J Chem Phys 1965; 42:860
$\Lambda^* = \frac{h}{\sigma\sqrt{m\epsilon}}$ · h = Planck's constant, M = molecular mass
ϵ = maximum energy of intermolecular attraction.

TABLE 4

Gas Solubilities

	H_2O	iC_8H_{18}	cC_6H_{12}	CCl_4	C_6H_6	CS_2
He	0.068	3.10	1.21	-	0.79	-
Ne	0.082	4.6	1.90	-	1.07	-
H_2	0.142	7.83	4.14	3.19	2.58	1.59
N_2	0.119	-	7.70	-	4.48	2.22
O_2	0.231	28.1	-	12.0	8.15	4.42
Ar	0.254	29.1	15.2	13.4	8.8	-

Data taken from Hildebrand, Prausnitz, and Scott, Regular and Related Solutions. New York, Van Nostrand Reinhold Co., 1970.

without invoking a detailed model of pressure-anesthetic antagonism by calculating the composition of the He-N_2 mixture that would be expected to have a narcotic potency equivalent to that of H_2. The results suggest that H_2 should behave like a 50% He:50% N_2 mixture. Such a mixture would be expected to lead to narcosis at approximately 200 m, and indeed, narcosis, as will be discussed later, has proved a problem in H_2 diving. Simple calculations and animal experiments suggest that a mixture of 20% N_2:80% He would be optimum in trimix diving (practical observations with men, where more subtle manifestations of narcosis are involved, would suggest an even lower concentration of N_2). Calculations on the same basis would indicate that a 40% H_2:60% He would be the optimum mixture for animal studies. A lower concentration of H_2 might be optimum in diving.

In reviewing the properties of H_2 I have tried to make general comments as to the expected consequences for diving practice. The degree to which experience supports these conclusions will be the subject of the papers that follow.

HYDROGEN AS AN ANESTHETIC GAS: APPROACHES TO PREDICTING SUITABLE HYDROGEN-HELIUM MIXTURES FOR DEEP DIVING

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INTRODUCTION

In the late 18th century, Sir Humphrey Davy noted that "there was every reason to suppose that hydrogen was not adsorbed or altered when respired; but only mingled with the residual gases of the lungs." (2). Although the accuracy of this statement would undoubtedly be challenged today, it is not a bad first approximation. Hydrogen is one of the least soluble gases; only helium and neon excelling it in this respect (see preceding chapter). Indeed, once the limitation to deep diving imposed by nitrogen narcosis was recognized, these were the gases to which people turned in search of physiologically inert diluents to be mixed with oxygen for deep dives. While in the United States Hildebrand advocated helium, in the United Kingdom, which lacked a strategic source for this gas, Haldane advocated hydrogen. In spite of his advocacy, most subsequent workers have shunned the use of hydrogen in both deep diving and laboratory studies. However, as dives with helium-oxygen were pushed to ever greater depths, a new phenomenon emerged. This was a hyperexcitability of complex etiology that is now known as the high pressure neurological syndrome (HPNS).

It is well known from work on aquatic animals and on liquid-breathing mammals that pressure per se causes such excitation. What is less clear is the extent to which relatively insoluble gases such as helium and hydrogen modify the effects of pressure. Thus, in a recent study, Harris et al. (4) showed that in dogs exposed to helium-oxygen or to an oxygenated fluorocarbon liquid while being compressed to a 1000 m of sea water "helium did not play a significant role in the etiology of HPNS." The question to be addressed here is: Does hydrogen merely act as a pressure-transmitting fluid like helium or as a narcotic gas like nitrogen? This question will be approached from the viewpoint of small animal research; experience with human diving will be presented by others later in this publication.

SMALL ANIMAL WORK

Because of the need for complex behavioral experiments to study subtle changes of the sort associated with inert gas narcosis, the work presented here will deal with general anesthesia in small animals. In general, it has always been observed that gases that cause anesthesia cause narcosis (e.g. nitrogen), whereas gases that do not cause anesthesia do not cause narcosis (e.g. helium). The work summarized here is not intended to provide a comprehensive review, but to present general principles.

The first comparison of the effects of hydrostatic pressure and hydrogen pressure was carried out using newts (*Triturus cristatus carnifex*) in small compression bombs (7,8). The data are presented in Figure 1.

Hydraulic compression causes loss of righting reflexes secondary to pressure-induced paralysis with onset at 140 atmospheres. At 200 atmospheres, paralysis is almost complete, whereas in hydrogen-oxygen (the partial pressure of oxygen was one atmosphere) only an insignificant loss of righting reflex was observed, suggesting that hydrogen exerts some protecting effect against pressure. However, no sign of anesthesia was reported. The data for helium (not shown) lie between the two curves in Fig. 1.

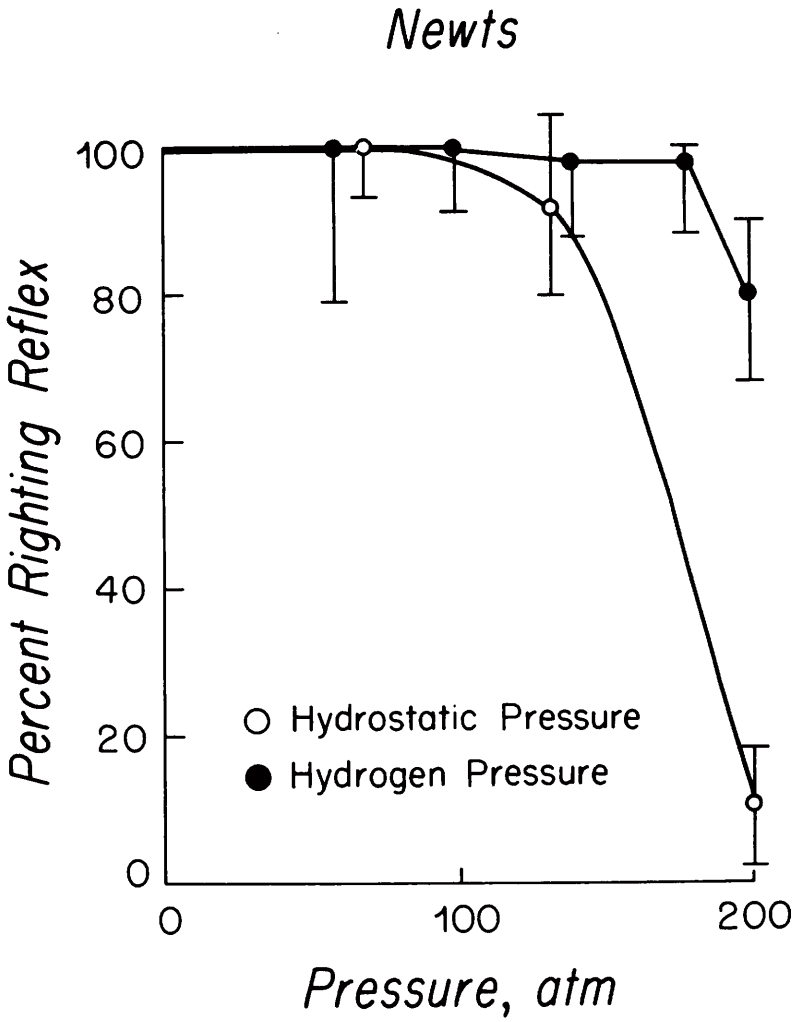

Fig. 1. A comparison of the effects of hydrostatic pressure (open circles) and of hydrogen pressure (closed circles) on the ability of newts to right themselves. Loss of response was caused by paralysis (7,8).

A much more definitive resolution of hydrostatic pressure effects from inert gas effects had been made recently using tadpoles (3). In these studies, the latent anesthetic effects of gases were revealed by studying

them in the presence of a second anesthetic. Figure 2 shows that even helium has anesthetic tendencies!

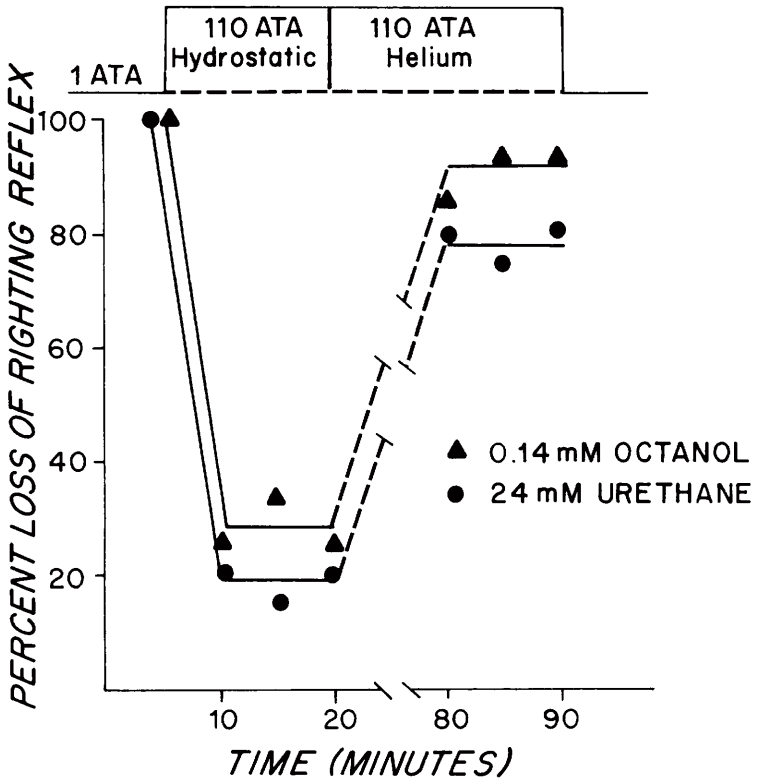

Fig. 2. The effect of pressure on a fixed anesthetic concentration. The mean loss of rolling response in animals exposed to 0.14 mM-octanol (triangles) or 24 mM-urethane (circles) drops from 100 to 25% with the application of 110 atmospheres of hydrostatic pressure. The isobar switching of hydrostatic to helium pressure increased mean loss of rolling response to 86%, revealing the hidden anesthetic potency of helium. Each point represents the mean response of five animals. Reproduced from (3) with permission.

The experiment was conducted in a small pressure bomb as follows. Anesthesia was induced either with 24 mM-urethane or with 140 μM octanol, doses in each case just sufficient to induce 100% loss of rolling response at ambient pressure. When these animals were compressed mechanically to 110 atmospheres, anesthesia was reversed (Fig. 2) and the mean loss of rolling response fell to 20%. Helium was then admitted to the chamber under isobaric conditions. Approximately 1 h was required for the helium to dissolve in the aqueous phase. During this period, anesthesia deepened progressively until a plateau was reached with 80% mean loss of rolling response. This is consistent with helium possessing a weak anesthetic effect. The magnitude of this effect can be quantified by determining the concentration-response curve for urethane anesthesia under various

conditions. Examples are shown in Figure 3. Here, we see that hydrostatic pressure causes a shift of the control 1 atmosphere curve to the right; there is about a twofold shift at 110 atmospheres. This is the well-known pressure reversal of anesthesia effect. What is not so well recognized is that helium does not cause such a marked pressure reversal (*dashed curve*). Thus, helium is an anesthetic, but we never observe anesthesia with it simply because as we raise its partial pressure to dissolve more helium we also raise the hydrostatic pressure. It is the latter's anesthesia-reversing ability the predominates. However, nitrogen behaves as expected, shifting urethane's ED_{50} to the left and, furthermore, causing anesthesia all by itself at 41.5 atmospheres.

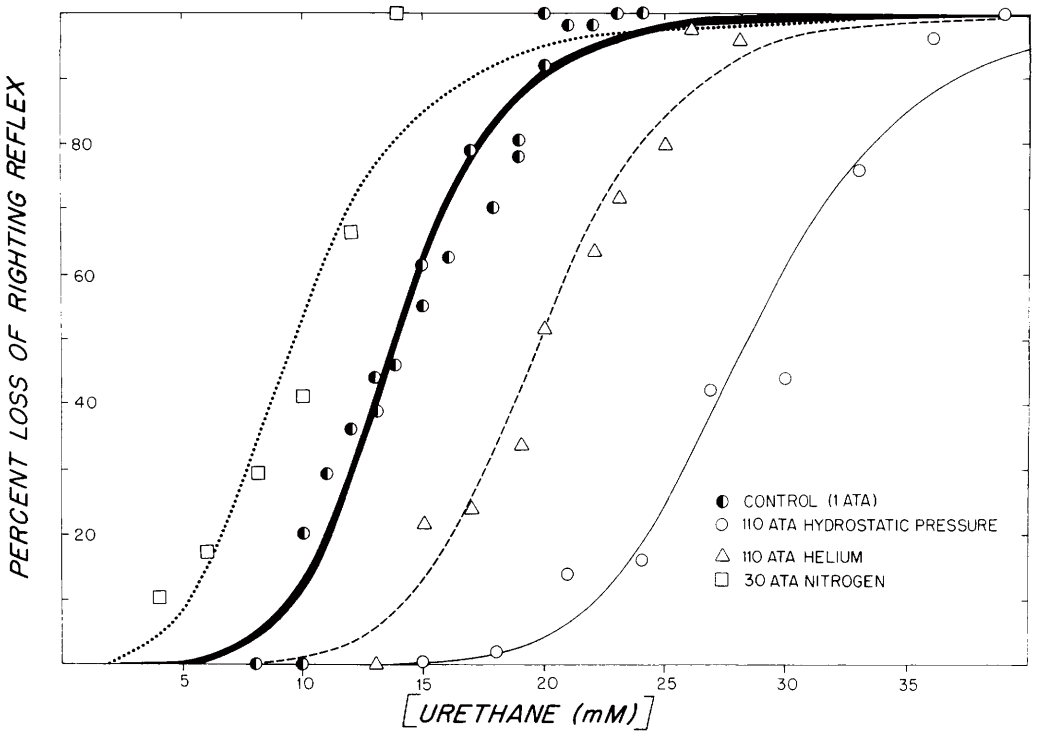

Fig. 3. Accumulative dose-response curves for urethane-induced loss of rolling response. The data were obtained under control conditions of 1 atmosphere of pressure (semisolid circles), 110 atm of hydrostatic pressure (open circles), 110 atm of helium (triangles), and 30 atm of nitrogen (squares). The greater degree of rightward shift by hydrostatic pressure as compared to helium is consistent with helium possessing an intrinsic anesthetic potency. The lines were drawn by eye. Reproduced from (3) with permission.

Given that helium modifies the effects of pressure per se, the next key question is: How does hydrogen behave? By two criteria, it is a weak anesthetic.

First, if we plot out the ED_{50}s for urethane (on a normalized scale, Fig. 4) we see that hydrostatic pressure produced the greatest reversal of anesthesia with an 107% increase in the ED_{50} of urethane at 110 atmospheres.

The gases all attenuate the ability of pressure to reverse anesthesia. The strength with which they do so increases with their lipid solubility. Thus, at the same pressure, helium increased the Ed $_{50}$0 of urethane by only 46%, whereas neon failed to produce a significant change (P = 0.05) from the 1 atmosphere base-line ED_{50} of urethane. At 110 atmospheres, the hydrogen-induced decrease in ED_{50} of urethane was minimal (significant at P = 0.05 but not P = 0.01). Nitrogen and argon both acted additively with urethane, decreasing the ED_{50} of urethane 26 and 37% at 30 and 20 atmospheres, respectively. The pressures of nitrogen and argon that could be studied were limited by their own anesthetic effects. In the absence of any other anesthetic, they caused loss of rolling response at median pressures (EP_{50}) of 42 and 24 atmospheres, respectively (Table 1). These values are somewhat higher than those reported for newts (8) but comparable to those reported for mice (10,12).

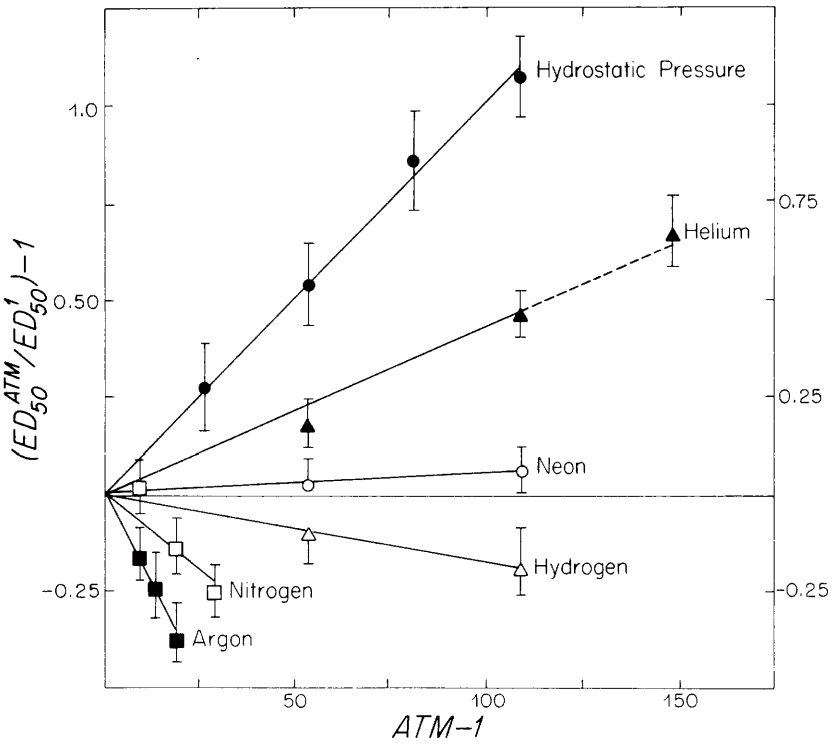

Fig. 4. The ability of mechanical compression and the gases to change ED_{50} of urethane. The ED_{50}s of urethane for each pressurizing agent are expressed as a function of increasing pressure by the ratio (ED_{50} at pressure/ED_{50} at 1 atm^{-1}). Reproduced from (3) with permission.

Second, when each of the agents in Fig. 4 was studied in the absence of urethane, we observed a loss of rolling response in all cases, except neon, where the maximum working pressure was limited to 120 atmospheres (Table 1). Hydrostatic pressure caused complete loss of rolling response in all cases, except neon, where the maximum working pressure was limited to 120 atmospheres (Table 1). Hydrostatic pressure caused complete loss of rolling

TABLE 1

The ability of pressurizing agents to cause loss of rolling response

Pressuring Agents	EP_{50} (atm)	Slope of Dose-Response Curve	Number of Animals
Hydrostatic	137 + 2.2*	28 ± 8.6*	50
Helium	172 ± 3.1	20 ± 5.5	50
Neon	Not determined	(No effect at 120 atm)	
Hydrogen	198 ± 12.5	6.9 ± 3.6	30
Nitrogen	41.5 ± 3.4	4.5 ± 1.1	55
Argon	24.4 ± 2.6	4.0 ± 1.2	50

* Values are means + SD.

response by 160 atmospheres, with an EP_{50} of 137 atmospheres. This is in the range observed with newts 4 (7) and can be unambiguously assigned as a pressure-induced paralysis effect. As with other species, nitrogen and argon both cause anesthesia in tadpoles (see above) with the slopes of the pressure-response curves of both nitrogen and argon not significantly different from, that of the anesthetic urethane ($P = 0.05$). Both gases also reduced the ED_{50} of urethane (Fig. 4).

The effect of helium alone is to cause loss of rolling response with and EP_{50} of 172 atmospheres, 35 atmospheres higher than that for hydrostatic pressure and in the same pressure range as the helium-induced paralysis in newts (7). The slope of the dose-response curve of helium is greater than that for the anesthetic gases ($P < 0.001$) and similar to that for hydrostatic pressure (Table 1).

We noted a mean loss of rolling response of 62% at the maximum pressure of 220 atmospheres of hydrogen and calculated an EP_{50} of 198 atmospheres (Fig. 5). On the basis of both, the slope of this dose-response curve and the slight additivity with urethane-induced anesthesia, *hydrogen appears to have a net anesthetic effect.* Conversely, we can conclude that hydrogen succeeded in postponing the paralyzing effect of pressure to well beyond 200 atmospheres, a performance unequalled by any single gas we have examined to *date.

How do the data with small mammals compare the those for amphibians? There are two studies in which mice were exposed to pressures of over 100 atmospheres of hydrogen. Both concluded that hydrogen was an anesthetic.

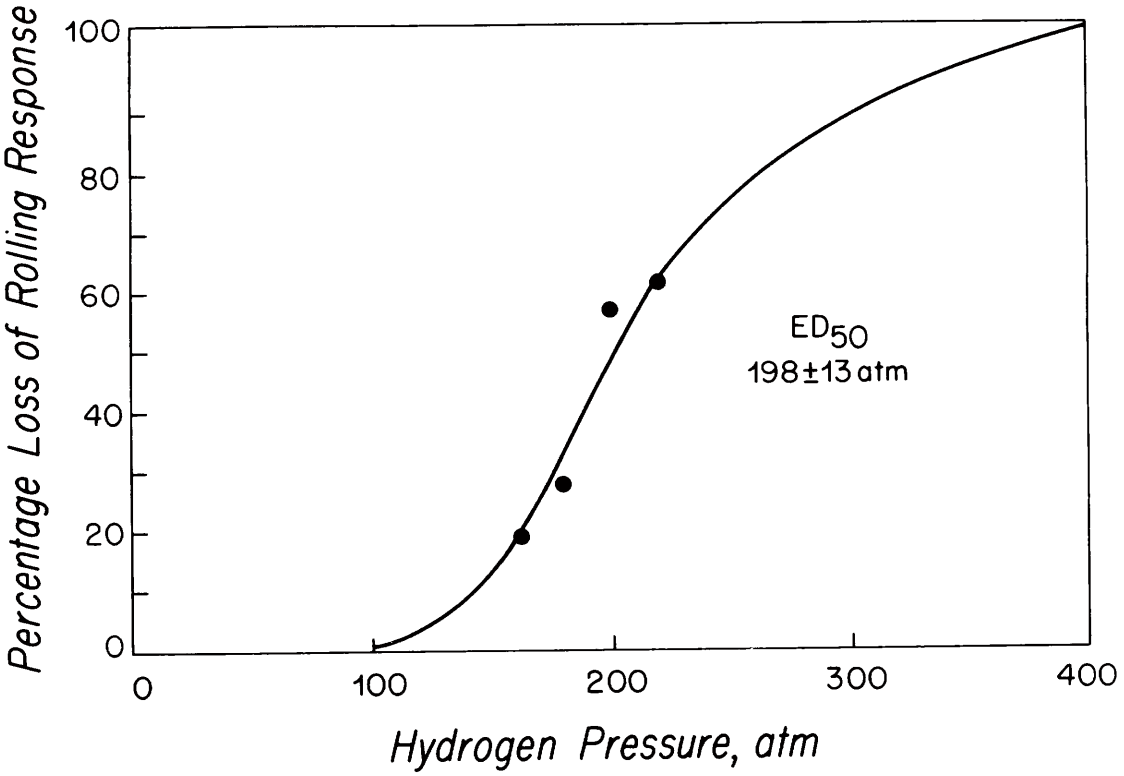

Fig. 5. High pressures of hydrogen cause loss of rolling response (equivalent to loss of righting reflexes). The slope of the pressure-response curve suggests this is due to anesthesia rather than to a pressure per se effect (Table 1).

In the first, Brauer and Way (1) determined that the righting reflex was lost at 129 atmospheres of hydrogen compared to a value of 32 atmospheres for nitrogen. They confirmed these values by studying the additivity of hydrogen-nitrogen mixtures. In the second study, Kent et al. (6) measured the ED_{50} of nitrous oxide as a function of the pressure of helium, neon, and hydrogen. Hydrogen was clearly synergistic with nitrous oxide, whereas neon, weakly, and helium, more strongly, antagonized nitrous oxide anesthesia. Their highest pressure in the presence of hydrogen was 100 atmospheres and they estimated hydrogen to have an anesthetic potency of 180 atmospheres. Their anesthetic potency for nitrogen was 39 atmospheres (12).

THE UNCERTAINTY IN HYDROGEN'S ANESTHETIC POTENCY

In summary, in newts no anesthesia was reported at the maximum pressure of 204 atmospheres (8) whereas in tadpoles at a similar pressure over half the animals were anesthetized (3). This discrepancy occurs in spite of the fact that nitrogen is more potent in newts than in tadpoles. A similar uncertainty is seen in the data for mice where the estimates of potency

differ by some 50 atmospheres. In the case of mammals this could be due to the experimental difficulties of maintaining optimum conditions under such high pressures of gas. For example, Brauer and Way (1) maintained their chamber at 32 $\pm$ 2° C, whereas Kent et al. (6) reported that in hydrogen at 100 atmospheres the chamber needed to be at 35-37° C in order to maintain rectal temperature at 37° C. However, this is an unlikely explanation for the observations in amphibians, suggesting there may be a more fundamental reason for the variability of hydrogen's anesthetic potency. Theoretical studies support this contention.

THEORETICAL CONSIDERATIONS AND PREDICTIONS

Our current understanding of the central nervous system does not provide an adequate framework for a detailed understanding of the physiological mechanisms underlying the actions of anesthetics or pressure. Nonetheless, certain theoretical models have proved reasonably successful in predicting the combination of mechanical pressure and inert gas partial pressure which will produce a given physiological end point. Such models, which we will call null models, get around our ignorance of the physiology by only considering animals in a given physiological state. They are useful, for example, for projecting at what combinations of hydrogen, helium, and pressure inert gas narcosis will occur, but they make no contribution to our understanding of the underlying physiology.

One such null model that has been successfully used to describe this interaction is the critical volume hypothesis in which anesthesia is said to occur when the absorption of an inert substance causes hydrophobic regions of an excitable membrane to expand beyond a certain critical volume. Pressure counteracts this expansion, thus reversing anesthesia (8). The relative expansion of the hydrophobic region at any pressure of an anesthetic gas, P_a, can be expressed as

$$\Delta V = V_2 \cdot P_a \cdot V_m^{-1} - B \cdot P_a \qquad (1)$$

Vm is the molar volume of the site of action and B its isothermal compressibility with units of (pressure)$^{-1}$. V_2, x, and P_a are the partial molar volume, the mole fraction solubility at 1 atmosphere partial pressure, and the partial pressure, respectively, of the inert gas used as pressurizing agent. When numerical calculations are carried out it is easy to correct for deviations both from ideal gas behavior and from Henry's Law (8,10). This is an advantage over empirical equations based on the concept of linear additivity.

The hypothesis assumes the critical relative expansion, ΔV_c, under those conditions causing anesthesia in half the animals should be a constant independent of pressure in the range studied.

For current purposes, it is sufficient to note the following:

1. The first term in equation (*1*) predicts the extent of the volume increase caused by any gas dissolving at its site of action. The magnitude of this effect is proportional to the gas's lipid solubility, x.

2. The second term in equation (*1*) defines the extent to which hydrostatic pressure compresses the same site. Since studies have shown that the compressibility of the site mediating general anesthesia is 3.0×10^{-5} per atmosphere (10), this site will be compressed 0.6% at 200 atmospheres in the absence of gas. Figure 6 illustrates this schematically. If a gas is present this volume decrease will be attenuated. With neon, which is a little more soluble than helium, the two effects roughly balance, but with hydrogen, which is more soluble still, the net effect is now expansion because anesthesia occurs. The important point to grasp is that the net effect of these sparingly soluble gases in this model is the difference of two terms of comparable magnitude. Thus, small changes in the physical parameters in either of the two terms in equation (*1*) will have a dramatic effect on the net volume change. This provides a rationale for the relative uncertainty in the anesthetic partial pressure of hydrogen.

PREDICTIONS FOR HPNS

The formalism of the critical volume hypothesis can also be applied to the HPNS (11). It then states that for a given HPNS end point the symptom occurs when some hydrophobic region is *compressed* beyond a certain critical amount by the application of pressure. Absorption of the inert gas or gases dissolved in a nonpolar medium always cause expansion, thus raising the pressure for appearance of the symptom (Fig. 6).

Similar considerations to those in the previous section explain why, in spite of its net anesthetic effect, compression with pure hydrogen also leads to HPNS in primates and mice (Brauer this volume). This follows from the fact that Miller et al. (10) showed that general anesthesia and the HPNS are mediated by different sites. The compressibility for the site mediating HPNS was much higher than for that mediating anesthesia. Using these figures we can calculate that at 200 atmospheres the net volume change is given by [(compression due to hydrogen dissolving) - (compression due to hydrostatic pressure)] = (net volume change), is (1.72-0.60) = +1.12% for the general anesthesia site and is (1.72-2.78) = -1.06% for HPNS (convulsion) site. Both these volume changes exceed their respective critical volumes; that is, a mouse at 200 atmospheres of hydrogen would be experiencing hyperbaric convulsions even though it was anesthetized. This is not a new situation; it has been explored in some detail in the case of helium-nitrogen mixtures (1,9,11).

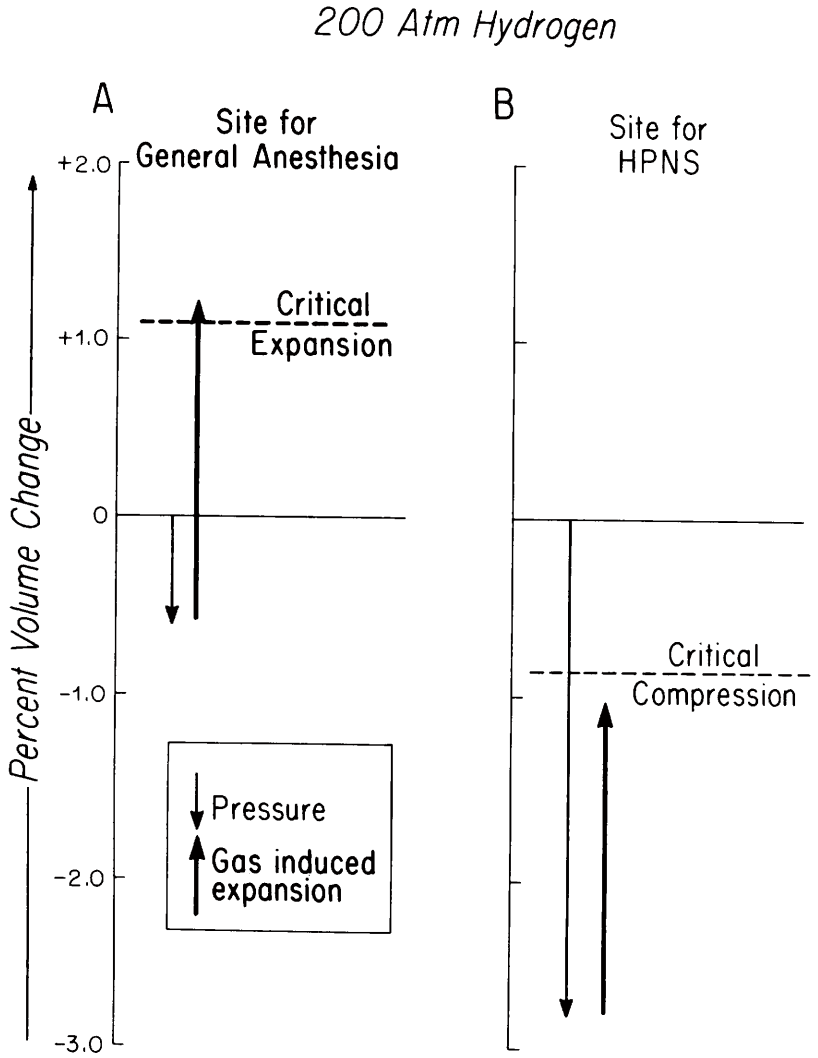

Fig. 6. *The predictions of the critical volume hypothesis for mice exposed to 200 atmospheres of hydrogen. A: The site for general anesthesia is compressed 0.06% by 200 atmospheres but the hydrogen dissolving at this partial pressure causes and expansion of 1.72%. The net volume change is thus +1.12%, which just exceeds the expansion required to cause anesthesia (i.e., the critical volume). B: The site for HPNS is more compressible than that for general anesthesia and is compressed 2.78%, but it has roughly the same solubility properties so is also expanded by 1.72%. The net effect is a compression of 1.06%, which just exceeds the critical decrease in volume required to cause HPNS. [For details see (10,11).] Benzene was used to stimulate the solubility of both sites.*

An important corollary of this discussion is that the use of hydrogen as a gas is neither more nor less *pharmacologically advantageous* than the equivalent mixtures of helium and nitrogen (trimix). There may well be other advantages in respiratory properties, avoiding decompression, problems with mixtures, cost, and so on, but the fundamental limitations of inert gas narcosis and HPNS remain. Hydrogen is probably the gas of choice when a single gas is required, but its pharmacology does not differ from the other gases. In all cases there will be a limiting pressure beyond which it will not be possible to proceed without encountering both inert gas narcosis and HPNS simultaneously (9,11).

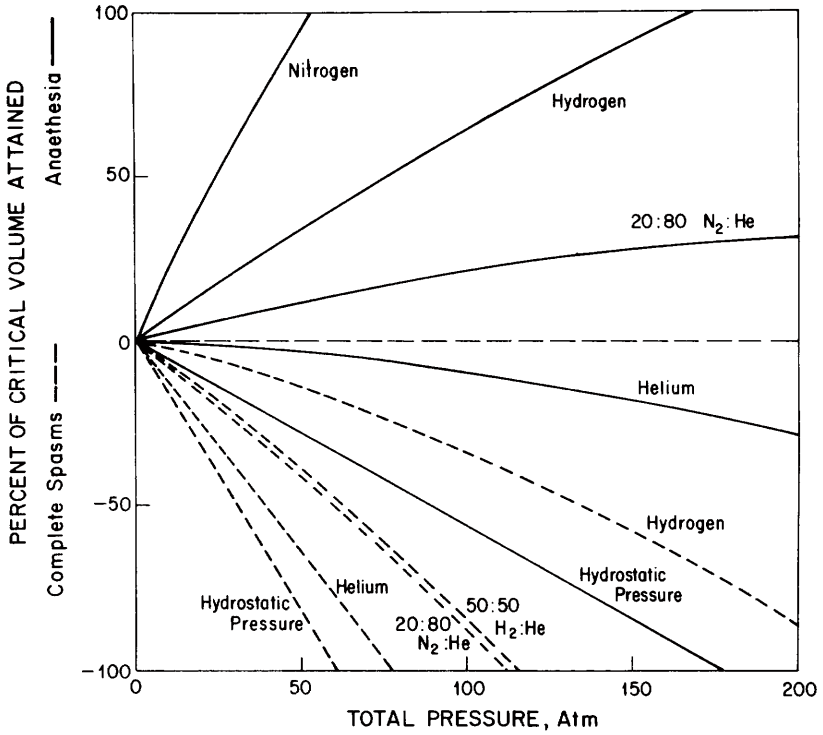

Fig.7. The ability of some gases and their mixtures to cause either general anesthesia (solid lines) or complete spasms (broken lines) has been calculated (11) with the corrections described previously (8,9). The expansion has been normalized to a percentage of the respective critical volumes. Parameters for the calculations have been given (10). Reproduced from (11) with permission.

SOME SPECIFIC PREDICTIONS

Theoretical calculations of the behavior of hydrogen are subject to large errors in the predicted pressure of anesthesia and the HPNS because the critical volume is achieved as the balance of two large opposing effects, as discussed above. Within these limits, however, the behavior of a number of gases and mixtures has been characterized in Fig. 7, in which the net volume change as a percentage of the critical volume for anesthesia and complete spasms (the earliest manifestation of HPNS in mice that is easily quantifiable) have been calculated as a function of pressure. The

results are in general agreement with the small animal data summarized above. The relative potency for causing HPNS is, in descending order, hydrostatic pressure, helium, neon (not shown for clarity), and hydrogen. The model also shows that the addition of two and a half times (in percentage terms) more hydrogen than nitrogen to helium produces equivalent mixtures for the postponement of complete spasms. So, one would predict that since 5-10% (by volume) nitrogen in helium is a useful mixture for the deepest human dive, 12.5-25% (by volume) hydrogen volume would also be beneficial. As more data for hydrogen gas narcosis in man becomes available these predictions could be improved. The range of mixtures that would avoid both narcosis and HPNS becomes smaller as pressure increases (9,11). Much larger percentages would be acceptable at lower depths. The advantage of hydrogen-helium mixtures would be a probable further reduction in flammability relative to undiluted hydrogen and a reduction in respiratory load relative to helium-nitrogen mixtures. We emphasize finally that the anti-HPNS efficacy of hydrogen would be no different from that of nitrogen; it is simply less potent, thereby allowing a greater dilution of helium. Thus the ultimate attainable depth will not be altered unless respiratory load proves limiting in practice.

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HYDROGEN NARCOSIS IN MAN

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Until 1983 no one had ever been in a position to observe H_2 narcosis in human beings because the H_2 partial pressure of the diving gas breathed by Zetterström, Edel, Fife, Delauze, and Bargiarelli was not high enough for the psychotropic effect of the H_2 to be perceptible. Brauer's research on mice, however, demonstrated that H_2 did have a narcotic effect on mammals.

OBSERVATIONS

In November 1983 our Hydra IV experiment consisted of heliox saturation with stops at 120, 180, 240, and 300 and, on ascent, at 150 msw, during which 6 subjects (3 professional divers, 1 engineer and 2 physicians) breathed various H_2 mixtures in the dry (30 min) under a Plexiglass dome and in the water (40 min). (See our report, EUBS Congress, 1984).

The first, very slight symptoms of narcosis became perceptible at 120 msw, with a (P_{H2} = 12.7 bar), to 2 of the 6 divers. At 180 msw (P_{H2} = 18.6 bar) 2 divers had insignificant signs of narcosis and the other 4 more or less definite symptoms. At 240 msw (P_{H2} = 24.5 bar) the picture of H_2 narcosis becomes clear and more or less complete, depending on individual variations. At 300 msw with the PH_2 reduced to 20.75 bar trimix with H_2 74%, He 24%, O_2 2%), the average degree of narcosis dropped noticeably in all the divers.

During the ascent, at 150 msw, with a P_{H2} of 15.7 bar, the 3 professional divers exposed for 2, 4, and 6 h, respectively, felt absolutely no difference between hydrox and heliox.

PICTURE OF SYMPTOMS

If we refer to the self-observation reports of the divers at the depth and PH_2 (240 msw - P_{H2} = 24.5 bar) at which the psychotropic effect of hydrogen manifested itself the most fully, we can say that hydrogen narcosis is characterized chiefly by sensory and somesthetic hallucinations which are accentuated by relative sensory rest of RSR and affect mood more than intellect.

Substantial variability occurred in these disorders among the different subjects, as can be seen in Table 1.

NARCOSIS SCALE

The degree of narcosis for which we have established a scale depends on the intensity, the associations, and particularly on the impact on behavior of the H_2 effect. We have tried to make the scale as simple as possible, and not descriptive (unlike Edmonds' N_2 narcosis scale) but pragmatic. It has 4 degrees which can be subdivided.

TABLE 1

Divers: 6. Depth: 240 msw. P_{H2}: 24.5 bar.

	Divers affected (out of 6)
1. Sensory hallucinations	
Gustative: taste of metal or chlorine	2
Auditory: sounds more intense, sometimes indistinct	3
Visual: light, more vivid (dazzling), colors tending toward orange	3
Tactile: cutaneous hypoesthesia, ± diffused	4
Hyperesthesia of the fingers	1
2. Somesthetic hallucinations	
A. At exercise	
Diffused warm flushed feeling	3
Easy muscular effort, without fatigue	4
B. In RSR position	
Disorientation, vertigo (sometimes nausea)	3
Distortion or loss of sense of bodily arrangement	3
3. Intellect and behavior	
Mental dispersion, interior dialogue	2
Instability, agitation, or impairment of alertness	3
4. Affective components	
Impression of increased muscular strength and endurance	3
Variable euphoria or well-being	3
Displeasure, anxiety about losing self-control	2
5. Other effects	
Tendency toward drowsiness	2
Breathing lapses!	1

Grades of narcosis:

0 - Not perceptible
1 - Barely perceptible
2 - Slight and controllable
3 - Apparent and capable of affecting behavior
4 - Incapacitating, evolutive and dangerous

SPECIFIC CHARACTER OF HYDROGEN NARCOSIS

We observed that the difficulties experienced by the diver are more or less acceptable, depending on the intensity of the combined effects. With degrees 1 and 2 they tend to be associated with euphoria, whereas at degree 3, self-control requires a mental effort which is disturbing or even agonizing. Finally at degree 4 we observed the case of a diver who, at relative sensory rest went rapidly from euphoria to sleep with breathing lapses!

It seems clear that while H_2 narcosis is not very disturbing at degrees 1 and 2, it is compatible neither with normal activity nor with the safety of the diver at degrees 3 and 4.

The "hydrogen effect" differs from the "nitrogen effect." Except in the final phases of drowsiness and loss of consciousness (a stage fortunately precluded in experimental conditions and, a fortiori, in operating conditions) H_2 behaves like a hallucinogen, perceived with a certain degree of lucidity and having little effect on reasoning power.

Nitrogen narcosis affects the intellect more and at the same time intensifies affectivity. We might say the "rapture of the deep" is comparable to alcoholic intoxication, whereas H_2 hallucinosis seems to be closer to the effects produced by LSD or mescaline (Annex 1).

The ratio of narcotic potency of the two gases appears to be quantified by virtue of concordant approximations substantiated by psychometry. Using our scale of degrees of narcosis as a reference, we estimate the narcotic potency of H_2 to be around 25% of the N.P. of N_2.

CONCLUSIONS

Hydrogen narcosis appears to be the primary deterrent to the use of pure hydrox for deep diving, for with this binary mix it would be hard to go beyond a depth of 160 msw.

But the "hydrogen effect" is neither absolute nor without usefulness, for two reasons:

1. As we shall demonstrate in our following paper, the hydrogen effect depends on the ambient pressure, which seems to act as an antagonist of narcotic potency;

2. The narcotic potency itself acts as an antagonist of the high pressure nervous syndromes, as is shown by our Hydra V experiment, the results of which we would like to present to you.

Gas narcosis characters:

NITROGEN (Edmonds et al.)	HYDROGEN (COMEX)
INCREASING MENTAL IMPAIRMENT	
with increasing depth, i.e., nitrogen partial pressure	with increasing H_2 partial pressure (different from depth)
INDIVIDUAL VARIATIONS	
marked	less marked in professional divers
DEVELOPMENT OF TOLERANCE	
noticeable	not evident up to now
NARCOSIS DEVELOPS WITHIN MINUTES OF REACHING	
the bottom	the maximum H_2 partial pressure and is not further progressive with time
RESIDUAL EFFECT	
No (?)	Yes ($\pm$)
RECOLLECTION	
very little and poor	copious and vivid
NUMERIC EVALUATION	
Martini Law	COMEX Law

DISCUSSION FOLLOWING PRESENTATIONS BY SMITH, MILLER, AND FRUCTUS

FIFE: I wonder if this diffused flushed feeling in the skin with hydrogen is due to vasodilation of the skin? Do you know the mechanism, Dr. Fructus?

FRUCTUS: No, this is a clinical and subjective impression.

LUNDGREN: It is fascinating to hear about this difference between the two gases in terms of the type of anesthesia they induce. I would like very much to hear any speculation as to why that would be. However I would also like to point to some similarities. These, to the best of my knowledge, came out only with the work of Dr. Adolfson who took some of us to 120 m on air. In some of these subjects both auditory and visual hallucinations were very vivid just as described in some of Dr. Fructus' work. Maybe one of the reasons that we haven't seen much of that in connection with nitrogen is that very few people have used sufficiently high pressures in laboratory studies.

SMITH: If there really was a fundamental difference in the narcosis between these gases this would have such enormous implications for theories of general anesthesia that the effect would really be quite profound. One has to wonder whether there isn't some HPNS mixed in with the narcosis at these high pressures. Until one has ruled out that explanation it is really hard to speculate further.

ÖRNHAGEN: We have had 3 subjects exposed to hydrox at 120 m, and we had the same story told to us. The narcosis was "different" from what they had experienced in air. We started to speculate a little on what this could be and we came to the conclusion that these divers were in a very new situation, an experimental dive, they had never experienced hydrogen before, and they showed some excitement in the face of this situation. After they had experienced narcosis and they both found that they could cope with the very light narcosis, they felt very much at ease and this might have influenced their interpretation. I mean, in our hydrogen dive a slight narcosis was the only thin causing them trouble while at pressure. Compressed air narcosis on the other hand comes with dense gas and maybe other problems that make the situation less pleasant.

BRAUER: It seems to me that the striking phenomenon before us is that both in your group, Hans, and your group, René, the divers themselves commented on the profound difference of the narcosis they perceived in hydrogen as against the nitrogen narcosis they were familiar with. Now one of the possibilities is clearly the one that you have mentioned, that nitrogen narcosis is something that most divers experience when they are very wet, have gone deeper than they ought to have, and there are all kinds of reasons for perceiving that they are in a threatening situation. So far as I know, and perhaps René, you may have something to add to this, we do not have what I think would be the only valid control experiment for what has been seen in these test dives: Namely, the experience of nitrogen narcosis using N_2 partial pressures isonarcotic with the hydrogen at the same high pressures attained in Hydra IV, and perhaps V, so that we may see the effect, if any, of HPNS effects overlying the nitrogen narcosis in the same kind of non-

threatening chamber environment. Some such experience may of course have been gained in the Duke Atlantis dives, but I am not sure whether we could compare those.

FRUCTUS: In the Atlantis experiments nitrogen concentrations weren't high enough to produce narcosis. We likewise didn't see any sufficient degrees of narcosis in our own trimix dives. Perhaps Dr. Youngblood may have something to add to that. He has been studying this.

YOUNGBLOOD: There is an observation that was not reported. Way back in the early rapid compression trimix dives at Duke we did a 1000-ft dive at a rapid compression rate (33 min), and compression HPNS was very marked. The atmosphere contained in excess of 10% nitrogen. Although the psychometric tests did not show it and the published papers failed to report it, I was on the dive, and at least 1 of the 4 divers reported to me later that he experienced hallucinations very similar to those Dr. Fructus mentioned. An interesting aside in this particular diver, again known to me only later, was that he was one who frequently used marijuana. This makes one wonder about these sensations: Could it be that one conditions oneself for different types of expression of what are perhaps the same pharmacological effects, giving different subjective interpretations to them?

EDEL: I know it is disturbing to think that two different types of narcosis should be manifested by two gases, but I thought that maybe I could muddy the waters a little further by speaking of three different types of narcosis. I have never had a hydrogen narcosis, but in one set of experiments we were making deep dives on helium and trying to make the shift to nitrogen as deep as we could to accelerate the decompression. I became very familiar with what I used to refer to as the "narcotic shock" of the shift from helium to the nitrogen narcotic effect. On one occasion I shifted to argon at a shallower lever, and in my recollections the effects of this were quite different from the nitrogen narcosis. In the nitrogen narcosis I was usually quite uncommunicative, while in the argon narcosis I couldn't be stopped from talking. Again, in the case of nitrogen narcosis, when I was tired from working long I really didn't notice any effect after the shift to the gas. In the case of the argon, before shifting I felt tremendous fatigue, as if I couldn't even lift my arm because of the workload, while after switching to the argon I could move in any direction and without any feeling of fatigue. I just wanted to throw that in to complicate things a bit further!

YOUNGBLOOD: One more observation, again one which we could not measure quantitatively. We had learned from the Atlantis series where the divers kept a log that on the trimix they had vivid dreams and nightmares. Perhaps these are merely a form of hallucination when less cortical control is exerted.

MILLER: It is well known that in behavioral studies it is very important to have exceedingly well-controlled experiments that would have to be done in a double blind fashion. The only diving experiments that may have been done like that were the ones that Lambertsen and colleagues tried, where they switched gases.

LUNDGREN: I would like to take this very brief moment to reemphasize what the chairman already said. It is probably extremely important to look for likenesses before we look for differences in these narcotic effects as long as we are to honor some idea of a common mechanism. In regard to what we have just heard about argon and nitrogen being different, one has to be concerned about dosage effects. In addition, I can think of more than a few people who would react very differently to different doses of alcohol, quite along the lines that Mr. Edel described, and yet it is obviously always the same stuff!

SMITH: If one looks at hyperexcitability caused by an anesthetic, and at what occurs under the conditions under which the diving experiments were done, one would conclude that they behaved in very different way. However, in very controlled experiments to look at the excitement caused by different anesthetics, one finds that it is in fact very reproducible and that the maximum effect occurs at roughly one-third the anesthetic dose. I would certainly endorse what Dr. Lundgren has said: It is only by controlled experiments that we can be certain that we are really dealing with fundamental differences. I think we could learn an awful lot about hydrogen narcosis and the mechanisms involved by studying a series of appropriate hydrogen-nitrogen-helium mixtures, because now we can match various properties other than the density, and the results could help up to discover how narcosis is affected by variations in the total pressure and in gas density.

HYDROGEN NARCOSIS IN MAN: PSYCHOMETRIC STUDIES

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Psychometric studies on hydrogen narcosis in man were carried out during three human experimental dives: Hydra IV, Hydrox A, and Hydra V. The characteristics of these dives are described in Table 1.

PSYCHOMETRIC TESTS

The psychometric tests used during these experiments were easy to use in a hyperbaric context and several of them had been used previously by Adolfson (1), Bennett and Blenkarn (2) for studying nitrogen narcosis, or by Bennett and Towse (3), Bennett et al. (4), and Lemaire (5) for studying HPNS.

Psychomotor Test

Manual dexterity (MD): The subject must insert 50 brass pegs in holes in a board as quickly as possible. The number of pegs inserted per minute is recorded.

Visual choice reaction time (VCRT): Reaction time measurement after light stimulations with choice in the response between 2 (2-VCRT) or 4(4-VCRT). The reaction time in milliseconds and the number of errors made are recorded.

Standing Steadiness: Recorded by means of a statometer, recorded during periods when eyes are open and closed.

Cognitive Tests

Multiplications test (M): The subject is asked to perform a maximum number of multiplications in 2 min. The number of multiplication solved in 2 min and the number of errors made are recorded.

Number similarities test (NS): The subject is asked to identify differences in series of numbers during a period of 1 min. The number of figures examined and the number of error made are recorded.

Paced auditory serial addition test (PASAT, a paced mental arithmetic test

involving a memory component): The subject is asked to add the last digit heard on a tape recorded to that previously heard. Thus, the 2nd digit is added mentally to the 1st, and the 3rd to the 2nd, and so on. The number of correct additions is calculated, and the number of omissions and the number of errors are recorded.

Number ordination test (NO): The subject is asked to arrange 9 digits in increasing order in as many random digit series as possible during 7 min. The number of series written per minute and the number of errors are recorded.

Mental and psychomotor promptness test (MPP): The subject is asked to write quickly on a sheet of paper letters or digits in squares determined by the instructions of the investigator recorded on a tape recorder. The number of squares filled up and the number of errors are noted.

TABLE 1
Characteristics of human Hydrogen dives

Dive	Hydra IV	Hydrox A	Hydra V
Date	November 1983	December 1983	May-June 1985
Place	COMEX, France	Swedish Defence Research Institute, Naval Medicine Division	COMEX, France
Depth	120-180-240-300-150 m	120 m	450 m
Gas	H_2/O_2 98/2 $H_2/He/O_2$ 74/24/2	H_2/O_2 98/2	$H_2/He/O_2$ 55/54/1
Number Subjects	6	3	6
Hydrox breathing protocol	Breathing hydrox under a dome after a switch	Breathing hydrox by a mask after a switch	Living on hydrox more than 2 days
Psycho-metric tests studied	Manual Dexterity (MD) Visual Choice Reaction Time (2-VCRT) Multiplications (M) Number Similarities (NS)	Visual Choice Reaction Time (4-VCRT) Paced Auditory Serial Addition Test (PASAT) Standing steadiness	Number Similar. Multiplications 4-VCRT 2-VCRT Manual Dexterity Number Ordination Mental and Phycho-motor Promptness

RESULTS

The results of the tests are expressed both as absolute scores and as the percentage of variation relative to the reference value which is the value of the test performed at the same depth in heliox (Hydra IV, Hydrox A) or the mean value of the two tests performed at 10 m in heliox (Hydra V).

Results of Hydra IV

The details of these results have been described at the Xth EUBS Congress in Marseilles in October 1984 (6). A summary of these results is shown in Table 2.

TABLE 2

Psychometrics during Hydra IV (6 subjects).
Variation of performance in percentage relative to the test performed on heliox at the same depth.

Gas Mixture	H_2-O_2	H_2-O_2	H_2-He-O_2	Air	Relative
$P_{Inert\ Gas}$ (Bar)	18.6	24.5	22.9	7.2	Narcotic Potency
Depth (M)	180	240	300	80	H_2/N_2
Manual Dexterity	+0.5%	-4.5%	-3.1%	-11.6%	0.11
Visual Choice Reaction Time	-10.3% (N=3)	-2.2%	+0.1%	-	-
Multiplications	-13.8%	-19.6%	-15.1%	-28.4%	0.21
Number	-4.4%	-6.4%	-8.7%	-12.6%	0.15

The conclusions were as Follows:

- The effects of H_2 were observed at 19 ATA and higher pressures in 2 of the psychometric tests; the multiplication and number similarities tests.
- The manual dexterity and visual choice reaction time tests were not significantly affected even with a P_{H_2} of 24.5 bar.
- The sensitivity to the H_2 effect appeared to be quite variable according to the individual subject.
- The manual dexterity test, the multiplications test, and the number similarities test showed greater deteriorations in air at 80 m than in Hydrox 98:2 at 240 m.

- The H_2 affects intellectual faculties (or cognitive processes) but less than N_2, which affects also the rapidity and precision of simple movement and the reaction time.

- H_2 and N_2 narcosis are not directly comparable but we can assess the narcotic potency of H_2 compared to N_2 for a given test (see Table 2). For the most sensitive test (multiplications) the narcotic potency has been calculated to 0.21 which is not very different from that mesaured by Brauer and Way (7) and Kent et al. (8).

- The safe limit for use of pure H_2 would probably be around 200 m-conditions similar to those of Hydra IV.

Results of Hydrox A

The details of these results have been described at the Xth EUBS Congress in Marseilles in October 1984 (1). As there were only 3 subjects and 2 tests run in this experimental dive, and the P_{H_2} was only 12.7 bar, the narcosis study of Hydrox A gave only preliminary results which were in accord with those of Hydra IV. A summary of the results is shown in Table 3.

The paced auditory serial addition test showed a tendency to deterioration in all 3 divers. This was pronounced (-78%) in one diver for one trial (this diver lost his power of concentration for a short while). The decrease of performance was due to an increase in the omissions rather than an increase in errors; the reduction in the number of correct answers on PASAT can be caused by a deteriorated memory alone or in combination with a slowing of the mental activity and a reduced power of concentration.

TABLE 3

Variation of Performance in Percentage Relative to the Test Performed at the same Depth Breathing Heliox (98/2) in Hydrox A (3 subjects)

Gas Mixture	H_2-O_2
P_{H_2} (bar)	12.7
Depth (m)	120
Visual Choice Reaction Time	No change
Paced Auditory Serial Addition Test	Tendency to Deterioration (-78%); -21%; -22%
Steadiness	No change (uncertain result due to experimental conditions)

Results of Hydra V

The Hydra V (May-June 1985) experiment was the first in which divers were saturated on a H_2-He-O_2 mixture (54:45:1) at a pressure of 46 ATA. Six divers participated in the experiment. Three of the divers were exposed to a switch of breathing gas without change of pressure (team A). The other 3 divers were decompressed to 200 m in the H_2 mixture (team B). H_2 narcosis was studied by clinical observation, subjective questionnaires filled in by the divers, and psychophysiological tests.

Dive Profile and Test Protocol

Fig. 1 shows the Hydra V dive profile with the schedule of the psychometric tests (NS, M, PASAT, 4-VCRT) given. Other psychometric tests (MD, 2-VCRT, NO, MPP) were also carried out during the dive but less frequently.

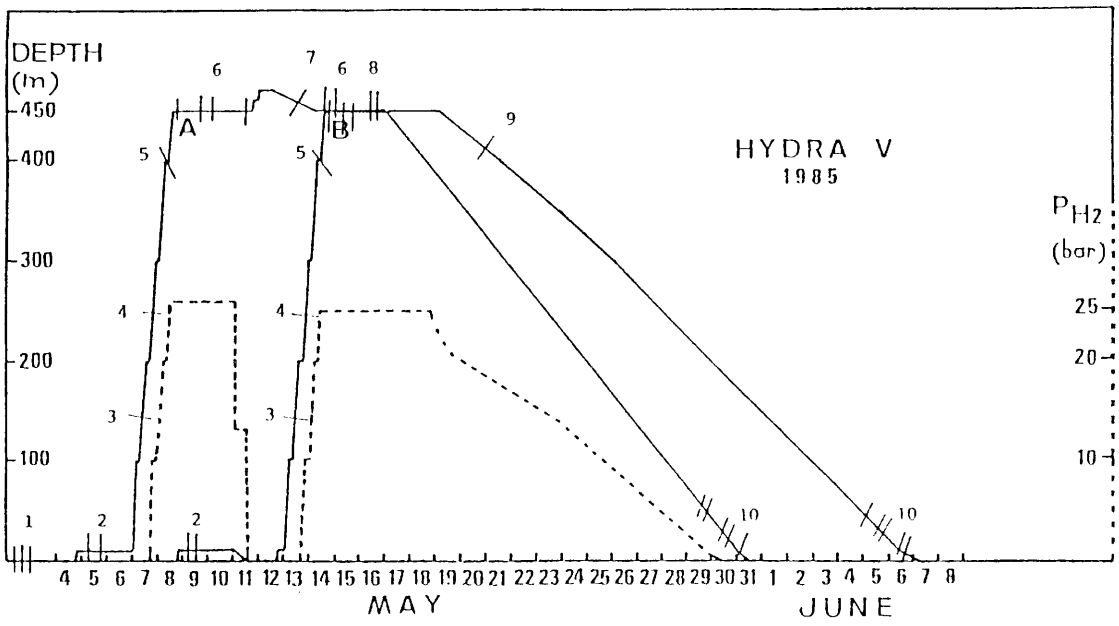

Fig. 1 Hydra V dive depth profile and hydrogen partial pressures. The occasions for the psychometric test are indicated:

- *1 learning tests at the surface;*
- *2 reference tests at 10 m;*
- *3,4,5 tests during compression at 142, 245, and 400 m;*
- *6 tests on hydrox at 450 m;*
- *7 tests on heliox at 450 m (team A);*
- *8 test on heliox, then on trimix with N_2 at 450 m with mask (team A), NS and M*
- *9 tests at the start of H_2 decompression at 420 m (team B);*
- *10 "postdive" control tests at the end of decompression.*

During the predive training period, dives to 66 m on nitrox 95:5 were carried out in a small chamber to obtain references for N_2 narcosis equivalent to 80 m on air (P_{N_2} = 7.2 bar). There were 3 test sessions in the chamber:

- at the surface before diving;
- during bottom time at 66 m;
- during the decompression stop at 15 m.

Results of Psychometric Tests

Fig. 2 (A-D) shows the mean performance of the 6 divers of Hydra V $\pm$ SD on 4 psychometric tests (NS, M, PASAT, 4-VCRT).

A: Performances on number similarities test expressed in number of figures examined in 1 min and number of errors.

B: Performances on multiplication test expressed in number of multiplications solved in 2 min and number of errors.

C: Performances on paced auditory serial addition test expressed in number of correct additions (*a*), number of omissions (*o*), and number of errors (*e*).

D: Performances on visual choice reaction time in milliseconds and number or errors.

Figure 2A. During the nitrox 95:5 dive to 66 m the mean deterioration for the divers, relative to the surface reference in the chamber, was 16% ($P<0.01$) but the reference value was higher than the average level of performance at the surface. The tests carried out during compression show noticeable deterioration from 400 m but did not become significant until the second test at 450 m ($P<0.02$). At the end of decompression, 4 of 5 tests show significantly higher performances than in the predive control situation.

Figure 2B. A deterioration averaging 16% is observed for this test during the nitrox 95:5 dive to 66 m ($P<0.05$), particularly clear for 4 of the 6 divers. The degree of deterioration appears less, however, since the reference test results in chamber were somewhat low. Diving hydrox saturation there was considerable individual variability from day to day as well as considerable variability among the individual subjects. But increasing the P_{H_2} at 400 and 450 m produced significant deterioration ($P<0.02$) only in one of the tests at 450 m.

At the end of decompression the 6 divers have recovered their performances with a more stable response to the test.

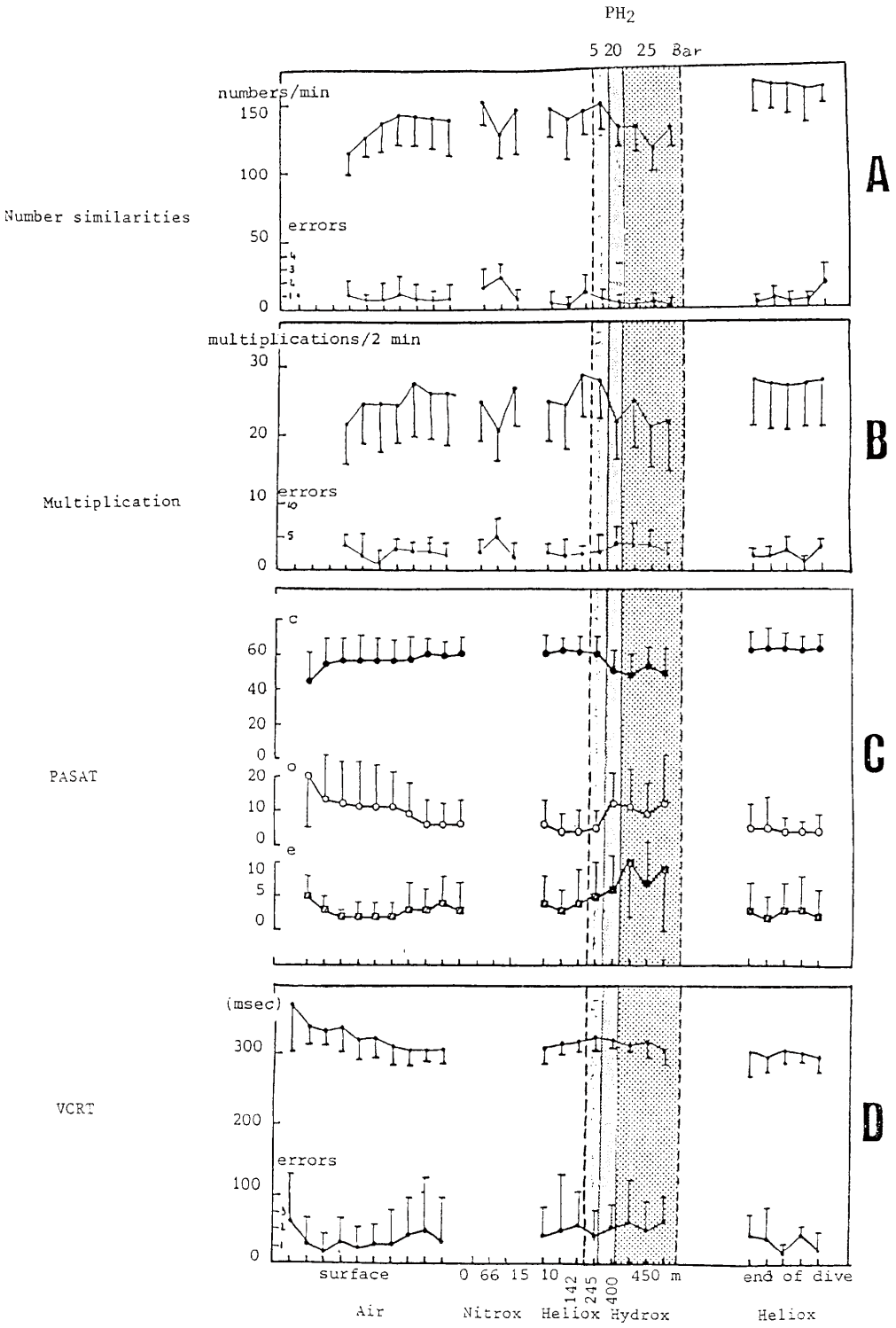

Fig. 2. Mean performance of the 6 divers of Hydra V ± SD in the 4 psychometric tests.

Figure 2C. We observed the following:

- good mastery of the test at surface;
- during compression, a gradual decline in performance, accentuated at 400 m (-17%, $P<0.01$) and then at 450 m on Hydrox (-23%. $P<0.01$) 24 h following arrival at 450 m the performance reduction was 21% ($P<0.05$);
- large individual variations and difference in the behavior of the subjects;
- at the end of decompression all 6 divers had completely returned to their earlier surface performances on the PASAT.

Figure 2D. We observed that:

- mastery of test on surface is gradual but clear;
- the slight variations observed thereafter during the dive are not significant (+ 2 to -1% at 450 m on hydrox). Remaining on on hydrox at 450 m did not significantly affect the VCRT results;
- at the end of decompression the performances were the same as for the predive surface tests.

Figure 3 gives the percentage of variation in performance for the 4 tests (NS, M, PASAT, 4-VCRT) as a function of the P_{H_2} of the breathing mixture compared to 10 m in heliox. The performance on the VCRT test is the least affected, and the PASAT the most affected. The performances on the NS and M tests are affected by the experimental conditions in about the same way. A summary of the results is given in Table 4.

The relative narcotic potency H_2/N_2 calculated for each cognitive test is on average 0.16, which is not very different from the results of Hydra IV.

On the basis of the H_2/N_2 narcotic potency ratio of 0.16 we estimate the narcosis experiences by the divers on hydrox at 450 m to be equivalent to that felt on air at 45 m. This narcosis was very slight and controllable.

Other psychometric tests carried out during Hydra V (MD, 2-VCRT, NO, MPP) have been used in previous experimental dives: Entex 5 (9), Entex 8 (10) and Entex 9 (10) in heliox or trimix at the same depth, 450 m. The results of these tests are shown in Table 5 and could be used to compare the heliox or trimix compression to a hydrox compression to 450 m with the same rate of compression (38 h).

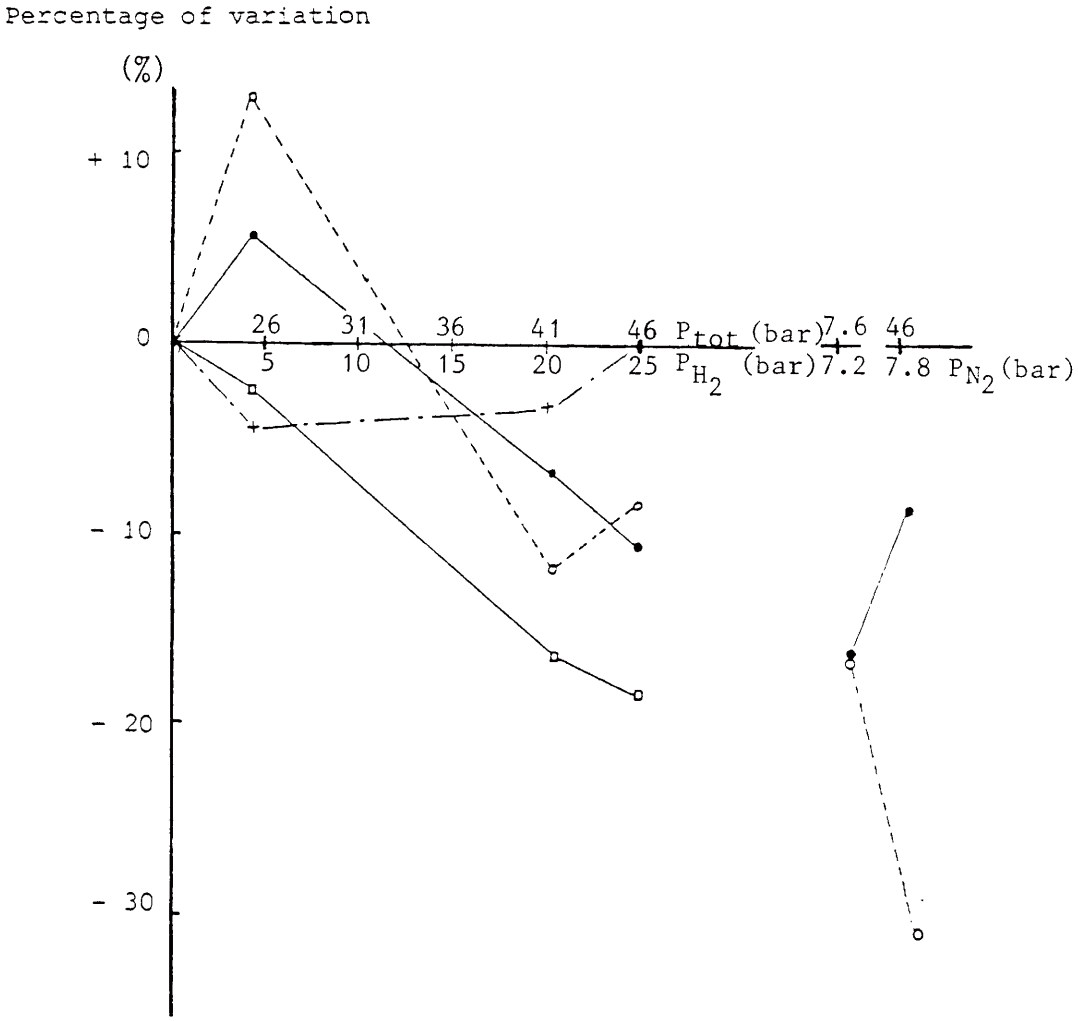

Fig. 3: Percentage of variation in performance for the 4 tests as function of the P_{H_2} of the breathing mixture compared to 10 m on heliox. For results obtained in N_2-containing atmospheres the performances are compared to the preceding test in non N_2 atmospheres. To the right, values obtained at low and high pressure 7.6 and 46 bar are indicated. The P_{N_2} were 7.2 and 7.8 bar, respectively.

• • *Number similarities test*

O=====O *Multiplications test*

□ □ *Paced auditory serial addition test*

\+ + *Visual choice reaction time*

TABLE 4

Variations of performance in percentage relative to the reference test (average of 2 tests at 10 m on heliox) from Hydra V (6 subjects).

Gas mixture	H_2-He-O_2	H_2-He-O_2	H_2-He-O_2	Relative narcotic potency	NITROX	
P_{H_2} (bar)	5	20	25		P_{N_2}	7.2	6.5
Depth (m)	245	400	450		H_2/N_2		66
Number Similarities	+6%	-5%	-10%	0.17	-16%	-
Multiplications	+15%	-10%	-8%	0.14	-16%	-
Paced Auditory Additional test	-3%	-17%	-19%	0.16	-	-29%
Visual choice reaction time	-4%	-3%	0%	-	-	-

In Hydra V the deteriorations of the MD and NO tests were less than in the Entex series. This shows that the compression in hydrox did affect the psychometric performances less than a heliox or trimix compression to 450 m. On the other hand the MPP test showed that there was a slight narcosis in hydrox.

DISCUSSION

It is rather difficult to interpret the results of these tests in view of the complex experimental conditions and the simultaneous influence of several different factors (compression, confinement, gas, etc.). It is also difficult to apply statistical methods to such a limited sample: 6, or even 3 divers, depending on the situation. The confinement, the test time, the length of time at maximum pressure, and the temperature are some factors that could have influenced the performance of the divers, but which can not be statistically tested in our study.

TABLE 5

Variation of performance in percentage relative to the reference test (average of 2 tests at 10 m on heliox) from Hydra V (6 subjects).

Gas mixture	H_2-He-O_2	H_2-He-O_2	H_2-O_2 or He-N_2-O_2
P_{H2} (bar)	25.5	25.5	0
Depth (m)	450 (arrival)	450 (24 h later)	450 (arrival)
Number of subjects	6	6	16
Name of dive	Hydra V	Hydra V	Entex 5,8,9
Manual dexterity	-5%	-4%	-10%
Visual choice Reaction time	-5%	+1%	- 7%
Number ordination	-3%	+1%	-15%
Psychomotor and Mental promptness	-20%	-14%	-

Rapid compression to a great depth is usually accompanied by a decrease in performance which is a part of the high pressure neurological syndrome (HPNS). The compression profile for this dive to 450 m was relatively slow and was used previously for:

- DRET 79/131 dive (11)
- Entex 5 dive (9)
- Entex 8 dive (10)
- Entex 9 dive (10)

Some psychometric tests which have been studied during three dives and Hydra V (MD, NO, VCRT) seem to show a better performance after the hydrox compression compared to the usually deteriorated performance observed after heliox or trimix compression.

It is known that helium has only little or no biological effect on the organism (12,13) and that H_2 has a certain narcotic potency (7,14). A narcosis more or less proportional to the partial pressure of H_2 was expected. Some of the tests we used for Hydra V (M,NS, PASAT, MPP) were chosen for their appropriateness for studying narcosis, and had been used previously by Adolfson (1). and Bennett and Blenkarn (2) for studying N_2

narcosis. The PASAT seemed to be the most sensitive of these tests (Fig. 3), but the NS also shows significant variations in 25 bar of H_2. The broad individual differences in the multiplications and number similarities test results could have been due to variations in the concentration of the subjects, which is corroborated by the divers' own statements.

The VCRT does not vary as a function of P_{H2} and P_{He}, which is in accordance with previous findings during exposures to H_2 (15,16). Kiessling and Maag (17) demonstrated that a VCRT with two choices deteriorated (i.e., the time increased) by 21% in 4 ATA of air. Unfortunately, in our study no measurements were made during the nitrox tests, but the same testing technique (4-choice VCRT) used in another laboratory (18) showed a significant time increase of 7.3% in air at 75 m depth.

It appears therefore that in so far as the cognitive psychometric tests and clinical observations are concerned, the divers experienced a "slight but controllable" narcosis at 450 m on hydrox 55:45:1 due to the action of the P_{H2} of 25.5 bar which was much lower than the narcosis observed at 240 m under a P_{H2} = 24.5 bar during Hydra IV.

CONCLUSION

Psychometric studies during human hydrox dives, Hydra IV (16), Hydrox A (Örnhagen, 1984) and Hydra V (COMEX, 1985, unpublished), allowed us to make some quantification of the H_2 narcosis, some differentiation in the effects of H_2 compared to N_2, and some evaluation of the narcosis level for a given breathing mixture.

The H_2 narcosis for an identical partial pressure is about one-fifth of the N_2 narcosis. H_2 affects the cognitive processes more than the psychomotor faculties. The narcosis level observed at 450 m, with a mixture composed of 55% H_2, 45% He, and 1% O_2, was found to be comparable to the narcosis level observed on air at 45 m.

Some speculations could be made about the pressure reversal effect of narcosis, but our results at 240 m with a P_{H2} = 24.5 bar and at 450 m with a P_{H2} of 24.5 bar are insufficient to draw any conclusions.

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DISCUSSION FOLLOWING PRESENTATION BY CARLIOZ

SMITH: Could I comment on Mme. Carlioz's interesting results on the hydrogen narcosis? I think it is too much to expect that we should get a constant potency ratio for the nitrogen and hydrogen, because at the pressures involved there is some pressure reversal of the narcosis. In other words, in Dr. Fructus' example there are two exposures, both involving 25 atm of hydrogen, one case showing narcosis and the other, nothing. That may simply arise because one was at 240 m and the other at 450 m, so there was a difference in the degree of pressure reversal. I don't think you should expect those pressures to be without effect and we must allow for that in the calculation.

CARLIOZ: During an experiment, the narcotic potency of an inert gas that you are measuring takes into account the pressure at which the experiment is carried out, and then the effect of the pressure. This narcotic potency measured is not the intrinsic narcotic potency of the gas but the relative net narcotic potency. This is described in a paper of Brauer et al. (1982).

BRAUER: In addition, of course, pressure drops out if you are comparing both at the same pressure as you would do when comparing $He\text{-}H_2\text{-}O_2$ and $He\text{-}N_2\text{-}O_2$, e.g., some of the Atlantis experiences with the Hydra V ones.

GIRY: If you look back at the plots, you will see that they were trying to find the same narcotic ratio for different tests measured under the same conditions to try to answer the question: Is any test equivalent as we go up on narcotic potency of the gas? They didn't try to get the exact figures for comparison with the pressure.

SMITH: In other words, that ratio would depend on the pressure.

BRAUER: I think the remarkable thing is that they came as close as they did. That's really the point, because with the psychometric tests--even if they are very carefully done as Dr. Carlioz's were--having the inherent variability they always show, by the time you calculate your ratios, those variations are quite enough to account for the differences that were seen even if everything had been the same.

SMITH: The question I am asking is: Should they be the same?

ÖRNHAGEN: Dr. Brauer has very well covered what I was planning to say, that is that these are psychometric tests. We have found that if you have a test where the subject is continuously asked to perform, you can get better, more stable, and more reproducible figures than if you leave the subject with a

test sheet for 2 min asking him to make as many multiplications or find as many numbers similar as possible. So before you draw any detailed conclusions or try to use elaborate equations I think you have to find a set of very good tests. Martine and I found in this study that, for example, multiplications and number similarities are less reproducible than PASAT, in which the subject is continuously paced. PASAT is a paced auditory serial addition test; we have a tape recording presenting a new figure from three to nine every second. The subject is asked to add the immediately previously given figure to the last given figure, respond verbally, memorize the previous figure, listen to a newer one, and then respond again. This means that the subject has to respond every 2 s with a sum of two digits. Doing it in that way, narcosis is easier to detect than if you just give him a sheet of paper as in multiplication tests, because then the voluntary action of suppressing narcosis could very well come into play and give a very pronounced variability. You can even have improvement at low partial pressures when you can easily suppress the narcosis. According to Fructus' scale, at a number 2 grade of narcosis it's very noticeable. But if you concentrate for a short period of time you can suppress this effect enough to make a good performance.

MILLER: That is a very important general point. When we are reading papers we should be putting more weight on certain tests than on others.

BRAUER: Well, you are really pulling out one error parameter by timing the subject. That is the key! Everybody who has observed their animals under light anesthesia knows that they slow down, and if they are thoughtful animals they can use that to correct their performance.

GIRY: I would like to speak of a problem encountered by some French scientists during the Hydra V dive. They got a very, very strange result; when during the cycle of a test the diver under hydrox had to choose between going fast and "no mistake," there was not always a choice. They didn't care about the exactitude of their answer. I think other people experimenting on hydrogen have got the same result, and that is an important point from an operational point of view.

SMITH: Everything we have seen today tends to fit in with what you might have expected. Roughly 50:50 hydrogen:helium would be very advantageous in terms of its lack of narcotic or HPNS effects. But a bit of evidence comes from Duke that doesn't fit in with this, and that is the significant euphoria that was observed at high levels of nitrogen up to 20% in the trimix diving. Now one wouldn't have expected that, and I wonder if that is an artifact related to the high compression rates used. In slower trimix diving we might find that 25% nitrogen:helium mixture would in fact be optimal. This would be consistent with the results we have heard today on the 50:50 hydrogen:helium mixture. Maybe then a picture would emerge and it would all come together. Is that a possibility?

BRAUER: I might have a point to add to that from animal observations. We have explored the effect of admitting the nitrogen in trimix experiments at various times during compression. The details of that work do not really affect us here--they match and amplify some of the things that Rostain has

done in the past. While doing that, however, we encountered a phenomenon that we termed the "student beer party stage"--and I think the term is descriptive enough. You have bunch of mice who are pounding on the window asking for more beer, or rather more nitrogen and generally looking terribly excited. This phenomenon characteristically comes on when you introduce sizeable amounts of nitrogen when the animals are at high pressures. Curiously enough, an analysis of the relation between the total pressures and the N_2 partial pressures at which this excitement stage is manifested suggests that pressure and inert gas effects act synergistically and not antagonistically to one another. I think this phenomenon of euphoria associated with anesthesia at high pressure needs more work, and that quite possibly it holds the key to our earlier discussion of qualitative differences between anesthesias as experienced by our divers.

ÖRNHAGEN: Returning to the question of euphoria, I have a slide showing two divers during the Hydra V dive. As I mentioned before they can perform well, and their performance on tests was very good when they were asked to perform. If you left them in the chamber undisturbed they were quite happy and felt very good. The slide shows those two divers trying to connect their EEG leads and asking for "Contact, do you read me?" That, I think shows very well the situation. There is narcosis but they can handle it, and if they are asked to perform they do well, as shown on tests.

MILLER: It seems to me that the hydrogen trimix school is using more narcotic mixtures than the nitrogen trimix school. During the early experiences at Duke with 10% nitrogen, narcosis occurred and the nitrogen was then cut by a factor of two.

YOUNGBLOOD: No, they started higher than that. It was 18% on the first dive and I was one of the drunken-mice inmates. For one thing it was a very rapid compression and it was very hot, 140° F, during the initial phase. Everyone in there suppressed their narcosis and performed their type of task. But this represents one of the dangers that Dr. Brauer mentioned earlier. There were only 4 of us on that dive, and only 3 taking the psychometric tests. Those decisions, of saying that was too much, were based on 3 subjects on a single dive, and all conclusions thereafter were taken from that point.

EDEL: I was just wondering if there were other considerations in the choice of the mixture. In the case of the nitrogen trimix you lean a trifle toward the HPNS whereas in the hydrogen trimix you are perhaps leaning a bit toward the narcotic end. I just wondered if both might not have the same reason, namely, that in both cases you are going toward the lower breathing resistance.

BRAUER: It seems to me some of the surprise and uncertainty expressed here with regard to pressure effects on depth of narcosis reflects little more than the traditional reluctance of doctors and man-oriented physiologists to pay attention to perfectly available results of animal experiments. The fact of the matter is that on the basis of data that are published in the literature, when I came to Hydra V I could say: Look, you are 3 or 4% too high on your hydrogen, I bet you will see narcosis. The published data

almost perfectly match the actual quantitative results of the human studies on both Hydra IV and Hydra V, always provided you take into account the effect of pressure. To do this you must avoid tying together pressure effects and pharmacologic effects as one big package, and separate them as we did in our multinational review of the interactions of these stress factors (Brauer, Hogan, Hugon, MacDonald, Miller, 1982). They can then be added linearly to match actual total pressures and actual partial pressures of each component of the atmosphere, and the predictions you can make, at least in the case of anesthesia, have proven to be very good. By the same token, as I shall show in the next session, the predictions that one can make for the HPNS are very poor because of species differences and because of nonlinear relations. Quantitative predictions for human HPNS effects on the basis of animal data have uncertainties of several hundred percent attached to them, and therefore are useless operationally. The qualitative differences in the observed narcosis also were unexpected, although in retrospect in our "animated" mice we already may have some data on interaction of pressure and narcosis with respect to euphoria that might have prepared us for them.

ÖRNHAGEN: Edel's comment is exactly what I was going to say. There are other reasons for putting the hydrogen in. I would say that in these experimental dives it was fortunate that we had some narcosis because without detectable narcosis we would not have reached one of our goals. Now we know exactly the point from which we can work down.

MILLER: I think I agree with Brauer that the anesthesia predictions are more reliable than the HPNS ones. You are probably much better off if you try to sail the ship near the edge of something, and you going to make better predictions about the edge where narcosis is than about the edge where HPNS is. Furthermore, your diver is probably familiar with narcosis and, of course, Edel's point about respiratory resistance is also pertinent here.

FRUCTUS (translated from tape): I would like to comment again upon the qualitative differences between nitrogen narcosis and hydrogen narcosis. Indeed, they probably are very different. All twelve divers who experienced both of them reported that they subjectively are. Some of them agree that a good description of nitrogen narcosis and hydrogen narcosis could be the following: With hydrogen one feels like someone driving a car whose steering doesn't respond anymore, who realizes it, and therefore stops. With nitrogen, he realized it as well, but keeps going because the idea of stopping just doesn't enter his head.

SECTION III
Interaction With the High Pressure Neurologic Syndrome

INTERACTION OF HYDROGEN WITH THE HIGH PRESSURE NEUROLOGIC SYNDROME

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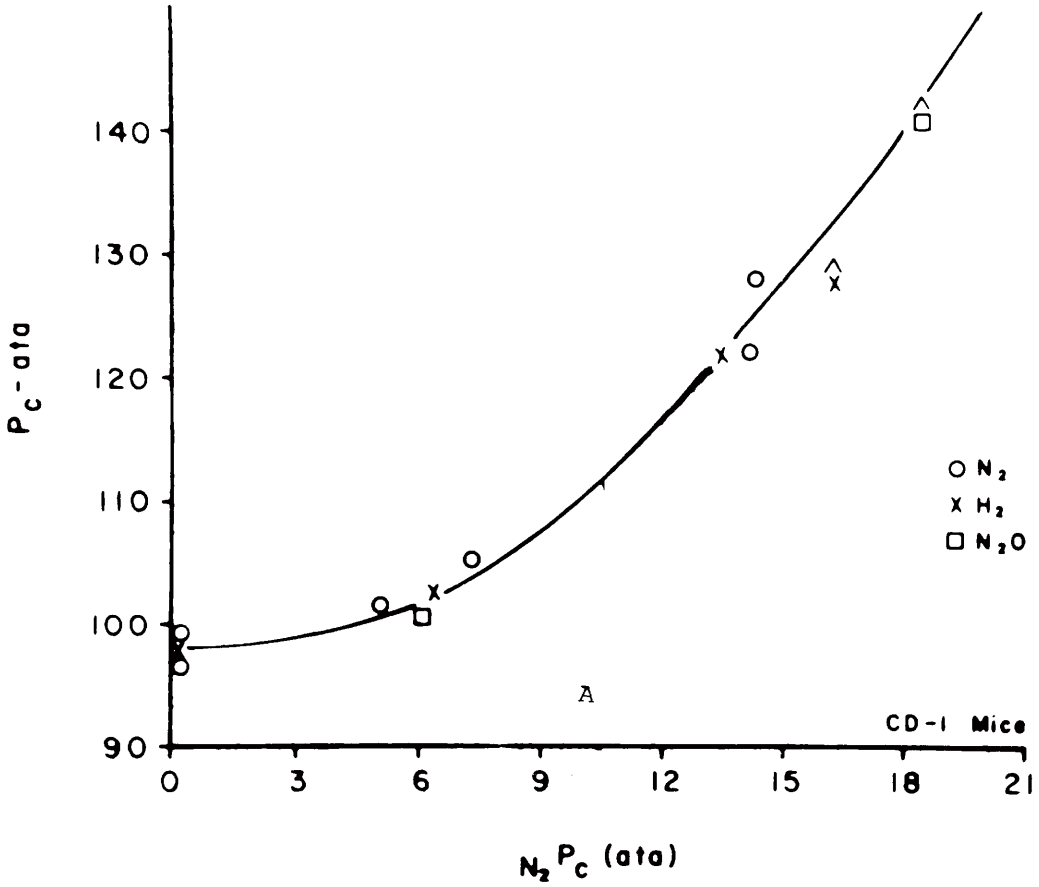
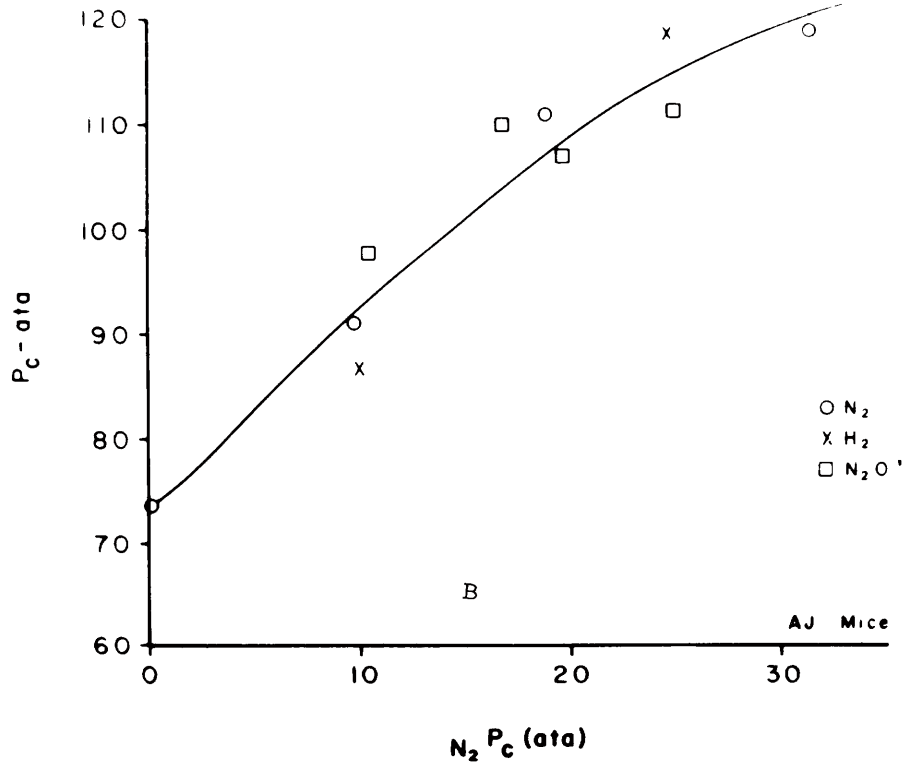
The very first report recognizing the high pressure neurologic syndrome (HPNS) as such was based on a comparison of the pressures giving rise to high pressure convulsions in mice and monkeys subjected to compression in He and in H_2-based atmospheres: Fewer animals of those exposed in H_2 atmospheres underwent convulsions than was the case with He, and the convulsion threshold pressures for these convulsions were higher (1). Coupled with the demonstration that H_2 is indeed a much more potent anesthetic than He (2), these observations put to rest the mistaken concept of "helium narcosis" as a basis of the tremors and seizures (3) and on the one hand, and on the other suggest the possibility that narcotically active gases like H_2 might provide a measure of protection against such high pressure convulsions. Subsequent work formally established this thesis (4,5). Table 1 shows data for two primates and two highly inbred mouse strains. For all of these the pressures required to elicit high pressure seizures in hydrox are higher than those for the same species compressed in heliox, the differences being well secured statistically. At the same time, Table 1 indicates that the ranges of individual variability of HPNS convulsion thresholds in all of these species are such that reliable conclusions can only be drawn from populations of adequate size and from experiments in which all animals are subjected to rigidly identical compression conditions, differing only in the one parameter being tested, i.e., in the present case, the effect of one of the metabolically inert gas constituents of the compression atmospheres.

More precise quantification of these effects is made difficult by the fact that, in general, the relations between convulsion threshold pressures and partial pressures of the narcotic component of the atmosphere at the time of convulsions are not linear (Fig. 1), differing in this respect from what appears to hold to a good degree of approximation for the phenomenon of pressure reversal of anesthesia (6). The most practicable approach to resolving this difficulty makes use of the observation that, at least in the two mouse strains where the most complete data are on hand, the shapes of the respective curves relating convulsion threshold pressures with partial pressures of narcotic gas appear to be the same for H_2, N_2, and nitrous oxide, gases that differ in narcotic potency by more than two orders of magnitude (2). For each strain, superposition of the curves for the several gases can be obtained by appropriate adjustment of the scales for the partial pressures of these gases at seizure onset, and th4e ratios of the scaling factors permit comparison of the relative potencies of the three gases as antagonists against high pressure convulsions.

A similar scaling tactic can be employed in the case of the squirrel monkey where, however, only a single data point is available for H_2, the convulsion threshold pressure for 99.5% H_2 [(5) and Brauer RW, Hinson WM, unpublished data]. The conformity of the dose response curves of three gases of such widely different properties to a common shape for each of the





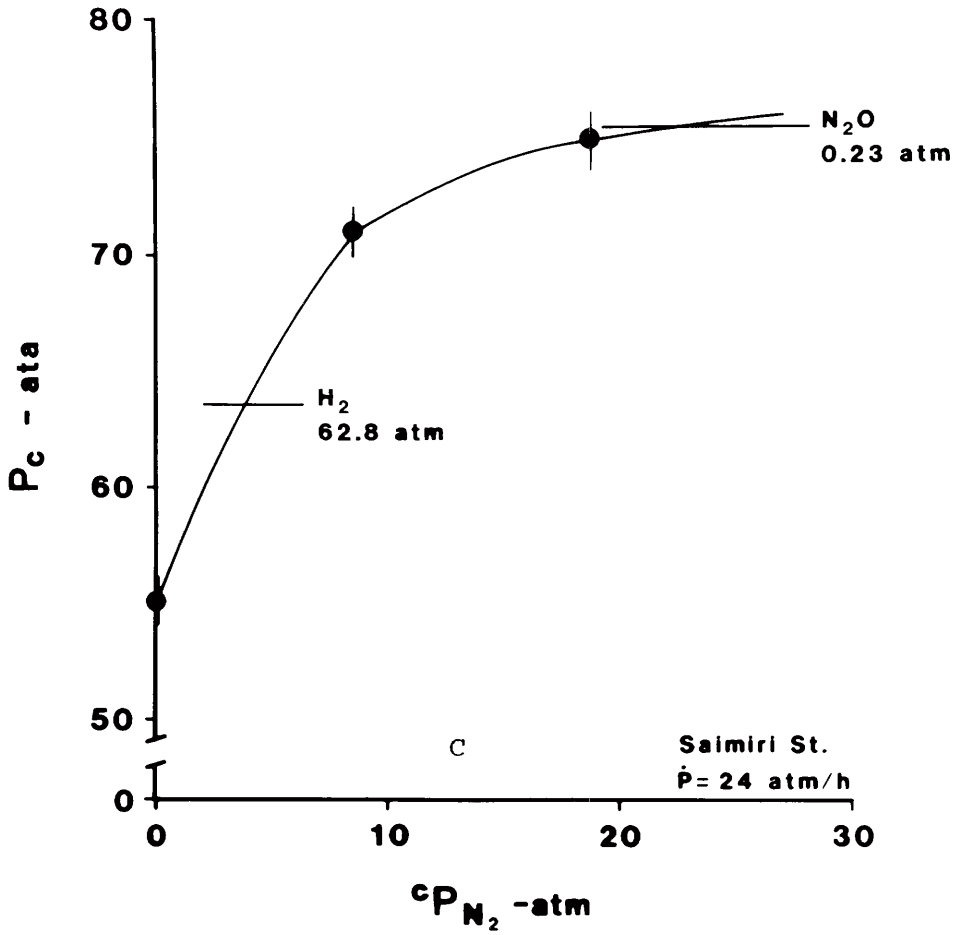


Fig. 1. Anticonvulsant effects of H_2, N_2, N_2O against type I HPNS convulsions. Abscissa - partial pressure of N_2 at seizure onset. Equivalent values for other gas scaled as in (6) to assure best fit. A. Results for CD-1 mice; B. Results for AJ mice; C. Results for squirrel monkey, Saimiri sciureus.

two mouse strains, despite the fact that the two curves are inflected in opposite directions (Fig. 1 *A* and *B*), makes it plausible to hypothesize that the actual anticonvulsant potency for each of the gases remains constant throughout the range tested for each of the models explores. This procedure therefore throws the entire burden of nonlinearity of the dose response curves of Fig. 1 to the charge of the convulsion-eliciting potency of hydrostatic pressure, which is assumed to vary with the concentration of the narcotic component of the compression atmosphere or more likely to vary in a nonlinear fashion with the absolute pressure attained at seizure onset, as illustrated for the case of the squirrel monkey in Fig. 2 (derived from Fig. 1 *C*).

On the basis of these considerations, then, one can estimate relative anticonvulsant potencies for these three gases for each of the three animal models for which adequate data are available. Table 2 shows these results, calculated taking the anticonvulsant effect of N_2 as the reference. Focusing on H_2 (Table 2, line 2), it is evident that the results reveal

TABLE 1

ANTICONVULSANT EFFECT (HPNS TYPE 1 SEIZURES) OF H_2

	P_c (in ATA) under: He/O_2	H_2/O_2
Macaca mulatta+		
P_c - EEG Seizure	57/7±4.1	(>)74.9±5.1
	t = 2.6, d.f. = 15, 0.025> P >0.01	
Saimiri sciureus+		
P_T	34.5±1.7	37.1±2.1
	t = 1.0, d.f. = 31, *P* > 0.4	
I_{P_c}	61.5±1.8	68.7±2.8
	t = 2.3, d.f. = 31. 0.05> *P* >0.025	
Mus musculus CD-1*		
I_{P_c}	91.4±2.3	(>)145±3.0
	t = 5.2, d.f. = 22, *P* <0.001	
Mus musculus AJ*		
I_{P_c}	73.5±3.0	(>)120±4.2
	t = 3.1, d.f. = 22,	*P* = 0.005

large and nonpredictable differences in anticonvulsant potency from one animal model to the next and are quite unrelated to species specific narcotic potency. Fig. 3 shows these results graphically, using a combination of physical properties of the gases that is in early correlated with narcotic potency as the independent variable (7). The resulting plots show the curve describing the squirrel monkey to be substantially steeper than the curves representing the two mouse strains, and all three probably somewhat steeper than the curve relating anesthetic potency to the same molecular property.

These data do not yet take into account differences in absolute HPNS susceptibility between these animal models. Because of the variability of the shape of the dose response curves, no single parameter can be expected to serve this purpose. We have computed four indices to serve this purpose as best possible: (a) The magnitude of ΔP_c, the increase in convulsion threshold pressure brought about by replacing He with H_2 in the compression atmosphere. (b) The same value expressed as the percentage increase in convulsion threshold pressure resulting from such substitution. The other two indices are based on the effect of atmospheres containing 25% H_2 in He. (c) The increase in convulsion threshold pressure per atmosphere H_2. (d) The same value recalculated as a percentage of the convulsion threshold pressure in He. These values are shown for the rhesus monkey, the squirrel monkey, and two inbred mouse strains (Table 3). Columns 2 and 3 of that

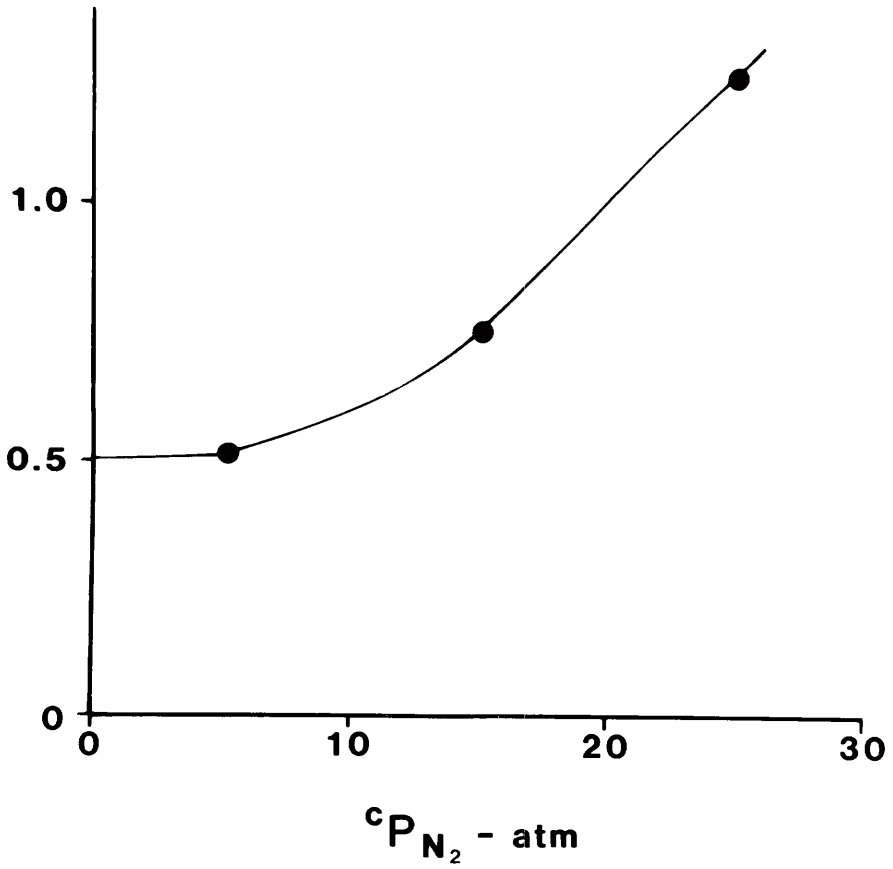


Fig. 2. Hypothetical variation of relative convulsant potency of pressure per se in the squirrel monkey as a function of N_2 concentration at seizure onset. assuming constant anticonvulsant potency -1.00 for N_2.

TABLE 2

$R_c^{N_2}$, RELATIVE INTRINSIC POTENCY, FOR ANTICONVULSANT EFFECT OF H_2, N_2, NO_2

	Saimiri Sciurcus	*Mus musculus* CD-1	AJ
H_2	0.11	0.23	0.45
N_2	1	1	1
N_2O	96	30	53

For mice $R_c^{N_2}$ is estimated to be [cF. (6)]: for He-O; for pressure as such, between -0.6 and -1.2.

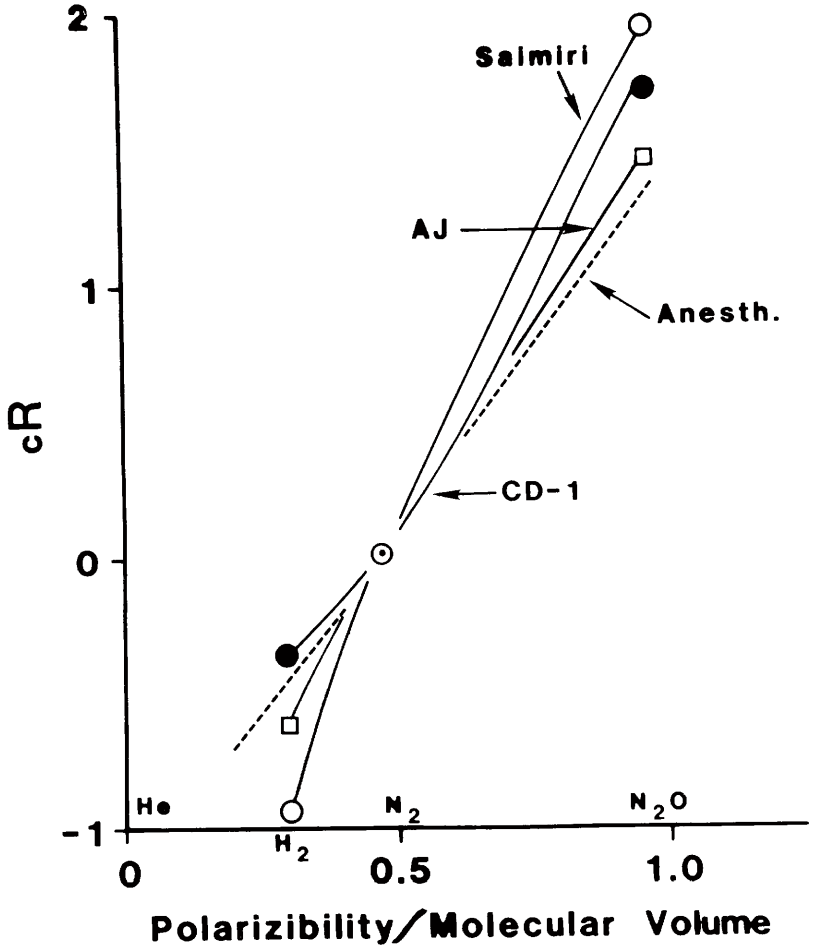


Fig. 3. Relative anticonvulsant potencies of H_2, N_2, N_2O in three animal models plotted against the ratio of polarizibility to molecular volume for each of the gases [cf. (7)] and compared to corresponding values for anesthetic potency [values from Table 2 and (6)].

table illustrate that the scope of the H_2 effect in the two mouse strains is very much larger than in either of the two primates, as well as the very substantial difference in H_2 susceptibility levels between the two monkey species. Column 4 and 5 reveal the importance of the shape of the dose-response curves by showing that at low concentrations of H_2 one of the two mouse models reveals only a low degree of anticonvulsant activity against HPNS seizures, but that this increases sharply as H_2 concentrations are increased to 30% or more.

Recapitulating the work report so far, the data allow us to conclude unequivocally that H_2 can be expected to have *some* antagonistic effect against HPNS manifestations in man. On the other hand, because of the large species differences, the magnitude of the effect to be anticipated can only be conjectured in broad limits: It is certain to be smaller, probably much

TABLE 3

EFFECTIVENESS OF H_2 AS ANTAGONIST AGAINST HPNS TYPE I SEIZURES IN DIFFERENT ANIMAL MODELS

	He vs. H_2		He vs. 25% H_2:75% He	
	ΔP_c	$\Delta P_c/P_c$	$\Delta P_c/P_{H_2}$	$(100\Delta P_c/P_{H_2})/P_c$
ANIMAL MODEL	atm			% atm
Macaca mulatta	17.2	0.30	----	----
Saimiri sciureus	7.3	0.12	0.20	0.36
Mus musculus				
CD-1	>53*	>0.58*	0.19 (0.45 and)	0.20 0.47 for 50% H_2)
AJ	>46.5*	>0.63*	0.68	0.91

*Values shown are for 50% H_2 in He.
xThe difference reflects the nonlinearity of the dose-response curves for CD-1 mice at low concentrations of narcotic gas.

smaller, than that for the same partial pressures of N_2. The scaling factor, in terms of ratio of the concentrations of N_2 to H_2 eliciting comparable effects, can be expected to fall somewhere between 0.1 and o.5. If HPNS seizures are taken as the end point, each atmosphere of H_2 in the chamber atmosphere can be expected to raise the threshold pressures by some value between 0.2 and 0.9 atm. Clearly all of these indications fall within ranges that are so wide that any operationally meaningful estimate of the effect of H_2 on severe HPNS symptoms in man can be established only on the basis of experiments involving human subjects.

Discussion so far has centered on the convulsion stage of the HPNS because little information is available regarding other manifestations of the HPNS. In the squirrel monkey both coarse and fine tremors have been seen under H_2 as well as He. As shown in Table, line 2, the mean pressure at which such tremors develop in the squirrel monkey in a H_2 atmosphere is somewhat higher than in a He atmosphere, the difference being proportionally as large as that for HPNS convulsions. Because of the variability of this end point from one animal to the next, however, this difference is devoid of statistical significance. Tremors in mice are a notoriously unsatisfactory end point and we do not believe that reliable data on this point are available at the moment [though some indications of this effect in mice are provided by data in (4)].

Rostain and Naquet (8,9) have reported extensive polygraphic studies on

a series of baboons subjected to compression in He and in H_2 atmospheres. Unfortunately, the eight experiments involving H_2 involved several different exposure schedules and, with the exception of two animals, were not carried to pressures high enough to establish high pressure convulsions. Thus, their data do not allow meaningful estimates of quantitative values such as mean convulsion threshold pressures for comparison with other species. They do however, provide important qualitative observations, especially at the preseizure stages of HPNS development in H_2-breathing baboons. In particular these authors describe in some detail changes in the EEG during the course of compression and note certain differences relative to similar compressions conducted in heliox. Increased theta wave activity and increase in microsleep and sleep activity were encountered at 30-35 atm pressures and disappeared during decompression, usually some time after passage to He. They describe marked monomorphism of the EEG and relatively increased frequency of stage 1 or 2 sleep for several hours of sojourn at 30 ATA of H_2. In deeper dives, muscular hypertonia was noted around 40-45 ATA. Brief bouts of paroxystic EEG discharges in the two animals tested at higher pressures put in a n appearance at 62-65.7 ata, and one full-blown EEG seizure was seen at 67.5 ata. These were concurrent with muscular jerks and, in the latter case, with a typical tonic-clonic seizure. Thus, qualitatively it would appear that in the baboon the picture of development of the severe stages of the HPNS in H_2 does not differ from that in He. Differences in the earlier stages, and in particular the marked somnolence observed, may reflect a peculiarity of HPNS development under H_2 in the baboon or, more likely it seems to us, may be attributed to the narcotic effects of H_2 at the high partial pressures employed in these experiments. It would be interesting to have control observations concerning development of EEG changes in the baboon during compression to equinarcotic levels in narcotically more potent atmospheres, such as in nitrox where the occurrence of HPNS-related changes could be excluded, permitting one to determine to what extent this latter hypothesis might account for the observed differences between the effects of He and of H_2 at pressures of 25 to 35 ATA in the baboon.

We should like, finally, to report briefly on recent findings concerning acclimation (or accommodation) to prolonged exposures to high pressures or to N_2--separately or simultaneously (10)[1] While not involving H_2 as the pharmacologically active gas we feel that these results do have a bearing on one particular aspect of recent human studies, namely, the phenomena observed during transfer of men from H_2-containing to H_2-free heliox.

The essential data are summarized in Fig. 4. The three graphs in the upper row (*A--C*) represent mean threshold pressures for HPNS type I convulsions in CD-1 mice, plotted as functions of acclimation time. Those of the lower row (*C--F*) represent mean partial pressures of N_2 inducing anesthesia

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[1]The contrary conclusion suggested in (10) with regard to anesthesia tolerance was based on incomplete data which have now been rectified by more numerous observations extending over larger acclimation times and to higher nitrogen concentrations.

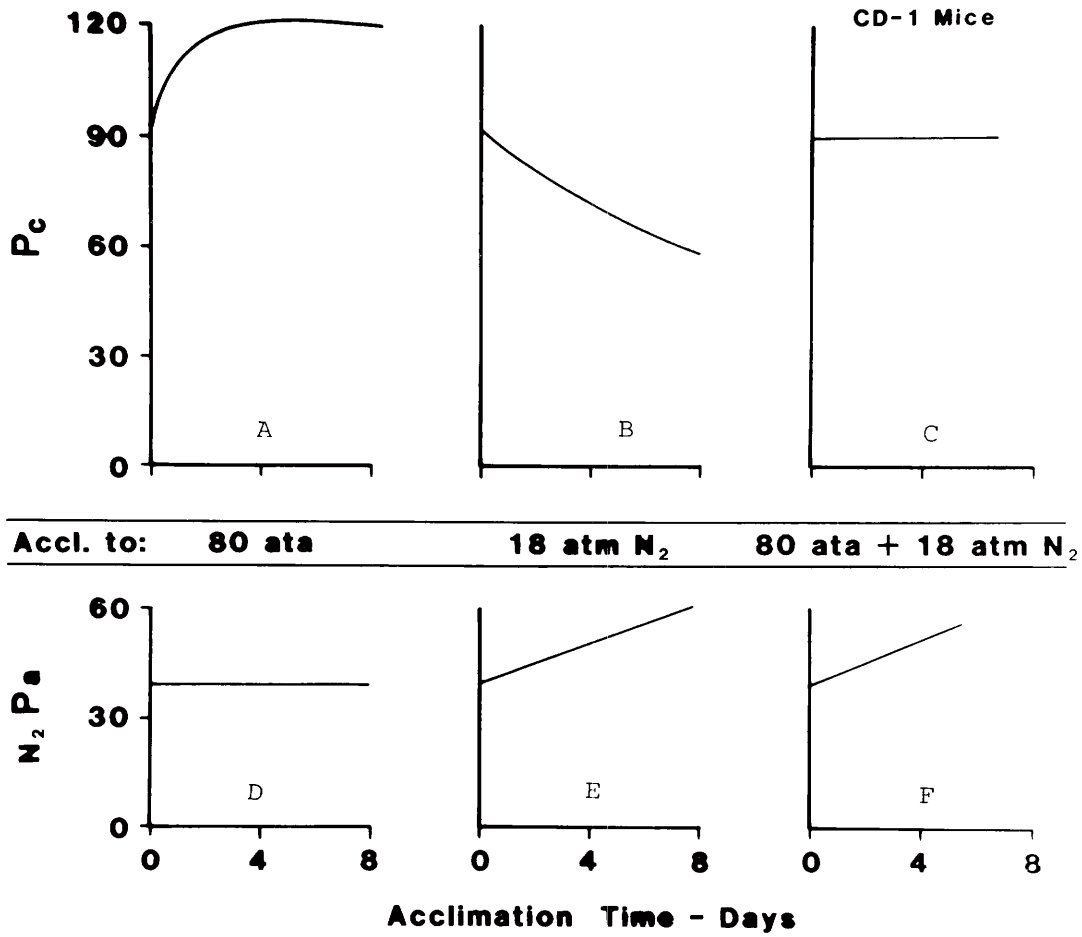

Fig. 4. Time course of acclimation to (A and D) high pressure (80 ATA He-O_2), (B and E) inert gas narcosis (18 ATA N_2, 0.5 atm O_2) or both simultaneously (C and F) (18 atm N_2, - 61.5 atm He - 0.5 atm O_2) on HPNS type I convulsion threshold pressures (A,B,C), and nitrogen partial pressure at anesthesia (D,E,F) (for details see test).

in the same strain of mice and plotted against the same time scale. Three types of experiments are summarized schematically: Acclimation to 80 ATA heliox for 1 to 8 d (Fig. 4A,D); acclimation to 18 ATA N_2 for the same length of time (Fig. 4*B,E*); and acclimation to 18 atm N_2 plus 61.5 atm He, i.e., at a total pressure of 80 ATA (Fig. 4*C,F*).

The results establish that prolonged pressure exposures result in increases in HPNS convulsion threshold pressures (determined 1 h after decompression of the animals to sea level). The effect comes on rapidly (less than 24 h for 95% change) (Fig. 4*A*) and, as shown by data not included here, is more or less linearly related to the acclimation pressure. Prolonged exposure to pressures up to 80 ATA does not result in detectable changes in anesthesia tolerance in these mice (Fig. 4*D*) (1).

Exposure to 18 atm N_2 results in a progressive fall in convulsion threshold pressures, with a halftime of 6 d, as well as a progressive

increase in anesthesia tolerance which is incomplete even after 12 d (Fig. 4*B,E*). All of these effects are comfortable secured statistically (P = >0.025 to P = >0.001). They are of interest theoretically because the contrast with the effects on anesthesia tolerance constitutes, to the best of our knowledge, the first instance where pressure and narcotic gas effects fail to be even qualitatively symmetrical in whole animal experiments. In addition, Fig. 4*A,B,D* indicate very large differences in the rate with which acclimation occurs to high pressure and to elevated N_2 concentrations, respectively.

Determination of the combined effects of these two types of stress factors thus became of considerable interest from the point of view of furthering our understanding of the nature of the antagonism between inert gas narcosis and high pressure effects on the CNS. The results of experiments involving simultaneous exposure of mice to a total pressure of 80 ATA and a partial pressure of 18 atm N_2 are shown in Fig. 4*C,F*: This mixture fails to produce any recognizable effect on the type I HPNS convulsion threshold pressure at any time during the acclimation exposure (Fig. 4*C*), a result that could not have been expected on the basis of the very different time courses of acclimation to narcosis and to high pressure alone if the effects had been merely additive. Thus, the observed lack of net effect on P_c must be taken to mean that in this respect the effects of the two stressors neutralize each other directly, either at the molecular level, in some such manner as envisioned by the critical volume hypothesis (1) or by a more complex physiologic antagonism.

On the other hand, anesthesia tolerance was increased by exposure to 18.0 atm N_2 in much the way as had been observed for the same partial pressure of N_2 in the absence of He, i.e., at a total pressure of 18.5 ATA (compare Fig. 4*E,F*). This complete absence of detectable interaction of effects on anesthesia tolerance during simultaneous exposures to high pressure and to narcotically effective N_2 partial pressure appears quite incompatible with any concept of mutual neutralization of the two agents, and contrast starkly--and, I might add a bit unexpectedly--with the situation just outlined with respect to high pressure seizures. Given the experimental fact that the relative values of total and partial N_2 pressure chosen just about neutralize each other with respect to the acute induction of anesthesia, these results imply either that acclimation in the sense of the term here employed is achieved in response to the presence of elevated N_2 concentrations in some tissue compartment rather than in response to a given level of CNS depression, or that pressure reversal of anesthesia does not imply true neutralization of all other effects on CNS activity, some of which are the ones triggering N_2 habituation.

Reasoning from pharmacologic data, both we (12) and Rowland-James et al. (13) concluded some time ago that interaction of high pressures with anesthesia suggests distinct--perhaps even anatomically distinct--sites of action for elicitation of high pressure convulsions and antagonism thereof by inert gas anesthetics, on the one hand, and for anesthesia and pressure reversal of anesthesia on the other. The present data extend these conclusions to indicate that the two "sites" accommodate to prolonged exposures to pressure or to inert gas narcotics in qualitatively distinct fashions.

The bearing of these data on the status of human subjects undergoing prolonged H_2 exposures can be anticipated by comparing Fig. 4*A,D.*: In He, pressure conditioning entails increased resistance to at least some HPNS symptoms. The process corresponds nicely to the familiar sequence in which HPNS symptoms in divers exposed to effective depths lessen or disappear in large measure during the first day or tow of sojourn at depth (14). By contrast, in an effective He-H_2 mix, as in our He-N_2 mix, HPNS symptoms can be expected to be suppressed at the outset corresponding to the increase of convulsion pressure in such atmospheres in our animal experiments (Fig. 1). Concurrently, as we have just seen, the accommodation process (shown by the rise in P_c in Fig. 4*A*) is also suppressed, probably to a degree corresponding to the product of potency and partial pressure of the narcotic gas in the conditioning atmosphere (this inference is based on comparison of the effects of equinarcotic He-N_2 and He-N_2O mixtures). As a result, He-H_2-O_2 mixtures which are very effective in suppressing HPNS manifestations can be expected to prevent partly or completely the desensitization of men to high pressure effects normally seen in heliox dives. When after a lapse of some days such men are then abruptly deprived of the H_2 umbrella by being returned to heliox, they should be no more pressure-resistant than they would have been at the very beginning of the dive and consequently can be expected to undergo HPNS symptoms as severe and as prolonged as those they would have encountered had they been compressed in heliox at the outset. These relations are illustrated schematically in Fig. 5*A,B*. Moreover, given the uncertainties in the evaluation of anti-HPNS potency of H_2 discussed above and the lowering of P_c during acclimation to a narcotic gas illustrated by Fig. 4*B*, one cannot rule out the possibility of more severe HPNS effects upon such switch over to heliox, i.e., of actual sensitization to pressure as a result of such prolonged exposures to He-H_2 at high pressures. We believe that such an effect was actually observed in man during the switch over from He-H_2-O_2 to He-O_2 at 45 ATA in the course of Hydra V, to abe described presently by Dr. Fructus.

Altogether, then, the results of the animal experimentation bearing on the interaction of H_2 with the HPNS can be summed up in a series of brief statements:

1. Hydrogen will provide some protection against HPNS symptoms.

2. While limits for the absolute and relative magnitudes of this effect can be deduced, the animal experiments do not allow one to anticipate the composition of mixtures giving the best compromise between the anesthetic and the anti-HPNS effects of H2 in man, not do they allow an estimate of the absolute magnitude of the pressures against which such He-H_2-O_2 mixtures might effectively protect man.

3. The nonlinear dose-response relations and marked species differences preclude the hypothesis that the mix of narcosis and anti-HPNS effects will follow any single pattern from one gas to another. Thus it seems certain that in man there will be qualitative differences

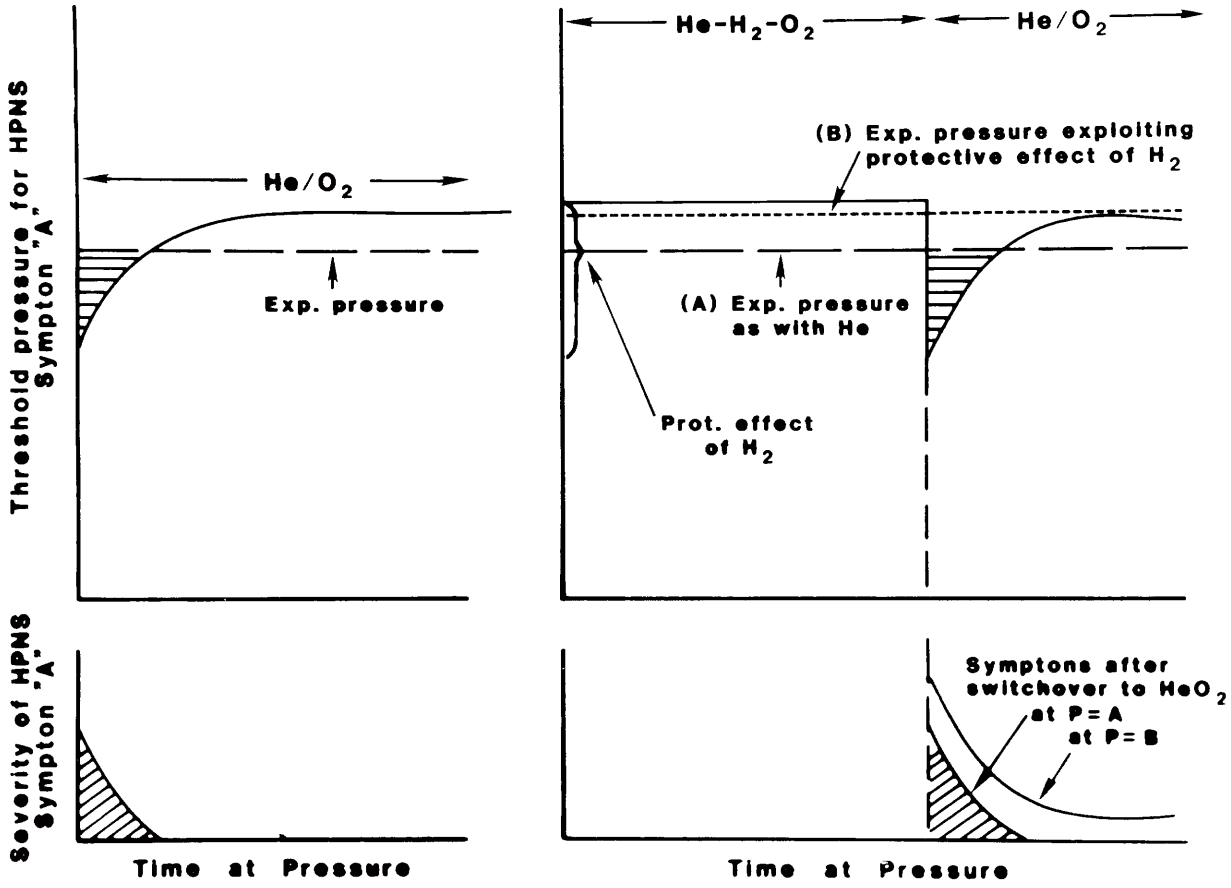

Fig. 5. Schematic representation of acclimation effects during prolonged exposure to He-O_2 (left panel) or the He-H_2-O_2 followed by switchover to He-O_2 (right panel) upon pressure tolerance (upper row) and severity to a hypothetical HPNS symptom (lower row) (for details see text).

between H_2 and N_2 which, even disregarding density effects, will provide a most favorable mix of narcotic and anti-HPNS properties for one or the other. Because of species differences a choice can only be based on experiments on human subjects.

4. The experimental data suggest that at least with respect to HPNS type I seizures, the antagonism between inert gas (IG) narcotics and high pressure (HP) effects is a true antagonism and not a mere masking of the pressure effects. This, however, does not apply to all aspects of IG/HP interactions, as shown by the persistence of anesthesia acclimation in combined HP and IG exposures.

5. Because of IG-HP antagonism with respect to pressure conditioning the results of the animal experiments suggest that transfer of men from He-H_2-O_2 to He-O_2 at pressure after some days of sojourn in the former gas mixture is likely to elicit transient but possibly severe HPNS symptoms, suppressed at the beginning of the dive by the anti-HPNS effects of H_2.

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DISCUSSION FOLLOWING PRESENTATION BY BRAUER AND DUTCHER

MILLER: You stated in regard to HPNS seizures that you really couldn't get decent dose-response relationships. My slide shows that in fact you can get a very good cumulative response pressure curve. The problem arises only if one calculates average seizure pressure from the observed individual pressures. This quantity may be biased, because usually in HPNS not every animal will be observed to respond. One gets more information by plotting the data the way pharmacologists do, as the fraction of all animals tested responding at a given dose, in this case, pressure. What you then expect to get is an S-shaped curve, defining the number of animals that have responded as a function of pressure. If all animals do not respond in a given experiment it doesn't necessarily matter if one knows the underlying distribution from experiments in which they all respond. If you look at our curve for complete spasms in mice (type II convulsions), you can see the individual points for the animals responding. In the case of helium, about 75% responded because some of them had other forms of HPNS earlier on, before the spasm; but nonetheless you can plot a very nice dose-response curve, assuming they all respond, and come up with a 50% pressure. If you do the same with a He-30% N_2 mixture, all the animals respond so that the complete curve is defined (this happens because nitrogen affect "complete spasms" more than "toxic convulsions," separating the two distributions). Although there are limits to this maneuver, the data are perfectly quantifiable.

BRAUER: There are two kinds of trouble with this--as you've been told before by us and by statisticians, I'm sure. In the first place, one has recourse to ED_{50} methods when, but only when, titration to an end-point is impossible. They are extremely inefficient, largely because all of your "nonresponders" fail to contribute data to the calculation. Looking at your data, it takes 50 animals to get the kind of reproducibility the end-point

linearity in the HP/IG relations that Halsey and his colleagues--and we and many others--find. In the second place, you pride yourself on the use of what is technically known as truncated populations--situations where significantly less than 100% of the animals respond, as for instance, in your slide on the rolling response of newts under hydrogen (see Miller, above, Fig. 5, where you calculate form fewer than 70% responders). I don't think you'll find many statisticians who will let you do that. It is generally considered inadmissible and likely to vitiate the validity of any population characteristics you would deduce from such data, including what you are pleased to call ED_{50} values. The sort of analysis you pretend to do on such data presumes that the distributions are nonskewed normal ones and, if so, your 50% value and mine (which is never based on incomplete seizure incidence) would coincide. When they are not normal--and your truncated populations will not necessarily show you that--your ED_{50} will cease to have any clear-cut meaning.

MILLER: The method is not particularly inefficient. The curve for nitrogen was defined with 10 animals. The curve for helium shows four separate experiments with 10 animals each (i.e., 40 animals). Obviously, if too few animals respond, the extrapolation becomes inadmissible, but this becomes apparent if the data are presented in this way. By drawing up such pressure-response curves, one checks automatically for skewed distributions. Potency comparisons are only meaningful if pressure-response curves are parallel. The only people who reported nonlinear effects are those who never do dose-response curves.

BRAUER: The fact of the matter is that none of the available data indicate that the dose-response curves are nonparallel and so this question--which would preclude many types of analysis--is hardly pertinent here as long as we recognize it and stay with a common endpoint. This has absolutely nothing to do with the question of linearity of HP/IG relations as determined on the basis of the available data. Indeed, your own people have published data which--as you will recall--showed nonlinear relations between narcotic concentration and mean HPNS convulsion thresholds; and so have we, and so has Halsey, and so has Eger. As we showed, there are profound strain and species differences (indeed, I showed some today), but I don't think there remains any valid doubt that linearity in the relations is the exception rather than the rule. As far as the statistics are concerned, this is a discussion that has been going on for many meetings, and I doubt we can settle it here. Your own data and your own remarks here show that you tend to use grossly truncated populations and that for and ED_{50} even you need 10 animals per point. Drawing an S-curve on fewer than five points seems clearly inadmissible, so we're back to 50 animals for you as against 10 for us.

SMITH: I must say that we have determined a considerable number of these curves in the presence of nitrous oxide, in particular, and do get well behaved dose-response curves. May I ask one more question about the curves? This morning we were talking about these responses and I think it was Keith Miller who said that he found the steepness was much greater than for anesthesia. That is an enormously steep dose-response curve.

MILLER: The pressure-induced paralysis in our tadpoles has a very steep dose-response curve. It is about five times steeper than the rather steep curve in rodents that you get with anesthesia. With opiates you get a very shallow dose-response curve; with general anesthetics a very steep dose-response curve. And if you take pressure-paralyzed tadpoles you get a steeper response curve than you have ever seen before in your life. With mice, on the other hand, slopes for general anesthesia are similar to those for "complete spasms."

GIRY: May we infer from your results that accommodation to pressure bears on the compression rate-dependent HPNS?

BRAUER: Personally, I think, and at the moment it is only personal thinking, that the distinction between compression rate-dependent and noncompression rate-dependent HPNS is a fictitious distinction. What we do have, and experimentally it seems to work out, is a pressure-dependent change in the functioning of the brain that elicits compensatory responses to pressure that take time. This is why I specified that in all of these observations we used standardized compression conditions, the same rate, the same temperature, same animal, and so on. I do have data for other curves and for other rates, and as we go to very high compression rates some of these phenomena change quantitatively though not qualitatively. With regard to the acclimation phenomena, I cannot yet answer you. We don't have the data yet.

UNIDENTIFIED SPEAKER: With regard to the HPNS site, you don't have an explanation why time at pressure would alter that?

MILLER: It's very hard to say that. In Brauer's mixture experiment, where the effects were balanced by using pressure and nitrogen, the results are quite definitely unexpected.

COLLIER: How about the pure IG situation?

BRAUER: The pure IG results are, I think, reasonably comfortable. We do have a reasonable degree of symmetry there. I would tentatively say that the two sites we are looking at could just possibly be quantitatively different enough to give you that. The combined HP and IG effects raise a much more complex picture and I am not prepared to predict what mechanisms might be involved to explain them. It is an exceedingly interesting phenomenon that needs more work.

YOUNGBLOOD: Observation. It is very interesting that you introduced us to acclimation phenomena after 4 d at 18 atm nitrogen. We tried in some of the early nitrox saturation experiments to measure whether acclimation to nitrogen narcosis takes place. We have never been able to conclusively demonstrate it, one of the reasons being perhaps that for economic reasons we have never been able to stay long enough. In looking through the previous dives I noted though that in the SHAD experiments, where heart rates were measured (although I don't think there was any mention of it), after about 6 d the pressure bradycardia began to go back toward normal. In my opinion this could be a change in the pacemaker cell function in which

the membrane which had been altered now has reexpanded to its normal configuration.

BRAUER: We have got Eger's old data on the nitrous oxide habituation. We first took off from there to see whether we could change the convulsion threshold pressure as well as the anesthesia susceptibility. Then, we worried, as did everybody else, about the possibility of nitrous oxide-induced biochemical changes, and redid the experiments with nitrogen, only to find that the results were identical. These are really quite dramatic animals. After 19 d of N_2 habituation, these are extremely convulsion susceptible; if you snap your fingers at them, some will go into convulsions.

SMITH: The question of the relationship between the compression rate-dependent and the compression rate-independent components of HPNS has been raised. Our results with rodents suggest very clearly that pressure has a subcortical site of action. Furthermore the pharmacology of high pressure and that of strychnine exhibit remarkably close parallels. Drugs effective against strychnine have, when tested, all been found effective against pressure, and vice versa. This is often not the case for drugs active against other convulsants. The rate-dependent effect appears to arise from a descending controlling mechanism that arises in the cortex. Ralph Brauer's early experiments with Reserpine, and many later studies, suggest that this inhibitory response is primarily mediated by noradrenalin. In view of the very different mechanisms involved it is not surprising that the two aspects of HPNS can respond in different ways to any particular drug.

ÖRNHAGEN: This is not really a question, just a comment. In Sweden a couple of years ago in a nitrox saturation dive to 60 m for 1 wk, we tried to trace down some kind of measure of adaptation to narcosis. It was very clear in subjective observations, and we also had some objective tests to show that there really was some improvement of performance.

MILLER: It is interesting to see how far acclimation will go. In general anesthesia, Eger's data suggest that we can get a factor-of-two shift in ED_{50} during tolerance. With pressure, I don't think we know yet.

BRAUER: With pressure it looks like a cutoff. We can take our animals as far as 80 atm, allow them to accommodate to that, and then raise them to 100 ata knowing that their convulsion thresholds at that point will be well above 120 ata. They don't quite convulse under those conditions, but they don't seem to do well and their pressure tolerance doesn't increase any more and even drops a bit. In our setting the optimum acclimation pressure seems to fall just below 80 ata, or at about 75% of the maximum convulsion threshold pressure. The limit of the conditioning effect thus is about 30% increase in P_c.

EFFECT OF HYDROGEN ON HYPERBARIC BRADYCARDIA

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One possible gain with hydrogen in dive gas mixtures is that, due to its narcotic potency, it is thought to offset some of the high pressure neurologic syndrome (HPNS) symptoms encountered during deep dives. The results from the COMEX Dive, Hydra V, are encouraging in this respect (see other chapters in this volume). However, the central nervous system is not the only vital tissue to be affected by high pressure.

Pressures over the range of 0,1-15 MPa (1-150) ATA have been shown to affect the electromechanical behavior of the heart. In isolated cardiac preparations, hydrostatic pressure has been shown to decrease spontaneous beating frequency (1), to slow conduction velocity and reduce excitability (2), and to increase contractile strength (3). Effects on cardiac conduction at elevated pressures have also been observed in intact hearts (4) and also in man (5). Inert or anesthetic gases can modify or counteract the pressure effects. The best studied modality with respect to inert gas interactions is pressure-induced bradycardia (6), where the ability to counteract the bradycardia is in proportion to the lipid solubility of the gases. In this respect, hyperbaric bradycardia is similar to other pressure responses, such as clonic pressure convulsions, liposome fluidity, and lipid phase transitions, as reviewed by Brauer et al. (7). At the time there were no data on the hydrogen effect on hyperbaric bradycardia. In this paper it is shown that hydrogen conforms to the general pattern of inert gases in this respect.

METHODS

The apparatus and methods have been described previously (3). The right auricles of female Wistar rats were suspended between a fixed hook and a strain-gauge transducer (Grass FT03). A bath containing the preparation was placed inside a pressure chamber. The temperature of the bath was controlled by a thermocontrol system to within 0.1°C during steady state and 0.2°C during compression and decompression procedures.

The main feature of the system is the ability to control the inert gas pressure in the fluid superfusing the preparations, irrespective of the pressure medium in the chamber. This is accomplished by means of hydraulically pumping liquid into the tissue bath. The outflow of the liquid is through a small slit in the lid of the bath. The chamber is pressurized with compressed air. However, the pumped liquid will convert the gas pressure in the chamber to hydraulic pressure.

The flow of the liquid through the slit is several times greater than the diffusion velocity of nitrogen and oxygen through the liquid, so the solution superfusing the preparation will be uncontaminated by air.

The bath solutions can be equilibrated with gas before being pumped into the chamber. It is thus possible to vary the inert gas pressure surrounding the preparations without changing the total pressure.

The inert gas-containing solutions were equilibrated with the appropriate gas phase for several hours before the experiments. All solutions were thoroughly bubbled with oxygen. After the experiments, the gas content in the solutions was measured by decompressing liquid samples in a graded syringe. In some cases the gas phase was analyzed with gas chromatography. N-Tris buffered solutions were used, with 2.3 mM Ca^{2+} (Fig. 1).

RESULTS AND DISCUSSION

At a temperature of 37°C a total of 13 preparations was compressed to 15 MPa. The beating frequency (BF) decreased from 172± beats/min at control pressure (0.2 MPa) to 120 ± 24 beats/min at 15 MPa. The mean reduction in BF was 30 ± 8%. At pressure, the effects of three different gases were tested: H_2, N_2, and He.

The results from seven experiments with 4.9 and 14 MPa H_2 are shown in Fig. 2. As can be seen, the BF falls during the compression and continues to decrease during the first 10 min at 15 MPa. In this series the fall in BF after 15 min at 15 MPa compared to the precompression BF was 52.7 ± 20.7 beats/min. Introduction of 4.9 MPa H_2 increased the BF by 9.4 ± 6.6 beats/min. Wash-out of the hydrogen with standard solution decreased the BF back to the earlier level. Superfusing the preparations with 14 MPa H_2 increased the BF with 24.8 ± 6.5 beats/min. Decompression with standard solution to 0,2 MPa brought the BF back to precompression level.

At pressure the preparations were exposed to 5MPa N_2, and 12 MPa of a mixture of 75% H_2 and 25% He. The results are shown in Table 1.

To compare the data in this study with previous results obtained on mouse sinus nodes at 27°C (6), three preparations were kept at 27°C during the experiments. Initial BF for these preparations was 93 ± 9.9 beats/min, which decreased to 55 ± 4.2 beats/min at 15 MPa. The mean reduction in BF was 37 ± 4%. This change was larger than for preparations kept at 37°C, but the difference failed to reach statistical significance ($0.1 > P > 0.05$). Örnhagen and Hogan (2) and Doubt and Hogan (8) have shown that low temperatures potentiate pressure effects on cardiac preparations.

At pressure the preparations were exposed to 5 MPa N_2 and 12 MPa of a mixture of 75% H_2 and 25% He. The effect of the hydrogen mixture was similar to the effect seen at 37°C. N_2 increased the BF more in the colder preparation ($P < 0.05$), and those results were close to those obtained in mine (6) (Table 1).

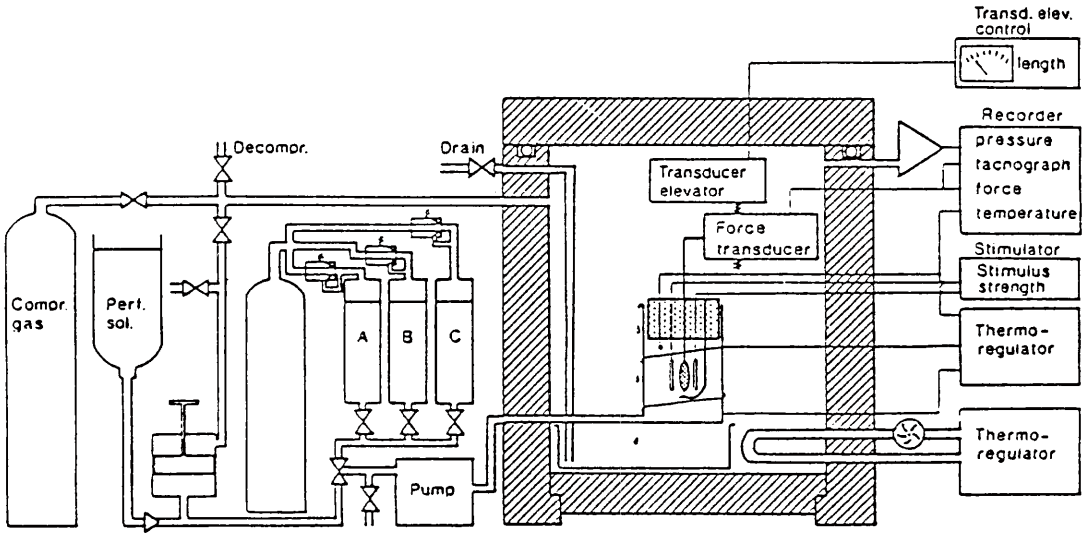

Fig. 1: Schematic drawing of experimental set-up.

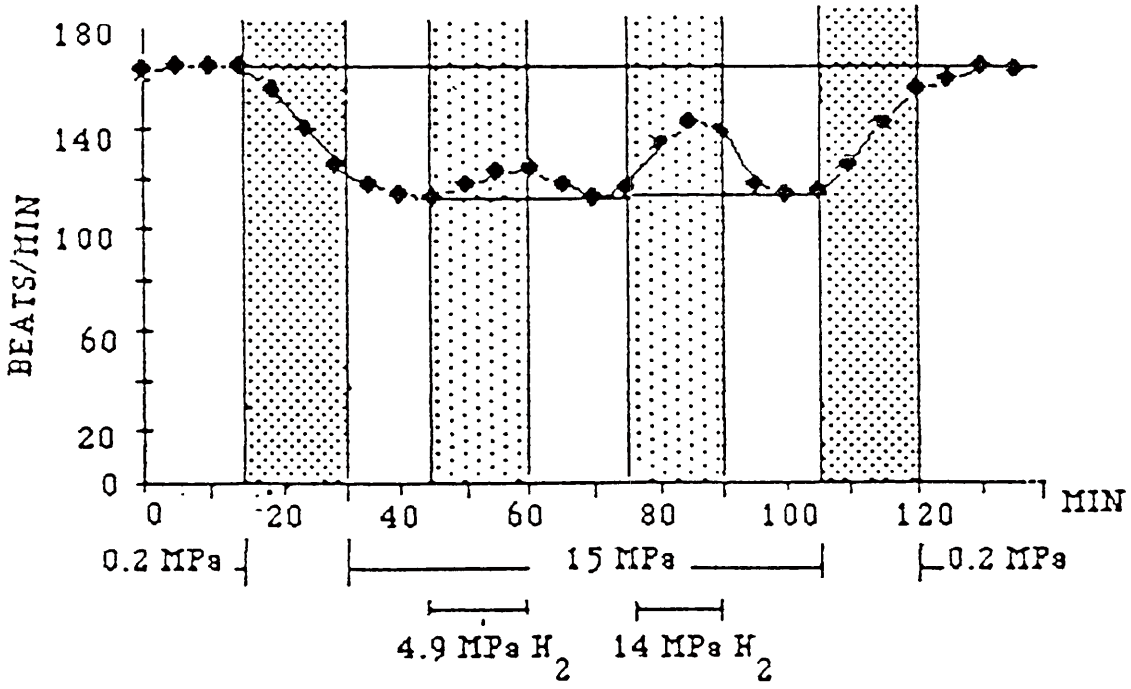

Fig. 2. Results from seven experiments with spontaneously beating rat atrial preparations, compressed to 15 MPa at 37°C, and tested with 4.9 and 14 MPa H_2. Dark shaded areas indicate periods of compression and decompression. Light shaded areas indicate hydrogen periods.

All data are related to the lines connecting the control periods (also shown in Fig. 2), to compensate for any time-dependent reduction in BF (1). The change in BF is assumed to be proportional to the total pressure (2). We have found that in rat auricles the BF is reduced by 25 $\pm$ 4.2% by 10 MPa,

TABLE 1

Inert gas effect on BF.

		$\Delta^{a}BF$	$\frac{a^{\pi}b}{p\pi b}$	N
Temperature 37°C				
$\Delta^{P}BF$ = -54	4.9 MPa H_2	9	0.51 ± 0.19	7
	14 MPa H_2	24	0.53 ± 0.22	7
$\Delta^{P}BF$ = -46	9.0 MPa H_2*	12	0.42 ± 0.15	3
	5.0 MPa N_2	8.5	0.51 ± 0.22	6
	13 MPa He	4.5	0.10 ± 0.05	4
Temperature 27°C				
$\Delta^{P}BF$ = -39	9.0 MPa H_2*	14	0.45 ± 0.12	3
	5.0 MPa N_2	12	0.85 ± 0.15	3
Data from Örnhagen (6)	3.5 MPa N_2		1.48	
Temperature 27°C	7.0 MPa N_2		1.16	
Mouse sinus nodes	14.0 MPa N_2		0.99	
	4.0 MPa He		0.18	
	12.0 MPa He		0.28	
	0.25 MPa N_2O		11.8	
	0.5 MPa N_2O		26.1	
	1.0 MPa N_2O		29.6	

Tabulated values for change in BF ($\Delta^{a}BF$) during inert gas exposure. $P < 0.05$ for all values.

$a^{\pi}b/p\pi b$ expresses the potency of the gas to reverse the pressure effect. For calculations *see Fig. 3*.

*Calculated from gas mixture H_2/He. Effect of the He subtract ed from the total change.

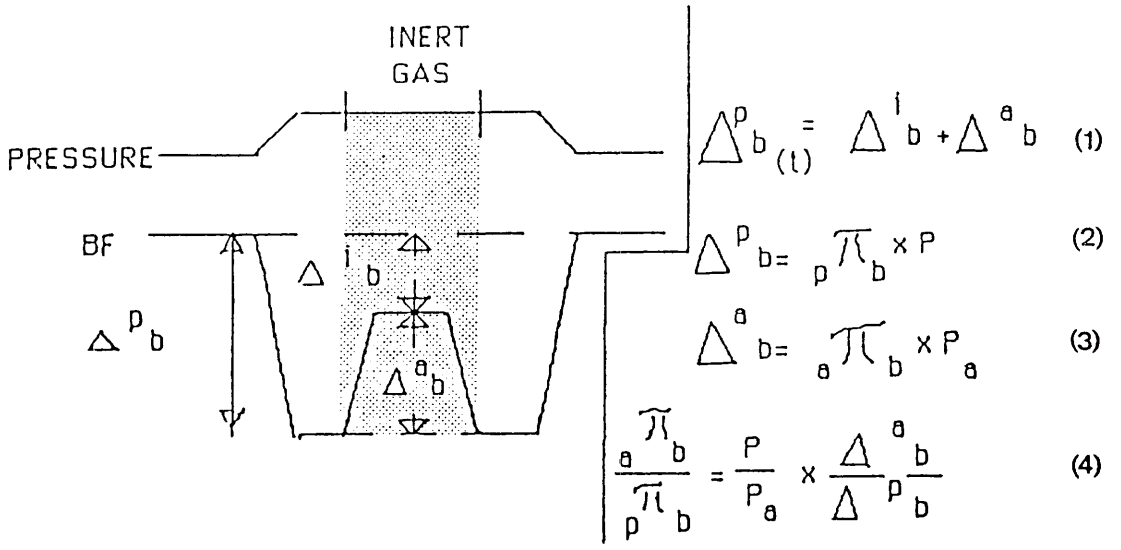

Fig. 3. Schematic drawing of experimental profile and BF changes. Nomenclature according to Brauer et al. (7). P = hydrostatic pressure; P_a = partial pressure of gas a. For other symbols see test.

and in this series 15 MPa reduced BF with 30 ± 8.2%. This is slightly less than the expected value, 37.5%.

According to the model of Brauer et al. (7), the effect of the inert gases is proportional to the partial pressure of the individual gases (3). This seems to be a good approximation for H_2 and for high concentrations of N_2 and N_2O. For the latter gases there is a substantial deviation at lower pressures (see Table 1). Finally, the potential of the inert gas, $a^{\pi}b$ (4), assuming linear additivity between pressure and gas effects.

In the present system $p^{\pi}b$ can be determined directly. In other experimental systems and with other biological end-points this is not always possible. The $a^{\pi}b$ and $p^{\pi}b$ values are then related to $N_2\pi b$ which is set to 1.00 (7).

The values for $a^{\pi}b/N_2\pi b$ were calculated, and corrections were made for pressure and concentration-dependent changes in solubility (9,10). In Table 2 these values are shown together with the values for other pressure responses that are similarly affected by inert gases. Arrows indicate the "neutral gas" for each response. Note that this gas is not the same for all responses. For hyperbaric bradycardia the pressure effect is balanced by an equal pressure of N_2.

The responses that are most like hyperbaric bradycardia in regard to the interaction between hydrostatic pressure and inert gases are HPNS convulsions and liposome fluidity. However for these end-points the N_2 effect is slightly larger than the pressure effect. The neutral gas for these responses lies between H_2 and N_2. The value for $H_2{}^{\pi}b/N_2{}^{\pi}b$ is higher

for hyperbaric bradycardia than for any of the other end-points.

TABLE 2

Pressure and inert gas interactions.

	Pressure-reversal of anaesthesia	Type I HPNS Convulsions	Liposome fluidity	Hyperbaric bradycardia	Lipid phase transition
HP	-0.2	-0.6	-0.7	-1.0	-1.6
He	0.07	0.00	0.12	0.14	0.2
Ne	0.18	-	-	0.28	-
H_2	0.39	0.34	0.25	0.48	-
N_2	1.00	1.00	1.00	←1.00→	1.00
N_2O	22.6	42	26	22.4	38

Relative potency of inert gases and hydrostatic pressure effects compared to N_2. Data in shaded columns from Brauer et al. (1982).

The potency of the gases to reverse hyperbaric bradycardia is related to their lipid solubility. When the potentials for the gases He, Ne, H_2, and N_2 are plotted against oil solubility, there is a good linear fit (Fig. 4).

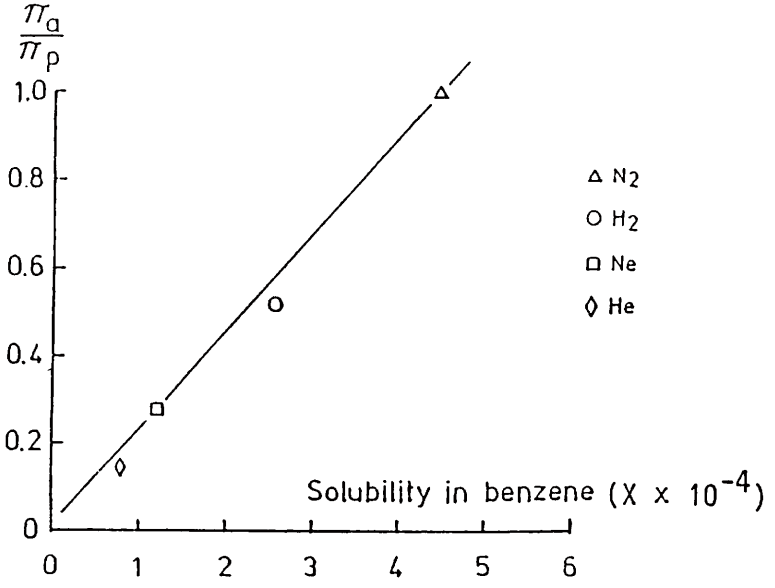

Fig. 4. Relation between gas solubility in benzene and pressure reversal potential. Solubility data from Wilhelm and Battino (11). $Y = 0.22X \pm 0.021$, $r = 0.996$.

The linear relationship between the pressure reversal potentials, $a^{\pi}b/p^{\pi}b$, and the oil solubility makes it possible to test the critical volume hypothesis (12) on this response. According to the theory, effect of anesthetics are caused by expansion of the membrane site due to the dissolved substance. The amount of pressure that precisely counteracts the expansion will abolish the anesthetic action. Similarly, the effects caused by pressure can be counteracted by a suitable amount of gas. Calculations were make for the theoretical volume change caused by the gases, using benzene as a model solvent (13). The membrane expansions was plotted against change in beating frequency caused by the gas. The compression effect for different hydrostatic pressures was calculated and also plotted against change in BF. Both relationships yielded straight lines that went through the origin, but the slope for the compression effect was more than twice that of the gas expansion effect (34.7 vs. 13.9; $P < 0.01$, Fig. 5).

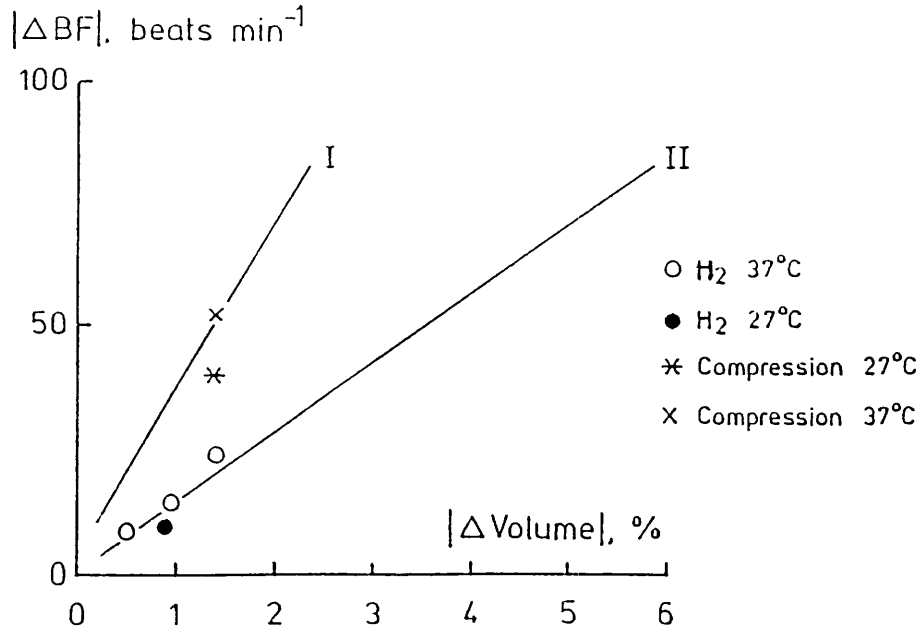

Fig. 5. Change in BF plotted vs. % volume change in benzene, compressed from 0.1-15 MPa (Line I: $Y = 34.7x \pm 5.0$, $r = 0.85$), or saturated with inert gases (line II: $Y = 13.9x \pm 2.1$, $r = 0.87$). Data on BFs are taken from Örnhagen (1977) and the present report.

The benzene model does not lend itself particularly well to describing the pressure/gas interactions on the BF. Some of the discrepancy could be caused by pressure-induced changes in solubility in the cell membrane. A pressure-related decrease in oil solubility has been reported by Gerth (14) for the olive oil system, but the observed deviations are too small to explain the difference between our results and the model.

Another possibility is that pressure and inert gases act at different "sites" with different compressibility. It has been shown by Finch and Kiesow (15) that the effects of both pressure and gases are different in different layers of the cell membrane. No other observations to support the

notion of different "sites" have yet been made on heart muscle. It has, however, been shown that pressure and gases do not exhibit a direct antagonism on the effect on the action potential in neurones (16.17).

CONCLUSION

In conclusion, hydrogen was found to behave as expected with regard to the pressure reversal of hyperbaric bradycardia. For the human diver the importance of hyperbaric bradycardia is probably only minor. Most of the pressure effects can be offset by autonomic or external factors. However, the pressure effects on conduction velocity and excitability could be more important insofar as these effects could predispose divers to cardiac arrhythmias, especially if the added effects of cold and high heart rates are present (Doubt & Hogan, 1981). Changes in impulse conduction and cardiac rhythm have been reported in divers both in heliox atmospheres (7) and in nitrox atmospheres at shallower depths (18). If hydrogen is as potent in reversing the effects of pressure on the impulse conduction as in reversing the bradycardia, addition of hydrogen in deep-dive gas mixtures could improve the divers' safety with regard to arrhythmias. Evaluation of the effects of H_2 on the arrhythmogenicity of high pressures ought to be important.

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DISCUSSION FOLLOWING PRESENTATION BY GENNSER AND ÖRNHAGEN

FIFE: Where did you do your recording from? The sinus?

GENNSER: We used part of the right auricle containing the SA-node.

FIFE: So you moved it in vitro and watched the temperature and all that while you were doing it.

GENNSER: Yes. The preparations were maintained in a controlled environment. The temperature was kept at 37° $\pm$ 0.1°C for most of the experiments. In some tests the temperature was kept at 27°C to compare with earlier measurements on mouse sinus nodes (6).

MILLER: Did I see in your first slide that 140 atm of nitrogen didn't completely reverse hydrostatic pressure, and then 140 atm of hydrogen also didn't completely reverse? It seems as though qualitatively they were both having the same effect.

GENNSER: You see, in that slide which shows effects of N_2 and N_2O on mouse sinus nodes (6), there is not only a reduction in beating frequency due to the compression but also a time-dependent drop in beating frequency. When the time-dependent component is accounted for, it is seen that 140 atm of N_2 almost completely reverses the effect of 150 atm hydrostatic pressure.

MILLER: Whereas the hydrogen is getting half? And the N_2O is much more potent?

GENNSER: Yes, about 30 times more potent than N_2.

MILLER: Can you make any guesses as to which ion channel underlies the slow rates that you see in your recordings?

GENNSER: High pressure seems generally to slow down the diastolic depolarization in cardiac tissue (1). According to the latest model of pace-maker activity, the diastolic depolarization in Purkinje fibers is caused by a Na^+ current, whereas in the SA-node the spontaneous rhythm is caused by a change in K^+ conductance (Noble, J Physiol 1984;353:1-50), although others claim that here, too, Na^+ currents play the major role (Maylie and Morad, J Physiol 1984;353). According to Kendig (Am J Physiol 1984;C84-C90), there is a generalized slowing of current kinetics in vertebrate neurons compressed to 100 atm. It is difficult to say which ion channel underlies the slowed beating frequency; although it seems that in neurons, Na^+ currents are most affected.

HYDRA IV AND HYDRA V: HUMAN DEEP HYDROGEN DIVES 1983-1985

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INTRODUCTION

The history of hydrox began with Sequin and Lavoisier, who in 1789 gave guinea pigs a mixture of "vital air" and "pure hydrogen gas" to breathe. The animals "remained [in the gas] a long time without appearing to suffer." A century and a half later, in 1941, Case and Haldane made the first tests on human beings. Then in 1944-45, Zetterström dove to sea depths of 40, 70, 110, and finally 160 m on hydrox, remaining some tens of min each time without any ill effects. In June of 1983, COMEX carried out Operation Hydra III in the sea, wherein 16 divers dove two-by-two to 70 m. Then H.G. Delauze, President of the COMEX group, and J.P. Bargiarelli, Director of COMEX Pro, dove to 91 m, all breathing hydrox for 5 min. There was no perceptible difference between hydrox and heliox breathing at these depths.

Operation Hydra IV took place in the Hyperbaric Research Center (HRC) of COMEX in Marseilles between November 14 and December 2, 1983. For the first time in history six divers breathed a hydrogen-rich mixture at a pressure depth equivalent to 300 m of sea water. The objectives of this experiment were basically to investigate:

- the toxic power of hyperbaric hydrogen
- the narcotic potency of hydrogen compared to nitrogen
- lung ventilation on hydrox under water, both at rest and during muscular exertion.
- underwater work capacity on hydrox as assessed by measuring the heart rate (HR)
- isobaric counterdiffusion on switching gases.

EQUIPMENT AND METHODS

Hyperbaric System

Part of the COMEX HRC installations in Marseilles were used, including Unit No. 1, the hydrosphere, a pool chamber 5 m in diameter comprising:

- a gas-filled area (heliox) above
- a heated (about 30°C) pool surrounded by a circular deck
- in the middle of the pool, a transparent plastic dome in which comparative tests were carried out in the wet or in the dry, on heliox and on hydrox;

and Unit No. 2, an eight-person living unit connected to the hydrosphere; and a control room outside these two units for controlling both. The hydrox mixture was supplied and exhausted via an independent circuit whose entire installation rigorously respected prevailing safety standards for the use of hydrogen.

Gases Used

The hydrox mixtures were prepared on the spot at COMEX with the assistance of AIR LIQUIDE technicians. Heliox was used as saturation gas with 400 mbar of O_2 at all storage depths, 120, 180, 240, and 300 m. For the comparative tests in the dry under the dome or under water on heliox and hydrox the following mixtures were used:

- helium/oxygen at 98/2
- hydrogen/oxygen at 98/2.

The PI O_2 varied therefore between 260 mbar (at 120 m) and 620 mbar (at 300 m) according to the depth, but was the same for both gases at the same depth.

Two special mixtures were tested at 300 m:

- $H_2/He/O_2$ at 74/24/2
- $H_2/He/O_2$ at 59/39/2.

The Divers

Six men (divers, engineers, doctors: mean age 36 $\pm$ 6; height 174 cm $\pm$ 8; weight 73 kg $\pm$ 6), divided into two teams of three each, participated in Hydra IV.

Methods

Compression to 300 m was progressive with stops at:

120 m for 14 h
180 m for 40 h
240 m for 46 h
300 m bottom time of 64 h.

Decompression from 300 m was not conventional in that there were two stops at:

- 150 m for the prolonged test exposures on hydrox of 2, 4, and 6 h, respectively, involving three of the divers.
- 80 m for comparison tests with air narcosis.

Dry Test Protocol

Each test session comprised two sets of tests, one on heliox followed by a second on hydrox, given as per the following schedule:

- "impregnation" and adaptation to medium	10	min
- manual dexterity test (MD), 1 hand	2	min
- visual choice reaction time (VCRT) test	2.5	min
- multiplication test	2	min
- number similarities test (NS)	2	min
- electroencephalogram	8-10	min
	30	min allotted

Upon returning to the heliox storage medium the divers were checked ultrasonically for circulating bubbles for 4 to 6 h.

Wet Test Protocol

The diver breathed heliox during the first half h of the tests and hydrox for the ensuing h. The test schedule was as follows:

HELIOX -	rest	10	min
	VCRT	2.5	min
	Cyclorower	7	min
	rest	5	min
	time allotted	25	min
HYDROX -	impregnation	10	min
	VCRT	2.5	min
	Cyclorower	7	min
	rest	5	min
	puzzle	0 to 30	min
	VCRT	2	min
	time alloted	30 to 60	min

HELIOX - diver leaves water
Doppler bubble detection for 4 to 6 h

During underwater dives the following parameters of the subjects were checked:

- ECG
- ventilation
- ventilatory pressures

Long-Term Exposure Protocol

Three of the divers underwent prolonged exposure to hydrox for periods of 2, 4, and 6 h respectively at 150 m. During these exposures they remained in the dry under the transparent dome and took the MD, multiplication, NS, and EEG tests at regular intervals. Complete blood tests were taken prior to exposure, immediately upon exit, and again 6 h after end of exposure.

The following table gives the hydrox exposures during the course of the experiment:

Depth(m)	Mixture	Time per Subject	No. subjects	Conditions
120	98/2	60 min	6	dry
180	98/2	30 min	6	dry
180	98/2	60 min	6	wet
240	98/2	30 min	6	dry
240	98/2	30 to 45 min	6	wet
300	74/24/2	30 min	3	dry
300	74/24/2	30 to 40 min	4	wet
300	59/39/2	60 min	2	wet
150	98/2	2, 4, 6 h	3	dry

THE GOALS OF HYDRA V

On a physiological level, the main goal of Hydra V was to study the anti-HPNS effect of hydrogen and diver's capability when breathing hydrox (H_2-He-O_2) in a dry or wet atmosphere at a pressure of 450 msw (46 ATA) and with a compression (38 h) similar to those of previous experiments (ENTEX 5, 8, and 9) using trimix (He-N_2-O_2) or heliox (He-O_2).

Other studies conducted were:

- toxic effects on man of long-term exposure under hydrogenated mixes
- narcotic effects compared with Hydra IV results
- study of isobaric counterdiffusion after switch of ambient inert gases from hydrox to heliox
- ventilatory and cardiac functions at rest and during muscular exercise, in either a dry chamber or in water
- hydrogen saturation decompression between 450 and 200 msw.

On the technical level, long exposures to hydrogen in large chambers necessitated the development of new techniques, which enable men to live in a hydrogen atmosphere with the same comfort and safety conditions as those afforded by helium.

A new generation system was developed to ensure in a hydrogen environment a high degree of safety:

- the elimination of contaminants produced by man
- the temperature and humidity regulation of the chamber's gaseous atmosphere
- The permanent reoxygenation of ambient gas to compensate for the divers' normal oxygen consumption.

EQUIPMENT

Hyperbaric Complex

Part of the COMEX hyperbaric research center facilities in Marseilles were used, including:

Unit No. 1: A system of three spherical chambers connected to the heliox chamber in which three divers can stay in hydrogenated gas mixture under physiological and medical controls and perform exercise tests in dry and wet conditions. This system was equipped for detection of H_2 exhausts with alarms and extraction outside hyperbaric center hall.

Unit No. 2: A chamber with lock under heliox, which can accommodate six divers.

Individual Equipment for the Dive

For the tests in the wet the divers were kitted up with:

- a one-piece COMEX Pro suit without hood made of 5 mm-thick neoprene with fastening
- neoprene boots
- safety harness
- weights
- emergency twin set (V = 3,33 1 x 2; p = 200 bar filled with bottom mixture
- new integral wet helmet COMEX Pro, with T8 demand/dump valve connected to the dry wall by an umbilical composed of
  - . life-line
  - . in-out breathing gas supply line
  - . communications line
  - . ECG and magnetometer lines
  - . mass spectrograph line
  - . oronasal temperature line
  - . mouth barogram line

Exercise tests were performed on cyclorower.

COMPRESSION TECHNIQUES FOR DEEP DIVES USING He-O_2, AND H_2-He-O_2 MIXTURES

After the human dives made in the Coraz series (1975): Rapid compression in 4 h to 300 msw with different percentages of nitrogen in heliox

Coraz I: 9% N_2
Coraz II,III: 4.5% N_2
Coraz IV: 0% N_2

we undertook a systematic study of the influence of nitrogen on the intensity of HPNS in the monkey *Papio-papio*. That was the Corasin series: Compression in 2 h to 600 msw. The results obtained have led us to develop a compression technique with the following characteristics:

- decreasing speed as depth increases
- short duration intermediate stages
- introduction of nitrogen before each stage, obtaining 8% at 600 msw

This method of compression minimized the HPNS at 600 msw (Corasin VIII) and reached a 1000 msw depth (Cornelius I).

Extrapolation of this procedure to man, during two compressions to 400 and 430 msw in Janus IV, phase II and III, showed an increase in modifications of the EEG in the first phase of the compression (the most rapid) between 0 and 300 msw.

This reduction of speed at the beginning of the compression in the experiments with the monkeys (Cornelius II and III) as far as 1100 msw using 5% N_2 minimized the clinical symptoms of HPNS and the modifications of the EEG.

A human dive to 450 msw was also carried out using this new procedure. Eight subjects were taken to 450 msw in 38 h (DRET 79/131) without clinical symptoms and without any important increase in there EEG activity. The same compression procedures were used in Entex 5 and 8 (450 msw, 12 d) with 4.8% of N_2, and in Entex 9 (450 and 610 msw) without adjunction of nitrogen in the heliox mixture.

ENTEX AND HYDRA V COMPRESSION PROCEDURES

- 0 - 10 msw, Heliox 0.4 b O_2
- 10 - 450 msw, 38 h

- with stops every 100 msw
  duration of each stop: 150 min (2.5 h)

- decreasing speed with depth

0 - 100	2	min/m
100 - 200	2.5	min/m
200 - 300	4	min/m
300 - 400	5	min/m
400 - 450	7	min/m

- gas mixture
  in DRET 79/131, Entex 5, 8
  $He-N_2-O_2$ / 4.8% N_2, adjunction of N_2 before 3.5 msw
  each stop: 2.2 bar of N_2 at 450 msw

  in Entex 9 (at 10-450 msw)
  $He-O_2$, without adjunction of N_2, PN_2 = 0.8 bar = 2% N_2

  in Hydra V
  He up to 200 msw
  H_2 at 200-450 msw

  H_2-He-O_2, 25 bar H_2 = 54%
  20.6 bar He = 45%
  0.4 bar O_2 = 1%
  (0.05 bar N_2 = 0.1%) elimination before compression at 0-10 msw

= compression duration
He: 14 h (10 - 200 msw)
H_2: 26 h (200 - 450 msw)

Gas Switch From H_2-He-O_2 to He-O_2

After 4 d at bottom depth, the three divers of team A were transferred from a hydrox atmosphere, 54% of H_2 at 450 msw (25 bar H_2) to a heliox atmosphere in 8 h with an intermediate hydrox mixture stop, 30% of H_2 at 450 msw (14 bar H_2).

Though the gas switch was progressive, it appeared to be too rapid and the divers on heliox were recompressed to 470 msw with an increase of PIO_2 from 0.4 to 0.6 bar. After a very slow decompression to 450 msw, they stayed at bottom depth for additional tests designed for comparison between heliox and hydrox.

Subsequently, the dive planning of Team B was modified and converted into a complete hydrox dive procedure that will certainly be adopted for future operations: compression with hydrogen when deeper than 200 m and stay under hydrox atmosphere at bottom. In the case of Team B, this made it possible to carry out tests in dry and in wet conditions, during dives in a wet pot chamber.

It was expected that the three divers would be able to appreciate the "extraordinary" breathing comfort under exercise on hydrox in water at 450 msw.

Hydra V
Bottom Time Duration

	Team A (3 divers)	Team B (3 divers)
H_2 He O_2 at 450 msw	72 h (3 d)	104 h (4 d 8 h)
He O_2 at 450 msw	128 h (5 d 8 h)	0
Total	200 h (8 d 8 h)	104 h (4 d 8

HYDRA V DECOMPRESSIONS

Team A: The three divers were decompressed on heliox from 450 msw to the surface in 14 d 10 h.

Speeds
450 - 15 msw = 45 min/m
15 - 0 msw = 60 min/m

PO_2
450 - 350 msw = 0.6 bar
350 - 120 msw = 0.5 bar
120 - 15 msw = 0.6 bar
15 - 0 msw = 24%

Hydra V
Hydrox Exposures in Water (T = 30 - 31°C)

Team B (3 divers)

	450 msw 54% H_2	415 msw 44% H_2	399 msw 42% H_2	395 msw 42% H_2
B_1	1 h 55 min			28 min
B_2	2 h 00 min		42 min	
B_3	1 h 58 min	38 min		
Total	5 h 53 min			

At the end of the decompression, near the surface (1 m), two divers had a slight pain in the knees. Team A was recompressed to 4 msw on oxygen, and then decompressed to the surface (speed = 30 min/m).

Team B: The decompression was conducted with progressive elimination of hydrogen from 450 msw to 200 msw. From there to surface, the ascent was carried out in a heliox atmosphere. This saturation decompression was the first ever performed with hydrogen and was closely monitored using ultrasonic bubble detector technique.

Decompression duration: 19 d 10 h
on hydrox: 11 d 17 h (450-157 msw)
on heliox: 7 d 17 h (157-0 msw)

450-350 msw = 70 min/m
350-300 msw = 65 min/m
300-250 msw = 60 min/m
250- 15 msw = 55 min/m
15- 0 msw = 120 min/m

450-100 msw = 0.5 bar
100- 15 msw = 0.6 bar
15- 0 msw = 2.4%

Team B arrived at surface on Friday, 7 June at 10:00 a.m. without problem.
Total time exposure on hydrox = 17 d 3 h

INVESTIGATIONS

Clinical observations	COMEX - GISMER - CEPISMER
- Tremor quantified EEG quantified EEG during sleep	GIS/CNRS
- Psychometric performances	OCTARES, Swedish Navy
Psychology	COMEX, CERB
- Ventilatory investigations in dry conditions, at rest and during exercise on bicycle ergometer	CERB
- Ventilatory investigations in wet conditions, at rest and during exercises on cyclorower ergometer	GIS, COMEX, CERB
- Cardiac adaptation to effort: dry and wet conditions	NMRI (U.S. Navy)
- Bubble detection	CERTSM
- Scintigraphy: lungs, skeleton, heart	CERB
- Biology in blood and in urine	CERB
- Ophthalmology	C.O.M.
- New regeneration systems with permanent reoxygenation of ambient gas to compensate divers' O_2 consumption	COMEX

Selection in nine professional divers: Clinical; scintigraphy; ventilatory and cardiac adaptation to effort (with respiratory resistance); ophthalmology.

Training: Psychometric tests; technical diving training.

Medico-physiological follow-up: Clinical; ventilatory function; scintigraphy; biology.

HPNS IN MAN
ELECTROENCEPHALOGRAPHIC AND TREMOR STUDIES
DURING HYDRA IV AND V EXPERIMENTS

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INTRODUCTION

Fifteen years ago, hydrogen-oxygen mixture experiments in monkeys gave contradictory results. Brauer and Way (1) reported an attenuation of the high pressure neurologic syndrome (HPNS) in mice and monkeys, but Rostain and Naquet (2) failed to find in the baboon *Papio-papio* significant changes between HPNS in helium-oxygen and HPNS in hydrogen-oxygen.

A few years later, in a study of the effect of helium-nitrogen-oxygen in monkeys, Rostain et al., (3-5) showed that the addition of nitrogen improved some symptoms of HPNS under several conditions. From these studies, it appeared that nitrogen did not reduce the HPNS if a speed of compression of 200 msw/h was used.

Consequently, with hydrogen-oxygen the use of compression speeds of 200 msw/h was probably too rapid and traumatic to allow a significant effect of hydrogen on the symptoms induced by such a rate of compression. The use of hydrogen in diving became interesting because of the low density of the mixture compared to helium of helium-nitrogen-oxygen mixture, and the narcotic potency which might reduce some symptoms of HPNS.

New investigations were carried out with hydrogen to study the effect on man of this gas under pressure.

METHODS

Two experiments were performed with hydrogen: Hydra IV and, recently, Hydra V. They are described in this book by Gardette.

During Hydra V, the divers breathed, during 30 min, hydrogen-oxygen mixture or hydrogen-helium-oxygen mixture with a mask in a special apparatus. The test was carried out at 180, 240, and 300 m. Our investigation was reduced to EEG analysis which was performed during 10 min in helium-oxygen before the switch to the mixture compounded with hydrogen and during the last 10 min of breathing the mixture composed of hydrogen. The EEG electrodes were put on by six divers before each test on the fronto-polar, central, mid-temporal, and occipital areas of the right hemisphere.

The second experiment was performed by two teams of three divers each. The two teams were compressed to 450 m in 38 h (same compression curve used in DRET 79/131, Entex 5, 8, and 9). The first 200 m of the dive was

performed using heliox. From this depth on, the divers were compressed with hydrogen. At 450 m, the percentage of H_2 was between 56 and 54%, and the partial pressure of oxygen was 0.4 bar. The first team, A, stayed 64 h with this mixture. A shift to helium-oxygen was performed with an intermediate stage of 8 h in helium-hydrogen-oxygen mixture with 25% of hydrogen. This team then stayed 5 d and 8 h in helium-oxygen mixture at 450 m. The decompression lasted 14 d 11 h.

The second group, B, stayed 4 d 8 h at 450 m and was decompressed to 200 m with a percentage of H_2 decreasing progressively from 54% to 0%. After that, the decompression was carried out in helium-oxygen. The total duration of decompression was of 18 d 22 h.

During Hydra V, we performed studies of tremor, EEG, and sleep disturbances. The EEG electrodes were composed of platinum wire fixed in the scalp for the entire duration of the experiment.

RESULTS AND COMMENTS

Hydra IV

During Hydra IV, the analysis of EEG activities and the power spectra showed a decrease in alpha activity in the posterior region when divers breathed hydrogen-oxygen, compared to the alpha activity recorded with helium-oxygen.

This decrease might be related to an effect of hydrogen but might also be a consequence of the rapid shift between the two breathing mixtures.

No significant difference between the various breathing mixtures was observed in slow wave activity (theta or delta).

Hydra V

Tremor. With group A, the compression to 450 m did not induce an increase of tremor. No tremor was observed during the stay in hydrogen-helium-oxygen mixture at the bottom. The switch to the helium-oxygen mixture induced tremor, which persisted during the entire stay at 450 m and during decompression until 200 m.

If we compare the increase of amplitude between the stay in heliox, with hydrogen and the stay in heliox without hydrogen, tremor activity increased only with helium mixture, between 50 and 100%. The Mann Whitney U-Test showed that differences between surface and stay with hydrogen-helium-oxygen mixture were not significant, whereas statistically significant differences were seen between surface and stay in helium-oxygen, and also comparing results at 450 m with the two different mixtures.

Particular attention must be given to the effects of the change of breathing mixture. The switch from 54% to 30% H_2 induced an increase of tremor activity which appeared in all the subjects though with different latencies. This increase persisted after the switch to 0% H_2 in at least two subjects.

With team B, the increase of tremor was not significant in two subjects during compression and stay at 450 m. In one subject the increase observed on the 2nd d of the dive was probably in relation to a thermal discomfort and not in relation to the compression in hydrogen-helium mixture. No tremor was recorded in this subject during the stay at 450 m.

EEG changes. With team A, compression with the hydrogen-helium oxygen mixture induced a decrease in alpha and beta activities in all the leads. This decrease persisted during all the stay at 450 m. The return to control value occurred during decompression after 300 m.

During compression, an increase of slow wave activity was recorded only in one subject, A3. This increase was around 200% and occurred between 400 and 450 m. The increase persisted at around 100% during the stay in the helium-hydrogen-oxygen mixture; it disappeared during the stay in helium-oxygen mixture.

A second subject, A1, presented an increase of theta wave activity around 100%, only during the stay in hydrogen-helium-oxygen mixture.

The third man, A2, did not present a significant increase of slow wave activity. Comparing the results before and after the switch, the increase in theta activity seems to have been recorded only in mixtures composed with hydrogen.

Comparison of the power spectra before and after the switch showed a decrease of the peak of theta activity, an evolution in helium-oxygen mixture never seen before. This decrease could be a secondary effect of the dramatic changes induced by the rapid switch from 54% to 30 % and 0% hydrogen.

Indeed the change of mixture induced an increase of slow wave activity, especially theta waves in the fronto-central and centro-temporal regions in all the subjects. This increase occurred during the first hour after the switch to 30 % H_2 and its maximum value (500% to 600% increase) was recorded in tests performed 3 h later.

The second switch, that to 0% of H_2, induced a new increase of theta waves in two subjects. Subject A2 seemed to have a depression of his EEG activities in all frequency bands analyzed.

The increase of theta wave activity was characterized by the occurrence of high amplitude slow waves and this type of activity recalled in some respects the EEG changes seen 18 years ago during the first description of HPNS in helium-oxygen during fast compression to 360 m (6).

With team B, which spent all its time at 450 m under 54% hydrogen, we recorded similar EEG changes.

Alpha activity decreased during compression; this decrease persisted throughout the stay at the bottom; return to control value was recorded around 300 m, i.e., before the disappearance of hydrogen from the mixtures.

The increase of theta waves was more consistent with this group. It appeared during compression in two subjects and during the stay in subject B1. This increase, which varied form 100% to 300% according to the subject, persisted throughout the stay at 450 m and disappeared during decompression at different times: rapidly in subject B1 around 430 m, and in subject B3 around 300 m; and still present in subject B2 when we stopped recording at 160 m.

CONCLUSIONS

The neurophysiological studies carried out during the Hydra V have shown that the hydrogen-helium-oxygen mixture did not induce tremor or other clinical symptoms of HPNS (dysmetria, fasciculation, microsleep). The comparison between these results and the results obtained with helium-nitrogen-oxygen breathing mixture shows that they are at the lower end of the range of increase recorded (7,8).

The increase in theta waves which appeared during compression or stay at 450 m are similar to the increases recorded in helium-nitrogen-oxygen or helium-oxygen with the same curve of compression (7,8). The depression of alpha waves and beta waves seemed to be more intense with hydrogen compared with the other mixtures. But the changes induced by the switch do not allow one to make any definitive statements.

An important observation is the increase of HPNS at constant pressure due to the rapid switch between two different gases. This effect might be the consequence of the disappearance of hydrogen which was necessary to prevent some HPNS symptoms; it might also be the consequence of the sudden increase of helium, and in this case it would be equivalent to a fast compression.

In conclusion, the use of 54% of hydrogen at 450 m induced EEG changes that were no more intense than those induced at the same depth by helium-nitrogen-oxygen and helium-oxygen mixture with the same curve of compression. It reduces or prevents clinical symptoms of HPNS, and this effect is probably in relation to its narcotic potency which antagonizes the pressure effect according to observations or hypotheses of several authors (1, 9-11). This mixture opens new perspectives for future deep diving.

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HYDROGEN, PRESSURE, AND HPNS

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During the Hydra V experimental saturation dive, two teams composed of three divers each (two professionals and one French Navy diver), six in all, went to a pressure depth of 450 msw.

One team spent 2.5 d and the other team 4.5 d on a mixture containing 55 $\pm$ 1% hydrogen (P_{H_2} = 25.3 $\pm$ 0.5 bar) at 450 msw, the P_{H_2} and depth having been reached in 26 h from the 200-m level.

According to the symptoms and signs observed, narcosis did not exceed grade 1 in the first team and grade 2 in the second team (appendix 1). Of the six divers, only LS had participated in the Hydra IV experimental dive. A professional diver who is not particularly subject to narcosis, he had on that occasion experienced a grade 3 hydrogen narcosis at 240 msw. With a P_{H_2} of 15.8 bar at a total pressure of 45 bar, he had no symptoms or signs of narcosis. Observation of the five other divers showed that with the same P_{H_2}, narcosis did not go beyond grade 2 and even that only for two of the six divers, whereas in Hydra IV, four of the six subjects had reached or exceeded grade 3 (appendix 2).

Our rough calculations for Hydra IV of the relationship between ambient pressure, gas pressure, and degree of narcosis led us to predict that, below 200 msw, for every additional 100 msw the P_{H_2} could be increased by 2 bar over the perfectly well tolerated 17 bar of hydrogen in the hydrox used at 160-165 msw (appendixes 3-6).

On the basis of this hypothesis we felt that the Hydra V divers would be able to tolerate a mixture with 50% H_2. To simplify things we decided to establish the "hydrogen depth" at 250 m, which gave a mixture with 55% H_2 and a P_{H_2} which was fairly well maintained at $\pm$ 1%. With the P_{H_2} of 23 bar originally planned on, instead of the 25.5 bar actually applied, it is quite possible that narcosis would not have gone beyond grade 1 for any of the six divers, but we would have had more difficulty in evaluating the limits.

It is quite possible that, even though the pressure reversal effect was not disproved, the tolerance to hydrogen at 450 msw could be due to another factor: the gradual increase in P_{H_2} from 0 bar at 200 m to 25.5 bar at 450 msw over a 26 h period, just as slow compression attenuates the HPNS.

A He-H_2 cross-over at 450 msw would have given us the answer. We had planned to do this, but the adverse effects of the opposite cross-over on Team A led us to abandon the idea. Therefore the question remains, albeit in our opinion: the pressure reversal effect, which we attempted with a certain degree of success to measure and utilize, is the explanation.

If the pressure reversal effect of H_2 narcosis has not been definitively demonstrated in human beings, the contrary (P_{H_2}/pressure) can no longer be doubted after the Hydra V experiment. To provide a basis for comparison we selected divers who had already participated in heliox saturation dives. Of our six subjects, five had participated in experimental dives to between 300 and 610 msw and had thus had experience with HPNS. Furthermore, the Hydra V compression profile to 450 msw was identical to the compression profile for the previous series of experiments (COMEX and French Navy).

None of the six divers had HPNS either in the 300-m zone or at 450 m. The clinical picture, now become classical, was completely absent. No tremor, dysmetria, nor prior to myclonia, the neuromuscular tension characteristic of the syndrome was apparent. Nasal respiration was normal, thus preserving appetite and resulting in relatively insignificant weight loss (an average of 2 kg, 4.5 lb, for team B, the one which did not switch to heliox), and there was a total absence of the "no joint juice syndrome" (NJJS). This was such a contrast with what the divers had experienced during heliox saturation that, in spite of the lack of comfort in their spherical chamber and the constraint of confinement, the unfailing characteristic of this hydrogen dive was well-being and good humor!

However, Team A, after 2.5 d of well-being, was switched over to pure heliox. The $H_2 \rightarrow$ He switch, in spite of being attenuated by 8 h in an intermediate mixture (with 30% H_2), affected two of the divers with a sudden onset of HPNS with postural tremor, vertigo, nausea, anxiety, agitation, and some myoclonia (appendixes 7-10). These disorders, along with the difficulties caused by gas counterdiffusion and the NJJS, gave us some problems but fortunately without lasting consequences.

We consider this delicate phase of the operation to have been a definite demonstration: switching from a hydrogen mix to pure heliox during deep saturation diving exposes the diver to inadmissible risks. This is why Team B remained on hydrox for 4.5 d until final decompression. This team showed no sign of either HPNS or NJJS. The hydrogen content of the mixture was gradually withdrawn during the first 250 m of decompression without the slightest incident.

CONCLUSION

If Hydra V did not definitively prove that it is the pressure reversal effect that limits the narcotic effects of H_2 at high pressure, it did prove that hydrogen can, at the right pressure, reduce the HPNS and NJJS.

APPENDIX 1

Hydra V Saturation Dive to 450 msw

H_2-He-O_2 Mix With 55 $\pm$ 1% H_2-P_{H_2} = 25.3 $\pm$ 5 Bar

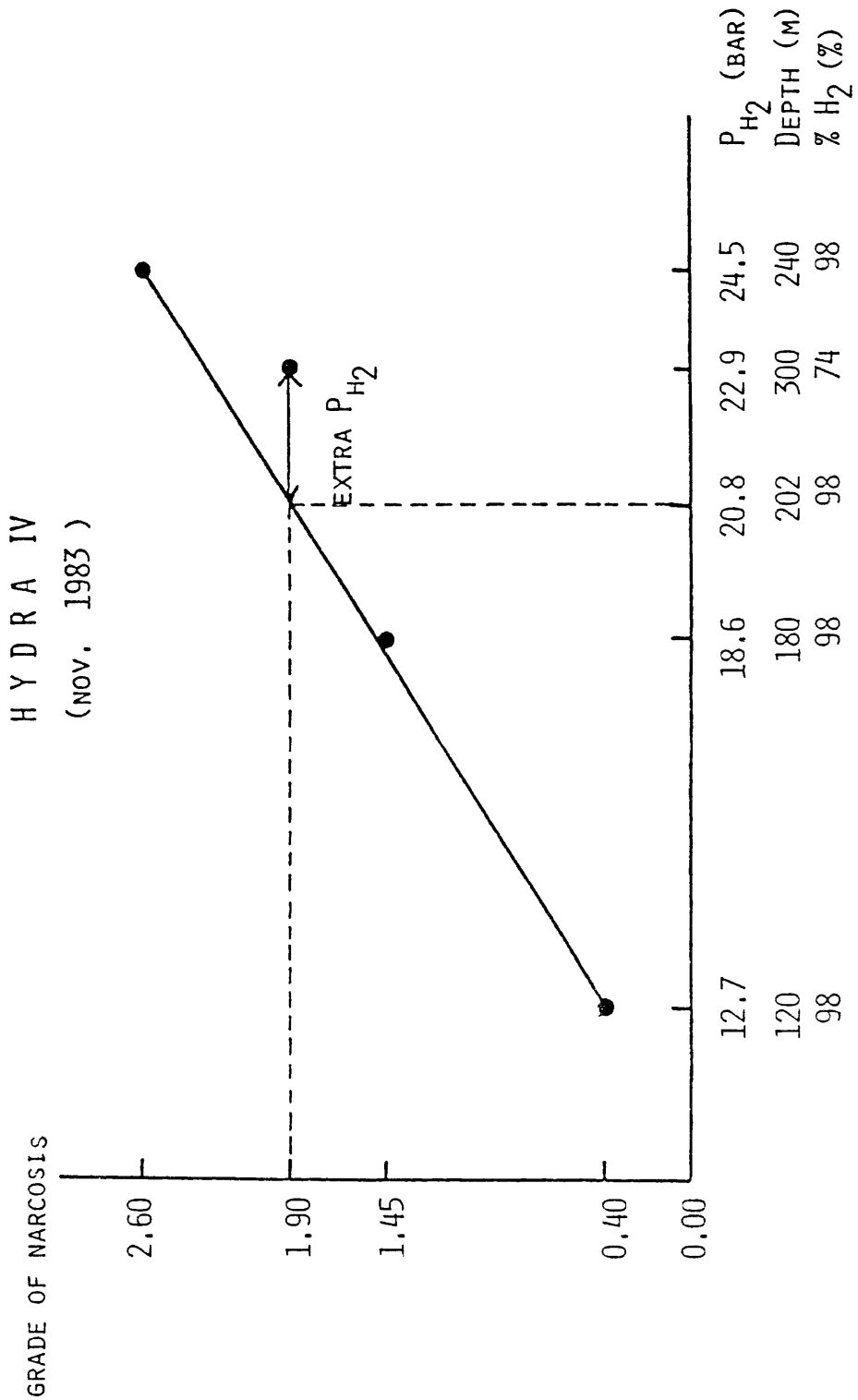
Diver	Symptoms	Grade of Narcosis
A_1, A_2	Euphoria, attributed to absence of HPNS	1
A_3	Well-being	0
B_1	Difficulty in concentrating. Upon rising slight vertigo at change of position	1.5
B_2	Cutaneous hypesthesia over entire body. Less to blows. Impression of pitching upon changing position	2
B_3	Thought process slowed down. Difficulty in concentrating. Some vertigo and nausea. Alternate euphoria and anxiety.	2

APPENDIX 2

Case of Diver L.S.

Exp.	Depth msw	P_{H_2} bar	Symptoms	Grade
Hydra IV				
	120	12.7	Some decrease in tactile sensitivity of fingers	.5
	180	18.6	Slight narcosis perceptible at R.S.R.	1
	240	24.5	Increase of tactile sensitivity and hearing. Mental effort for self-control giving rise to anxiety. Subject felt normal during activity. Impairment of alertness during R.S.R.	3
	300	22.9	Same symptoms as at 240 m but attenuated	2
	300	19.3	Narcosis scarcely perceptible	1
	150	15.7	(Stop during the ascent) - No symptoms	0
Hydra V				
	450	25.8	Nothing to be noted	0
	450	11.5	Nothing to be noted	0
	450	0.00	Slight tremor. "No joint juice" syndrome (knees)	HPNS !

APPENDIX 3



APPENDIX 4

HYDROGEN PRESSURE AS A FUNCTION OF DEPTH
(predictive equation)

$$P_{H2} = 17 + .02\ \Delta D$$

where

P_{H2} = recommended hydrogen pressure (bar)

17 = basic allowable P_{H2} (bar)

0.02 = overpressure coefficient (bar/msw)

ΔD = depth - 160 (msw)

(160 msw is the depth limit of pure hydrox diving
with a narcosis level not to exceed grade 1)

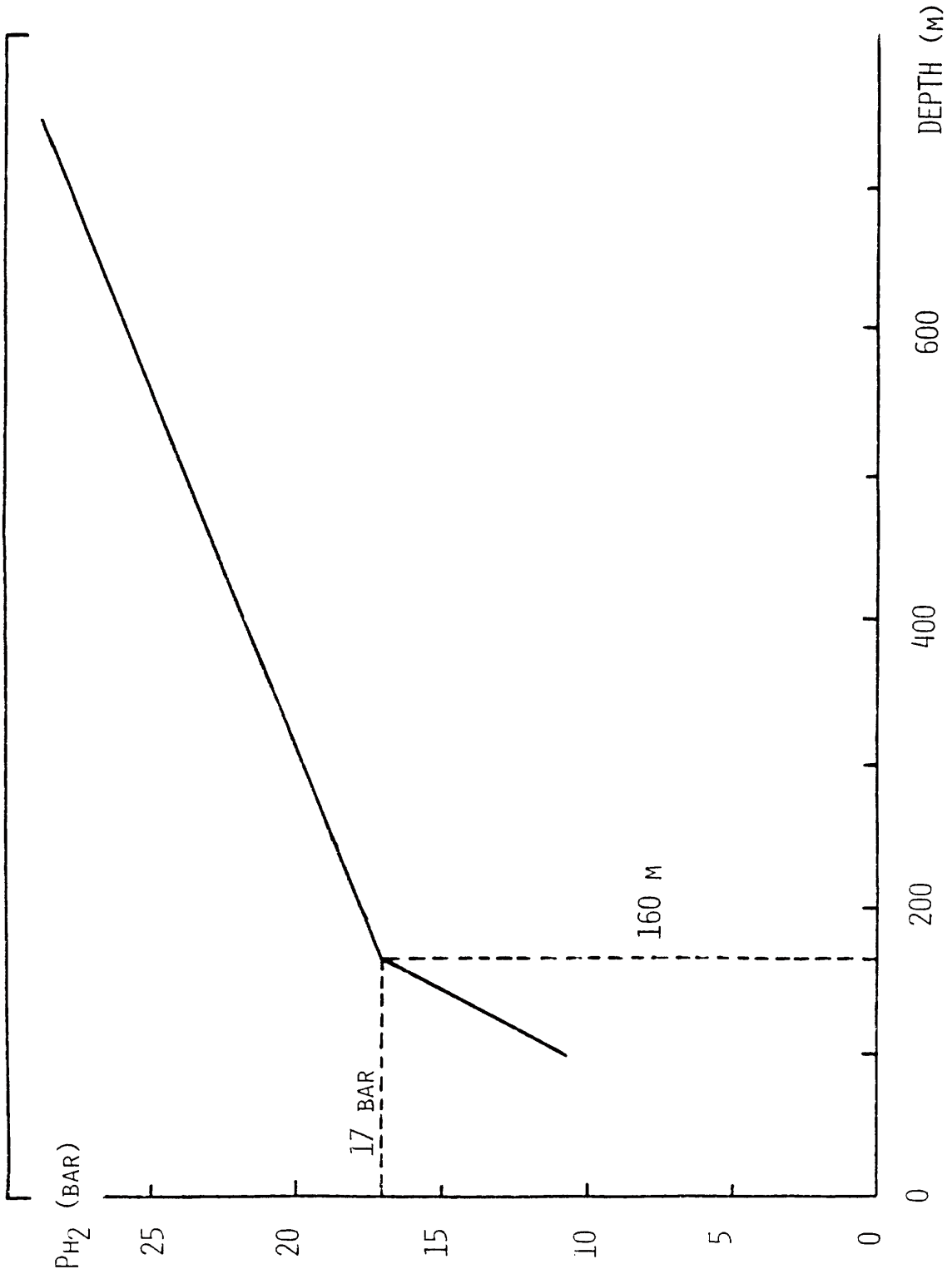
APPENDIX 5

Allowable P_{H2} and F_{H2}

According to the Depth of the Dive

Depth msw	P_{H2} bar	F_{H2} %
200	17.8	85.0
250	18.8	72.0
300	19.8	63.8
350	20.8	57.8
400	21.8	53.0
450	22.8	49.5
500	23.8	46.5
550	24.8	44.3
600	25.8	42.3
650	26.8	40.6
700	27.8	39.0

APPENDIX 6



APPENDIX 7

Switch H_2 - He - May 11 & 12 - Diver A_1

Time	
08:05	450 msw - Switch to 30% H_2 Nothing to be noted
16:05	Switch to 0% H_2 (Heliox 99-1)
17:30	Pallor - Severe fatigue with precordial pain - Nausea Tremor - slight myoclonia - Painful right knee and wrist
17:47	450 to 460 msw - (0.5m/min) - Heliox 2% O_2 by mask
18:07	460 msw
18:40	Cannot bear mask - Takes it off. Anxiety, pallor. Persistence of articular bends (knees, wrists). Slight general improvement - Attenuated myoclonia
19:30	Better at rest laying
20:30	Dinner Eats little - No appetite but no nausea
22:20	460 to 470 msw - P_{O_2} : 0.6 bar When laying at rest, symptoms and signs are attenuated
23:00	
23:25	470 msw
00:30	Falls asleep
10:00	Asthenia - Persistence of tremor
12:00	Ascent to 450 msw

APPENDIX 8

Switch H_2 - He - May 11 & 12 - Diver A_2

Time	
08:05	450 msw - Switch to 30% H_2 Nothing to be noted
15:05	Switch to 0% H_2 (Heliox 99-1)
17:30	Vertigo (without nystagmus) - Nausea Tremor - Pain in his left shoulder
17:47	450 to 460 msw - (0.5 m/min) - Heliox 2% O_2 by mask
18:07	460 msw
18:40	Itching all over his body Articular pains (left shoulder, knees) Tremor. Takes 1 g of Aspirin
19:30	More and more intense itching. Excitement Articular pains reach his ankles
20:20	460 to 470 msw - P_{O_2} : 0.6 bar Pruritus and pains are getting worse - Takes 1 tablet of Valium 5 mg
20:30	Dinner Scarcely eats. Takes his mask again - 2% O_2
23:00	Exasperated by pruritus - Takes Polaramine 6 mg
23:25	470 msw Very excited as itching increases when lying
00:30	Falls asleep
10:00	Pruritus dying down - Tremor - Arthralgia (rather NJJS)
12:00	Ascent to 450 msw

APPENDIX 9

Switch H_2 - He - May 11 & 12 - Diver A_3

Time	
08:05	450 msw - Switch to 30% H_2 Slight tremor
16:05	Switch to 0% H_2 (Heliox 99-1)
17:30	Slight indisposition - Tremor Pains in both knees
17:47	450 to 460 msw - (0.5 m/min) - Heliox 2% O_2 by mask
18:07	460 msw
18:40	Finds the change unpleasant NJJS (knees) exactly like after Heliox compressions
19:30	Nothing new
20:30	Dinner Appetite almost normal
22:20	Takes 1 Valium 5 mg and falls asleep
23:00	Sleep
23:25	470 msw Sleep
00:30	Sleep
10:00	NJJS in both knees
12:00	Ascent to 450 msw

DISCUSSION FOLLOWING PRESENTATIONS BY ROSTAIN ET AL. AND FRUCTUS

UNIDENTIFIED SPEAKER: I would like to ask Dr. Fructus whether or not subject A2 had a rash. He was very itchy, but did he have a rash?

FRUCTUS: No.

LUNDGREN: I would like to raise briefly another operational aspect that is likely to strike anybody who has had clinical responsibility for human subjects in a chamber. I can't hold back my curiosity but have to ask Dr. Fructus or anybody else who was there and wants to comment: You had one of your subjects at depth pale, sweating, with precordial pain; could you fill us in a little more on the clinical situation and the considerations that must have gone through your mind when the subject presented these symptoms? How did you resolve it so as not to be concerned that you actually had a heart condition to deal with?

FRUCTUS: In this situation we were pretty sure that this could not be the case.

ÖRNHAGEN: I share that opinion, but I think the situation is very difficult. I just want to point out the possibility that Dr. Gennser mentioned, that we have a reduction of the carrying off of the conductivity of the cardiac myocardium, and Stokes-Adams-like attacks at these pressures could happen, based on the animal research we have. In some deep dives, a diver has passed out, and we are now operating at depths where it could happen again and we have to look out for it.

YOUNGBLOOD: On this same vein of speculation, if we are looking at counter-diffusion problems, there is no reason to think that as you have the surface of the skin with the lighter gas and the more dense gas in solution, we could not have at the alveolar capillar membrane also counterdiffusion which might create the microbubbles in the pulmonary vascular bed, which in turn could cause microbubbles in the coronary circulation. These would respond to recompression and not to an isobaric change.

ÖRNHAGEN: Could we leave this question for Dr. Masurel who monitored the divers and will talk about his work tomorrow?

GIRY: I would like to say that exercise performance of the divers, tested two days after the gas switch, was not affected, and that the ECG was perfectly normal.

IMBERT: I would like to make a further comment on behalf of Dr. Fructus, related to the accident. The most important problem they were thinking about then was a possible vestibular accident and that was the true reason for the recompression, and not the narcosis or the HPNS problems.

GIRY: Have you any means of predicting individual susceptibilities?

FRUCTUS: That is very tricky, but still in the two divers we carried out we have made a number of observations. In Hydra IV, we had a group of intel-

lectuals--an engineer and two physicians, and on the other hand three professional divers, well accustomed to saturation dives. The least degree of narcosis clearly was seen with the professional divers. In Hydra V we had a group of divers, all of whom were amply experienced and had already made deep dives, one of them all the way down to 610 m. We have certainly gained the impression that these experienced divers showed substantially smaller degrees of narcosis. Of the six divers the two who showed a degree of narcosis of approximately two on my scale and who didn't perform well were the two subjects we had taken into Hydra V only after a good deal of discussion.

FLYNN: Are there any long-term health consequences of either Hydra IV or Hydra V?

FRUCTUS: We haven't talked here about toxicologic, largely because Dr Giry was supposed to bring results with him but didn't. The blood chemistry so far has been totally negative--no indication of toxic effects of any kind--transient or residual. Nor have we seen any EEG abnormalities relatable to the Hydra experience. From the point of view of body weight, we had one diver who went into the chamber hoping to lose weight and who we put on a special diet. He lost 5 kg. The remaining divers didn't lose more than 1-2 kg. This seems to be due to the fact that they were in a physiologically much more favorable situation than divers on heliox at the same depth. Perhaps in part this is related to the absence of HPNS symptoms, but more particularly, in my opinion, because of the absence of my favorite symptom--nasal congestion. This plugged-up nose is typically seen in saturation dives at considerable depths under heliox and was completely absent in the divers on hydrogen-helium during Hydra V. In helium this business shows up at 300 to 360 m and is associated with a loss of appetite, not only because they can't smell their food but also because you can't breathe through the mouth while chewing your food, and with a badly congested nose this can make eating very uncomfortable. As a result, the weight losses in heliox saturation dives may very well be a mechanical problem as much as anything else. I have seen exactly the same kind of sequence during Dr. Bennett's Atlantis IV dive--from about 450 m on his divers refused to consume anything but liquid foods. Since then these divers of ours have regained their normal physical condition and have already left for other diving sites.

BRAUER: I don't think you should write off the loss of appetite during the high pressure exposures purely to the plugged-up noses. We have experiments with mice whose tastes are fairly catholic, who show to an exaggerated degree this loss of appetite and in whom the loss of appetite in the chamber can be overcome by offering them either a cafeteria or "Julie's pet breakfast food." In either case, on these altered diets the weight loss disappears or becomes very small, and that does not sound as though our mice had drippy noses. I think you are looking at something much more interesting related to the brainstem or subcortical effects of high pressures on appetite that I don't think we should neglect.

FLYNN: Were there any clinical studies 2 w after surfacing including of phychomotor testing, EEG and ultra responses, neurologic examinations to ensure that everything was intact?

GIRY: Extended and professional medicine has been done on the commercial divers and none has been found affected in any way.

FRUCTUS: The divers were asked to give their own evaluation of their experiences during Hydra V and said essentially: "We feel ourselves as comfortable at 450 m on heli-hydrox as we are used to feeling on heliox at 250 m."

SECTION IV
Respiratory Exercise and Cardiovascular Physiology

THEORETICAL CONSIDERATIONS OF HYDROGEN AS A BREATHING GAS IN DIVING

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This is a brief introduction to the session on the respiratory aspects of hydrogen as the diver's breathing medium. One of the expected advantages of H_2 is derived from its low density as it relates to respiratory flow resistance. Another aspect--a concern, is the potential that H_2 has for disturbing thermal balance. There is also the narcotic potential of H_2 which had two sides, a negative and a positive.

We can begin with the thermal problem. The problem of respiratory heat loss is dominated by the specific heat of the gas mixture that is being breathed rather than its heat conductivity. For comparison, consider the specific heat values of H_2 and He, which is the other important inert gas alternative in very deep diving.

Volumetric specific heat at ATA:

$He = 8.39 \times 10^{-4}$ kJ x L^{-1} x $°K^{-1}$*

$H_2 = 1.16 \times 10^{-3}$ kJ x L^{-1} x $°K^{-1}$

Assume that the diver is at a pressure of 50 ATA and is breathing at a rate of 65 liter x min^{-1}; and that the breathing gas is being warmed from the ambient water temperature of 4° C (277° K) to body temperature, i.e., 37° C (310° K). (This assumes thermal equilibrium between the gas and the body which may not fully occur. Moreover, evaporative heat loss and heat loss from the body surface have not been taken into account). The respiratory heat loss will then be:

$Q_{He} = 8.39 \times 10^{-4} \times 65 \times (310-277) \times 50 = 8.98$ kJ x min^{-1}** or 1.5kW***

$Q_{H2} = 1.16 \times 10^{-3} \times 65 \times (310-277) \times 50 = 126$ kJ x m^{-1} or 2.1 kW

These numbers should be compared with the metabolic heat generation during heavy exercise of about 1.0 kW. Clearly the diver would, under these conditions, experience a net loss of heat which would potentially be about 45% more rapid during H_2 breathing than during He breathing.

It may therefore be concluded that, in the absence of sufficient respiratory gas heating, such as may occur in connection with equipment malfunction, H_2 will pose a significantly greater danger to the divers' heat balance than He. The specific risks connected with excessive respiratory heat loss are:

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* Kilojoules per liter and degree Kelvin.
** Kilojoule per min. *** Kilowatt.

- Whole body cooling;
- Severe mucus production in the airways (1);
- Cold-induced bronchospasm;
- Intense discomfort.

Spaur et al. (2) recorded the maximal voluntary ventilation (MVV) in subjects breathing a He-O_2 mixture at 49.5 ATA (PiO_2 = 0.3 - 0.5 ATA) to be about 100 liter x min^{-1} (ATP). When their submersed subjects performed subjectively heavy exercise (at a $\dot{V}O_2$ of 119 liter x min^{-1}, the ventilation was calculated at 56 liter c min^{-1}, i.e., 56% of MVV. Given that MVV is proportional to the square root of the relative gas density, one may predict the MVV for H_2 breathing at this pressure at be:

$$\frac{MVV_{H2}}{MVV_{He}} = \frac{D_{He}}{D_{H2}}$$

where D_{He} is 0.1625 kg x m^{-3} and DH_2 = 0.08078 kg x m^{-3}. The $MVV_{H}2$ then would be predicted at 142 liter x min^{-1}, i.e., about 40% higher than for He and, given the same $\dot{V}_E$ to MVV relationship (56%) as for He, the $\dot{V}_E$ for H_2 would be predicted at 89 liter x min^{-1}.

Taking the analogy with the results of the study mentioned above one step further, one may assume that a proportionality in the sustainable O_2 consumption also exists such that

$$\frac{\dot{V}O_2(H_2\text{-breathing})}{\dot{V}O_2(He\text{-breathing})} = \frac{\dot{V}E\ He}{\dot{V}_E\ H_2}$$

which yields a sustainable O_2 consumption during heavy work and H_2 breathing of about 2.7 liter x min^{-1}. This is a metabolic level which allows a considerable useful power output. A similar reasoning may be applied to measurements performed by Salzano et al. (3) in He-O_2 breathing subjects in the dry pressure chamber at 47 ATA. Their subjects were able to perform 6-min exercise bouts of up to 800 and 900 kpm with ventilation levels between 60 and 80 liter x min^{-1} supporting a $\dot{V}O_2$ of about 2 liter x min^{-1}. If, again a 40% higher ventilation can be achieved with H_2, and if the $\dot{V}O_2$ is correspondingly increased, the respective numbers would be for $\dot{V}_E$ 85-110 liter x min^{-1} and for $\dot{V}O_2$ 2.8 liter x min^{-1}, i.e., the same as was predicted from the observations of Spaur et al. (2).

Finally, the maximal pressure at which H_2 can be inhaled is most likely not going to be set by restrictions that it may impose on pulmonary ventilation but by its narcotic potency. If the narcotic potency of a gas is proportional to lipid solubility then H_2 is about 4.5 times as narcotic as N_2 (4). Extrapolating from the U.S. Navy air diving limit of 190 ft, the limit for H_2 would be about 900 ft. However, this disregards the possible ameliorating effects that high hydrostatic pressure may have on narcotic effects. In this context it is worth noting the suggestion that tissue respiration may be compromised at high pressure per se as evidenced by

abnormal lactacidemia. If such a pressure-induced disturbance could be counteracted by narcotic gases in the same way as they counteract some pressure effects on the central nervous system, then H_2 may be of interest because of its higher narcotic potency than He. It would add justification for further experimentation with He-H_2-O_2 trimix for very deep diving.

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HYDROGEN IN BREATHING GAS REDUCES WORK OF BREATHING

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During the Swedish saturation dive to 1.3 MPa (120 m) when hydrox (98% hydrogen:2% oxygen) was tested as a breathing gas, we recorded work of breathing, lung resistance calculated from the work of breathing, and some other respiratory parameters (1). Since ventilation might limit physical performance during deep diving, quantifying the respiratory load and ventilatory performance become of great interest.

WORK OF BREATHING AND FUNCTIONAL LUNG RESISTANCE

The work of breathing was measured in three divers sitting at rest by measuring the esophageal pressure with a balloon and the volume changes with a following seal spirometer (Fig. 1) (2). There was a tendency toward lower work per breath when breathing hydrox (0.3 J) compared with heliox breathing (0.6 J) at the same depth. Owing to the large variations in minute ventilation, the difference was not significant. By using the instantaneous respiratory flow and the work of breathing, we calculated the functional lung resistance [$R_f(1)$], which is a value that can be used to estimate the respiratory load due to flow resistance at different ventilations (3). Functional lung resistance was 35% lower ($P = 0.01$) during hydrox breathing (Fig. 2). We also measured $R_f(1)$ after the dive breathing air at 0.1 MPa (Om). This value was 35% lower than the $R_f(1)$ during hydrox breathing.

The pressure drop in the larger airways (diameter > 2mm) depends on area changes, bends, and turbulent friction losses. A very simplified relationship for this drop can be written as follows:

$$\text{Pressure drop} = \text{density}/\text{diameter}^4 * \text{flow}^2 * F.$$

The factor F is dependent on the viscosity. Exercise and increased ventilation increase airway diameter probably due to sympathetic activities in the airway smooth muscles (4). By even further simplifying the above relationship, we tested the assumption that the increase in diameter which is a result of the increase in flow can allow the use of the following linear expression:

$$\text{Pressure drop} = \text{density} * \text{flow} * F_1$$

where Fl is a constant. The flow resistive work during one inhalation can be calculated by integrating the pressure drop over the inhaled volume, V_{in} Fig. 3:

$$\text{Work} = \int_0^{V_{in}} \text{pressure drop} * dV_{in}$$

which is equal to:

$$\text{Work} = \int_0^{T_{in}} \text{pressure drop} * \text{flow} * dt$$

where T_{in} is the time for one inhalation.

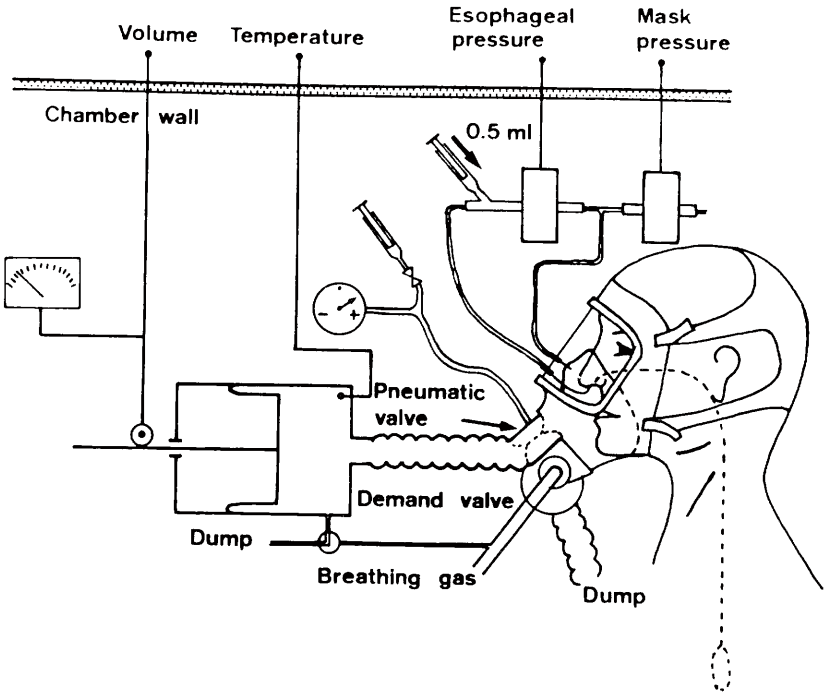


Fig. 1 *Schematic drawing of the experimental set-up used in pulmonary function studies during heliox and hydrox breathing.*

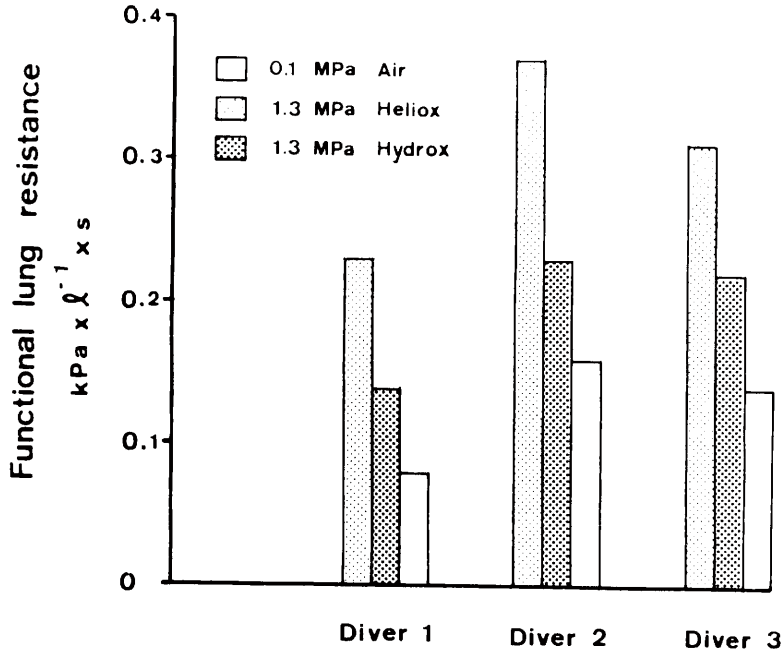


Fig. 2. Functional lung resistance during resting ventilation Each histogram bar is a mean of three breathing cycles.

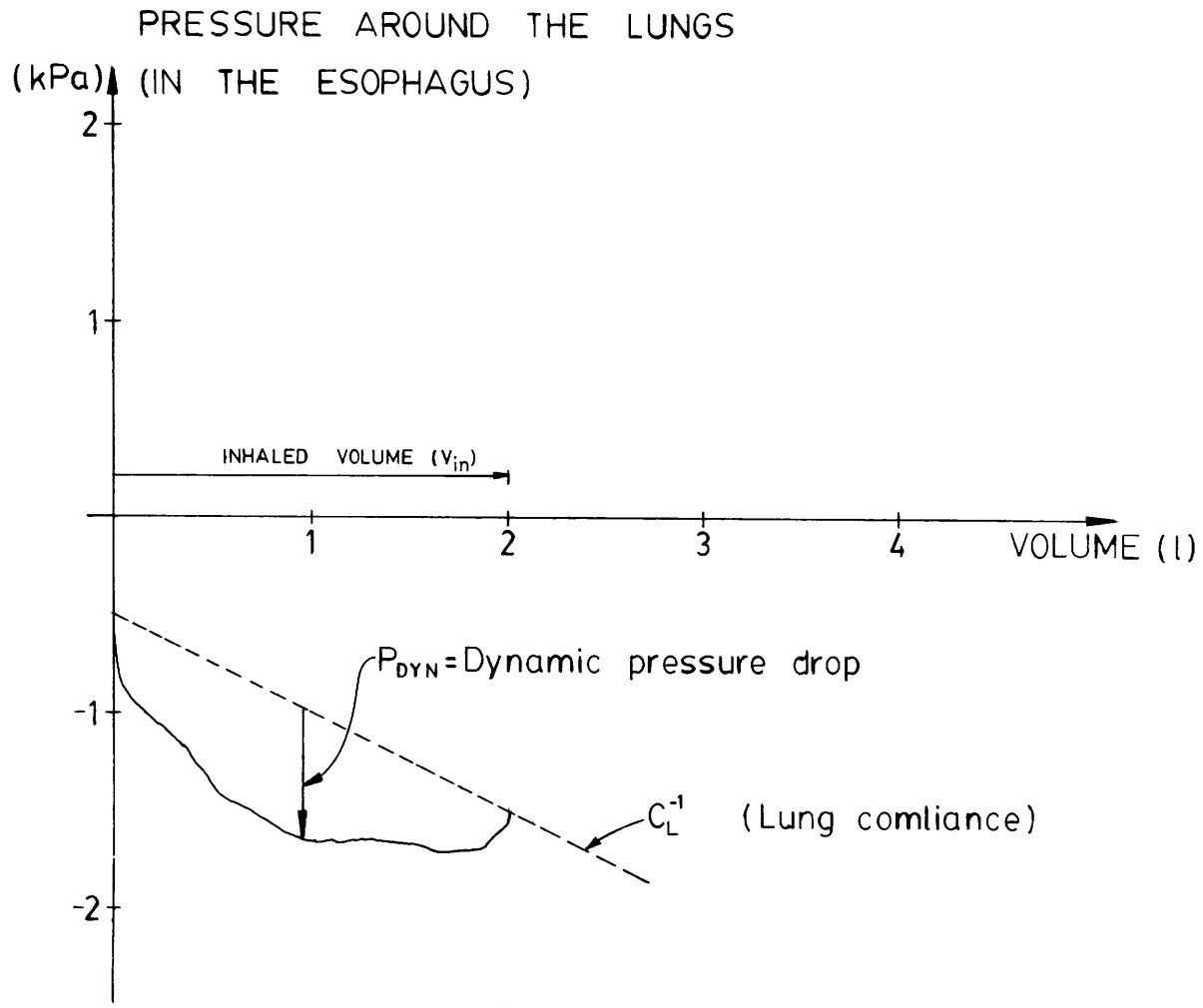


Fig. 3. Volume-pressure registration of the lung. Pressure is normally measured with an esophageal balloon. The area within the curve and the broken line is the flow resistive work of breathing during inhalation.

By using the two expressions above, the following will apply:

$$\text{Work} = \text{density} * F_1 * \int_{\circ}^{T_{in}} \text{flow}^2 * dt.$$

Density times the factor F_1 which is assumed to be constant for a certain gas at a certain ambient pressure is the above-mentioned $R_f(1)$. Several hundred patient investigations [(5) and personal communication, L. Jorfeldt, Clinical Physiology, Linköping University, 1984] have shown that the above assumptions give a useful resistance value which only varies between narrow margins during rest and exercise. If a sinusoidal flow is assumed, then:

$$R_f(1) = \text{Work}/T * 2/(V'_E * P_i)^2.$$

The density of the hydrox gas was 42% lower than the heliox gas at 1.3 MPa (Table 1), which correlates well with the reduction in $R_f(1)$ which was

35%. After the dive in air $R_f(1)$ was however 35% lower although density of air at 0.1 MPa was only 17% lower than hydrox at 1.3 MPa. This discrepancy could be due to the fact that the Reynolds number (Re) was 125% higher for the hydrox gas compared with air at the surface, since the density of hydrox was higher and the viscosity almost half that of air. This means that the flow of air could stay laminar up to a somewhat higher flow, thus reducing $R_f(1)$ further than would be expected if the density decrease alone was responsible.

TABLE 1

	Air 0.01 MPa		Heliox 1.3 MPa		Hydrox(98/2) 1.3 MPa	
	in	out	in	out	in	out
Density						
(kg x m-^{3})	1.14	1.19	2.39	2.42	1.38	1.40
Rel %	100	100	210	203	121	118
Viscosity						
(Pa x s x 10-^{6})	18	18	21	21	9	9
Rel %	100	100	124	124	53	53
Rel % Re (Reynolds tal)	100	100	170	160	230	220

In Fig 4., we have plotted the actual measured power of breathing (work per time unit) during inhalation and exhalation as a function of minute ventilation. The pooled $R_f(1)$ values calculated from the data achieved during rest for the three gases have then been used to estimate the power that would be required during harder work. For these calculations according to the equation above, we have assumed the ventilation and thus the flow to be sinusoidal. The divers also performed some measurements during hyperventilation and these $R_f(1)$ values are also plotted in Fig. 4. From these data, an estimate can be made of the power of breathing with a specific gas mixture for different ventilations by using the $R_f(1)$ concept.

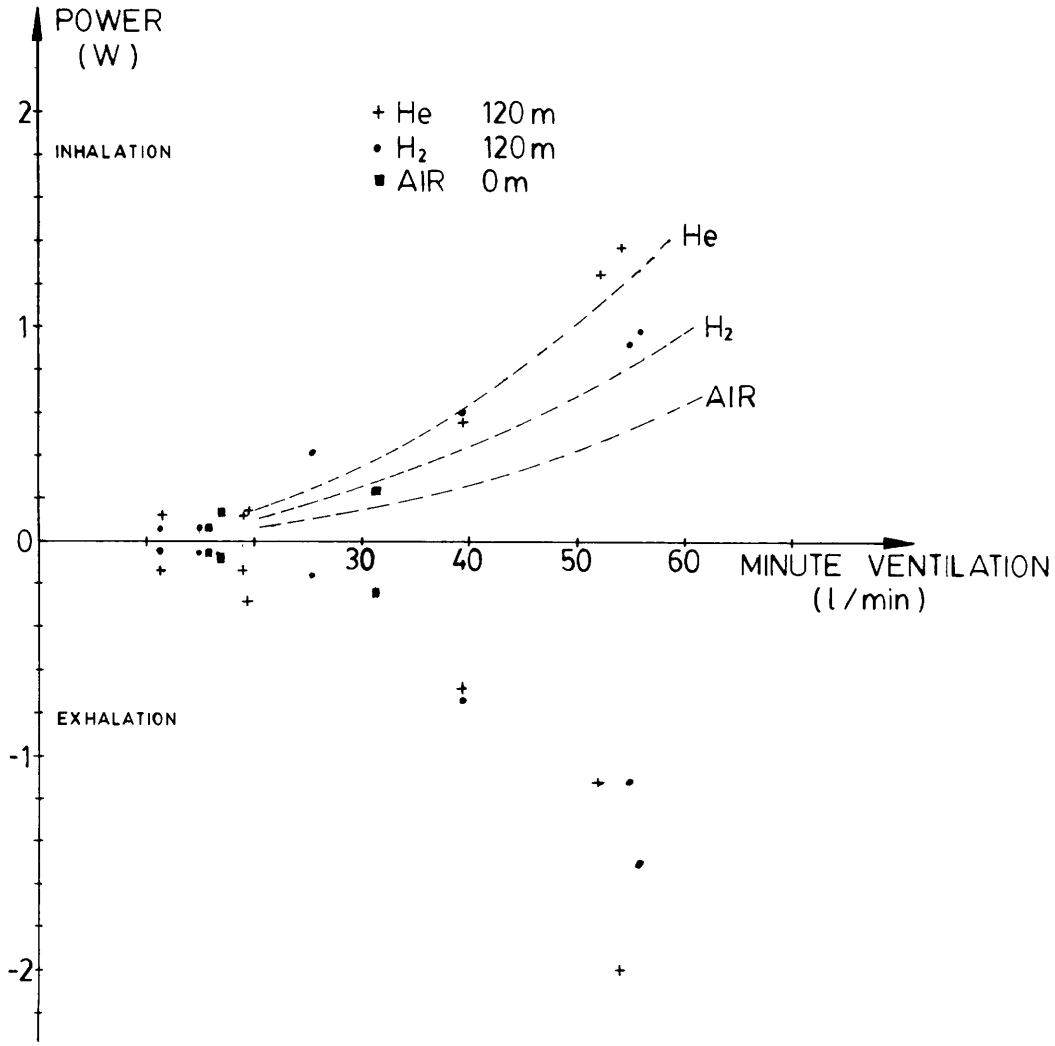


Fig. 4. Absolute and relative densities and viscosities for the breathing gases.

SPIROMETRY AND DYNAMIC LUNG COMPLIANCE

Vital capacity (VC), forced vital capacity (FVC), and forced expiratory volume after 1 second ($FEV_{1.0}$) were all somewhat higher at depth compared with the values in air before and after the dive (Fig. 5). We have proposed that this could be due to a sympathetic drive caused by the mental stress surrounding the hydrox dive. The divers' heart rates were 5 to 11 beats higher at depth compared with air breathing before the dive. Such a sympathetic drive could perhaps keep some bronchioles open a little longer during exhalation, thus decreasing residual volume and increasing VC. The VC after the dive was not reduced compared with the VC before, which was perhaps a positive effect of the low O_2 partial pressure (P_{O_2}) of about 26 kPa used in the chamber system throughout the dive.

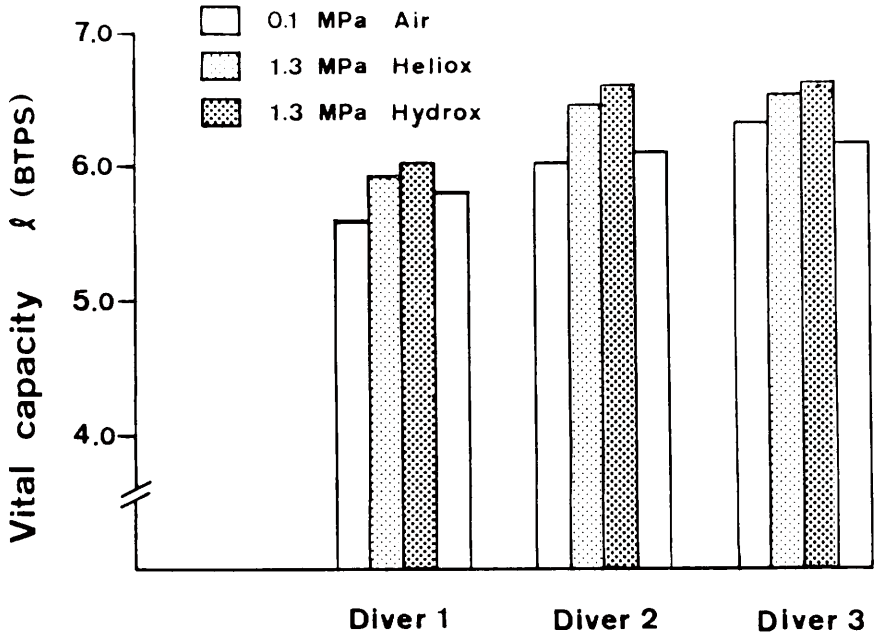


Fig. 5. Power of breathing measured at different ventilations during rest. The broken lines are calculated from the measured values at low ventilations according to the formula given in the text.

Maximal voluntary ventilation (MVV) with hiliox was about 25% lower than both the air MVV before and after the dive and the hydrox MVV (Fig. 6).

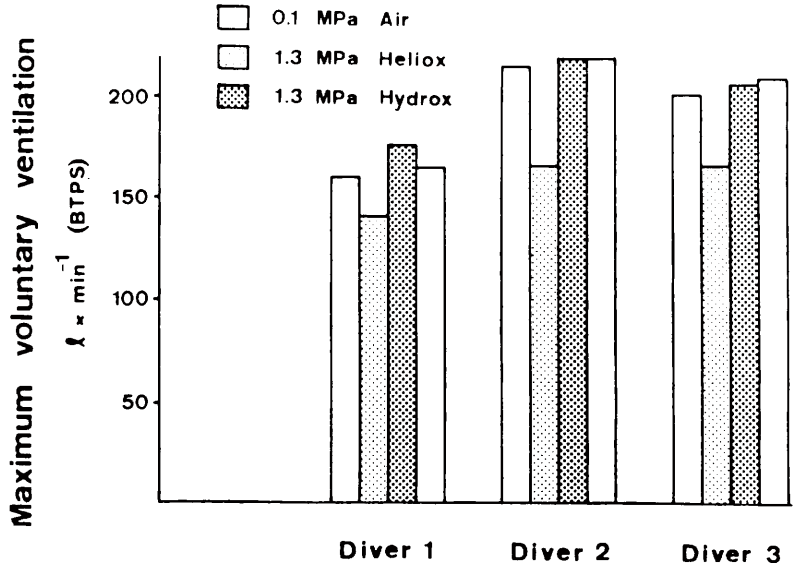


Fig. 6 Forced vital capacity. Each histogram bar is a mean of two measurements in air and four measurements in heliox and hydrox. Forced vital capacity. Each histogram bar is a mean of two measurements in heliox and hydrox.

The dynamic lung compliance increased with rising density (Fig. 7). The difference between the values at depth compared with the surface value could perhaps also be an effect of the above-mentioned stress. Sympathetic drive might keep more airways open and thus increase compliance. An increased compliance will reduce the elastic work of breathing.

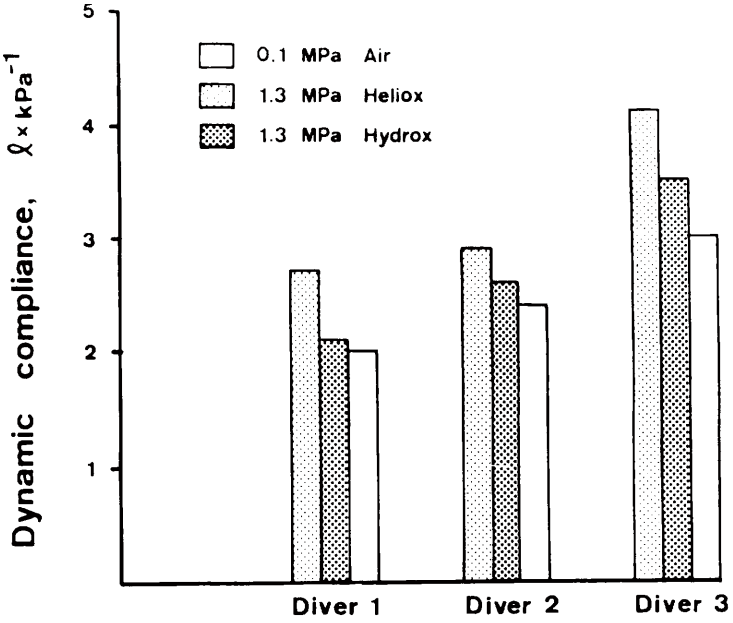


Fig. 7. Maximum voluntary ventilation. Each histogram bar is a mean of two measurements.

VENTILATION CAN LIMIT PERFORMANCE

An increased load on the respiratory system and limited expiratory flow will lead to hypoventilation, carbon dioxide retention, and dyspnea. Thus the restricted ventilation could reduce both mental and physical performance. This load is both flow restrictive and elastic. The elastic load is due to the compliance (C) of the system. The total load is also the sum of the effects of the diver's respiratory system and his personal diving equipment. A badly designed rebreathing bag or a tight-fitting suit and harness will add to the internal compliance and thus increase the elastic work of breathing. As shown in Fig. 8, the elastic work of breathing is:

$$Work_{elast} = V_{in} * P_{elast}/2, \text{ as } C = V_{in}/P_{elast}$$

$$Work_{elast} = V_{in}^2/(2*C).$$

When we add the different elastic works together, we get:

$$Work_{elast} = V_{in}^2 * (1/C_L + 1/C_T + 1/C_{DS})2$$

and the elastic power of breathing during inhalation:

$$Power_{elast} = Work_{elast} * 2/T$$

where T is the time for one breathing cycle and the inhalation time is T/2. V_{in} is given in l/s.

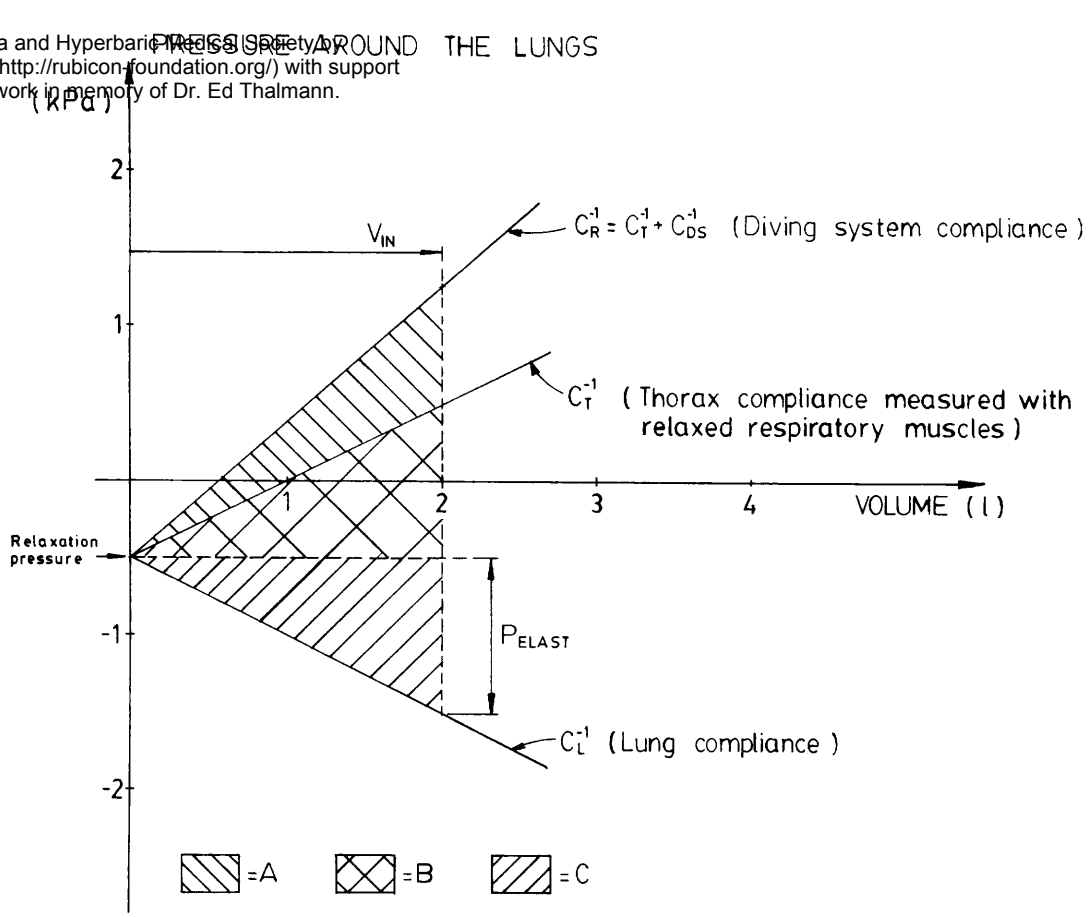
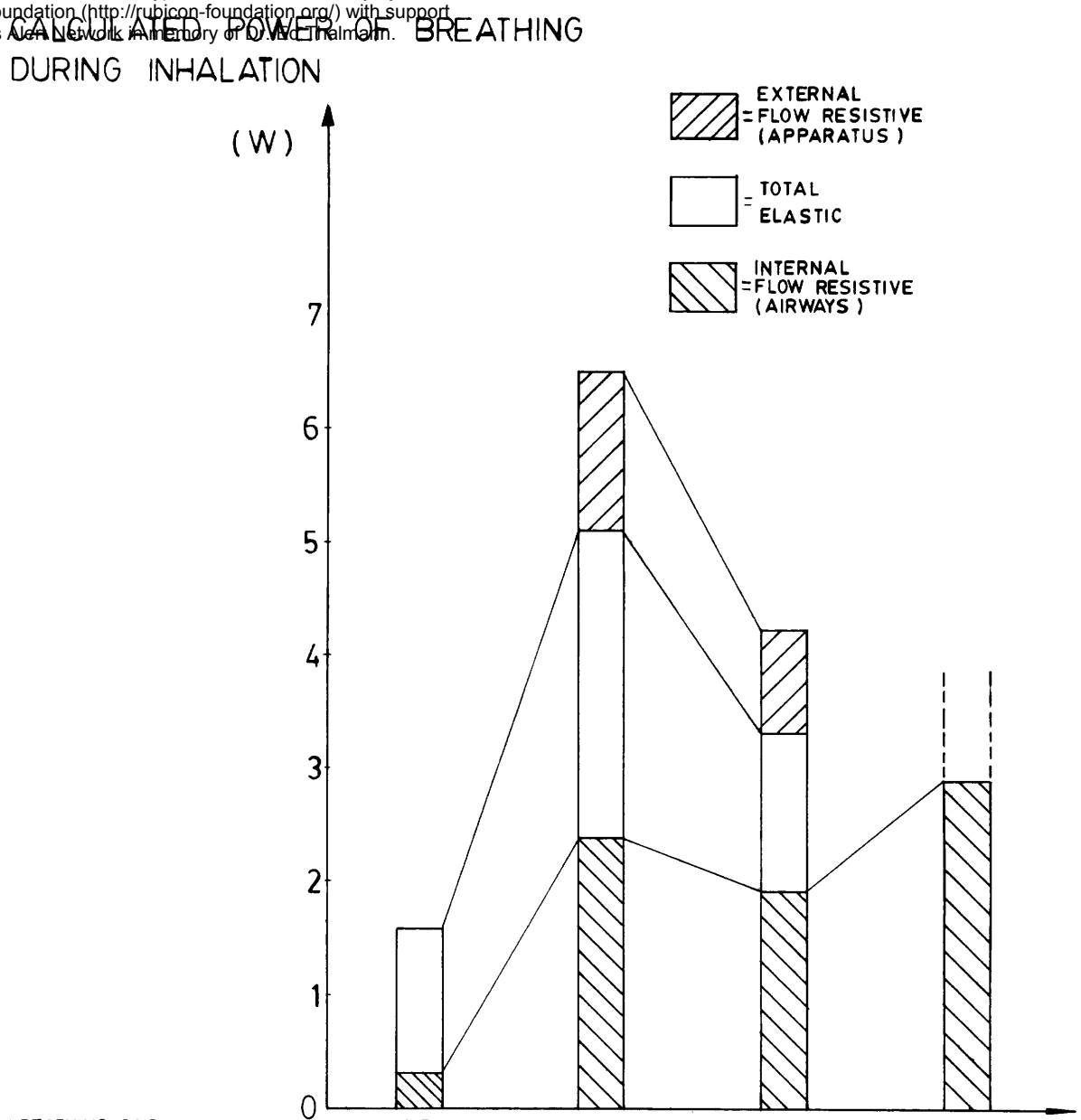


Fig. 8. Dynamic compliance. Each histogram bar is a mean of three breathing cycles.

A hydrostatically unbalanced bag placed on the diver's back will almost halve the dynamic lung compliance by reducing the lung volume (3). Normally, the total compliance of the lung and thorax, is about 1 liter/kPa. n a diving situation with a hydrostatic load of -2 to -3 kPa, which can induce dyspnea, compliance may well have been reduced to 0.5 liter/kPa (6).

TOTAL POWER OF BREATHING

In Fig. 9, we have theoretically calculated the mean power exerted by the inspiratory muscles, assuming that the whole of the elastic load is taken up during inhalation and that the minute ventilation is 40 1/min. In all calculations sinusoidal flow has been assumed. Three situations involving diving at 450 m in water are compared with calculations at the surface in air; heliox (99% He:1% O_2); a mixture of 49% He:50% H_2:1% O_2; and H_2 trimix (94% He:5% H_2:1% O_2). The $R_f(1)$ at 450 m was calculated from the actual measured $R_f(1)$ at 120 m by linear extrapolation. This value is probably an underestimation in the heliox diving situation, where a hydrostatically imbalanced breathing system was assumed, since it has been shown that this imbalance will increase $R_f(1)$ by about 20% (3). The total compliance in line with the discussion above was set to 0.5 1/kPa in the heliox dive.



BREATHING GAS	:	AIR	HELIUM 99% OXYGEN 1%	HELIUM 49% OXYGEN 1% HYDROGEN 50%	HELIUM 94% OXYGEN 1% NITROGEN 5% (TRIMIX)
DEPTH	:	0 m DRY	450 m IN WATER	450 m IN WATER	450 m IN WATER
LUNG RESISTANCE (kPa/l·s)	:	0,13	1,10	0,9	1,30
APP. RESISTANCE (kPa/l·s)	:	—	0,64×	0,40+	—
TOTAL COMPLIANCE (l/kPa)	:	1,0	0,5++	1,0	—

Fig. 9. Volume-pressure curve exemplifying different compliances for the lung, the thorax, and the diving system (for example breathing bag, harness, and suit). Area A is the internal elastic work caused by the lung, Area B is the work caused by the thorax, and Area C is the elastic work caused by the diving system.

The flow resistance in the breathing apparatus [$R_f(app)$] was calculated from Morrison's tolerance and comfort curves regarding the work of breathing (9).

$$R_f(app) = (0.5/V'_E + R) * 2/Pi^2$$

where V'_E is given in 1/s and R is 2.4 kPa/1/s for the tolerance curve and 1.2 kPa/1/s for the comport curve.

In water at 450 m breathing heliox, the total power of breathing during inhalation with a minute ventilation of 40 1/min will be about 6.5 W, which could induce respiratory muscle fatigue and cause dyspnea. The addition of H_2 will reduce the internal power of breathing by 18%. If the breathing system is hydrostatically balanced by, for instance, putting lead weights on the breathing bag when placed on the diver's back, the total elastic power will be reduced by 50% (8,9). This balancing will also reduce the internal resistive power by about 20% by increasing airway diameter (3). A design with the breathing bag on the diver's chest will also reduce the total power of breathing as subjectively rated by the divers (10). Finally the use of Morrison's comfort criteria for the breathing apparatus instead of the tolerance criteria will reduce the external resistive power of breathing by 36%. This criteria will also be easier to fulfill when using hydrox.

By adding all these improvements together, a total reduction of 35% in the power of breathing can be achieved. Further reduction can probably be achieved by the increased airway diameter caused by hydrostatic balancing of the breathing apparatus.

Compared with the He-N_2-O_2 trimix dive, internal resistive power will be reduced by 32% when using the He-H_2-O_2 mixture.

SUMMARY

The resistive power of breathing seems to be linearly related to the density of the gas. Using H_2 in the gas mixture will thus reduce both the internal and external resistive power. With a breathing bag on the diver's back, the hydrostatic imbalance of the breathing apparatus could be about -2 to -3 kPa. Correcting this imbalance will achieve an even greater reduction in the required power of breathing, reducing both the elastic power (by increasing compliance) and the internal resistive power (increasing the diameter of the airways).

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DISCUSSION FOLLOWING PRESENTATION BY DAHLBÄCK

LUNDGREN: I would like to make one point that takes on additional interest given what you mentioned about the problems you had with continuous hyperventilation in your subjects. Sometime ago, in regard to hyperventilation under physiological conditions, we did some measurements on maximum voluntary ventilation both at rest and during exercise. We found you can have something like a 15% increase in maximum voluntary ventilation if you perform the maneuver during exercise. This seems to be due to a modification in the autonomic control of the bronchial smooth muscles. One could perhaps predict that in your situation your subjects may have been at somewhat of a disadvantage when they were hyperventilating at rest and thereby not inducing in themselves the lower resistance that would have been present if they had been exercising at the same time.

DAHLBÄCK: But I also mentioned that at the same time we had this mental stress which could have had some impact on the airways.

LUNDGREN: That's true, but what the balance of that is we don't know. If the problem is general stress, with hyperventilation caused by stress, that would be the case. If hyperventilation occurred for other reasons perhaps then it would go the opposite way.

GIRY: Did you try to calculate what could be the increased resistance in the breathing apparatus registered due to chamber gas?

DAHLBÄCK: Well, I thought about it. As I said before, there seems to be a linear relation between the pressure drop and the flow in the airways. In the breathing apparatus that is not necessarily true. But in the breathing apparatus the square of flow will prevail. In that way you could calculate the increase in resistance. But we have not enough data yet.

GIRY: In most work which is done on the actual diver in the water, changing the inhaled gas will result in changes of the external resistance which are much smaller.

DAHLBÄCK: Yes, I can agree with you. Modification of the breathing apparatus would promise much greater benefit.

PHYSICAL WORKING CAPACITY IN DIVERS BREATHING HYDROX AT 1.3 MPa (13 ATA)

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Reduced ventilatory capacity, due to an increased gas density, is one of the most important factors that restrict the physical working capacity at depth (1,2). Despite the ventilatory limitations to maintain a normal oxygen uptake, breathing air, at 0.6 MPa (6 atm) is possible (3,4). At greater pressures the use of helium instead of nitrogen had made possible performance of heavy work even at pressures exceeding 3 MPa (eg. Ohta B. et al., 1981). At still larger pressures, symptoms of respiratory insufficiency during work tests, and even during rest, have been observed (6,7).

From the theoretical viewpoint H_2 with its low specific density, can be expected to give even lower breathing resistance than He (2). The few data on H_2 breathing by man at pressure, published before this dive were consistent with this hypothesis. It has been shown that MVV (maximal voluntary ventilation) at 200 ft pressure (0.6 MPa) was increased by 30% when a 97% H_2:3% O_2 breathing mixture was used instead of a 97% He:3% O_2 mixture (8).

Because of the relatively shallow depth of the present dive (120 m), no large effects on the work capacity could be expected. Heliox gas (98:2) at 1.3 MPa (13 atm) has a gas density 2.1 times that of air at 0.1 MPa (1 atm), and hydrox gas (98:2) has a density 1.2 times that of air at 0.1 MPa. Earlier chamber dives showed that one can tolerate more than twice the normal breathing resistance without any effect on the maximum work capacity (9). However, by switching between the different gas mixtures during the work tests, we hoped to be able to note small differences in breathing pressures, respiratory frequency, and possibly changes in heart rate and end-tidal CO_2. Subjective estimates of breathing resistance and work load were also of interest.

METHODS

The results discussed in this paper were obtained during a 120 m heliox saturation dive with hydrox exposures in December 1983. Technical details of the dive have been presented earlier (10).

The divers were tested on a mechanically braked bicycle ergometer modified to fit into the trunk between the chambers, with the diver sitting on a chair behind the bicycle. A speedometer on the ergometer enabled the subject to keep the correct pace.

The divers were breathing through the dive mask (AGA Spiromatic II) during all the tests. The mask had a safety pressure (positive pressure

inside the mask, with respect to the chamber pressure) of 0.2 kPa (2 cm H_2O). The difference between the pressure inside the mask and the chamber atmosphere (differential mask pressure) was recorded continuously with a pressure transducer (Validyne DP 15TL). This pressure reflects the mouth pressure of the diver. Calibration with a water manometer inside the chamber was carried out before each test.

During the tests at 1.3 MPa a dump system was connected to the expiratory outlet of the mask. Since the system was only designed for resting ventilation, the expiratory breathing resistance was quite large during the heavier work loads (1.5 kPa; 15 cm H_2O).

Samples of the expired gas were continuously drawn from the inner mask (50 ml/min at chamber pressure) and analyzed with respect to O_2, CO_2, He, and H_2 with a mass spectrometer (Centronic 200 MGA).

Single lead ECG and pulse rate were monitored throughout the tests (Siercust 311 S, Siemens). The subjects were asked to estimate breathing resistance and leg work on a 10 degree scale during the tests (11).

Before the dive each of the subjects had to perform two work tests on an electrically braked ergometer, to obtain their maximal O_2 uptake, estimated from tables in Åstrand and Rodahl (12). They also performed one OBLA-test (onset of blood lactic acid) each. These values were used to choose three suitable submaximal loads for the chamber tests.

During the chamber tests the loads were 75, 150, and 225 W. The divers pedaled at a constant load until "steady-state" was reached. This was defined as a level of constant end-expiratory CO_2, and less than 4 beats/min difference in pulse rate, between measurements at 2-min intervals.

At pressure the breathing gas (either 98:2 heliox or 98:2 hydrox) was changed once at each load, without the divers being told. Each diver had three predive tests in the chamber. The tests during pressure were longer than the predive tests, but the two postdive tests were carried out with exactly the same profile as the test at 1.3 Mpa. On the second postdive day the divers went through an OBLA-test.

RESULTS

Predive tests showed that the divers were physically very fit, with maximal O_2 uptake of 4.7-5.0 1/min (Table 1).

The resting heart rates both on heliox and hydrox at 1.3 MPa were not significantly different from the surface values. Heart rate during work also were similar to the pre- and postdive values, and there were no differences in the mean heart rates during work, between heliox and hydrox periods (Fig. 1).

Results for Individual Divers

Diver 1 had initially slightly lower pulse during work at 1.3 MPa, but during the second hydrox-exposure (at 150 W) he had a period of tachycardia. This coincided with a feeling of narcosis. No change in respiratory

pattern

TABLE 1

Results from predive tests.

Workload (W)	0	75	150	225
Heart rate (min^{-1})	68 ± 4	93 ± 5	122 ± 12	156 ± 11
F_{CO_2} (%)	5.1 ± 0.2	5.7 ± 0.3	6.0 ± 0.4	6.4 ± 0.3
Breathing frequency (min^{-1})	10 ± 2	13 ± 2	18 ± 3	23 ± 4

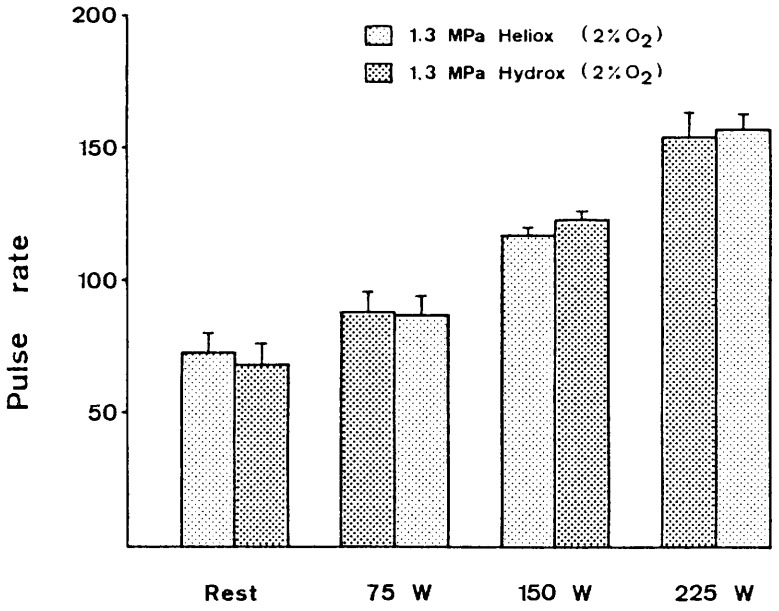

Fig. 1. Heart rates during rest and bicycle ergometer test during heliox and hydrox breathing. Bars indicate means ± 1 SD for the minute immediately preceding and the minute immediately after the shift of gas. No significant differences were observed between heliox and hydrox breathing. Note the order in which the divers were exposed to the two gases.

or end-total CO_2 was seen during this period. The diver continued to pedal, and the heart rate returned to the earlier level. The subject worked on the highest load without any symptoms (Fig. 2).

Diver 2 had similar results during his test at 1.3 MPa as those during the surface tests (Fig. 2 center). Breathing frequency and end-tidal CO_2 were also similar to their surface values. Diver 3 (the off-shore diver) was the only subject who showed a tendency to lowered heart rate during the test at 1.3 MPa. There was still no obvious difference between the heliox or hydrox gas (Fig. 2 bottom). For all three divers, respiratory frequency and end-tidal CO_2 were unchanged with respect to pre- and postdive trials, and did not show any differences between heliox and hydrox periods (Figs. 3 and 4). Because of the dump system connected to the expiratory outlet of the mask, there was an increased expiratory resistance. The mask pressure during expirations at the highest work load was ca. 15 H_2O. This pressure was significantly lower when hydrox was used. Also the inspiratory pressures were reduced when hydrox was used. This was most pronounced at the highest work loads, indicating a lower breathing resistance with hydrox (Fig. 5).

The subjective estimates of the breathing resistance during the tests showed that this was experienced as less pronounced during hydrox compared with heliox (Fig. 6). Leg work estimates on hydrox and on heliox did not differ.

The postdive onset of blood-lactate tests did not differ from the predive values.

DISCUSSION

Since we had no previous experience of hard physical work during hydrox breathing, the work at 1.3 MPa was limited to submaximal loads. However, all three divers performed very well at the highest load, 225 W, both during heliox and during hydrox breathing. Measurements of heart rate, respiratory frequency, and expired CO_2 did not show any significant differences between the gases. The response to the work was essentially the same as during the pre- and postdive trials.

The measurements of the mask pressure showed smaller fluctuations during hydrox breathing than during heliox breathing, especially during the high loads. This indicates a lower breathing resistance with hydrox. The subjects reported that they noted an obvious difference between the two gases. It was experienced both at rest and during work, and the divers were well aware of which gas they were breathing. Temperature difference, lower breathing resistance, and occasionally a slight feeling of narcosis were mentioned as reasons for the quick identification of the gases.

Divers' subjective impressions of hydrox as a breathing gas, based on questionnaires and spontaneous comments, were generally very favorable. All of them noted that the breathing resistance was astonishingly small even during hard work, and the work felt easier than with heliox. The feeling of lowered breathing resistance is consistent with smaller fluctuations in mask

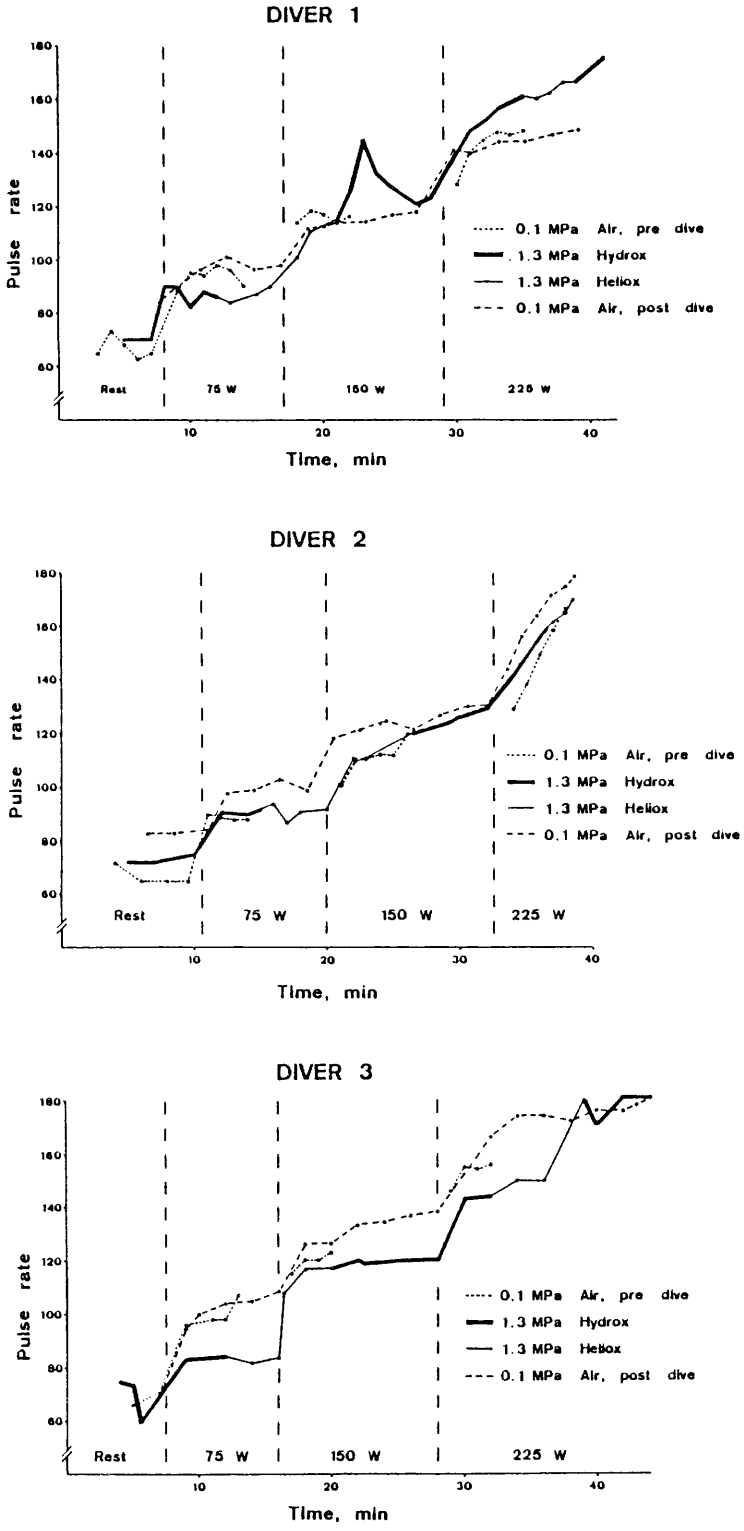

Fig. 2 A, B, and C. Mean recordings of heart rates for divers 1, 2, and 3.

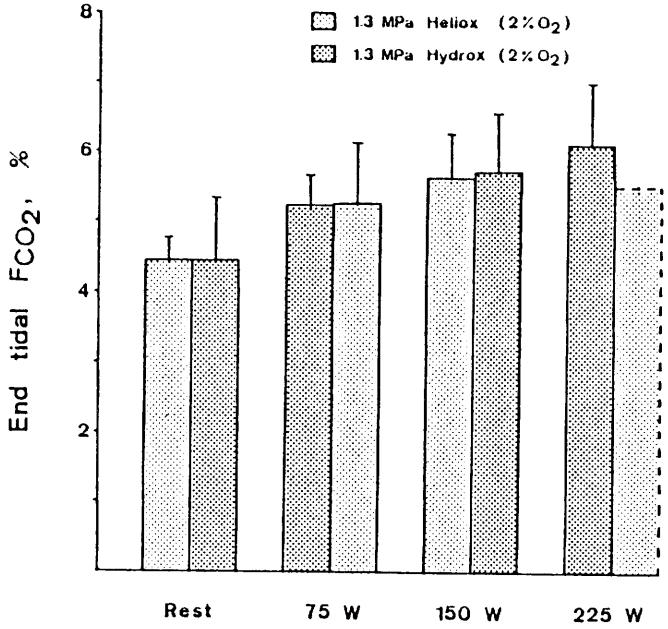

Fig. 3. *End expiratory CO_2-concentrations in the oro-nasal mask at rest and during bicycle ergometer work while breathing hydrox and heliox. Values are expressed in surface equivalent %. Mean values ± SD are based on three measurements in all bars except the hatched bar where the n value = 2. Measurements were made during the last min before the first min after a shift of gas. No significant differences were found between hydrox and heliox breathing. Note the order in which the divers were exposed to different gases (for protocol of the measurement, see Figs. 2 A, B, or C).*

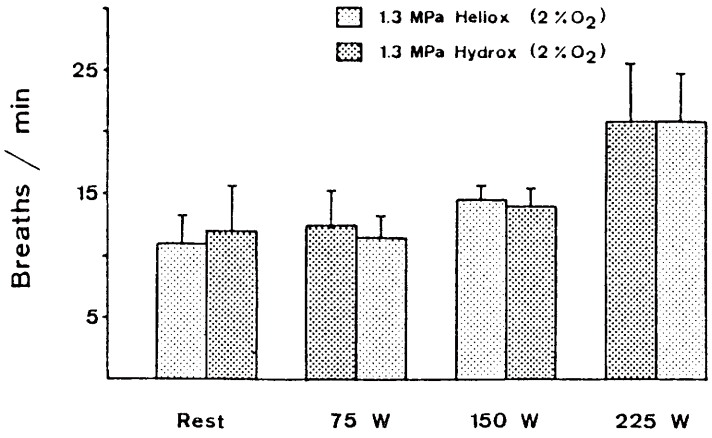

Fig. 4. *Breathing frequency during rest and bicycle ergometer work at 1.3 MPa during heliox and hydrox breathing. Bars indicate means ± 1 SD measured during the last min preceding and the first min after a shift of gas. Note the order at which the divers were exposed to different gases (for an experimental protocol, see Fig. 2).*

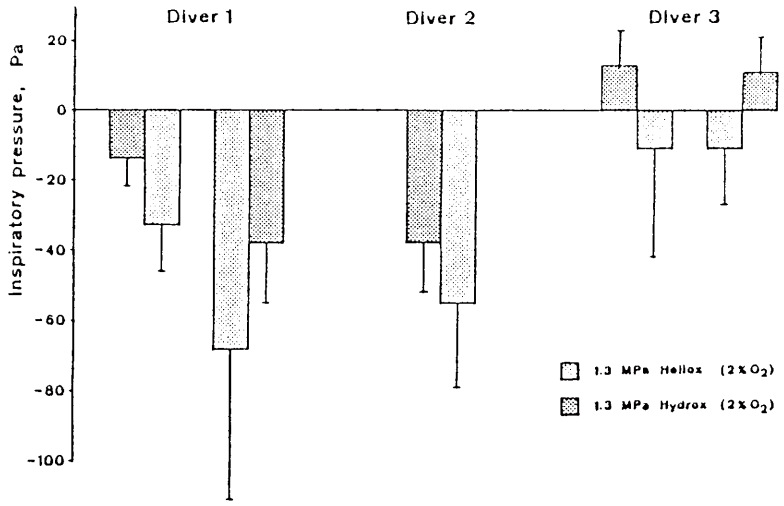

Fig. 5. Breathing mask pressures during inspiration (means ± 1 SD) for divers 1-3 during 225 W. Measurements are made during the last minute before and the last minute after the gas shift. The safety pressure in the mask was +100 Pa.

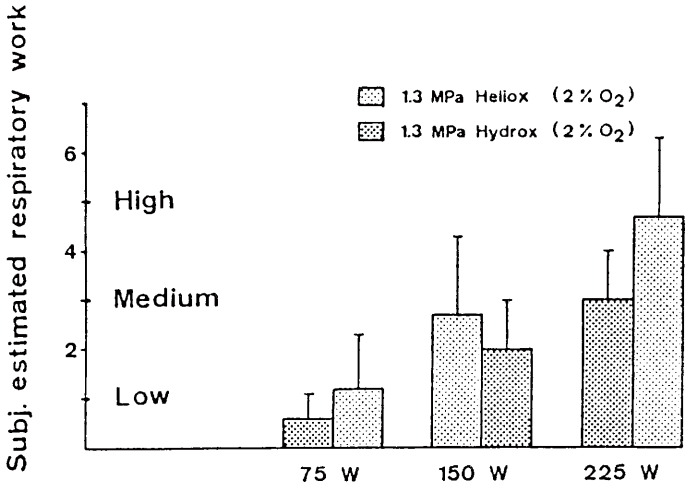

Fig. 6. Subjective estimates of work of breathing compared to resting values close to zero during bicycle ergometry at 1.3 MPa. A 10-point scale according to Borg was used. Paired t test showed a significantly lower estimate during hydrox breathing ($n = 9$, $P < 0.01$).

pressure, which was expected because of the lower density of H_2. Interestingly, this feeling was obvious even at relatively moderate pressure.

These observations make it difficult to draw conclusions about the suitability of using hydrox for deep sea diving. Although no conclusions can be reached as to the maximal physical performance during hydrox breathing compared with heliox, all the divers felt they could work more easily during the hydrox exposures.

Deeper dives with hard work test are needed to further test the effects of hydrox on physical work capacity.

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DISCUSSION FOLLOWING PRESENTATION BY GENNSER ET AL.

FIFE: During the shift from He to H_2 did you say that they noticed a difference in the temperature?

GENNSER: Yes, but the H_2 tanks were kept outside and the gas was only warmed when it was brought through the chamber.

FIFE: Well, do you think they were actually seeing a difference because of the difference in specific heat of the gas?

GENNSER: I don't know. We did not monitor what the temperature of the gas was when it came into the chamber. The divers said that they felt a cooling on the face.

WELLS: It was probably a difference in the sources of the two gases--one stored with high pressure, the other recirculated.

ÖRNHAGEN: For safety reasons that I am going to discuss later we stored the hydrox mix outdoors; the heliox was stored indoors. These experiments were run in December, and in Sweden we have snow at that time. That's one difference. The storage temperature was 20° C for the heliox and it was something around -2° C for hydrox. We had a gas heater on the line used during hydrox breathing. You also have to take into consideration the difference in the adiabatic effects of the two gases. When you expand heliox it cools down; when you expand hydrox its temperature doesn't change. Our impression was that with this system we would come up with a temperature in the mask of something like 10-15° C. But since we didn't have a thermistor in the mask, we can't be sure about the gas temperature. The divers were able to notice the difference between the gases, and the feeling of a cooling of the face was one of these. They were very quick to pick up the narcosis; it didn't take more than, say, 30 s until they felt the narcosis. To me that's a very interesting question: Which tissue is operating that fast, and where is "narcosis" located? That's been puzzling me for a long time. Why can you experience narcosis that quickly?

LUNDGREN: We all know that the circulation time from the lung to the brain is only a few seconds. It is still worth nothing that at least under resting conditions there is a wash-out time, or wash-in, if you want, of the lungs in order to completely change the inert gas in the lungs, of about 5 min. It is shorter of course when you exercise and have increased ventilation.

MILLER: I think it is recognized that the rate of uptake of anesthetic gases into the brain increases as their solubility in the blood goes down. Since you are dealing with a very insoluble gas it can be expected to be quick. Whether it would be that quick I don't know, but it would certainly be quicker than a more soluble gas, like nitrous oxide, but about the same as a gas of more nearly the same solubility properties as N_2. The solubility of H_2 in the blood is low, therefore the mass transport is low, but the mass that has to reach the brain to saturate it is also low, in direct relation to the solubility level of the blood. The important thing is whether you are depleting what is in the lung: The nitrous oxide filling up the lung will be quickly dissolved in the blood and carried away from the lungs, so the partial pressure drops a lot--whereas with H_2 there is very little uptake from the lung although you still saturate the blood and so the partial pressure in the lung isn't falling.

SMITH: There is another secondary factor of the same general type just described by Dr. Miller. Often the partial pressure in any tissue can be affected by the uptake in fatty regions before it reaches equilibrium so that if you have a gas that is of low water solubility and high fat solubility you get a very long period of equilibration but if the reverse is true it equilibrates quickly. So establishing local equilibrium can depend on the oil:water ratio in the circumstances.

FLYNN: In the old days of compressions of 500 ft of sea water in 16 s using air, followed by immediate ascent to the surface at 9 ft/s, the narcosis hit at about 150 ft in ascent; while on the bottom at 500 ft they were still essentially free of any narcotic symptoms. Thus the narcosis lagged behind the dive profile about one to two circulation times in the brain.

LUNDGREN: Does anybody have a figure for H_2 solubility in the gray matter? How does it compare to, say, olive oil?

SMITH: The paradox with H_2 solubility is that in water it is greater than that of N_2. Yet in oil they are very different; H_2 has one half the solubility of N_2 in most fatty substances, olive oil, for example. The paradoxical water solubility relations of H_2 to N_2 were pointed out by Haldane, if I am correct, for the first time.

GIRY: I was quite interested in the fact that in H_2 when they were working at almost maximum O_2 consumption, 225 W, they wouldn't stop when you told them to. Is that true?

GENNSER: Well, this was the case with one of the divers. He felt that he could work for another 10 min. Whether that was a case of narcosis or whether he wanted to test hydrox to its maximum limit, I can't tell.

ÖRNHAGEN: But I think you should notice here that these divers were in very good physical condition and 225 W was not close to their maximum. There was a reason why we couldn't go above 225, of course: that was the maximum of our bicycle ergometer.

GENNSER: This diver did 1.5 min at 450 W during the predive and postdive tests, so he was at roughly half his maximum performance.

GIRY: The point I want to make is that they didn't worry about the clock. Under heliox they would have stopped as soon as you said to stop.

GENNSER: That's probably correct.

LUNDGREN: May I bring up one question that has to do with the diver's subjective evaluation of fatigue? In conjunction with your slide on respiratory fatigue I am curious how the question was put to the divers, or what they were asked to describe or answer. The reason for my question is that it is very difficult to get objective measurements of respiratory fatigue on the basis of information from the subjects themselves. If you ask a person to tell whether he is fatigued, it could be that his legs are hurting, or whatever. So how the question is phrased is very important.

GENNSER: There were actually three questions: How tired are you legs? How tired do you feel generally? How tired are you of breathing?

LUNDGREN: Respiratory fatigue is what you showed on the slide.

GENNSER: For the other questions, there were no differences between helium and hydrox at this depth, but the estimate of respiratory fatigue was always lower during hydrox breathing.

LUNDGREN: Do you feel that there was any problem in getting the divers to understand what you mean by respiratory fatigue? What did you say in Swedish? I want to see if I agree with the translation.

GENNSER: In Swedish, "Andfåddhet."

LUNDGREN: That is roughly "short of breath"; that is better than "respiratory fatigue." I have no objections.

RESPIRATORY STUDIES DURING EXERCISE, ESPECIALLY UNDERWATER

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NMRI, Bethesda, Maryland, USA

A major benefit expected from adding hydrogen to a diving mixture is to lower its gas density, thereby reducing the total resistance to breathing in the diver's airways, as well as in the circuits of his breathing apparatus. In designing respiratory studies to evidence such a benefit, three important factors must be kept in mind:

- The measurements must be comparative, with hydrox and with heliox used under identical conditions.

- The experiments are to be conducted preferably underwater, to take into account all factors of breathing resistance.

- The studies are to be conducted at moderate depths, because the H_2 percentage would be lower at greater depths.

METHODS

As detailed in Mr. Gardette's presentation, two different chamber complexes were used. Figure 1 shows the experimental set-up for Hydra IV. The diver was exercising on an arm ergometer in the lower part of a large sphere filled with water. The upper part was filled with heliox. The diver was supplied first with heliox, then with hydrox and the expired gas was collected in the dome for direct spirometry. After each 15 min run, including 7 min of exercise, the dome gas was evacuated into the free atmosphere. The O_2 expired pressure was recorded with a fuel cell at the exhaust of the line. This enabled us to assess the minute volume of ventilation, the O_2 consumption, and the respiratory equivalent of O_2. A differential pressure transducer allowed recording of tidal variations in mouth pressure associated with breathing.

Figure 2 shows the set-up for Hydra V at 450 m. The wet pot could not be equipped with the dome, and since direct spirometry was no longer possible, we had to imagine another way to measure ventilation. The quantity of hydrox that the diver inspired was measured through a mass flowmeter incorporated in the supply line, and pressure drops in the storage tank were also recorded. Also, respiratory movements were recorded using NMRI's magnetometer method. However, all measurements were indirect, and thus less accurate than in Hydra IV.

The expired gas O_2 content and the mouth pressure were assessed in the same way as in Hydra IV, and new monitoring systems were added. Gas temperature at mouth was measured using a thermocouple. Tidal carbon

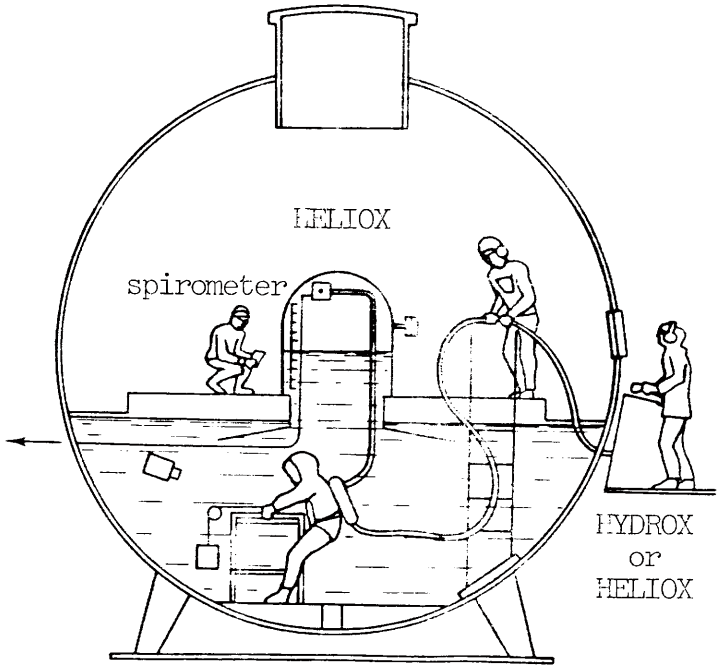

Figure 1: Experimental set-up for Hydra IV (wet studies) 180 to 300 m.

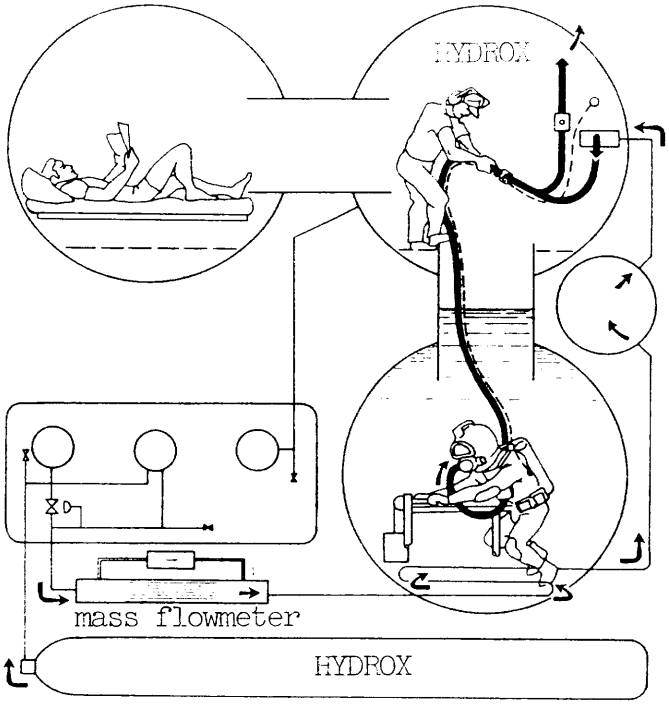

Figure 2: Experimental set-up for Hydra V (wet studies) 450 m.

dioxide was recorded by mass spectrometry, by means of the CERB system. Note that the Hydra V divers were saturated with hydrox instead of heliox, and that comparison with heliox was not available.

Figure 3 is a plot of gas density as a function of H_2 pressure in the diving mixtures used in underwater studies. At the far left, with no H_2, are the values for heliox at 180, 240, and 300 m (approximately 3.4, 4.4, and 5.4 g/liter). At the far right, with no He, are the values for binary hydrox at 180 and 240 m (approximately 1.9 and 2.5 g/liter). At 300 and at 450 m, ternary gas mixtures were used. The 300-m plot shows a linear decrease in the gas density with increasing H_2 pressure. In the ternary mixture used at 450 m, the gas density was 5.6 g/liter, very close to heliox density at 300 m. The H_2 pressure (24.8 bar) was very close to the H_2 pressure with binary hydrox at 240 m. By drawing a line from this point toward the upper left, you would be able to find the value for heliox at 450 m, approximately 7.5 g/liter.

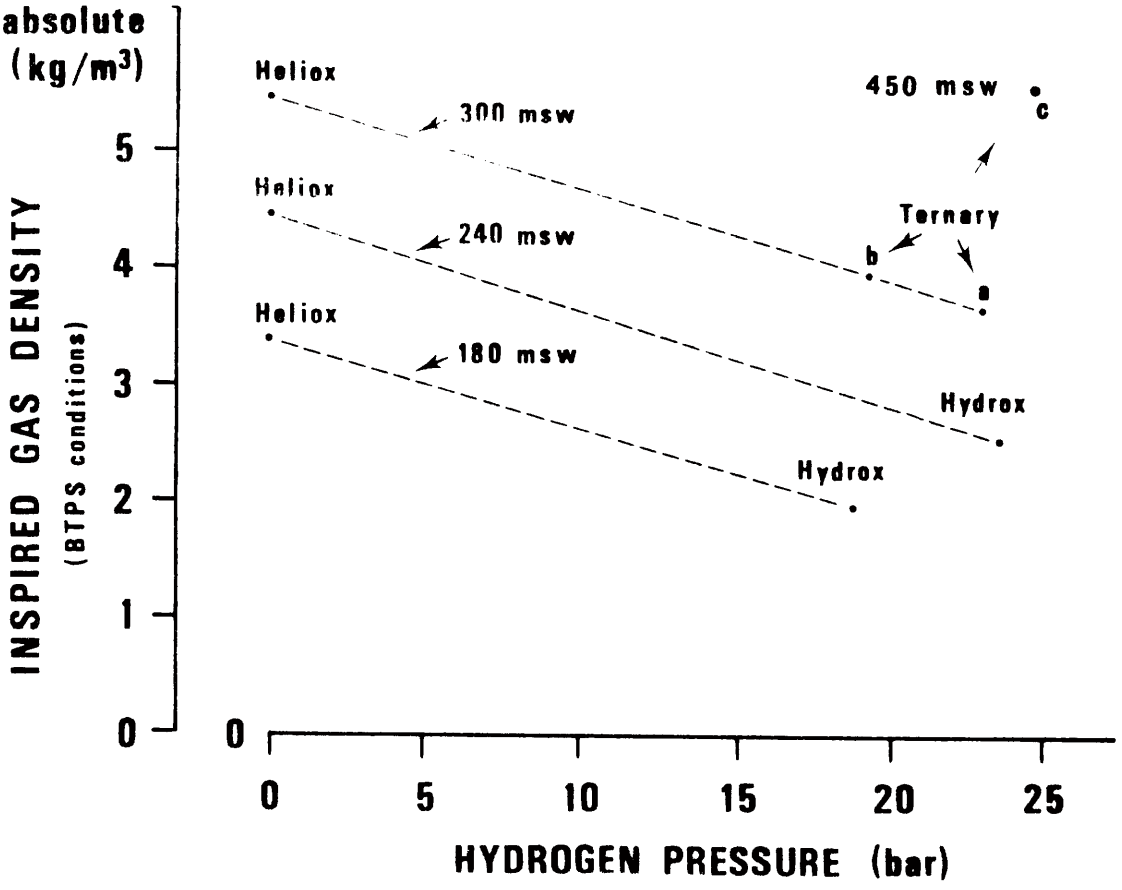

Figure 3: Absolute gas density as a function of hydrogen pressure in respiratory mixtures used in Hydra IV and Hydra V (binary heliox at far left, binary hydrox at far right).

RESULTS

We would like to focus on four results, which we believe to be the most significant:

1. At 180 m, all six subjects in Hydra IV could exercise for 7 min, breathing heliox, then repeat the same exercise breathing binary hydrox. Exercise consisted of moving up and down a 20 kg load at a rate of 15 strokes/min. Figure 4 shows the mean value and the standard errors for four respiratory variable:

- Minute volume expressed in liters BTPS ($\dot{V}E$)
- Respiratory rate expressed in cycles per minute (f_R)
- Oxygen consumption in liters STPD per minute ($\dot{V}O_2$)
- Respiratory equivalent of O_2 in liters BTPS per liter STPD (ERO_2)

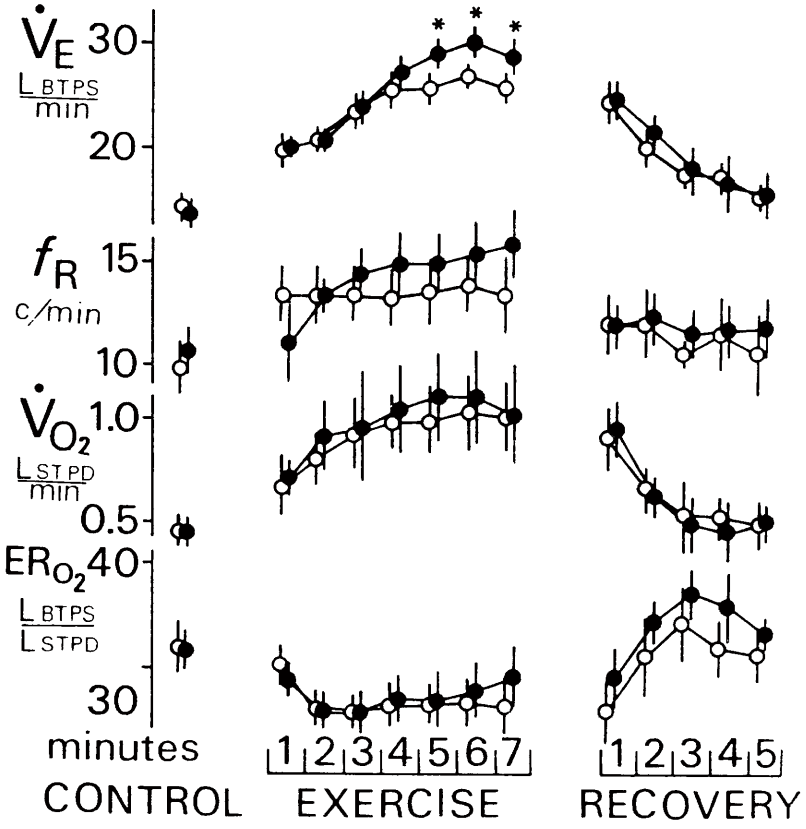

Figure 4: Comparison of binary hydrox (black dots) and heliox (open circles) in six subjects at 180 m. Note higher ventilation during the last 3 min of exercise with hydrox.

In figure 4 black dots represent binary hydrox; *open circles*, binary heliox. Values are plotted every minute, during the 7 min of exercise and the next 5 min of recovery. Control values at rest are plotted at the far left and are similar for both gas mixtures.

During exercise, there is a tendency to breathe at a higher rate with hydrox, and at a higher minimum volume. The differences in minimum volumes are significant at *P* lower than 0.05 during the last 3 min of exercise. Note that O_2 consumptions were higher than 1.2 liters/min, which could correspond to a work load higher than 80 W.

The ventilatory improvement observed with hydrox at 180 m appears to be due to its lower gas density. The interpretation seems pretty easy, since H_2 pressure is still rather low, and the complications that will occur with its further increase are still avoided.

2. At 240 m with binary hydrox, the divers' performances were by H_2 severely impaired narcosis but we will discuss only the respiratory effects.

The divers experienced difficulties starting the exercise at the right time, following the correct rate, and stopping when they were asked. In such circumstances, data dealing with exercise and cardio-respiratory performance are of little value.

The divers reported that the resting periods at the beginning of each run tended to enhance the narcotic effects: subjective feeling of inebriation, over-confidence, and tendency to drop off to sleep. This was associated with changes in the breathing pattern.

Figure 5 shows mouth pressure recordings in one of the subjects who proved to be the most sensitive. Each sequence represents 1 min of breathing, and the vertical bar at the left stands for 30 cm of water. The upper line is the control record with heliox. After 2 min of breathing hydrox there is little change but a slight increase in respiratory rate, which is usual. The 5th min displays characteristic changes, present in most of the divers but normally without further deterioration afterwards. In this particular case, respiration slow down far too much during the min that followed, with expiratory pauses, and we decided here to switch immediately back to heliox. During the 7th min, after a short time lag, the diver aroused and ventilation returned promptly to normal, with compensatory hyperventilation. This is a clear demonstration of what we described as the respiratory depressant effect of H_2. Hence at this point it may be stated that H_2 has a somewhat double-edged action:

Improving pulmonary ventilation by a decrease in breathing resistance owing to its 10 w molecular mass.

Hindering respiration by a depressant effect at the central level due to its narcotic potency.

3. There is, however, a pressure reversal effect, which is of primary importance for hydrox diving. Other speakers have commented upon the neurophysiological aspects, but it is also significant for the respiratory physiologist.

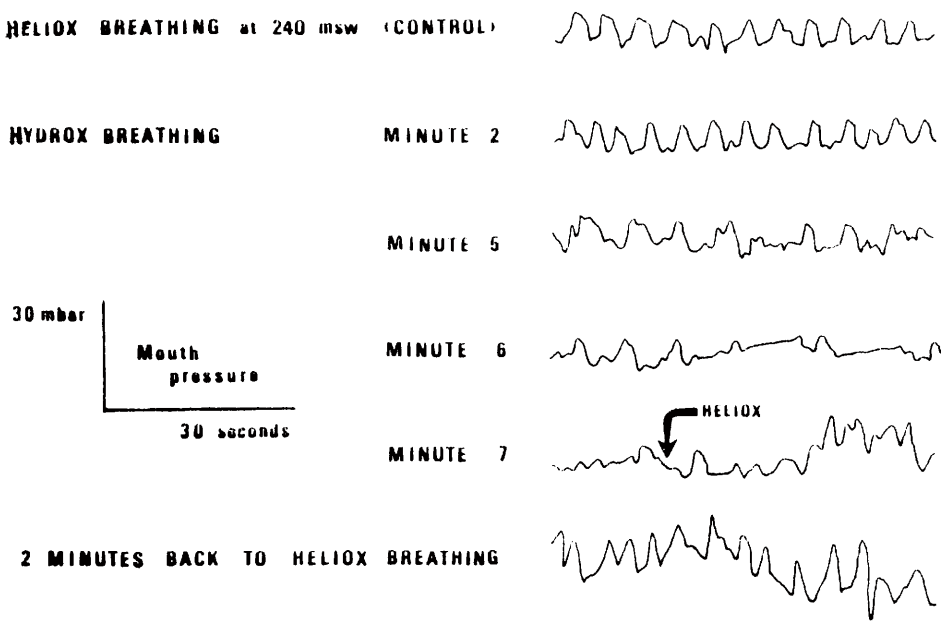

Figure 5: Respiratory depressant effect of binary hydrox at 240 m. Not the quick recovery after switching back to heliox, which indicates merely a narcotic effect of H_2 rather than a toxic one.

During Hydra V, at 450 m, the partial pressure of H_2 was 24.8 bar, almost identical to what it was during Hydra IV, at 240 m with binary hydrox. But in Hydra V the divers were able to perform underwater successfully. The rate of exercise was 25 strokes/min instead of 15 as in the Hydra IV dive, and the load varied from 10 to 15 kg. Minimum volumes ranging from 40 to 50 liters were recorded, with heart rates averaging 100 beats/min (90 to 120) and O_2 consumption close to 1.5 liters/min. For the three divers of team B, the duration of submerged activity was 2 h with an average pulmonary ventilation of 26 to 28 liters/min.

All divers carried out four exercise runs. The first three lasted 6 min, and the last, even longer. The first was referred to as Light because the load was only 10 kg instead of 15 as in the following runs. The second was referred to as Standard. The third was performed with a breathing load. Using a control that acted on the demand valve, the diver made it more resistive, to the level he was able to tolerate, to check his ability to bear an eventual malfunction. Finally, for the last run the diver was asked to sustain the exercise for as long as he felt comfortable.

They did this for 8 to 13 min, and hence the total exercising time during these individual 2-h dives ranged from 26 to 31 min. When the divers were asked the reason for stopping, none of them reported respiratory distress as the cause, but some other reason such as hand

pain or boredom. The improvement is striking is we compare these performances to those observed during Hydra IV at 240 m with binary hydrox and the same H_2 partial pressure. The difference may be caused primarily by the addition of 20 bar of He and the pressure reversal effect. Mass spectrometry performed by the CERB during these exercises showed no evidence of carbon dioxide retention.

4. Finally, the last point deals with the feeling of breathing comfort reported by all subjects during hydrox dives. Many factors have to be considered besides the simple reduction in respiratory resistance. Narcosis, lesser pain sensitivity, and overconfidence may be potential factors in facilitating breathing efforts. Also HPNS may hinder breathing by impairing respiratory muscle function, and H_2 may prevent it, as N_2 in trimix might have prevented dyspnea in deep Atlantis dives, as reported by Salzano and Bennett. However the mechanical factors seems to be the primary one.

Figure 6 compares mouth pressure recordings in the same diver, at the same depth, under four conditions: breathing either heliox or ternary hydrox, either at rest or during exercise. Negative waves correspond to inspiration; and positive, to expiration. At rest as well as during exercise, peak to peak amplitudes are much smaller with hydrox than with heliox.

CONCLUSION

Four results are prominent:

- An increase in breathing comfort within the limits of activity the divers were asked to perform, which was well within the range of professional diving: ventilation averaging 30 liters/min.

- Hydrogen may have some depressant central effect on respiration. However its narcotic power may counteract HPNS, and thus avoid impairment of respiratory muscle function at pressure.

- Pressure exerts a reversal effect on H_2 narcosis, and in theory this allows a correct ternary mixture to be adapted to depths in excess of 180 m, for optimal performance.

- In hydrox diving, the reduction in respiratory resistance and in breathing efforts appears to be a major factor in improving performance at depths greater than 300 m.

To summarize, these results indicate that hydrox, defined as a $He\text{-}H_2\text{-}O_2$ ternary mixture, may be of value for improving divers' performance during underwater work at great depths.

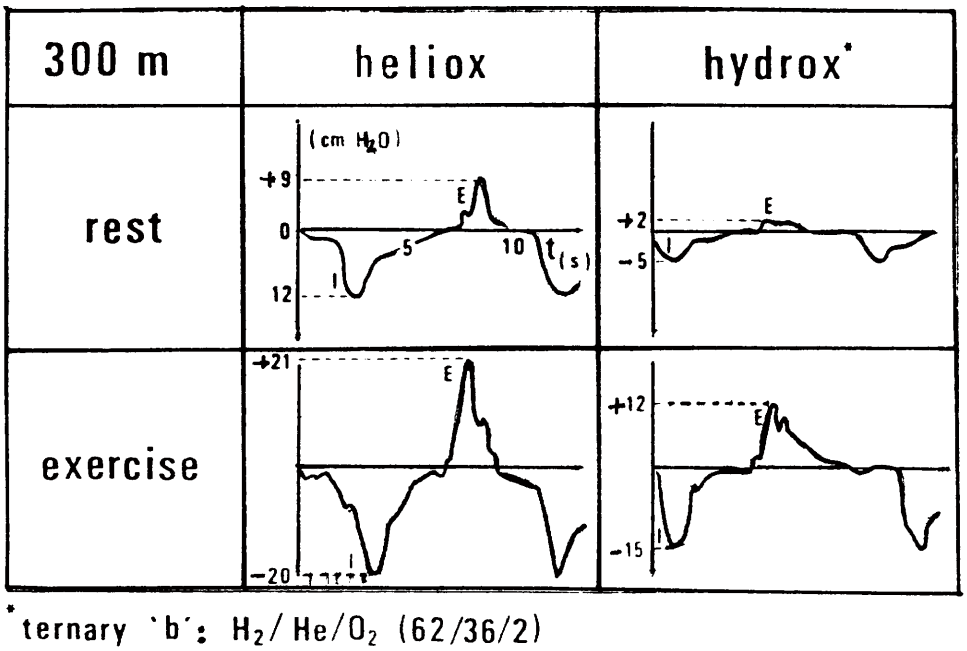

Figure 6: Comparison of mouth pressure recording during heliox or ternary hydrox breathing at rest and during exercise.

Subject: LS--Positive peaks correspond to expiration, negative peaks to inspiration (the recorded pressures are those developed by the diver to fight against flow resistances in his underwater breathing apparatus). Note the lower amplitudes under hydrox for similar ventilatory flows, explaining the feeling of breathing comfort reported by divers during underwater exercises.

DISCUSSION FOLLOWING PRESENTATION BY IMBERT ET AL.

FIFE: What problem, if any, did you have with gas being collected in the dome? Did you drain it off and measure?

IMBERT: No. The fuel cell itself was located in the dome.

FIFE: So you didn't have to worry about the gases dissolving in the water. You measured it before it contacted the water.

IMBERT: That is correct.

DAHLBäCK: Is there a linear relationship between flow and pressure drop in your breathing apparatus?

IMBERT: We have not enough data to plot this relationship.

FIFE: But what you measured was mostly pressure.
LUNDGREN: You are measuring pressure in the mask, but you just said something about the breathing apparatus.

IMBERT: We estimated the average rate of flow through the breathing apparatus by dividing tidal volume by expiratory time.

LUNDGREN: But you are not saying anything about internal resistance?

IMBERT: I cannot do that. We have not measured internal resistance.

LUNDGREN: It was a clarification of a statement, and I think we have to agree on this. Surely mouth pressure will always reflect resistance of the breathing apparatus.

DAHLBäCK: My question was: Do you think there is a linear relationship between mask pressure and the flow?

IMBERT: We can't say, because we have not performed a specific study of that. We do not have sufficient data to plot out a complete regression line and to compute it. The diver is in a given condition and what we are able to record is the average value of flow, and the average of pressure or pressure drop; and that's exactly what we plot.

LUNDGREN: I understand that the work load you imposed was a weightlifting type of work. What was roughly the wattage output?

IMBERT: From the O_2 consumption?

LUNDGREN: No, from the actual mechanical work.

IMBERT: It's hard to say with this kind of ergometer.

LUNDGREN: No, I realize that. What I am trying to say is, did you try to estimate it?

IMBERT: Well, we can try to estimate the diver's level of activity from their minute volumes. What we can say is that during Hydra V the average was around 26 to 28 liters/min, which is close to the average minute volume of a diver at work. At times the minute volume rose to 45 or 50 liters/min.

LUNDGREN: Ah, you are anticipating my question in a sense. I wanted to ask do you feel that this was the limit of their output, or could they have pushed further? You mention that when you asked them to go on for as long as they could, some stopped from sheer boredom.

IMBERT: Yes.

LUNDGREN: So I am asking, could you, from what you have measured and seen, say anything about maximal output?

IMBERT: No. We cannot estimate the maximal output. The only thing we are certain of is that respiratory fatigue was never a cause for stopping work during Hydra IV or V.

VENTILATORY TOLERANCE TO EXERCISE DURING A HYDROGEN-HELIUM-OXYGEN SATURATION DIVE (HYDRA V)

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Using hydrogen as a diluent gas for diving has been thought of since 1930 (1). The first actual human experimental dives using this diluent gas for oxygen have been performed by the Swedish Navy (2). A series of bounce dives has been achieved by Edel's team (3) and by Fife (4).

Most of the animal experiments dealt with the neurologic effects of the gas (5) or the decompression problems (6). In this field, a French communication (6) described a "toxic effect" attributed to the mixture, and further work in this area was postponed. Recent experiments did not find this toxicity [Risso et al. on rats (7), Rostain et al. on monkeys (8)]. It now seems that in the experiments of Michaud et al.(6) (dive under H_2-O_2 at 30 ATA with a temperature of 29° C), the results observed may have been due to the combination of high narcotic potency of the gas (P_{H_2} = 29.5 ATA) and hypothermia. The use of He for deep diving for a time stopped the urge to find a new diving mixture.

The evidence of a density-related limitation to ventilation (9,10) induced a search for a breathing gas lighter than He. Looking at Mendeleev's table, it appears that the only candidate is hydrogen. In the 80s, interest in H_2 was renewed by this aspect of the problem as well as by the high price of He. Two series of human experiments have been conducted in this field, one by the French diving company COMEX, the Hydra series (11), and the other by the Swedish Navy (12.13). All the work performed in this area evidenced narcotic effects of this gas at pressure. However, none of these teams studied the putative improvement in exercise tolerance provided by the H_2-containing mixtures. The Swedish team did not observe any drastic increase in vital capacity (VC), forced expiratory volume in 1 s (FEV1), or tolerance to exercise.

The present experiment (Hydra V, sponsored by IFREMER and DRET) is the first saturation dive using H_2 as part of the diluent gas. It was intended to test the modifications in exercise tolerance induced due to the use of a H_2-He-O_2 breathing mixture (hydrox) at 46 ATA, as compared to a He-O_2 mixture (heliox). Because of the narcotic effects of H_2, P_{H_2} was maintained at 25 ATA. According to the theory of respiratory mechanics, the expected gain afforded by the ternary hydrox-heliox mixture could be on the order of 10 to 15% at maximum ventilation rates (10).

This situation is the only one known in which narcotic effects due to elevated P_{H2} (which may interfere with the regulation of ventilation) are combined with decreased gas density (which should lead to increased ventilation). Therefore, no prediction could be made regarding the resulting ventilation during the performance of work.

MATERIAL AND METHODS

The Dive

Hydra V was a saturation dive at 46 ATA. It was planned to involve two teams of three divers each, teams A and B. It included a control period of 3 d at 2 ATA, breathing a heliox mixture (Confin); compression to bottom pressure in 39 h using hydrox mixture; a stay in hydrox mixture for 3 d; switch to heliox for another 3 d; and decompression on heliox. Because of counterdiffusion and HPNS problems during the gas switch for team A, team B was not submitted to the heliox part of the experiment (Table 1)

TABLE 1

Experimental situations originally scheduled for both teams (performed only by team A)

Pressure ATA	Stay d	PO_2 atm	PH_2 atm	PHe atm	Temperature °C	Code
2	3	0.4	nil	1.6	28	Confin
46	2+1	0.4	25	20.6	32	Hydrox
46	3	0.4	nil	45.6	32	Heliox

The Divers

Six divers volunteered for the for the experiment, three commercial divers from COMEX, two military divers, and one civilian diving instructor (Table 2). Table 2 gives the characteristics of the divers.

The Exercises and Breathing Resistances

The protocol for the exercise tolerance tests was identical to the one used during the previous 46 ATA French saturation dives, ENTEX series (14, 15, 16).

To demonstrate any ventilatory benefit, the ventilatory load has to be great enough. This was achieved through 6-min muscular exercise on an electrically braked bicycle ergometer (Siemens) at present workloads of 0, 75, and 110 or 150 W. Due to a defect in the regulation module of one of the bikes, the workloads imposed in hydrox were 1.4 times greater than in heliox.

TABLE 2

Anthropometric data for Hydra V divers

Diver Code	Age y	Height m	Weight kg	$\dot{V}O_2$ max* $ml \cdot mn^{-1} \cdot kg$	VC L	FEV1 L	MVV $L.mn^{-1}$	Origin
A1	40	1.89	88	39.0	6.32	4.10	196	M.N.
A2	35	1.83	80	44.1	5.53	3.60	192	COMEX
A3	34	1.76	74	40.9	6.25	5.01	171	COMEX
B1	32	1.76	73	50.8	5.60	4.16	156	M.N.
B2	31	1.79	75	36.0	5.40	4.11	134	COMEX
B3	34	1.72	75	44.0	4.61	3.57	177	INPP

* indirect measurement according to ASTRAND (*)
M.N. : Marine Nationale (French Navy)
COMEX : COMEX commercial diver.
INPP : Institut National de Plongée Professionnelle (Diving Instructor).

To attain the ventilatory limits of the subjects, external breathing resistances were added, identical on inspiratory and expiratory sides of the breathing apparatus. These were Plexiglas diaphragms, 1-mm thick, perforated by a calibrated orifice. The diameters were chosen in such a way that the external resistances should be identical in CONFIN, HYDROX, and HELIOX. The goals were breathing resistances of 0 (R0), 10 (R2), and 15 (R3) cm $H_2O \cdot (L.s^{-1})^{-1}$ for sinusoidal breathing regimen of 40 $L \cdot mn^{-1}$ (Vt = 2.0 liter, $f = 20.mn^{-1}$) at the gas density used.

The different combinations tested are given in Table 3.

TABLE 3

Actual workloads and resistances imposed on the subjects

Situation	Workloads Code	W	Diaphragms Code	W
CONFIN	W0	0		
	W0'	28	R0	40.0
	W1	105	R2	10.0
	W2'	154	R3	8.0
	W2	210		
HELIOX	W0	0	R0	40.0
	W1	75	R2	12.5
	W2'	110	R3	11.5
	W2	150		
HYDROX	W0	0	R0	40.0
	W1	105	R2	12.0
	W2'	154	R3	10.5
	W2	210		

(W0' used during CONFIN; W2' used for R3)

Ventilatory Measurements

The ventilatory measurements were performed using a "bag-in-box" system previously described (14-16) equipped with a rolling seal spirometer. The system has been modified in such a way that it allowed P.1 measurements and breathing of pressure chamber gas during the first 4 min of exercises. Recording the ventilatory parameters was done during the last 2 min of the exercise reus (steady state period). A gas sampling port in the mouthpiece allowed continuous sampling of the breathing gas to determine $PetO_2$ and $PetCO_2$ by mass spectrometry (Riber QSX 200). A gas sampling line for gas analysis was also set in the box (inhaled has analysis) and in the bag (exhaled gas analysis) for computation of O_2 consumption ($\dot{V}O_2$) after completion of the run.

We measured:

Tidal Volume:	Vt (in L BTPS)
Respiratory rate:	f (in mn^{-1})
Duration of inspiration:	Ti (in s)
Mouth pressure:	P (in mb)
FO_2 and FCO_2.	

The organization of a session is given in Table 4.

TABLE 4

Organization of exercise runs

Diver	Workload	Resistance
A1	W 0	R 0
	W 1	R 0
	W 2	R 0
A2	W 0	R 0
	W 1	R 0
	W 2	R 0
A3	W 0	R 0
	W 1	R 0
	W 2	R 0
A1	W 0	R 2
	W 1	R 2
	W 2	R 2
	And so on...	

We computed:

Ventilation: $\dot{V}E = Vt \times f$ (in liter·mn^{-1})

Oxygen consumption $\dot{V}O_2 = \dot{V}E\ (FiO_2 - FeO_2)$ (in liter·mn STPD)

End tidal partial pressure of CO_2: $PetCO_2 = FCO_2 \times$ Total pressure (in Torr)

Flow rates ($\dot{V}$) by numerical derivation of the volume signal;

Actual breathing resistances: P/V.

The P.1 Measurement

The technique used for P.1 measurements was identical to that described by Lind (17). P.1 was measured at random, never more frequently than every three breaths, and the average of the measures made during the last 2 min of exercise was considered as the true P.1.

Monitoring Subjects

Immediate monitoring of the subjects was attained in two ways:

Instantaneous $PetCO_2$, and control of the capnigram;
Measurement of heart rate by a three-lead ECG.

RESULTS

Only A-team results will be presented here, because they are the only complete set. Team B subjects were not submitted to the heliox situation at 46 ATA. Therefore, a comparison between hydrox and heliox is not possible for them.

All subjects except B3 were slightly euphoric in the hydrox situation. The exercises were considered easier in hydrox by all subjects, even when the actual workloads were greater than in heliox. However, some behavior modification let us presume that there was a slight degree of narcosis in H_2 (difficulty calibrating transducers, burst of laughter during MVV measurements, etc.).

In team B, for a workload of 105 W and the medium range resistance R2, subject B did not feel that he had reached his limits (fc = 170, $PetCO_2 > 70$ Torr). He requested (but was not allowed) to perform the highest workload. Subject B3 was unable (for psychological reasons) to perform any exercise. The full set of results is given in the appendix.

Lung Function

The results of the ventilatory clinical investigation of the subjects are given in Table 5.

Tolerance to Exercise

To compare the values between heliox and hydrox, it was decided to interpolate the hydrox values for workloads of 110 W and 150 W. Table 6 gives the main results obtained for a workload of 150 W in HELIOX (actual measurement) and HYDROX (interpolated).

In Hydrox (as compared to Heliox):

- $\dot{V}O_2$ is not different.
- $\dot{V}E$ is slightly decreased (not significant).
- $PetCO_2$ is increased ($P < 0.05$).
- P.1 does not vary.

If CONFIN is considered as a reference situation, ventilatory measurements in heliox are closer to "normal" than the ones collected in hydrox.

TABLE 5
Lung volumes and flows

Diver	Volumic Mass $g.L^{-1}$ (0°C)	Air 1ATA 1.23	HYDROX 46 ATA 6.4	HELIOX 46 ATA 8.7
A1	VC	6.32	6.20	6.03
	FEV1	4.10	3.10	2.90
	MVV	202.	33. (*)	78.00
A2	VC	5.53	5.60	5.60
	FEV1	3.60	3.14	2.91
	MVV	192.	58.	66.
A3	VC	6.25	5.93	5.93
	FEV1	5.01	2.43	2.43
	MVV	171.	42.	45.
B1	VC	5.60	5.62	
	FEV1	4.16	2.53	not exposed
	MVV	156.	72.	
B2	VC	5.40	5.32	
	FEV1	4.09	2.60	not exposed
	MVV	138.	68.	
B3	VC	4.61		
	FEV1	3.57	not measured	not exposed
	MVV	177.		

Team B was not exposed to heliox.
(*) bursts of laughter during all trials

VC(Hydrox)/VC(air)	=	0.90 ± 0.02 (m ± sd),
VC(Heliox)/VC(air)	=	0.97 ± 0.03 ,
VC(Hydrox)/VC(Heliox)	=	1.01 ± 0.02 ,
FEV1(hydrox)/FEV1(air)	=	0.67 ± 0.15 ,
FEV1(Heliox)/FEV1(air)	=	0.67 ± 0.11 ,
FEV1(Hydrox)/FEV1(Heliox)	=	1.05 ± 0.04 ,
MVV(Hydrox)/MVV(air)	=	0.33 ± 0.14 (with A1)
	=	0.37 ± 0.12 (except A1)
MVV(Heliox)/MVV(air)	=	0.33 ± 0.07 ,
MVV(Hydrox)/MVV(Heliox)	=	0.75 ± 0.28 (with A1)

There was no difference in VC between HYDROX and HELIOX. The increase in FEV1 is at the limit of statistical significance. The decrease in MVV is not significant.

TABLE 6

Ventilatory measurements without added external breathing resistances, for a workload of 150 W in Heliox (actual) and Hydrox (interpolated between 105 and 210 W) (team A)

		$\dot{V}E$	$\dot{V}O_2$	$PetCO_2$	P.1
CONFIN	m	42.7	2.76	53.7	5.6
	sd	8.9	0.34	7.0	0.8
HELIOX	m	43.6	2.24	57.0	3.8
	sd	14.5	0.33	4.0	2.3
HYDROX	m	37.6	2.28	60.0	3.9
	sd	3.6	0.04	5.3	1.2

Table 7 gives the same results for the 110 W workload with the maximal breathing resistance.

TABLE 7

Ventilatory measurements with maximal external resistance for a workload of 110 W in heliox (actual) and hydrox (interpolated between 105 and 154 W). Team A.

		$\dot{V}E$	$\dot{V}O_2$	$PetCO_2$	P.1
CONFIN	m	29.9	2.00	57.6	4.9
	sd	1.0	0.12	8.2	0.3
Heliox	m	32.9	1.76	56.7	13.2
	sd	8.3	0.14	2.9	1.8
Hydrox	m	29.6	1.94	62.3	9.3
	sd	6.5	0.19	7.1	2.3

The results are the same as those without resistance except that P.1 is significantly decreased in hydrox. $\dot{V}E$ is identical in Confin and in hydrox. $PetCO_2$ is higher in hydrox than in the two other situations. P.1 decreases with gas density. Pooling all the measurements and comparing the hydrox situation with the heliox using Student's paired *t* test gives:

$\dot{V}E$ decreases by $8 \pm 8\%$ ($P = 0.2$)
$PetCO_2$ increases by $9 \pm 3\%$ ($P < 0.05$)
P.1 decreases by $27 \pm 10\%$ ($P = 0.02$)

The analysis of the $\dot{V}E = f(\dot{V}O_2)$ relationship on all results obtained are given in Table 8.

TABLE 8

Relationship $\dot{V}e = a0 + a1(\dot{V}O_2)$
a0 in liter.mn^{-1} (BTPS)
a1 in liter.mn^{-1}/(BTPS) liter.mn^{-1} (STPD) of O_2

		Team A				Team B				
R	*n*	a0	a1	r	*P* <	*n*	a0	a1	r	*P* <
CONFIN										
R0	9	10.5	11.1	0.83	0.01	18	5.2	13.1	0.98	0.01
R2	6	4.7	14.8	0.95	0.01	15	3.5	14.9	0.97	0.01
R3	8	4.1	13.1	0.98	0.01	17	4.2	13.0	0.98	0.01
HELIOX										
R0	9	3.4	18.7	0.94	0.01					
R2	8	6.3	12.2	0.97	0.01		nonexposed			
R3	9	8.4	13.9	0.86	0.01					
HYDROX										
R0	9	3.2	15.3	0.98	0.01	14	3.1	15.0	0.98	0.01
R2	9	5.4	12.2	0.98	0.01	15	5.8	12.1	0.98	0.01
R3	9	3.6	13.2	0.95	0.01	12	4.0	13.2	0.96	0.01
All Resistances Polled										
CONFIN										
	22	5.8	13.2	0.94	0.01					
HELIOX										
	26	8.1	12.3	0.92	0.01					
HYDROX										
	27	3.7	13.8	0.96	0.01					
All Environments Pooled										
R0	26	6.3	14.2	0.92	0.01					
R3	26	7.2	12.1	0.93	0.01					

The slopes do not differ depending upon the medium. The ordinate for $\dot{V}O_2 = 0$ is greater in heliox than hydrox.

Neuromuscular Command of Ventilation

The neuromuscular control of ventilation has been assessed by a multiple correlation technique. Results are given in Tables 9 to 12.

TABLE 9

Relationship $\dot{V}e = a0 + a1\ (\sqrt{P.1})$. All results.

		Team A					Team A + B			
R	*n*	a0	a1	r	*P* <	*n*	a0	a1	r	*P* <
CONFIN										
R0	9	-00.2	17.3	0.94	0.01	18	-9.3	20.0	0.92	0.01
R2	6	-24.2	22.0	0.93	0.01	18	-4.0	16.8	0.77	0.01
R3	8	-11.6	19.2	0.87	0.01	17	-7.3	16.3	0.87	0.01
HELIOX										
R0	9	- 1.6	20.8	0.69	0.01					
R2	8	-23.4	52.4	0.94	0.01		nonexposed			
R3	9	5.0	7.5	0.88	0.01					
HYDROX										
R0	9	- 4.8	21.2	0.78	0.01	14	-6.6	22.8	0.68	0.01
R2	9	6.9	8.1	0.89	0.01	14	7.8	10.7	0.75	0.01
R3	9	- 2.6	10.6	0.97	0.01	12	6.3	8.3	0.79	0.01
All Resistances Pooled										
CONFIN										
	22	- 6.8	17.8	0.83	0.01					
HELIOX										
	26	10.6	7.1	0.58	0.01					
HYDROX										
	25	9.2	8.4	0.68	0.01					
All Environments Pooled										
R0	26	15.1	9.8	0.76	0.01					
R3	24	3.2	9.6	0.78	0.01					

a0 in $L \cdot mn^{-1}$ (BTPS)
a1 in $L \cdot mn^{-1}$ (BTPS)/mb.

The efficiency of control estimated by the relationship between $\dot{V}E$ and $\sqrt{P.1}$) is greater in CONFIN than in HYDROX, slightly greater in HYDROX than in HELIOX.

As shown in the preceding section, P.1 was decreased in HYDROX as compared to HELIOX. We tried to analyze the influence of external parameters (role of the workload and of the diaphragms) and the influence of endogenous parameters (the actual inspiratory resistance ResI), and the breathing pattern (Vt/Vc and Ti) and P.1. The analysis was done on log-log transforms.

TABLE 10

The log(P.1) and environmental parameters

	n	constant	log(W)	log(dia)
CONFIN	22	(r = 0.68 =)		
coef.		1.4	0.22	- 0.25
t stat.		3.40 (*)	3.97 (=)	- 1.71 NS
HELIOX	26	(r = 0.86 =)		
coef.		2.5	0.33	- 0.68
t stat.		4.19 (=)	6.52 (=)	- 3.52 (*)
HYDROX	25	(r = 0.84 =)		
coef.		2.0	0.33	- 0.58
t stat.		4.40 (*)	6.74 (=)	- 2.99 (*)

NS = not significant.
(+) $P < 0.05$; (*) $P < 0.01$; (=) $P < 0.001$.
W actual workload in Watts.
dia: diameter of resistors in millimeters.

It appears that the role of the mechanical workload is not different in hydrox or heliox, even if it is greater than in CONFIN. The influence of the diaphragm is greater in heliox than in hydrox, which had to be expected.

Only the actual inspiratory resistances show any differential effect. It is greater in HELIOX than in HYDROX. The same external charge will give greater P.1 in heliox environment.

The role of the CO_2 stimulus on P.1 (log-log transform) is described in Table 12. Even if the slope of the relationship is greater in hydrox than in heliox, the origin ordinate (which represents a multiplicative coefficient) is greater in heliox. If one recalculates P.1 for a given $PetCO_2$, it is always greater in heliox than in hydrox.

TABLE 11

The log(P.1) and respiratory measurements

	n	constant	log(ResI)	log(Vt/VC)	log(Ti)
CONFIN	22	(r = 0.90 =)			
coef.		3.5	0.18	0.84	1.6
t stat.		14.1 (=)	3.89 (=)	4.68 (=)	8.22 (=)
HELIOX	26	(r = 0.88 =)			
coef.		3.6	0.47	1.30	1.60
t stat.		8.7 (=)	5.75 (=)	4.13 (=)	5.96 (=)
HYDROX	25	(r = 0.89 =)			
coef.		3.9	0.36	1.40	1.70
t stat.		9.66(=)	4.69 (=)	4.69 (=)	5.67 (=)

(*) $P < 0.01$; (=) $P < 0.001$.
ResI in cm H_2O. $(L \cdot s^{-1})^{-1}$.
Ti in seconds.
Vt/VC dimensionless.

DISCUSSION

Lung Function

The Swedish team (25) observed a slight increase in VC at 1.3 MPa, which they attributed to the effects of the stressful situation. We did not observe the same increase. However, our subjects had been under saturation conditions for two days, so that much of the stress effect was deleted.

The increase in FEV1 is at the limit of statistical significance, in favor of hydrox. These results are comparable to those observed by Dahlbäck during the Swedish dive and agrees with the predictions of a purely mechanistic theory (18).

MVV in our situation does not vary significantly. This does not correlate with Dahlbäck's results nor with the theoretical predictions (24). It seems that the behavior of our divers (mainly in subject A1) did not allow them to perform the test correctly, and this may explain the discrepancy. MVV is a test which depends largely on the breathing pattern of the subject. Obtaining reproducible results needs training and repetition of the test in order to choose the best value. In the present experiment, while the subjects' cooperativeness cannot be doubted, their self-control does not appear to have been as strict as in the 1 ATA or CONFIN measure-

ments.

TABLE 12

Relationship: $log(p.1) = a0 + long(PetCO_2)$

Situation	*n*	a0	(t stat)	a1	(t stat)	r	*P*
CONFIN	22	0.68	0.73	0.017	0.98	0.21	NS
HELIOX	26	- 1.36	1.69	0.054	3.59	0.57	(*)
HYDROX	25	- 2.86	3.80	0.075	5.73	0.76	(=)

(*) <0.01; (=) <0.001

Ventilation During Exercise

It appears from these results that in hydrox, $\dot{V}E$ tends to be smaller and $PetCO_2$ is greater than in heliox. This can be interpreted as an alveolar hypoventilation.

According to the purely mechanistic theory of the limitation to ventilation (18-23), the intrathoracic resistances should be smaller in hydrox than in heliox. Therefore, breathing should be easier, and ventilation near the physiological limits of the subjects should be greater.

The exercise runs were reported by the divers less difficult in hydrox than in heliox. This is in agreement with the observations of Dahlbäck et al. at 13 ATA (25). Örnhagen (13) reported a slight degree of narcosis in the Swedish dive.

During exercise runs without added external breathing resistances, in HYDROX, we observed a tendency to alveolar hypoventilation ($\dot{V}E$ tends to decrease, $PetCO_2$ is increased) as compared to heliox. In such a situation, the only breathing resistances are intrathoracic, which should be lower, according to the mechanistic theories of the limitation to ventilation. P.1 is identical in both situations. The impedance of the thoracopulmonary system (estimated by the slope of the $\dot{V}E$ versus $\sqrt{P.1}$ relationship) is slightly smaller in hydrox than in heliox. The mechanical situation at the lung level therefore is not the cause of these results. Because of elevated $PetCO_2$ in HYDROX, P.1 ought to have been decreased. Such a phenomenon has already been described in rats for PH_2 as low as 8.3 ATA (29) and might be explained by the pharmacological effect of H_2 on the CO_2 sensitive structures. The Swedish team did not observe any modification in exercise tolerance at 13 ATA. However, the exposure duration to the H_2 mixture was very short (less than 0.5 h), PH_2 was in the low narcotic potency range, and total pressure was low, so that the ventilatory limit to exertion was far from being reached.

With added external resistance, we observed the same phenomena as without resistance, but more in the presence of a significant decrease in P.1. The multiparameter regression analysis shows that the actual inspiratory resistances are of less importance in HYDROX than in HELIOX. This, with the subjective reports of the subjects and the clinical observation of their behavior, supports the hypothesis of a H_2-induced narcosis, as previously reported for lower PH_2 by Fructus (11) and Örnhagen (12). This narcosis diminishes the reactivity of the CNS (28), even on the vegetative system (29); and, for a given combination of exercise and workload, the ventilatory control (P.1) resulting from the different stimuli is less than in heliox (a situation in which HPNS may induce a hyperexcitability of the same structures). Even with a decreased impedance of the respiratory tract, $\dot{V}E$ is less, and a slight alveolar hypoventilation appears, leading to increased $PetCO_2$. Apparently, the feed-back of $PetCO_2$ on P.1 is included in the structures affected by this narcosis.

It is questionable whether there is a decreased ventilation in hydrox or an increased ventilation in the heliox situation. Comparison of $\dot{V}E$ and $PetCO_2$ measurements obtained without resistances at depth with the one obtained at 2 ATA (CONFIN) shows that the HELIOX situation is closer to CONFIN than the HYDROX one. This implies that pressure modifies the reactivity of the respiratory system (P.1 is lower in the two sets of measurements at depth). H_2 depresses this system (decrement in the $P.1/PetCO_2$ relationship as compared to heliox).

With added external resistances, the situation is more complex. It seems that in HELIOX, there is a hyperexcitability of the respiratory system (increased P.1 and $\dot{V}E$ as compared to CONFIN). This does not lead to alveolar hyperventilation ($PetCO_2$ remains at the same level). This increased ventilation may be a compensatory reaction to the decreased gas diffusion at the alveolar level due to increased gas density (23). The gain in alveolar diffusion due to a lighter gas (H_2) is too small to compensate for the narcotic effects of the gas.

CONCLUSION

The first H_2-He-O_2 saturation dive to 46 ATA gives results which cannot be explained by the purely mechanistic theories of the limitation to ventilation in hyperbaric environments. It is the only known situation in which an increased narcotic potency combines with a decreased gas density.

It seems that the high PH_2 (25 ATA) encountered is responsible for a level of narcosis which could be detected by clinical observation of the subjects. This H_2-induced decrease in CNS reactivity has implications for the neurologic control of ventilation. For the same exercise load and breathing resistance, in hydrox, P.1 is smaller than in heliox. The density-related decrease in thoracic impedance is not sufficient to compensate for the decreased control, and a slight hypoventilation, with increased $PetCO_2$, occurs. It seems that the neurological modifications completely masked the expected theoretical benefits of the lighter gas mixture.

It is questionable whether the same phenomena would occur with lower PH_2 and whether any kind of narcosis may have the same effects on the

respiratory system. What is the optimal PH_2 not to be exceeded to retain the mechanical benefits of this lightest gas?

APPENDIX

Individual results of the measurements done during the Hydra V experimental dive (hydrogen-helium-oxygen, 46 ATA, PO_2 = 0.4 ATA).

Res	:	diameter of the diaphragms inserted in both the inspiratory and expiratory part of the breathing system
W	:	actual mechanical workload imposed (in W)
fc	:	mean cardiac frequency (in mn^{-1})
$\dot{V}O_2$	:	mean oxygen consumption (in $L \cdot mn^{-1}$ STPD)
$\dot{V}E$	:	min ventilation (in liters.mn^{-1} ATPS)
Vt	:	tidal volume (in liter ATPS)
fr	:	mean breathing frequency (in mn^{-1})
$PetCO_2$	:	mean $PetCO_2$ (in Torr)
P.1	:	mean occlusion pressure (in mb)
Vt/ti	:	mean inspiratory flow (in liter APTS.s^{-1})
Pi	:	mean of the average inspiratory pressures (in mb)
Pe	:	mean of the average expiratory pressures (in mb)

These results shown are the mean of the values of the corresponding parameter measured during the last 2 min of 6 min of exercise.

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DISCUSSION FOLLOWING PRESENTATION BY GIRY ET AL.

YOUNGBLOOD: I would just like to ask Dr. Giry his opinion regarding the operational significance. I understand the reason for caution in going deeper, but would you agree at least that at 450 m we have shown that high work rates can be achieved without dangerous increase in heart rate or changes in respiratory parameters?

GIRY: Well, before saying that, I would suggest trying an experiment with say 20 bars H_2 first to know exactly what the role of narcosis is in all this. But anyway, if you could get from the surface some kind of control over the divers I would say, "Well, let's try it." But personally I wouldn't recommend trying it at this stage.

LUNDGREN: When you say the control of the divers, do you mean the ability to intervene if something should go wrong?

GIRY: Yes, and we also want to know that things are going well.

MILLER: Surely you could test some of this by making He-N_2 mixtures of equivalent narcotic effectiveness?

GIRY: Well then you would get increased internal resistance and that is precisely the brand-new situation. Usually, with different gases the heavier they are the more narcotic they are. With H_2 we have the only situation where you get a lighter gas that is more narcotic, so here you can differentiate between the two things as you cannot with N_2-He-O_2.

BRAUER: Should the next experiment in pursuing this interesting line of reasoning be the one in which you use breathing mixtures containing a greater amount of CO_2 to look at CO_2 sensitivity?

GIRY: That should be done, but then I am not sure that would be realistic from a safety point of view inside the pressure chamber.

LUNDGREN: We are already looking at relatively high CO_2. How high should it be?

GIRY: During these dives we have observed partial pressures of CO_2 under hydrox of more than 70 Torr because some of the divers went to 210 W. We did measure some parts of end tidal CO_2 sensitivity. You will tell me that there is greater sensitivity to CO_2 in hydrox than in heliox in this situation. But that is a log-log plot, and so this constant term is not just additive. There is a basically decreased sensitivity to CO_2, and if I were to draw this line on a linear plot, you would see the sequence from high CO_2 sensitivity to low: CONFIN-HELIOX-HYDROX. That is to say the sensitivity is lower.

DAHLBäCK: So you are saying that the subjective feeling of the divers, when they say that they perceive a reduced respiratory effort, is due to two factors, both this reduction in resistance and also this hypoventilation?
GIRY: Well, there is something else. We tried to find out among all of these factors which could be tested, which one would be most sensitive, the endpoint being always P.1 just in case there are neurological problems. So, we plotted log P.1 versus the actual workload and the actual diameter of the resistance. When comparing heliox to hydrox, you don't find any difference on the workload nor a very drastic difference in terms of the diameter. The problems of the relationship of the reaction due to the gases were moderate upon the change of the exposure. When we looked at the breathing pattern of two of the divers at the time when they spontaneously alluded to respiration, we saw the tidal volume versus vital capacity ratio and the external expiratory resistance they allowed us to create, and you can see that expiratory time has no influence on the P.1. The preliminary inspiration at depth shows no effect, but then as you go through the resistances you can see that there is in hydrox a decreased sensitivity, that is to say that as you increase the resistance, P.1 will not increase, or the diver allows the resistance to increase, but then P.1 will not go over. And that is the same as to say that the problem is based on some kind of feeling, on the diver feeling the effect of the gas. All of them felt very happy with the hydrox gas. You have seen them going down and up between two spheres 3 m high? Well, during a previous dive, Entex VIII, we had exactly the same set-up, but the divers during Entex VIII (which was trimix heliox-N_2) requested, "Please don't let's go up and down--that's exhausting!" In Hydra V, they were happy; "You want us to go up, we go up; you want us to go down, we go down." They were happy with the mixture. So when you were speaking to them, everything was fine. But when you look at what is really going on within them, that's not so.

YOUNGBLOOD: Given what we know about the blunted CO_2 response in some commercial divers, and particularly those who make a practice of breathhold diving as a sport, do we know in these subjects that CO_2 response curves are normal for this experiment?

GIRY: Yes. One of our divers allowed less of a CO_2 buildup when doing 60 or 70 W work than the other two, before his ventilating effort increased, and yet reversed when he reached a high level. That's why in my presentation I never talked about 0, just because of this diver in this range. I couldn't conclude my data because of the reaction of this one.

LUNDGREN: You painted a nice picture of the rationale why the divers all hypoventilated on H_2, giving the reduced P.1 as an expression of the supposedly reduced respiratory drive. What is the possibility that your P.1 measurements were biased by changes in mean lung volume? When you measure the effect of respiratory muscle pull as a drop in mouth pressure, you have to be concerned about which lung volume this is done at because the respiratory muscle would work at a mechanically different advantage depending on what volume you do it at. There is also the concern of gas compliance which is clearly less at these high pressures. Have you any handle on that question?

GIRY: Well, no, it was impractical to do that and check the exact level at which the divers were breathing. But perhaps you can get the answer in another way; looking at the mean inspiratory flow, we got a 0.99 correlation without P.1 measurements. So, we believe what we have done was the best we could do, and yielded real and not fanciful data.

CARDIOVASCULAR STUDIES DURING HYDRA V

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Human work tolerance at depths of 300 m and beyond can be limited by factors related to the increases in gas density, deranged neurological function, or impaired cardiovascular performance. Several paradigms for deep diving have evolved to suggest ways to overcome these physiological disturbances. Slowed kinetics of heart rate and cardiac output responses to exercise at 300 m can be partially overcome by transient elevations in PO_2 (1). Use of inert gases with narcotic potency have been employed to reverse membrane effects of pressure on the heart (2) and nervous systems (3).

Hydrogen has been suggested as a deep diving gas because of its low density and its specific effects on the cardiovascular and nervous systems. The 300 m Hydra IV dive conducted by COMEX in November 1983 demonstrated that men could perform light exercise safely while breathing H_2 gas at very high partial pressures. The divers of Hydra IV had a normal cardiovascular response to exercise and were free of any dangerous cardiac arrhythmias (4). With the COMEX Hydra V dive in May 1985, we were afforded the opportunity to extend these observations to a higher absolute pressure, to a longer duration of hydrogen exposure and to a significantly higher workload.

Two teams of three men each, A-team and B-team, were saturated for several days on a H_2-He-O_2 mixture (HYDROX) at 450 m. The mixture contained approximately 56% H_2 and had an O_2 partial pressure of 400 mbar. At depth, each team performed graded bicycle ergometer exercise in the dry while measurements of ECG, heart rate, and cardiac output were obtained. The data form the basis of this report.

METHODS

The studies were performed in conjunction with the French Navy (Marine Nationale). The details of the dive and of this specific experiment are given in papers by Gardette and Giry in this workshop.

Briefly, the protocol called for studies to be performed at a control depth of 10 m on heliox and then at 450 m on hydrox. In addition the A-team was studied at 450 m on heliox. In all cases, the O2 partial pressure was controlled at 400 mbar. The subject sat on an electronically braked bicycle ergometer and breathed chamber atmosphere through a mouthpiece. Respiration was either unimpeded (R = 0) or impeded by insertion of orifice resistors of progressively decreasing caliber (R = 2 and R = 3) into the breathing circuit. The subject rested for approximately 11 minutes, then performed two 6 min periods of work, first at light to moderate intensity (75 or 105 W) and then a moderate to heavy intensity (110, 150, 154, or 210 W). The

subject rested between the two work periods for a variable period of time while gas analysis was performed and also rested for a minimum of 5 min after the second workload to allow heart rate recover to be assessed. The exercise protocol is shown in Figure 1.

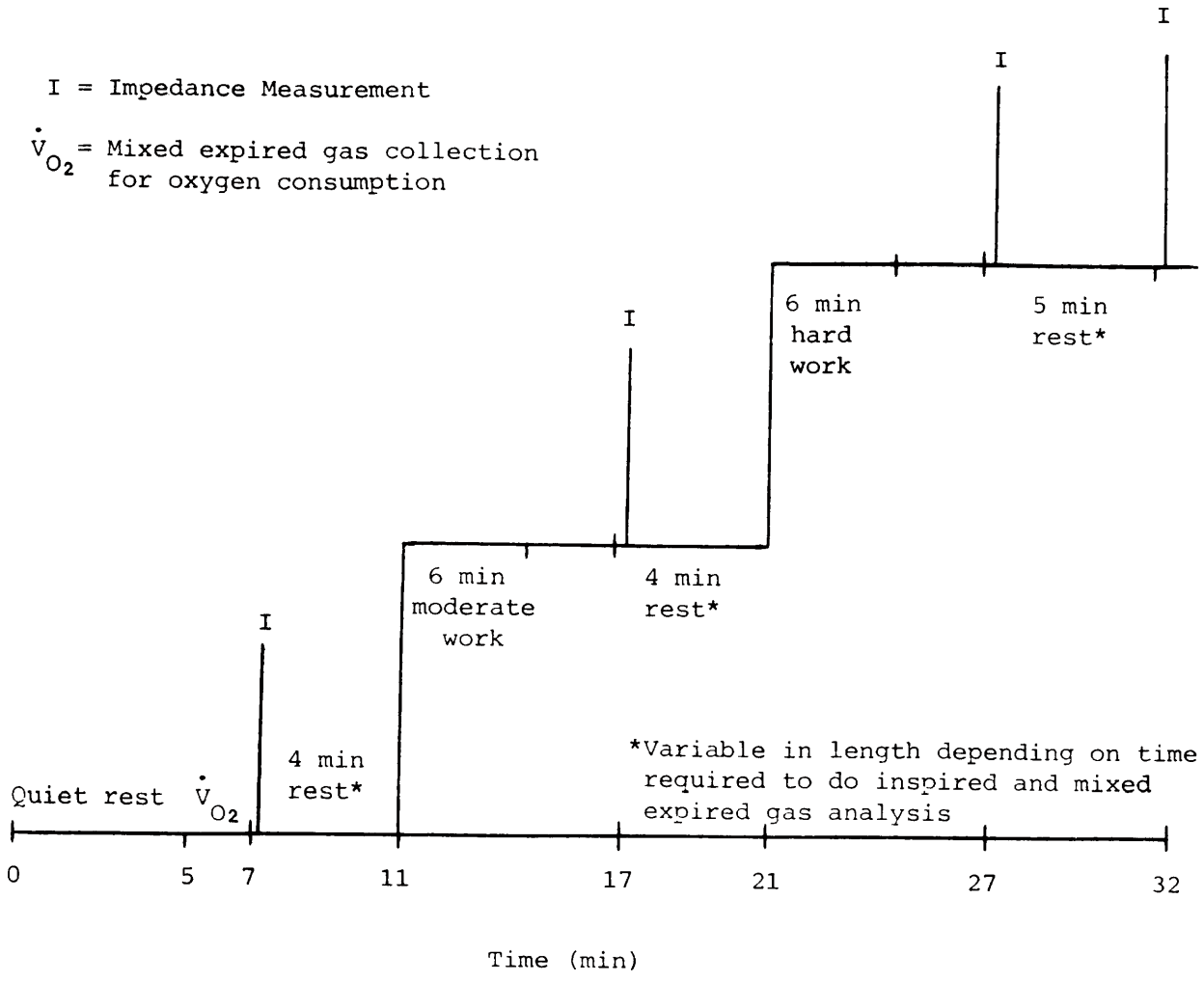

Fig. 1. Experimental Sequence. Following an initial rest period, two 6 min periods of moderate and heavy exercise were performed. Mixed expired gas was collected between 4 and 6 min of each exercise period for determination of oxygen consumption ($V(O_2)$). Impedance cardiographic measurements (I) were obtained immediately following cessation of work.

During the experimental sequence, ECG was obtained continuously form patch electrodes placed on the chest. To obtain cardiac output, pairs of 1 cm wide aluminized mylar strip electrodes were placed circumferentially around the neck and around the lower thorax. A 4 mA current at 100 kHz was applied to the outer neck and thoracic electrodes. The inner neck and thoracic electrodes recorded the changing thoracic impedance from which cardiac stroke volume was determined.

For the measurement of cardiac output, the subject was instructed to stop work and hold his breath at the end of a normal expiration. In this way, both motion artifact and respiratory variation in thoracic impedance were eliminated. All measurements were completed within 10 s of stopping work.

From the impedance wave form, cardiac stroke volume was derived using the following equation (5):

$$SV = A \cdot L \cdot \Delta Z/Z_o$$

where: SV = stroke volume in ml;

A = the area of the thorax derived from the circumference of the inner thoracic electrode;

L = mean distance between the inner thoracic and inner neck electrodes;

ΔZ = the change in thoracic impedance with each cardiac stroke;

Z_o = mean baseline thoracic impedance.

Cardiac output was computed as the product of the stroke volume and the simultaneously determined heart rate.

The heart rate was also determined by direct counting for the last minute of each rest or exercise period. These count values are the ones shown in Figs. 2 and 3.

The results of the heart rate and cardiac output measurements are shown in Figs. 2 and 3. The A-team and B-team will be considered separately because of the differences in response.

At 450 m on hydrox, the A-team was able to complete and assigned workload of 210 W at R = 0 and R = 3. The workload was reduced intentionally to 154 W and this was also completed successfully. In heliox at 450 m, the A-team was able to complete assigned workloads of 150 W at R = 0 and 110 W at R = 3. They were unable to complete and assigned workload of 150 W at R = 2.

Preliminary analysis of the data from A-team showed no clear effect of added respiratory resistance on heart rate or cardiac output, so all resistance conditions were combined to illustrate the effects of gas mixture

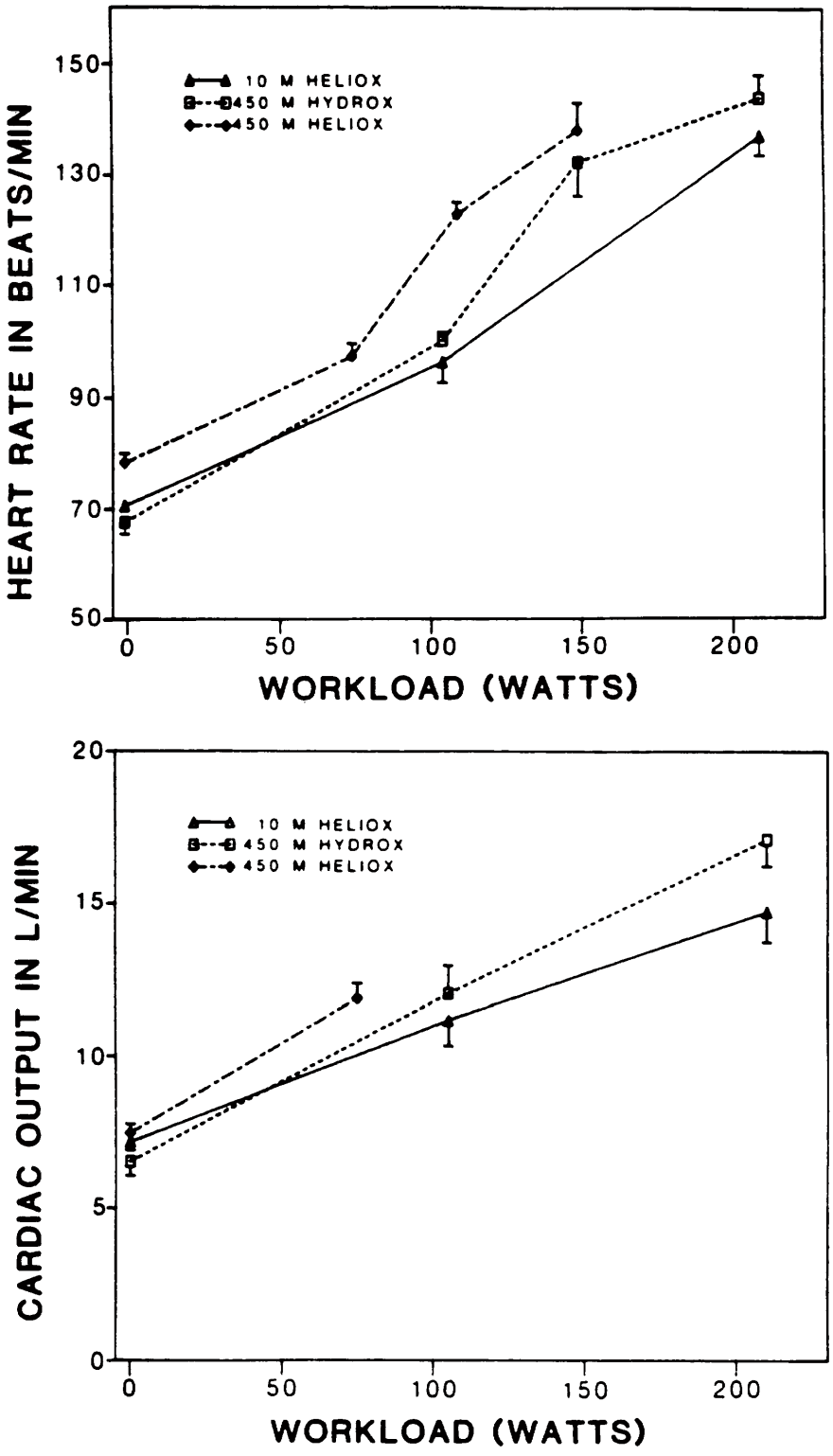

Fig. 2. Cardiovascular responses to exercise in A-team. All resistance conditions are included. Vertical bars indicate 1 standard error of the mean.

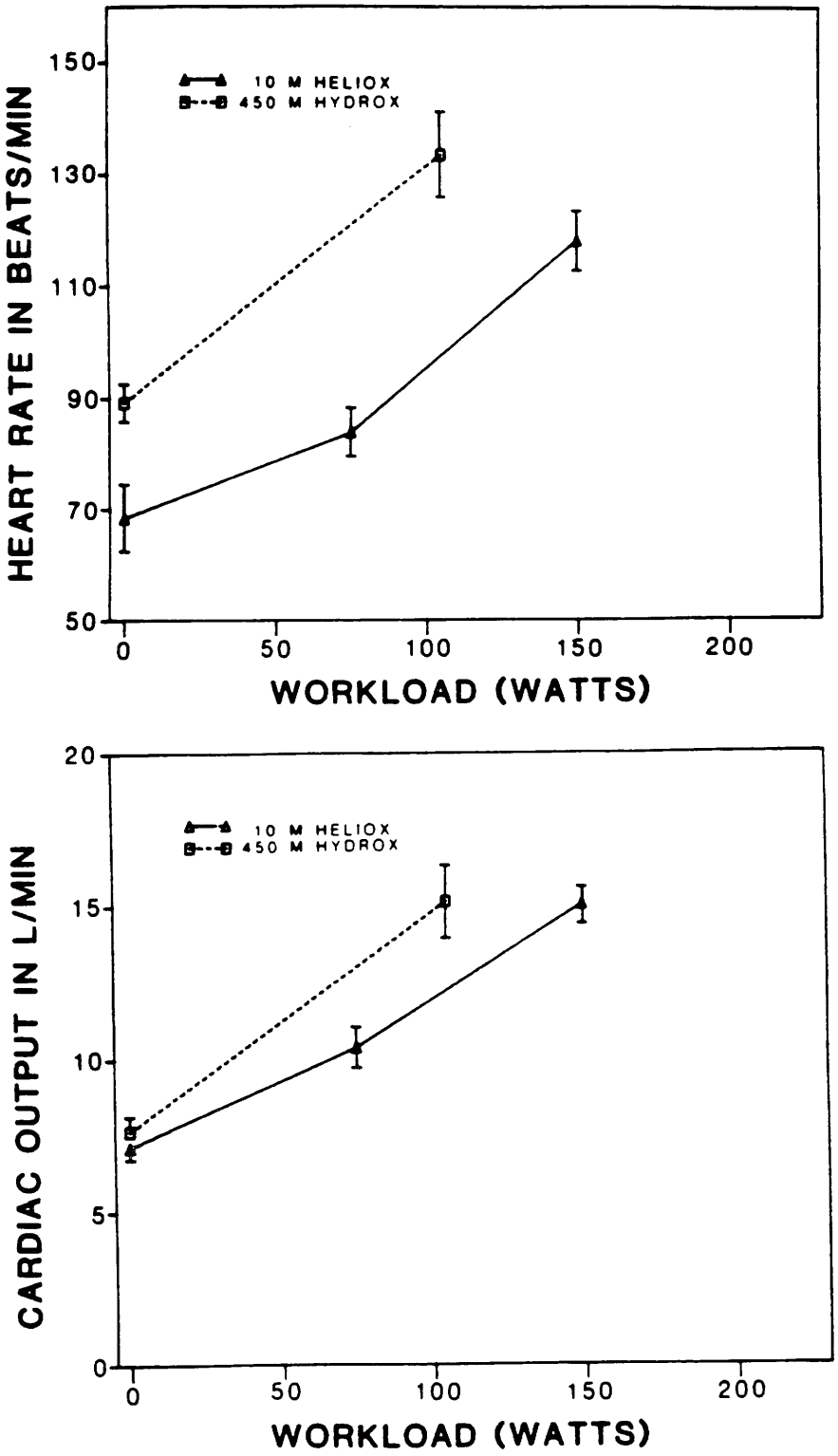

Fig. 3. Cardiovascular responses to exercise in B-team. All resistance conditions are included. Vertical bars indicate 1 standard error of the mean.

and depth. Under all conditions, heart rate and cardiac output increased with exercise as expected (Fig. 2) At 450 m, heart rate and cardiac output were elevated with both hydrox and heliox when compared with 10 m control values. Heart rate and cardiac output, however, were slightly lower than hydrox at 450 m than with heliox at the same depth. Statistical analysis of these results has not yet been completed.

The B-team's heart rate response to exercise with heliox at 10 m was nearly identical to that of the A-team indicating that both groups were relatively evenly matched. However at 450 m on hydrox, only one subject performed at the level of the A-team. This subject completed assigned workloads of 210 W at R = 0 and R = 2, and 154 W at R = 3. The second subject completed the lighter 105 W workload at R = 0 and R = 2, but was not allowed to attempt the higher workload or the R = 3 resistance condition because of the relative tachycardia observed during the lower workloads. The third subject was ill at 450 m and stopped after 1 min and 50 s on the 105 W workload at R = 0. He did not perform any further experiments.

Resting heart rate was elevated in the B-team at 450 m in hydrox when compared to the 10 m heliox control. This is in contrast to the slightly lower heart rate seen at 450 m on hydrox in the A-team. The data from the B-team contained more technically unsatisfactory traces than did the data from the A-team and this fact, coupled with the fewer conditions available for study in the B-team, limited the conclusions that could be drawn about the heart rate and cardiac output responses to exercise. As shown in Fig. 3, however, it appeared that the performance of a given level of exercise at 450 m in hydrox required a substantially higher heart rate and cardiac output.

Both A- and B-team members showed a normal supraventricular rhythm on ECG under all conditions tested. For the most part, this was clearly distinguishable as a normal sinus rhythm, although in some tracings the P wave was not apparent. These tracings may have been sinus or nodal in origin. The QRS duration appeared normal. A marked respiratory sinus arrhythmia was noted in all subjects under all conditions. Isolated premature supraventricular or ventricular beats were noted in some subjects at rest or in the resting period following work both at 10 and 450 m. Some isolated premature contractions were also noted during work at depth. The conditions under which premature beats appeared during work are shown in Table 1. No dangerous arrhythmias were noted at any time.

Conditions under which cardiac arrhythmias appeared during exercise

Time constants for the rate of rise and fall in heart rate with heavy exercise in A-team without added respiratory resistance (R = 0) are shown in Table 2. Compression to 450 m slowed both the rate of rise and fall of heart rate. Hydrox appeared to have a faster rise than heliox at depth. The off-time constants, however, were identical. Statistical analysis of the data has not yet been conducted.

TABLE 1

Subject	Depth (m)	Gas	Resistance Condition	Workload (W)	Arrhythmia Type	No.
A1	450	Hydrox	3	154	VPC	2
					VPC couplet	1
A1	450	Heliox	2	150	VPC	3
A3	450	Hydrox	2	105	VPC	2
					VPC couplet	1
				210	VPC	1
A3	450	Heliox	3	75	SVPC	2
B2	450	Hydrox	0	105	VPC	1

VPC = ventricular premature contraction; SVPC = supraventricular premature contraction; VPC couplet = 2 ventricular premature contractions in a row.

TABLE 2

Time constants (min) for rise of heart rate with heavy exercise and subsequent fall with rest. A-team, no added respiratory resistance.

Subject	10 Heliox		450 Heliox		450 Hydrox	
	τ_{on}	τ_{off}	τ_{on}	τ_{off}	τ_{on}	τ_{off}
A1	0.86	0.54	2.20	0.85	1.24	1.32
A2	0.53	0.73	0.65	1.09	0.95	0.76
A3	0.96	0.73	1.36	1.40	1.29	1.22
Mean	0.78	0.67	1.40	1.11	1.16	1.10
SEM	0.13	0.06	0.44	0.16	0.11	0.17

CONCLUSIONS

The A-team was capable of performing hard work in hydrox at 450 m. Heart rate and cardiac output increased uniformly as the exercise load was

increased and no significant arrhythmias appeared. The absolute values of heart rate and cardiac output were slightly lower on hydrox at 450 m than on heliox at the same depth. Thus the hydrox values at depth appeared closer to the baseline 10 m control values than did the heliox values. These differences, however, were relatively minor.

Compression to 450 m slowed heart rate kinetics in the A-team significantly when compared to the rise and recovery times at 10 m. At 450 m, the rate of rise in heart rate with heavy exercise was faster in hydrox than in heliox. Thus the hydrox values, although prolonged, appeared closer to the 10 m control values than did the heliox values. The rate of recovery post-exercise with hydrox at 450 m was identical to that with heliox. H_2 may be of some benefit in reversing those effects of pressure that degrade the onset characteristics of the cardiovascular system. The failure of H_2 to also speed cardiac recovery at depth may relate to basic differences in the mechanisms controlling onset and recovery functions.

The B-team behaved differently at 450 m on hydrox than did the A-team. The reasons for these differences are still unclear. Only one member of B-team was capable of doing hard work. Both at rest and for a given workload, heart rate and cardiac output in B-team appeared substantially higher on hydrox at 450 m than on heliox at 10 m. These changes, particularly in heart rate, were out of proportion to those seen in the A-team. Importantly, no significant cardiac arrhythmias occurred even though these subjects appeared under significant stress.

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DISCUSSION FOLLOWING PRESENTATION BY FLYNN

LUNDGREN: Could you briefly mention whether there were any physiological or methodological reasons why you had more problems getting the data from the B-team?

FLYNN: There were methodological problems, for instance, in putting the electrodes on correctly. There may also have been some wiring problems. As the experiments went on we tended to have more and more noise in the signals. The physiological or psychological reasons for problems with the B-team I can't assess completely. I don't speak French and I wasn't always completely knowledgeable about the exact condition of the subjects.

GENNSER: You say you didn't have any arrhythmias. Did you check for conduction times in the ECG?

FLYNN: That has not been done yet. If you look at the ECG traces, there are no substantial aberrations of rhythm. There were a few premature contractions. For the most part it was a very monotonous supraventricular rhythm. Some subjects showed more sinus arrhythmia than others did. There is nothing to suggest any kind of a dropped beat. Looking at the P-R intervals and Q-T intervals and EC coupling intervals they all look very reasonable. There was nothing grossly abnormal that jumped out.

Yesterday we heard that in the isolated node preparation bradycardia would be induced by pressure and that narcotic gases would then reverse that, He not being too hot in that respect and certainly H_2 being better. Our results appear to my way of thinking to be exactly the opposite, in terms of relative tachycardia at depth. We saw the highest heart rate in He as opposed to H_2, and so it seems to be the limited data against that kind of theory.

FIFE: How much of that could have been psychological?

FLYNN: I imagine a lot of it.

LUNDGREN: There is of course the possibility that there was a difference in respiratory work load. Let me see, would that work the right way? If less work were being done, you would expect that H_2 would help to keep heart rate down.

FLYNN: Well, that's what happened. The heart rate skipped a beat or two. So, that's right--the work is nullified out.

Now there is an interesting point. Dr. Giry told me last night that the divers said it was harder to work in $He:O_2$ than in $H_2:O_2$ yet they were at the same ergonomic load but had higher heart rates and higher cardiac outputs. So this matches the statement that it is harder to work in He.

LUNDGREN: Any difference in terms of respiratory work is very difficult to catch by measuring O_2 consumption under these conditions. Even under very

hard respiratory work, the total amount of O_2 consumed is modest, and it takes very special and careful measurements to catch that under the conditions of exercise. One could speculate perhaps that the strain on the respiratory muscle could have a secondary effect on heart rate, and then certainly on the perception of the work load. What were the main reasons for those divers in the B-team who couldn't go any higher than 75 W not being able to continue?

FLYNN: The reason I think was an elevated heart rate, which was seen on the outside. Wasn't that about 160 beats/min?

LUNDGREN: So they were stopped from the outside. It was not that they themselves threw in the towel.

FLYNN: They were not allowed to do the higher workload because of the findings.

LUNDGREN: But weren't they complaining?

GIRY: One of the divers didn't complain at all, but we stopped him from the outside. The other diver stopped short of breath as soon as he got on the bike and it appeared afterwards that the problem was not physiological.

LUNDGREN: In retrospect, would there be anything in the workup of that diver to explain why that diver would suffer shortness of breath when the others didn't?

GIRY: As far as I know, no.

IMBERT: All the divers on the B-team performed well under wet conditions. Under dry conditions, something occurred that stopped one of them, perhaps for some technical reason; he said, "I can't do that." He was able to perform two days later under wet conditions.

GARDETTE: Also there was special problems for the B-team. The temperature in the sphere was not correct. It was too high by about 2° C.

LUNDGREN: Two degrees under these conditions is a very substantial difference.

FIFE: This may be kind of farfetched, but is it possible that the difference between the H_2 and the He is a difference in the temperature of the blood leaving the heart? If that's the case, could that play a role in these results?

FLYNN: That's a possibility because there are some temperature changes in blood associated with O_2-CO_2 exchange.

FIFE: The question is whether or not this might have had an effect on such things as PO_2?

LUNDGREN: We have tried some very preliminary experiments to influence

heart rate by cooling breathing gas and it's not easy, but that doesn't mean that it could not happen, with the right circumstances.

CARLIOZ: For that one diver one problem was that during that first day he was very anxious. After the second day he was in better shape; he was not anxious.

SECTION V
Operational Considerations
Safety and Systems Design

HYDROGEN FLAMMABILITY AND IGNITABILITY IN DEEP DIVING ATMOSPHERES

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INTRODUCTION

The use of hydrogen-oxygen atmospheres or hydrogen-helium-oxygen atmospheres for deep diving operations may be feasible if the mixture composition is safely outside the flammable range. This has been achieved in the human and animal studies described in this conference by maintaining O_2 partial pressures at levels that are physiologically viable but sufficiently small compared to the mixture total pressure so as not to support combustion.

Since this is a unique application of H_2 flammability considerations, the conference organizers have requested a review of relevant flammability data and test methods. The review will emphasize published flammability data and does not include the COMEX data obtained in preparation for the Hydra IV and V experiments (1). H_2-air flammability data are reviewed, along with H_2-O_2 and H_2-He-O_2 mixture data, because of the need to avoid flammable mixtures in support operations outside the diving vessel. A brief review of H_2 ignitability data is provided for the benefit of operations having a double goal of eliminating ignition sources as well as avoiding flammable mixtures.

FLAMMABILITY TEST METHODS

Flammability data at atmospheric pressure are usually obtained in a vertical cylinder, typically 5 cm in diameter and 1.0-1.5 m long (2,3). Upward flame propagation limits, which are wider than those for downward or horizontal flame propagation, are usually based on spark ignition near the open, bottom end of the tube. The lower and upper limits of H_2 flame propagation in air using this method are 4.0 and 75.0 vol % H_2 (2). When the equivalent tests are conducted in a closed tube, the H_2-O_2 limits are reported to be as wide as 3.9 to 95.8% H_2 (2).

Flammability data at elevated pressures have been obtained in a variety of cylindrical and spherical pressure vessels. For example, Holmstedt's data on the H_2 upper flammability limit were obtained in two cylindrical vessels with volumes of 1.5 and 5.2 liters (4). Fig. 1 is a schematic drawing of Holmstedt's apparatus. H_2-He-O_2 gas mixture components were metered into the test vessels according to their desired partial pressures. A mechanical agitator mixed the gases in the vessel prior to ignition. Electric sparks or fused wires, located axially 5 to 3 cm, respectively, above one end of the vessel, served as the ignition source. Holmstedt reports that the energies associated with the fused wires were 5-8 J, while the spark energies were 0.15-3.7 J depending on the mixture's total pressure.

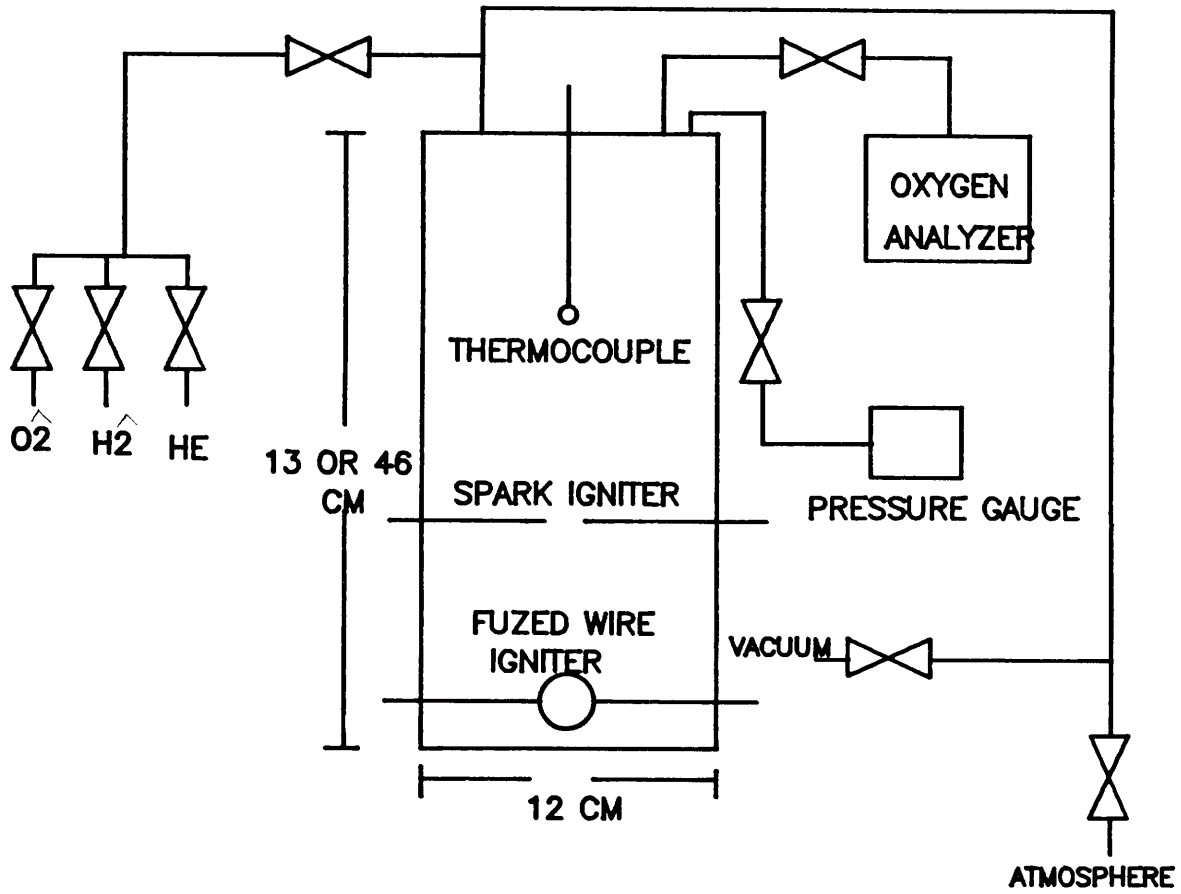

Fig. 1. Holmstedt Flammability Apparatus

Test vessels and ignition sources used in various H_2-O_2 mixture flammability experiments are listed in Table 1. Holmstedt reports that the flammability data obtained in his larger (5.2 liter) vessel were identical to the data from his smaller (1.5 liter) vessel. Other vessels listed in Table 1 have comparable volumes. The igniter energies listed in Table 1 span a range of two orders-of-magnitude, which may cause some slight difference in measured flammability limits. According to Bartknect, increasing the ignition energy from 1 J to 100 J caused the lower limit of methane to decrease from 4.9 to 4.25 vol % (5).

Another important difference among various flammability determinations is the method used to detect combustion. Possible combustion criteria for closed test vessels include temperature increases, pressure increases, and O_2 consumption. Holmstedt relied primarily on thermocouple responses and measurements of pressure decreases when the gas mixtures cooled. He reports that the temperature/pressure data were consistent with the O_2 consumption data, and that there was a sudden transition from no combustion to complete O_2 consumption as the mixture O_2 concentration was increased by at most 0.2

Table 1

Flammability Determination at Elevated Pressures

Reference	Vessel	Igniter
Holmstedt (4)	12x13 (or 46) cm cylinder	0.2-3.7 J spark, 5-8 J fuzed wire
Yantovski & Chernyak (6)	5x30 cm cylinder	spark
Kagarko & Ryabikov (7)	16 cm diam sphere	14 J pulsed wire

vol %. Other experimenters, for example, Yantovski and Chernyak, report a wide range of O_2 concentrations in which only partial combustion occurs, as measured by O_2 consumption (6).

Oxygen (or H_2) concentration at which some combustion first occurs is called the flammability limit, while the somewhat higher concentration at which the rate and extent of combustion becomes sufficiently large to produce a pressure rise is sometimes called the explosive limit. Since the difference between flammability limits and explosive limits are apparatus dependent, it is more prudent to associate the explosive limits with the broader flammability limits reported in the following section.

FLAMMABILITY DATA

Holmstedt's data on the H_2 upper (fuel rich) flammability limit for H_2-He-O_2 mixtures at 2 atm are shown in Fig. 2. Holmstedt measured the upper limit at), 20, 40, 60, and 80% He, and assumed the lower limit was 5 vol % H_2 at all concentrations. The intersection of the upper and lower limit as plotted in Fig. 2 represents the minimum O_2 concentration required to support H_2 combustion at any He dilution level. Holmstedt called the O_2 concentration determined as shown in Fig. 2 the critical, or maximum safe O_2 concentration.

Figure 3 shows Holmstedt's maximum safe O_2 plotted as a function of mixture total pressure. As the pressure is increased form 1 to 29 atm, the maximum safe O_2 concentration increases from 3.4 to about 4.3 vol %. An explanation for this pressure effect is not apparent since pressure can simultaneously affect the combustion reaction rate, the rate of heat loss from the reacting mixture, and the efficiency of energy deposition form the ignition source.

Hydrogen-oxygen mixture upper flammability limit data are shown in Fig. 4 plotted against pressure. Data from four different experimenters span a range from 4.5 to about 6.0 % O_2 at pressures on the order of 10 atm (4,7,8). These differences are probably attributable to igniter strength and location in the test vessels as described previously.

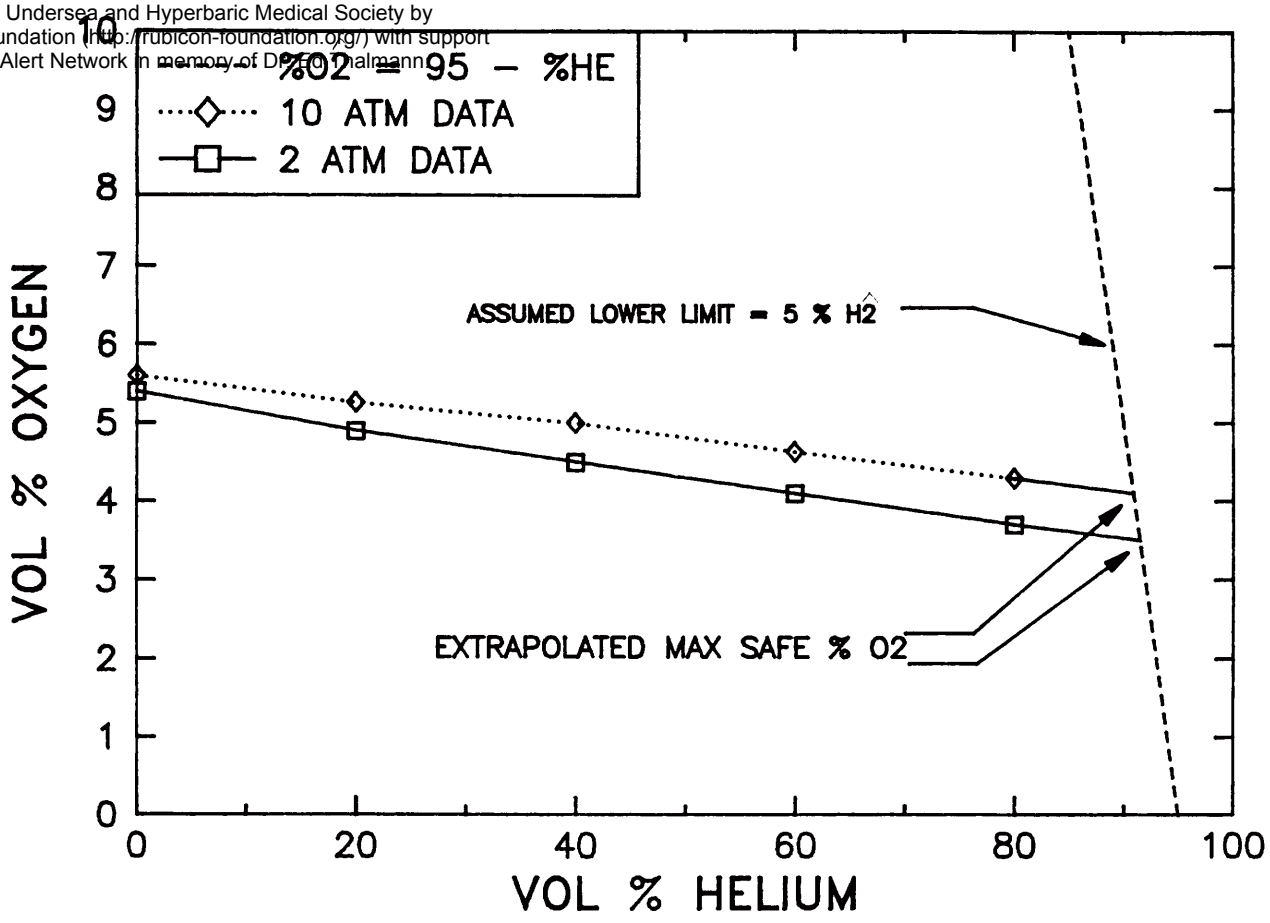

Fig. 2. Holmstedt Upper Flammability Limit Data

Kagarko and Ryabikov's data on the lower flammability limit of H_2 in O_2 are shown in Fig. 5 as a function of pressure (7). The lower limit increases from 4.5 vol % H_2 to about 6% H_2 as the pressure is increased from 1 to 100 atm. Lower limit data reported by Coward and Jones for downward propagation indicate a roughly constant value of 8-9% H_2 at pressures up to 122 atm (2). Thus, downward propagation limits are significantly narrower than upward flame propagation limits at all pressures.

Flammability limits for H_2-He-air mixtures are reported by Coward and Jones and by Koren et al. (2,9). The reported maximum amount of H_2 for which a H_2-He mixture is nonflammable at any air concentration is 8.7% H_2 (He/H_2 = 10.5) and 10.5% H_2 (He/H_2 = 8.5) (2,8). These limits (which correspond to 5.6-6.1 vol % H_2 in the H_2-He-air mixture) are relevant to the design of air locks between the diving vessel and an air atmosphere.

IGNITABILITY DATA

Two common accidental ignition sources are hot objects and electrical sparks. Some of the available data on the conditions required for these sources to ignite H_2-air and H_2-O_2 mixtures are reviewed here.

Surface temperatures required to ignite an H_2-air or H_2-O_2 mixture depend on the mixture composition and on the size and shape of the hot object. The minimum ignition temperature, which is called the spontaneous ignition temperature, refers to a situation in which the gas mixture is heated slowly and uniformly so that it is at the same temperature as the vessel walls. The spontaneous ignition temperature for a stoichiometric H_2-

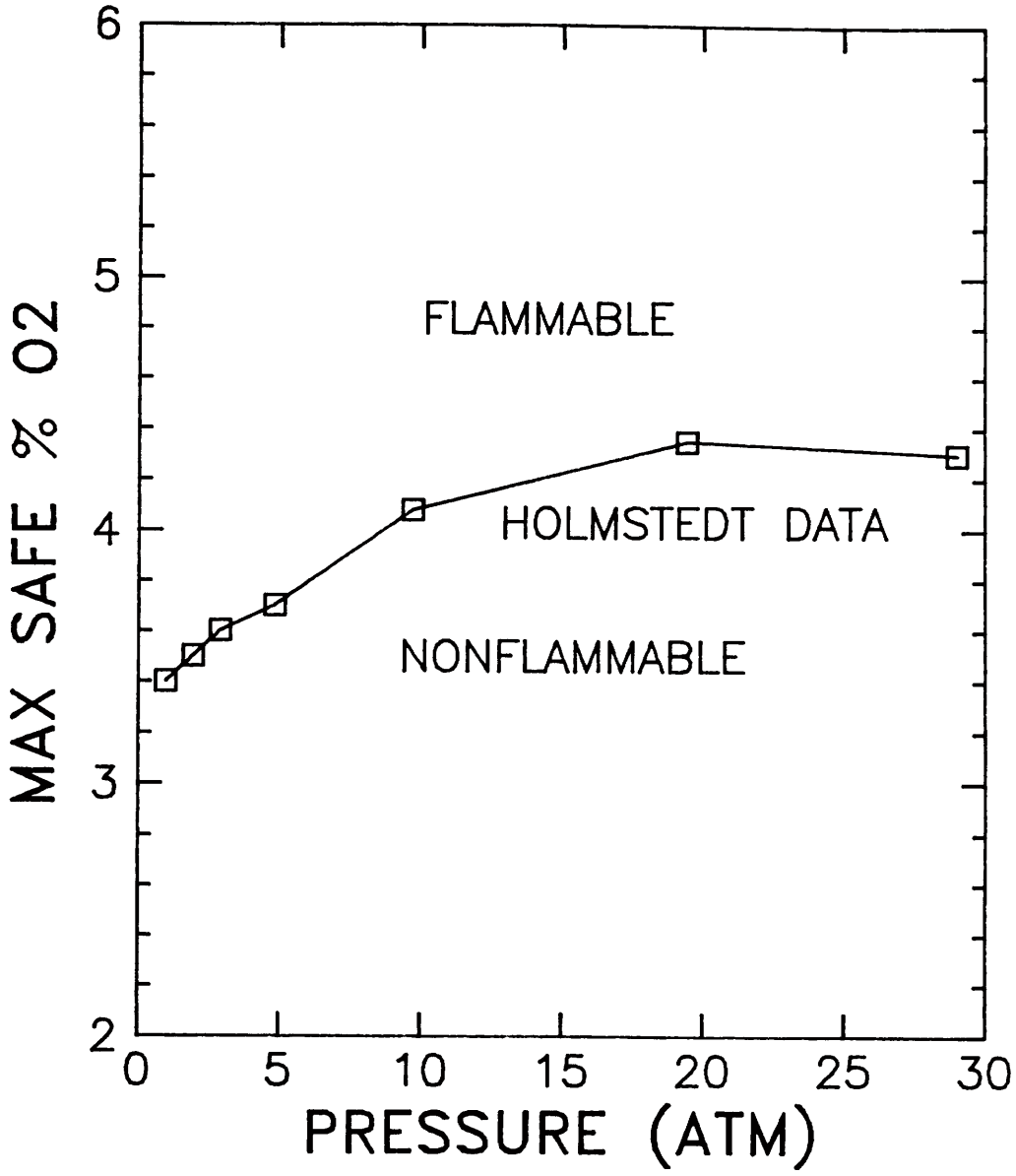

Fig. 3. Max Safe % O_2 vs Pressure

Electrical spark ignition energies have been measured for a variety of air mixture (30 vol % H_2) is 515° C. This value increases sharply as the H_2 concentration deviates from its stoichiometric values or as diluent gas is added (10).

Surface temperatures required for small thermal igniters to ignite lean H_2-air mixtures have been measured recently in an extensive series of tests conducted for the nuclear power industry and regulators. Required surface temperatures are in the range of 640-800° C depending on the size and shape of the igniter and the concentration of stream in the mixture (10). Surface temperatures required to ignite H_2-O_2 mixtures would presumably be lower but published data apparently are not available.

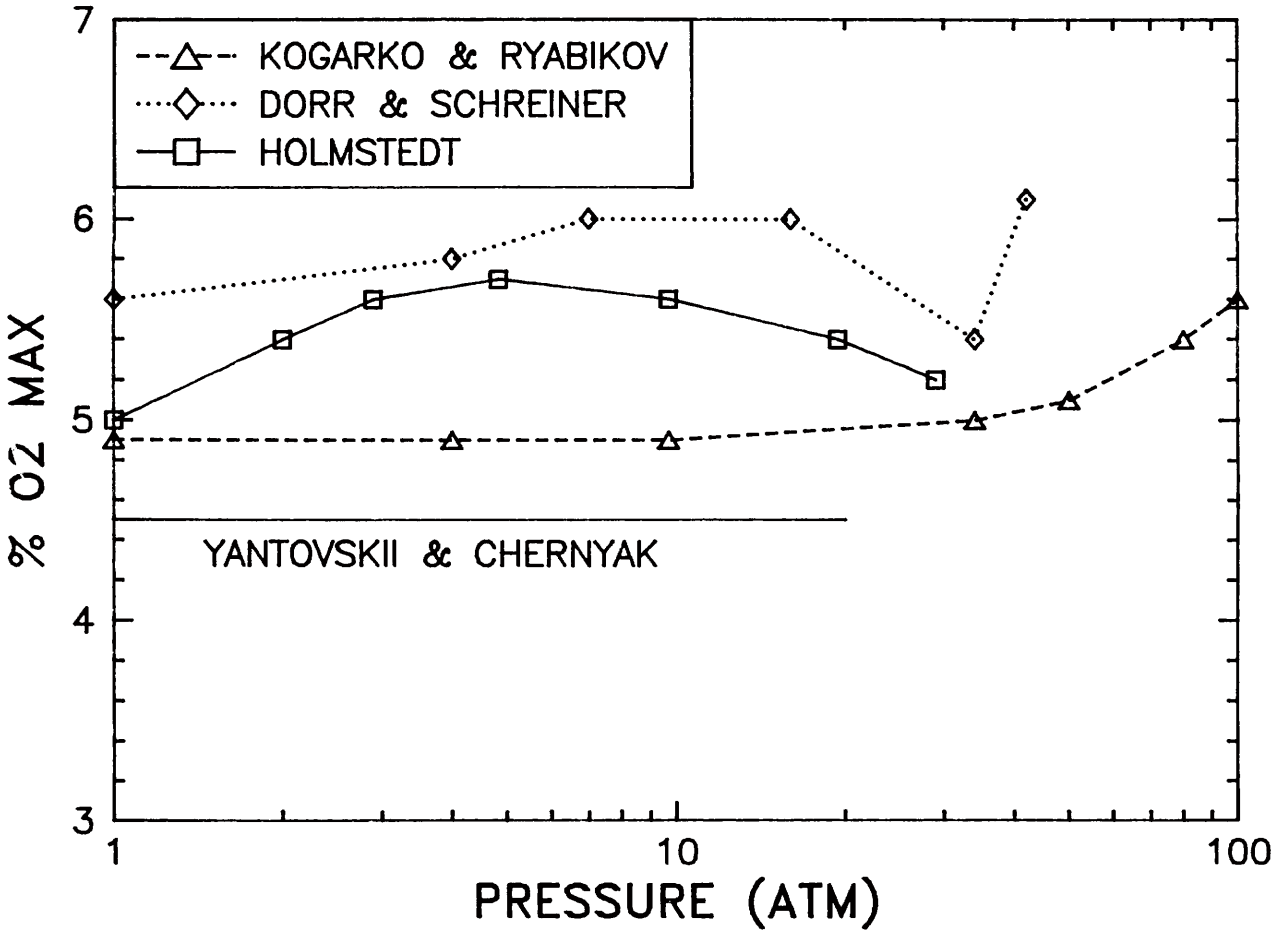

Fig. 4. H_2-O_2 Upper Limit Data

H_2-O_2-diluent gas mixtures. Minimum required spark energies for various H2concentrations and for the O_2:diluent ratio corresponding to normal air are shown here as Fig. 6 (11). The minimum ignition energy for a stoichiometric H_2-air mixture is 0.02 millijoules, which is a value easily exceeded in many accidental electrical and electrostatic discharges. On the other hand, spark ignition energies required to ignite gas mixtures near the flammability limits are on the order of 10 J. The data in Fig. 6 shows that a more energetic spark is required to ignite a H2-He-O_2 mixture than to ignite a H_2-air mixture in the same H_2-O_2 concentration.

Figure 6 also shows data for quenching distance, which is defined as the minimum separation between two parallel plates that will allow a flame to propagate in a specified gas mixture between the plates. The quenching distance for near-stoichiometric H_2-O_2-diluent mixtures is less than 1 mm. When the diluent is removed, or when the mixture pressure is on the order of 100 atm, the quenching distance can decrease by and order-of-magnitude or more compared to the values shown in Fig. 6. Therefore, flame arrestors designed for H_2-air service may not be suitable for deep diving gas mixtures.

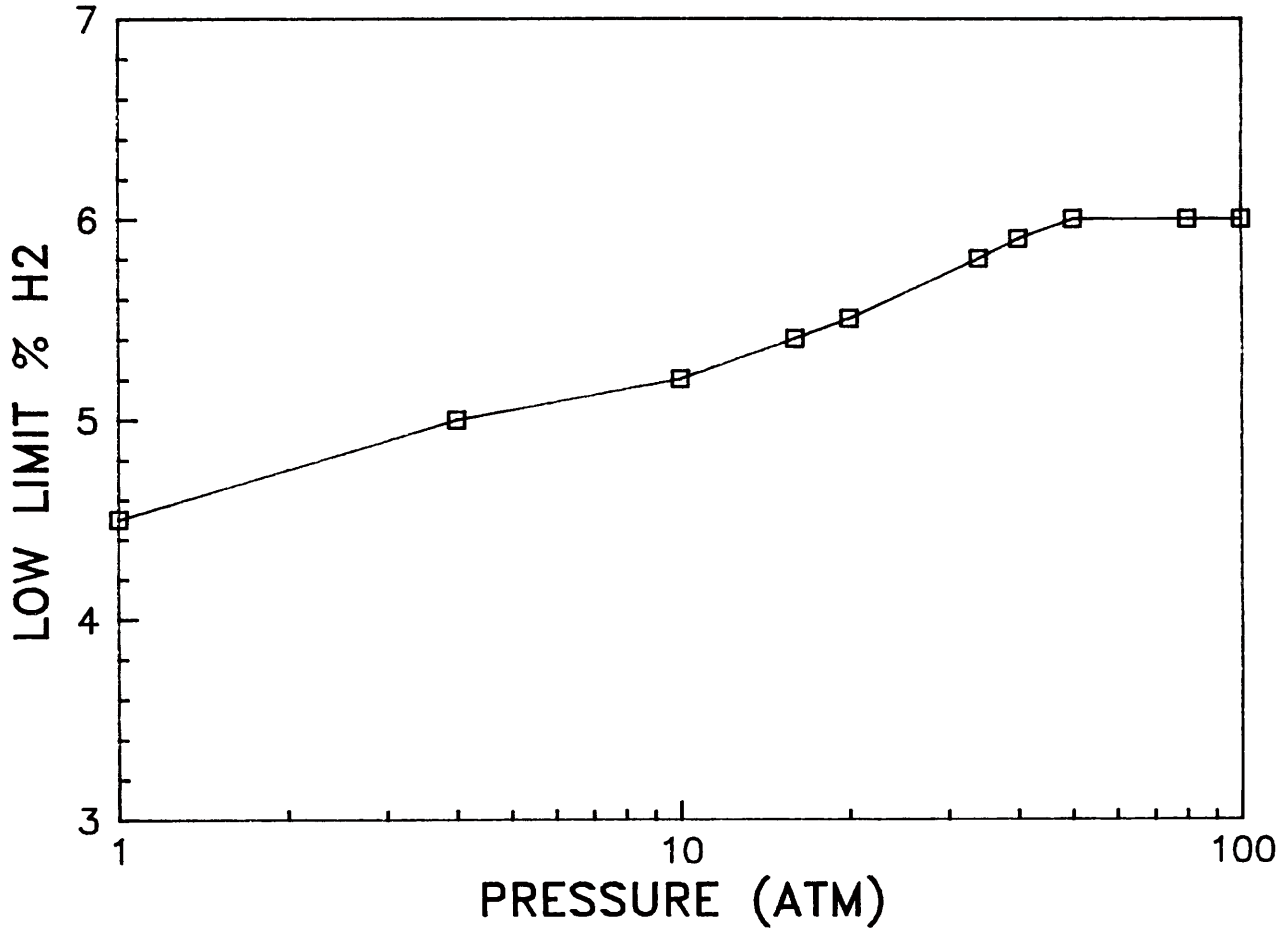

Fig. 5. Kogarko Data on H_2-O_2 Lower Limit

The flammability and ignitability data presented here are not sufficient to determine reliably whether a specific piece of electrical equipment will or will not ignite a H_2-O_2 or H_2-air mixture, and whether or not the resulting flame will propagate from the equipment into the surrounding gas mixture. This type of equipment-specific information is best obtained from approval testing organizations that ascertain whether a particular piece of equipment is suitable for use in a particular category of hazardous environment. Two nationally recognized approval testing organizations in the United States that determine equipment compliance with the flammable gas atmosphere sections of the National Electric Code (Article 500) are Factory Mutual Research Corporation and Underwriters Laboratories, Inc.

CONCLUSIONS

The minimum O_2 concentration required for flame propagation in H_2-He mixtures is reported to be in the range 4.2-6.0 vol % O_2 depending on the experimental apparatus and the pressure of the gas mixture.

Holmstedt's data on the maximum safe (i.e. nonflammable) O2 concentration for H_2-He-O_2 mixtures of any proportions show the concentration increasing from 3.4 vol % O2 at 1 atm to 4.3 vol % at 29 atm. In view of the scatter in the flammability data obtained from different test facilities, it would be helpful to compare the Holmstedt data to the data obtained recently by COMEX.

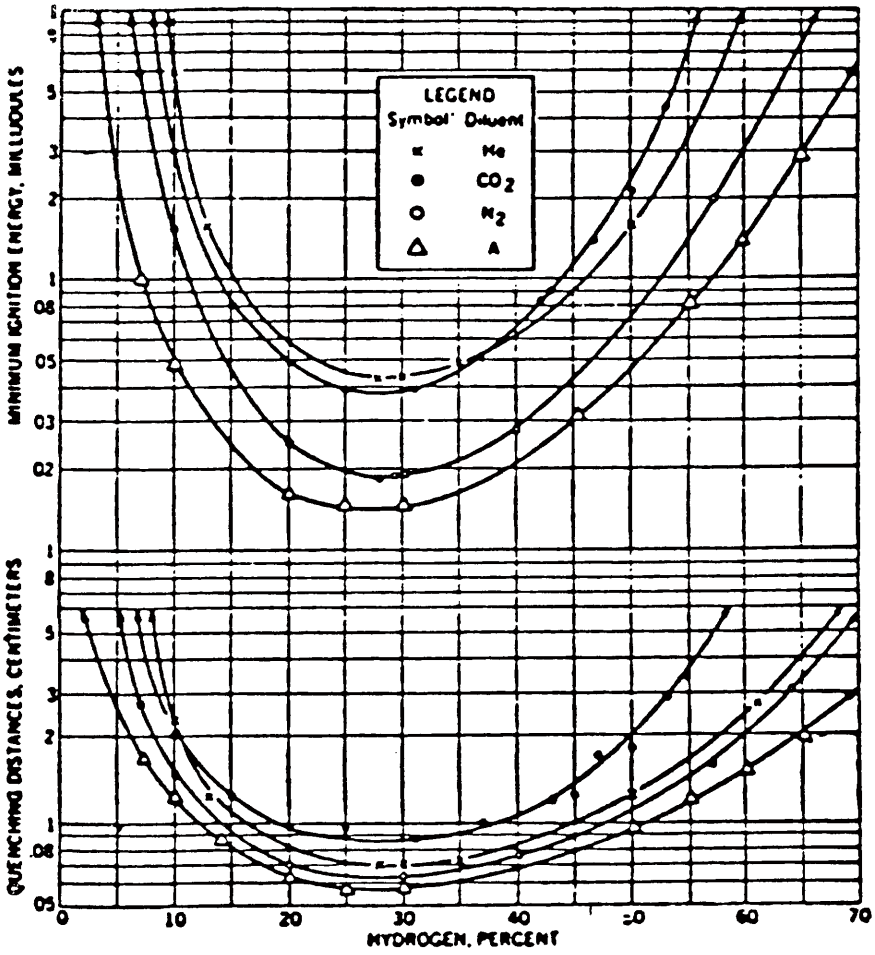

Fig. 6. Minimum Ignition Energies and Quenching Distances for Hydrogen-Oxygen-Inert Gas Mixtures at Atmosphereic Pressure. $O_2/(O_2$ + inert gas) = 0.21 (11; Copyright Academic Press).

Thermal and spark energy ignitability data are available for H_2-air mixtures and, to a lesser extent, for H_2-O_2 mixtures. The data for H_2-air mixtures appear to be conservative compared to the comparable data for H_2-O_2-He mixtures of equivalent concentrations.

Approval testing facilities are readily available for verifying that a particular piece of electrical equipment will not ignite and/or will contain an explosion of an H_2-air mixture. However, equipment approved for H_2-air service at 1 atm should be retested for H_2-O_2 mixtures and for service at deep diving atmospheric pressures.

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DISCUSSION FOLLOWING PRESENTATION BY ZALOSH

YOUNGBLOOD: How does that ignition spark energy relate to sparks generated by static electricity?

ZALOSH: Static sparks are relatively strong. It's well known from people who dealt with H_2 in the early days in the laboratory that in several instances it was ignited just by people removing synthetic garments. The

charge generated by shoe leather on a carpet certainly would be well above the million Joule I showed you. It's more usually interpreted from the standpoint of leakage currents in electrical equipment. If you look at the National Electrical Code there are certain maximal allowable leakages to ground for electrical equipment. One can provide some allowable leakage paths if one really wants to be conscientious about electrical apparatus.

YOUNGBLOOD: Some of us are interested in how insurance codes in this country may affect the introduction of H_2 diving into the offshore industry. Do you have any thoughts on that?

ZALOSH: Yes, first of all I represent the research interest not the underwriter interest of the insurance companies. I am familiar with industrial property insurance, since the organization I represent is a consortium with industrial property insurance. We deal with several companies so we don't have the liability and personal interest considerations. From the property standpoint we insure a few companies that are in the business of high pressure H_2-O_2 mixtures. For example we insure a few companies that are in the business of high pressure water electrolysis at several thousand psi and over the course of the years we have worked out acceptable conditions to run those experiments. They require special conditions in terms not only of the device itself, but also the building in which the device is located. The latter has to be acceptable from an insurance point of view. This can be done if one is willing to take pains in the construction of the laboratory or test structure built around the apparatus.

LUNDGREN: Are you talking about electrolysis for commercial purposes or for experimental purposes?

ZALOSH: The units I am familiar with were developed for the Navy and contracted for the Navy and are being used in naval applications and submarine applications. Our insurance interest has not been submarine; it has been the industrial buildings in which the devices were built and tested.

FLYNN: I heard the terminology hot spark and cold spark. Does that mean anything?

ZALOSH: I don't use that term myself, and I don't know of any thresholds above which one could go from a cold spark to a hot spark. The quantitative data make more sense to me than any such descriptive terms.

BRAUER: When one discussed this subject in the past, one tended to make a distinction between flammability limits and explosive limits. Is that worth perpetuating?

ZALOSH: That's a good question. The distinction is disappearing in combustion circles these days. The reason there was a distinction particularly in the case of H_2 was that in these flammability tests one could ignite H_2 without measuring much of an overpressure. And the reason for that was that they either ignited it near the top of the vessel so the flame

didn't propagate throughout the mixture, or the apparatus was so narrow that the flame was quenched on the way up. And then the third reason was that even in a 12 ft diameter sphere some classical experiments were run and they found that between 4% H_2 which is the lower limit of flammability and 8% H_2 which is the limit for downward propagation, one would get negligible pressures. People who wanted to emphasize that point then would say "4% is the flammability and 8% is the explosive limit." Since then there have been a number of experiments where people have ignited in different geometries and different size apparatus, particularly with regard to what happened at Three Mile Island. There was a H_2 gas mixture that ignited during the accident, and now it's clear that under the proper conditions one can generate overpressures of three or four times the initial pressure even in the 4-8% range. So when dealing with flammability you really have to be careful if you want to make that distinction as to when you'll get an explosion in the pressure generation and when you will just get a flame. In the absence of really knowing what you are doing, one should take the lower of the two limits to be safe.

ÖRNHAGEN: Can you expand on the idea that leaking H_2 can self-ignite?

ZALOSH: I just came from a meeting at the National Academy of Sciences on Tuesday and the mechanisms giving rise to that kind of event were identified as posing one of the key remaining unresolved questions. The information is that H_2 definitely does ignite at high pressures when there is a low gas mixture, even with relief valves.

ÖRNHAGEN: What kind of pressure range is that?

ZALOSH: I can answer two ways. From an anecdotal viewpoint, in terms of accident reports, one hears about pressures of at least a few hundred pounds per square inch. From the standpoint of the physics involved, there is just a speculative and hypothesized mechanism, shock wave heating. In shock wave heating all one has to do is be above the critical pressure of chokeflow. From that standpoint one needs only a few atmospheres. We are not sure that is the right mechanism. There are others and this event certainly has been observed at a few hundred atmospheres. One thought relevant to point of ignition on high pressure release: Sometimes this sort of ignition occurs in the form of a jet flame attached to the leak site. That's not too bad, since it's a well-defined flame. What is more worrisome is that when you have a large gasket let go then you don't necessarily get the ignition at the leak site. There is some accumulation of H_2 and a delayed ignition, and that's the worst situation. We have just heard a story a few days ago about a situation in the plant where these leaks occurred inside buildings, and the ignition didn't occur until the mixture had a chance to accumulate in the building. There are two kinds of explosions, an ordinary explosion with gradual pressure rise and a detonation where you have a flame front propagating along a shock tube. This is an important distinction because in one case you can vent the building, in the other case you can't. In the case of this large sudden release of energy of ignition, there is definitely detonation.

BRAUER: If any of you want to see an example of jet effect as you walk down the hallway, you will find that one of the doors is suspiciously large. It is suspiciously large precisely because 12 years ago we had a visiting scientist, who as a special courtesy exception, was allowed to bring an H_2 tank inside the laboratory. We had a jet blowout on that tank which put a flame 20 ft across the room, melted every fixture on the ceiling, blew out the door, and caused some other damage but left the building as a whole intact.

ÖRNHAGEN: Regarding flash back into tubes, am I to understand that it is impossible to have a flashback in a tube with a diameter below 10 mm?

ZALOSH: At atmospheric pressure, that is correct. That quenching distance decreases rapidly with pressure. It goes like pressure to the minus second or third power. So don't use that number under high pressures; it is much smaller.

FIFE: I would like to get your view concerning the use of ionization as a measure of radiation or ignition. You mentioned that as a possible way of measuring ignition or explosion but there is some work that shows that you can see ionization and have current flow and use that as a way of measuring the ionization before you get the gas. Can you speak about that as a way of measuring whether or not you got ignition?

ZALOSH: Yes, flame ionization detectors are very good for hydrocarbon gases but not for H_2.

FIFE: Why?

ZALOSH: There are not as many free radical ions in the H_2 as there are in the hydrocarbon. You are really relying on the presence of impurities. If you want to see H_2 in the air or int the H_2-O_2 mixtures, thermal conductivity detectors are much more reliable.

FIFE: Those aren't going to work until after you already have the fire.

ZALOSH: Just a minute, do you want to see H_2 gas detectors or...?

FIFE: No, I am not thinking about gas detectors. Heinz Schreiner and Door did a large series of studies on which H_2-O_2 mixtures are safe. Their technique was to use a high voltage battery in series with a spark gap and the resistor shunt across an shunt across an oscilloscope so that when you got ionization you had a flow of current across the sparkgap and the resistor. That was the basis on which all of the tables were constructed.

ZALOSH: I hate to be critical after the fact but that relies on the impurities of the experimental apparatus. At what thresholds you get ionization to cause that spark is not a fundamental property of the H_2 gas mixture but of how dirty your apparatus is.

FIFE: But every one of the techniques you are using is an after the fact measure. What is important is whether or not it occurred, isn't it?

ZALOSH: Yes, it depends on the response, in the case of the pressure you can have a respondence from micro...

MILLER: The most dangerous thing in the laboratory is a leak in your chamber or in your pipes valves not being mended properly. Are there detectors that can help in that situation?

ZALOSH: Yes, those detectors are being used commercially.

GIRY: Thank you, Dr. Zalosh. After that, we shall have no more explosions in our labs.

SYSTEM DESIGN AND SAFETY CONSIDERATIONS FOR "HYDRA" EXPERIMENTS

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COMEX
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The experimental saturation dive Hydra V could only be performed after an extensive study of risks relevant to the handling of hydrogen and of its specific use in the confined atmosphere of facilities initially designed for containing inert gases.

This study involved the following:

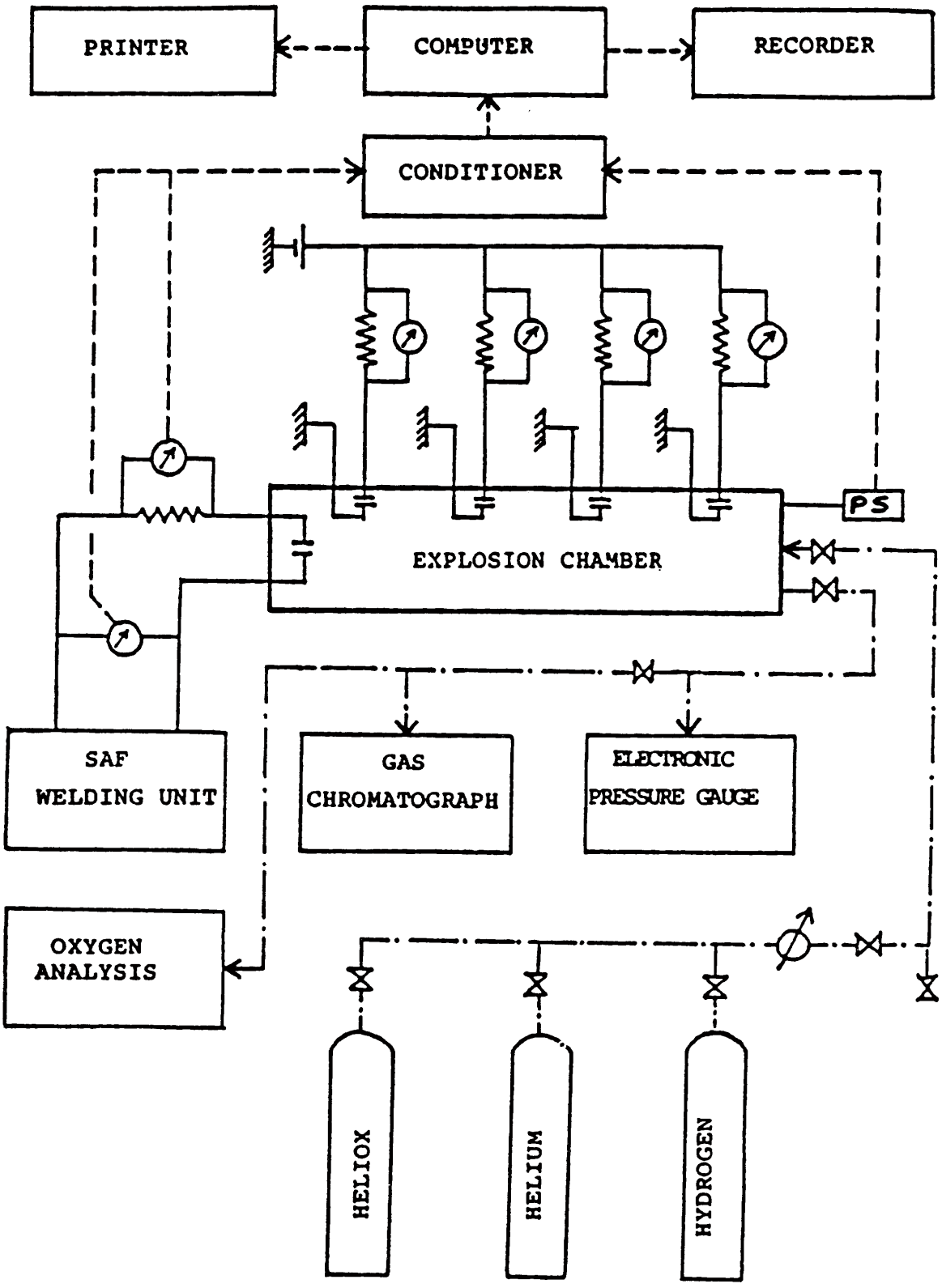
- Experimental research on the explosivity limits under pressure of ternary mixtures H_2-He-O_2;
- Search for a H_2 of breathing quality;
- Testing the compatibility of H_2 with different materials constituting COMEX Hyperbaric Center heavy equipment.
- Development of a regeneration system for hydrogenated gases with automatic readjustment of the O_2 injection rate;
- Ensuring the conformity of all gas circuits;
- Providing ample safeguards to guard against any accidental H_2 leak in the hyperbaric center.

EXPERIMENTAL RESEARCH ON THE EXPLOSIVE LIMITS UNDER PRESSURE OF TERNARY MIXTURES: H_2-He-O_2

Experimental Installation

The device presented in Fig. 1 includes:

- A cylindrical explosion chamber that can resist pressures up to 1000 bar. This chamber is equipped with electrodes to ignite and to measure the velocity of flame propagation;
- A welding unit SAF supplying current of high amperage (up to 320 A);
- A chromatograph for analysis of gas mixtures;
- An O_2 analyzer;
- A pressure transducer
- A data acquisition system that enables recording of 7 parameters every 2 ms, during 3 s.



MEASUREMENT OF EXPLODABILITY LIMITS

Fig. 1 Lay-Out of the Installation

Experimental Protocol

- The tests have been carried out at the following pressures: 15, 30, 45, 60, and 75 bar relative.
- The minimum O_2 concentration, below which H_2 combustion no longer occurs in the H_2-He-O_2 mixture, for H_2 concentration of: 20, 30, 40, 50, and 60% by volume was determined at each pressure.
- The ternary mixture is prepared directly in the explosion chamber, from pure H_2, pure He, and heliox.
- Subsequently, it is analyzed by gas chromatography before and after ignition by means of 13, 16 welding electrodes, connected to a SAF 320 welding unit.
- The combustion energy is very high (50 to 300 J) for an electric arc of 30 to 300 msec duration.
- For each H_2 concentration and at each pressure level, various tests were carried out, varying the O_2 concentrations above and below the estimated explosive limit.

Measurement of the O_2 concentration before and after ignition allows one to trace the graph of the ratio of consumed O_2/initial O_2, as a function of the initial O_2 concentration. In Fig. 2, the point of inflexion of the curve corresponds to the O_2 limit below which there is no more combustion or flame propagation.

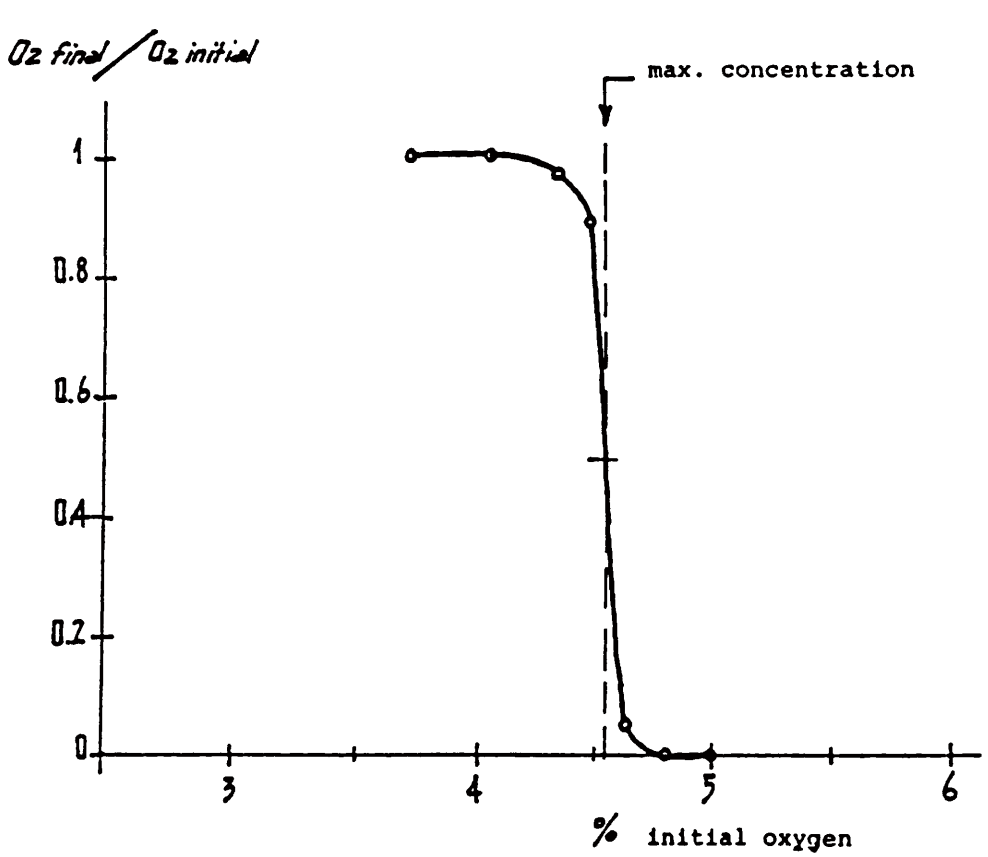


Fig. 2. Explodability of Ternary Mixtures: H_2-He-O_2

Test Results

One-hundred and forty-two tests have been carried out. Table 1 shows the distribution of tests as a function of pressure and H_2 concentration. When the pressure of the ternary mixture H_2-He-O_2 is increased, the maximum O_2 concentration is distinctly reduced (Fig. 3). On an average, we note a relative decrease by 15 to 20% of the maximum O_2 concentration, for a pressure increase of 60 bar. When the quantity of neutral diluting gas is increased--in this case, helium--the maximum O_2 concentration is also distinctly reduced (Fig. 4). For a total pressure between 15 and 75 bar, the maximum O_2 concentration tends to be asymptotic at approximately 4.4% (Figs. 3 and 4).

TABLE 1

The Distribution of Tests as a Function of Pressure and Hydrogen Concentration

Pressure (bar)	Total Number of tests	Hydrogen 20%	30%	40%	50%	60%
15	50	13	12	8	8	9
30	33	6	7	9	7	4
45	22	6	5	3	4	4
60	22	6	4	3	4	5
75	15	4	3	3	3	2
	142	35	31	26	26	24

The triangular diagram on Fig. 5, based on the results obtained by SEP and by us, shows that in a ternary mixture H_2-He-O_2, risks of explosion arise only beyond 8% H_2 for O_2 concentrations lower than 10%. Even though the O_2 concentration required for flame propagation is very definitely reduced upon increase of the He concentration and of the total pressure, this leaves sufficient scope to envisage the performance of Hydra experients, as we can quantify the risks and, therefore, control them.

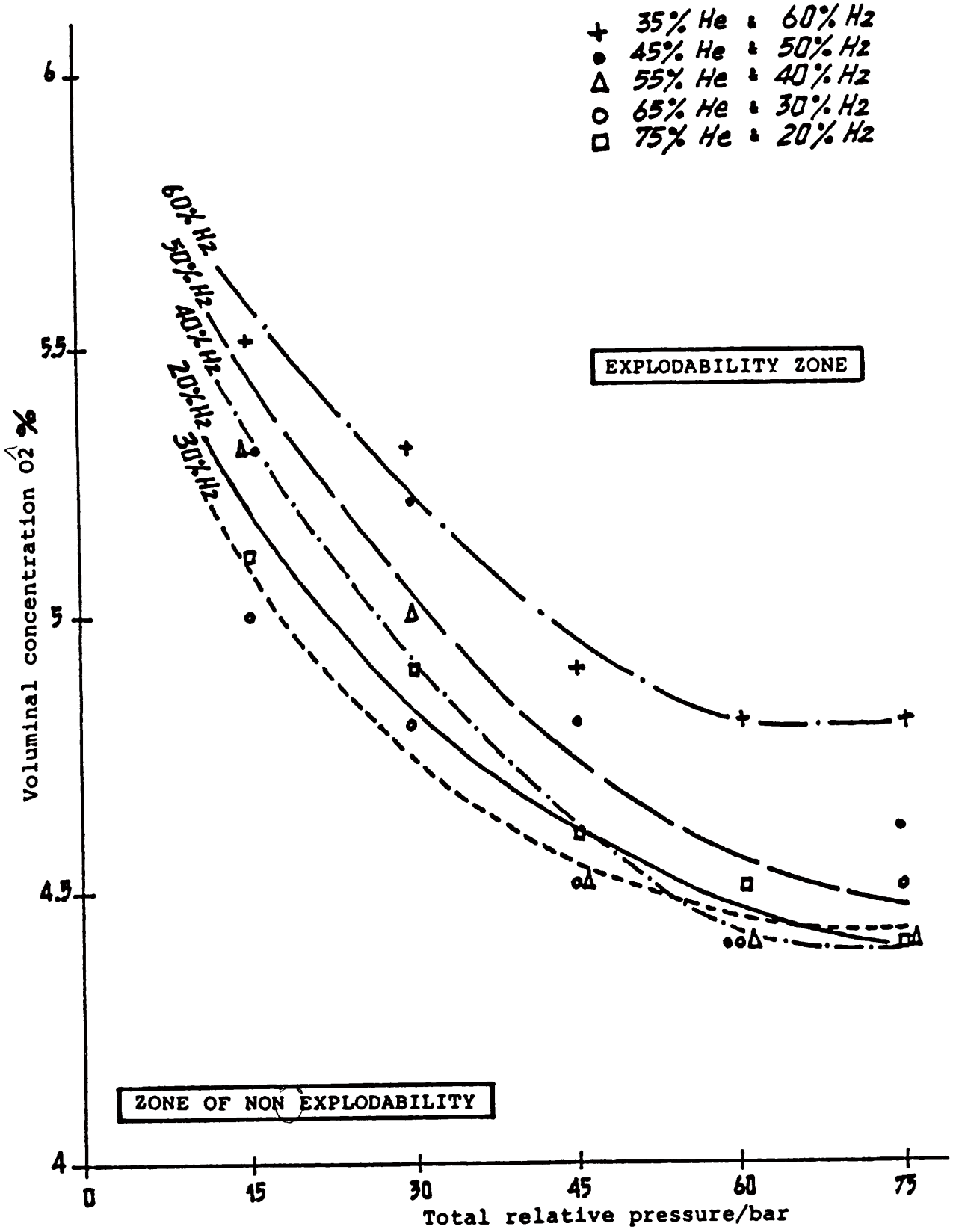


Fig. 3. Explodability of H_2-He-O_2 Mixtures

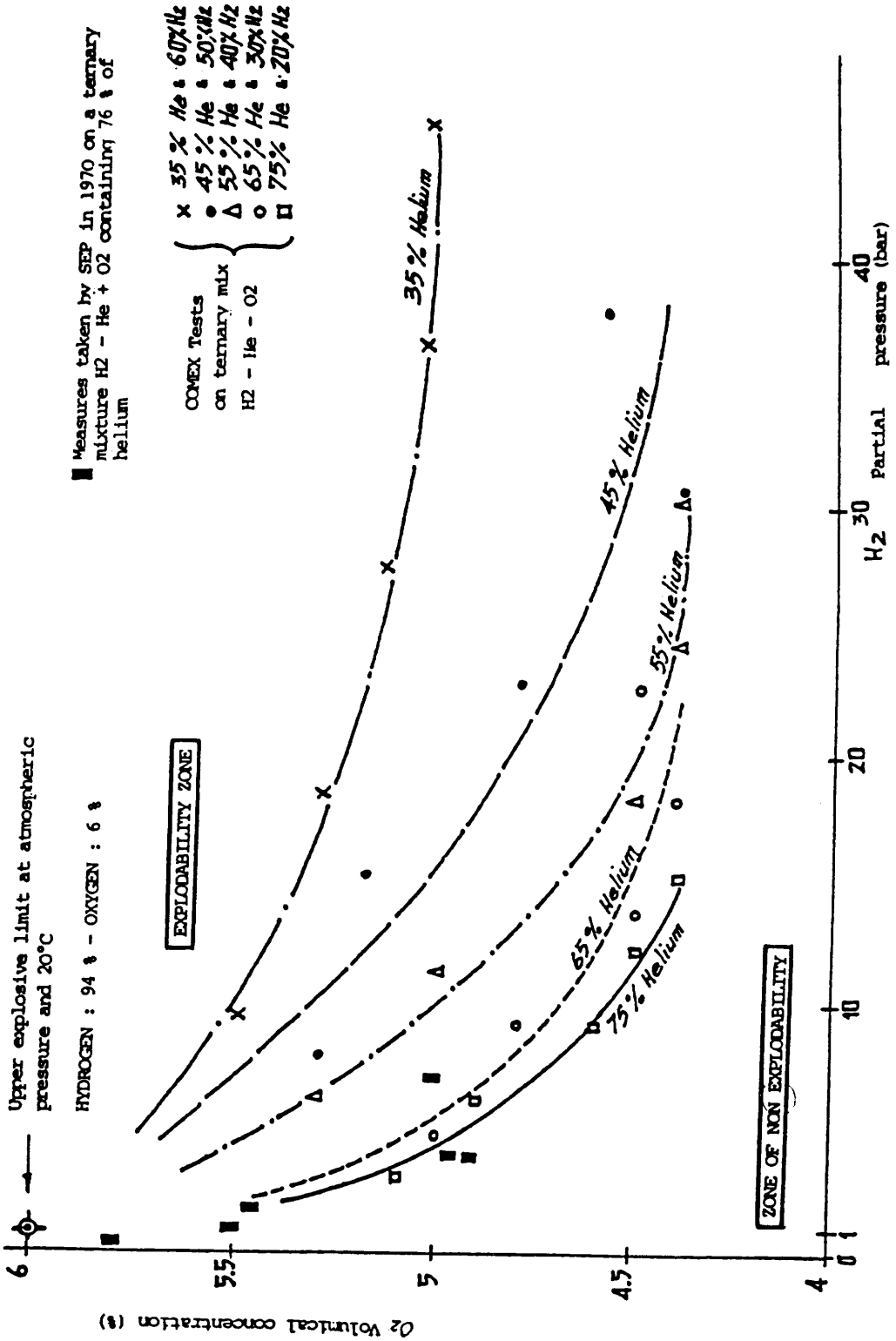


Fig. 4. Explodability of Mixtures H_2-He-O_2

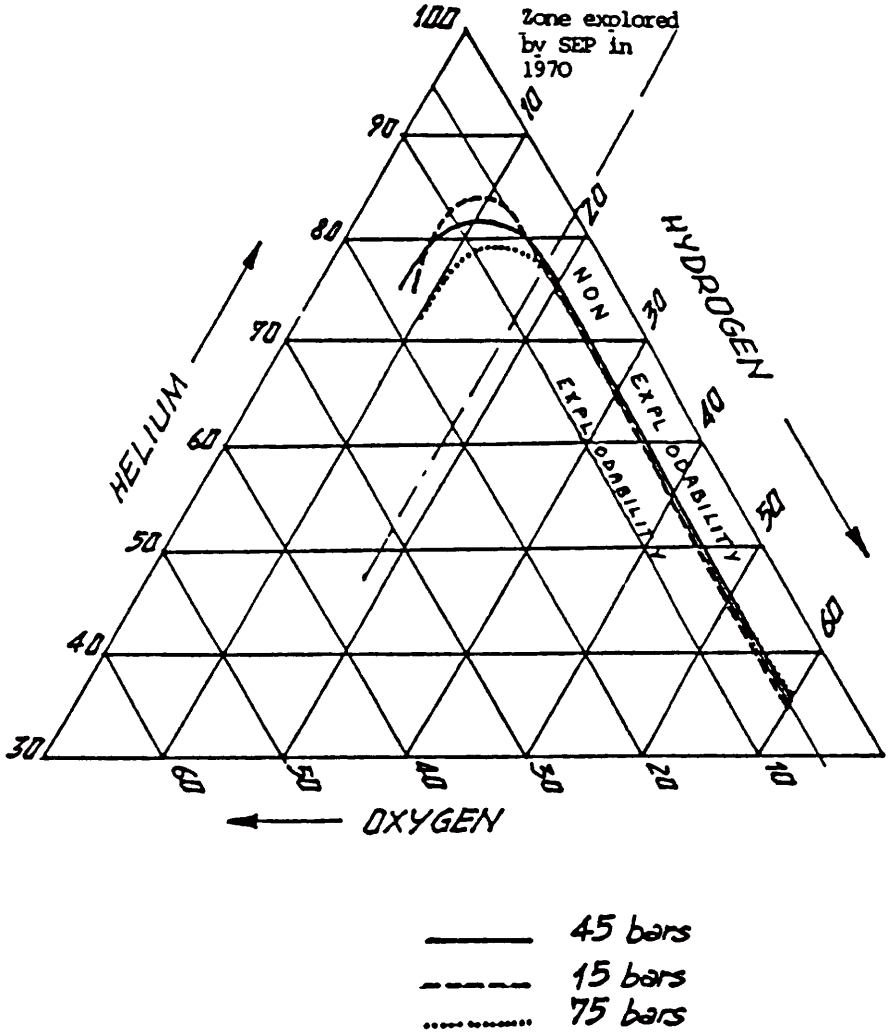


Fig. 5. Explosive Limits of Pressurized Mixtures of H_2-He-O_2

HYDROGEN QUALITY

As for all other gases used during diving, H_2 must meet certain quality criteria to be acceptable as a breathing gas.

Traces of nitrogen, argon, water, hydrocarbon, carbon dioxide, carbon monoxide, and so on, within reasonable limits, do not pose serious risks for current utilization depths. This is different in the case of certain pollutants that, even in infinitesimal concentrations, at great depths may present high risks of serious intoxication. In H_2, such contaminants are certain hydrides, in particular arsine and phosphine, and, to a lesser degree, hydrogen cyanide. The possible presence of these components in H_2 is mainly related to certain manufacturing processes or, in some cases, with purifying methods using catalysts.

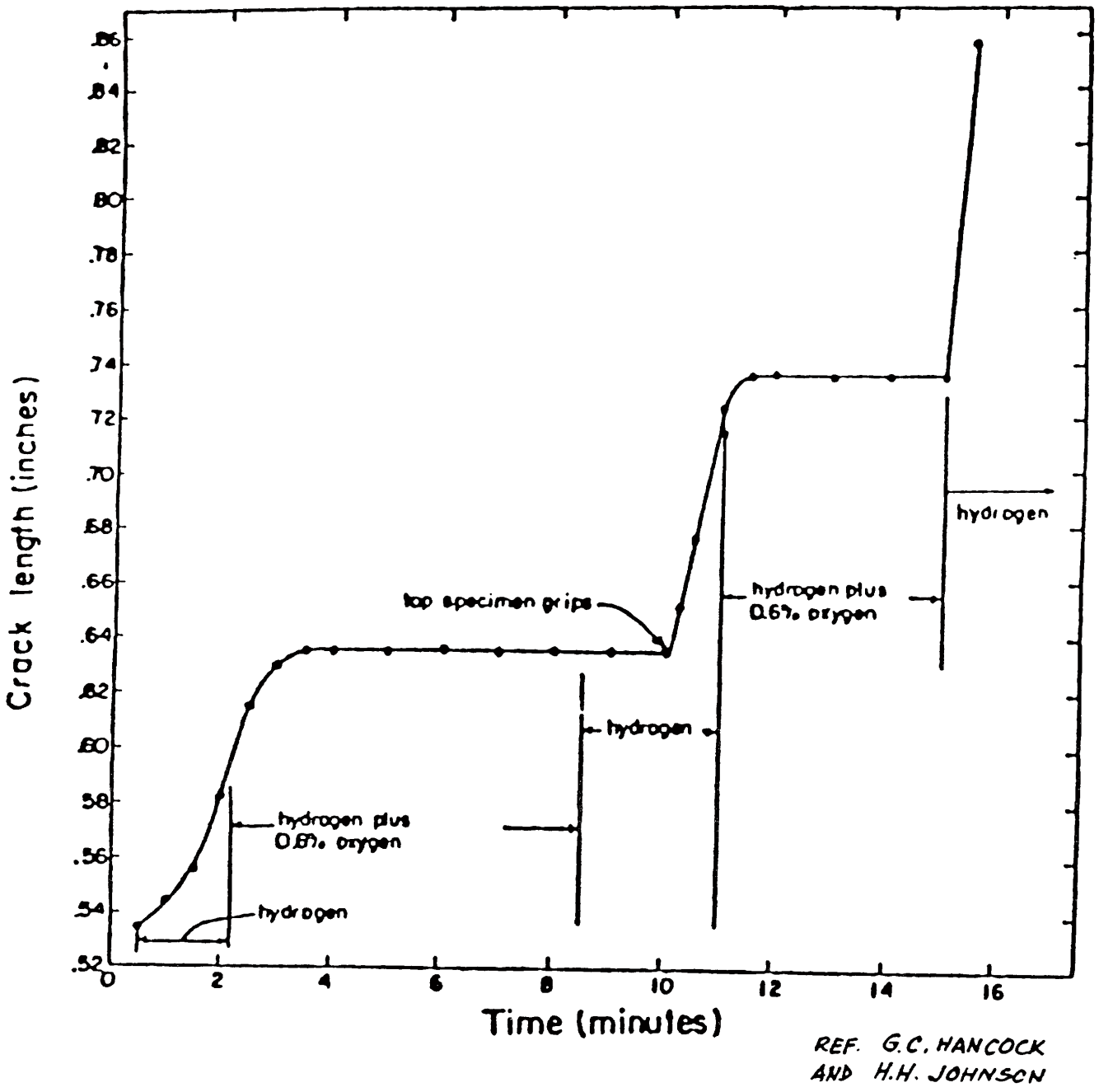


Fig. 6. Subcritical Crack Growth in Hydrogen and an Hydrogen-Oxygen Mixture

Actually, H_2 of catalytic origin may present the highest risk of presence of toxic hydrides. In this respect, electrolytic H_2 would seem to be more acceptable, but in either case only final purification through cryogenic adsorption will fully guarantee its quality as a breathing medium.

The stipulated threshold limit values (TLV) of hydrides are:

- *arsine ≥ 0.05 ppm*
- *phosphine ≥ 0.3 ppm*
- *hydrogen cyanide ^ 10.0 ppm*

For Hydra V the contaminant limit for H_2 is at 0.0015 ppm (expressed arsine + phosphine). At 46 ATA, the concentration in the ternary mixture would give a maximum partial pressure of 0.037 microbar, considerably lower than the TLV.

The H_2 used for HYDRA V presented the following characteristics: (Table 2).

TABLE 2

Hydra V Experiment
Hydrogen Purity

- Origin:	Catalytic
- Special treatment:	Cryogenic purification
- Purity:	> 99.995%
- Impurities:	Hydrocarbon < 1.5 ppm Arsine and Phosphine: < 0.0015 ppm

Risks of Steel Fatigue Caused by Hydrogen

Steel fatigue caused by gaseous H_2 is a phenomenon that has been on known for approximately 20 yrs. It has been the subject of many studies that showed the specific influence of the presence of certain contaminants in H_2 (O_2, H_2O, CO, H_2S, and so on).

- O_2, even in small concentrations, has a considerable inhibiting action, explained by the high iron/oxygen affinity (Fig. 6); traces of O_2 would be adsorbed on the steel surface, thus limiting penetration of H_2.

- Water vapor contributes to fatigue, but, in association with O_2, it increases the inhibiting action of the latter.

In the case of a H_2-He mixture without O_2, the steel fatigue would be related to the H_2 partial pressure. Fatigue becomes noticeable only when the H_2 pressure is above 100 bar and the total pressure above 200 bar (Fig. 7) Therefore, in the saturation chambers, the risks of fatigue are practically nil as, for evident physiological reasons, there will always be both O_2 and water vapor. Moreover, in future deep diving, the H_2 partial

pressure will hardly ever be greater than 30 bar, reducing the risks even further.

Within the scope of experiments with animals at very great depths (1500-2000 m), the H_2 partial pressure could approach 100 bar and involve a slightly higher risk of fatigue but, there again, the O_2 and water vapor can be counted upon to have a considerable inhibiting action.

GAS REGENERATION SYSTEM

This system was designed for regeneration of hydrogenated gases, providing a very high degree of safety.

The system consisted of:

- blowers;
- purifying filters;
- heat exchangers;

and was housed in one sole compact container (Fig. 8).

This choice allowed all exterior connections between filters to be suppressed and, consequently, the risks of leakage to be reduced. The blower providing gas circulation is connected to an external electric motor by means of a magnetic coupling. The variable speed engine allows one to regulate the gas flow between 30 and 300 m^3/h and thus to optimize the system's efficiency at each pressure level.

Thermohygrometric control is automatic, as a function of temperature and relative humidity measurements effected inside the chamber via special probes.

The normal O_2 consumption by the divers is continuously compensated by means of an automatic O_2 addition system. The latter system has been designed to add pure O_2 to the H_2 without ever exceeding the explosive limits. The addition system is provided with several safety levels that automatically stop O_2 addition in the following situations:

- Abnormal increase of the O_2 concentration in the injection zone;

- Temperature increase in the injection zone;

- Breakdown of the blower.

During Hydra V, the physiological comfort parameters (humidity, temperature, partial O_2 pressure) were maintained at fixed values with almost perfect accuracy (Fig. 9).

SAFETY PROBLEMS

Within the scope of Hydra V, we demonstrated that H_2 can be adequately controlled by observing some simple rules, the most essential of which is never to exceed the explosive limits at any point of the installation.

The start-up procedures for the chambers and their annex installations were established taking into account the above rule in every possible situation. All gas circuits were flushed with inert gas prior to pressurization with H_2. Ternary mixtures H_2-He-O_2 were prepared from pure H_2 and binary H_2-O_2 mixes containing less than 4% O_2. H_2 was introduced into the chambers only beyond 200 m as, at this depth, the O_2 concentration was less than 2%.

In the test center, we installed additional facilities to enable us to cope with any accidental H_2 leak. The H_2 pressurized chambers were equipped with a hood linked to the exterior by means of a powerful extractor (Fig. 10). Eight H_2 detectors were placed in areas where leakage was most likely to occur. These detectors were individually hooked up to one of the electronic modules with two pre-set levels for alarms at 0.15% and 0.5% H_2. The first level would automatically trigger the first extraction speed providing a flow rate of 20,000 m^3/h. The second level doubled the extraction speed which at 40,000 m^3/h would create a slight negative pressure in the center, draining the entire H_2 leak into the extractor.

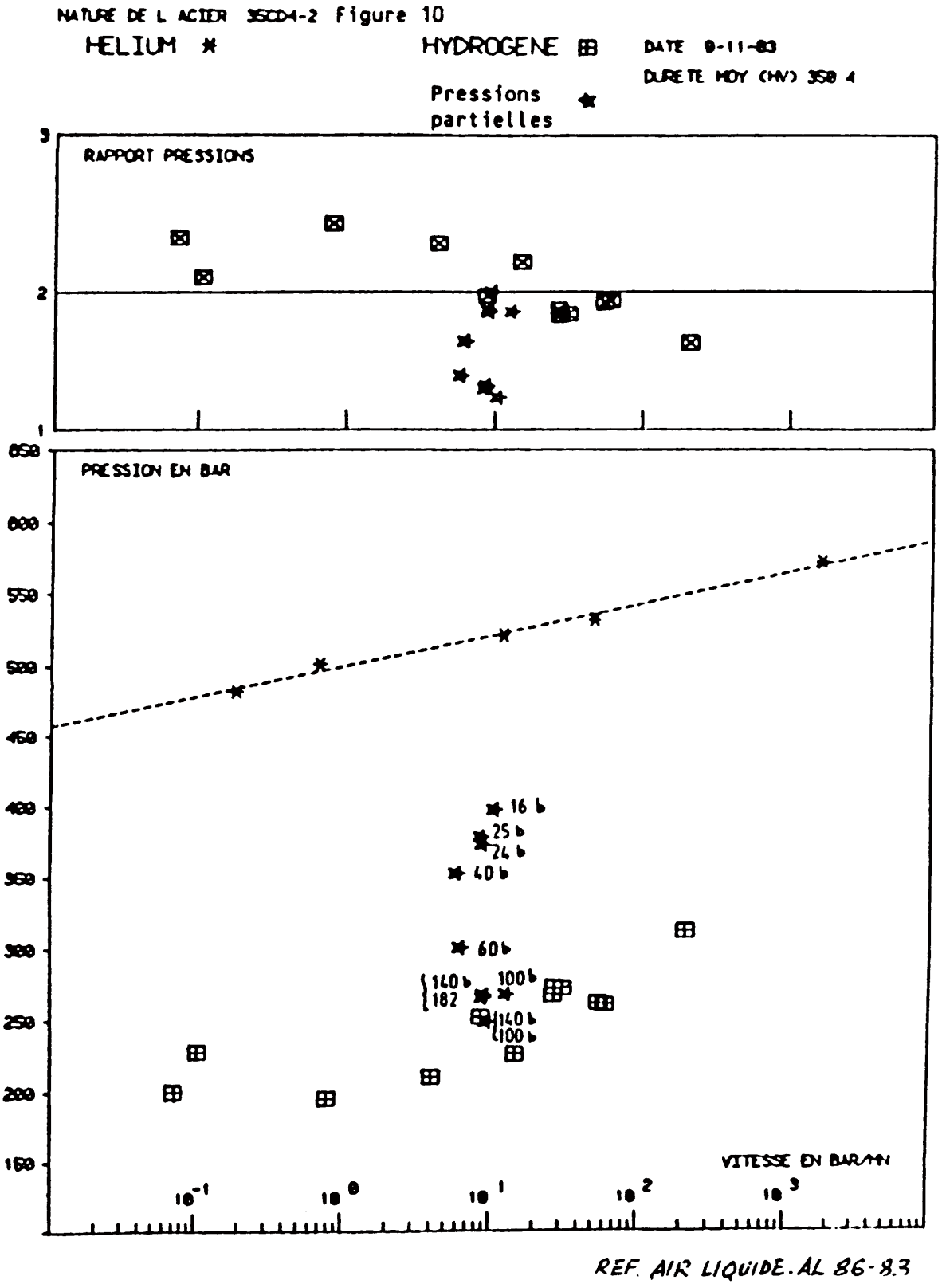


Fig. 7. Dynamic Rupture Test--CRCD/SEPG

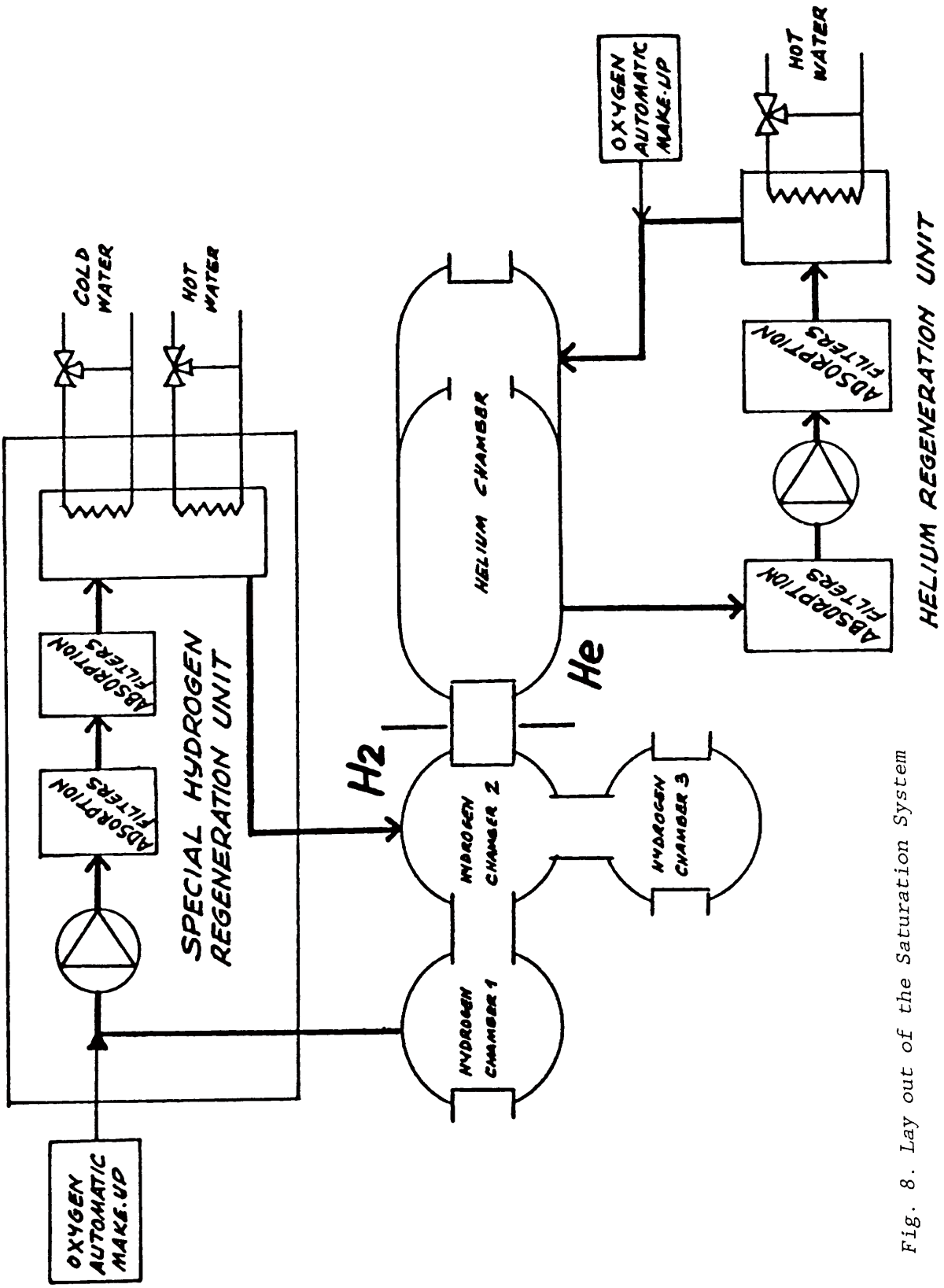


Fig. 8. Lay out of the Saturation System

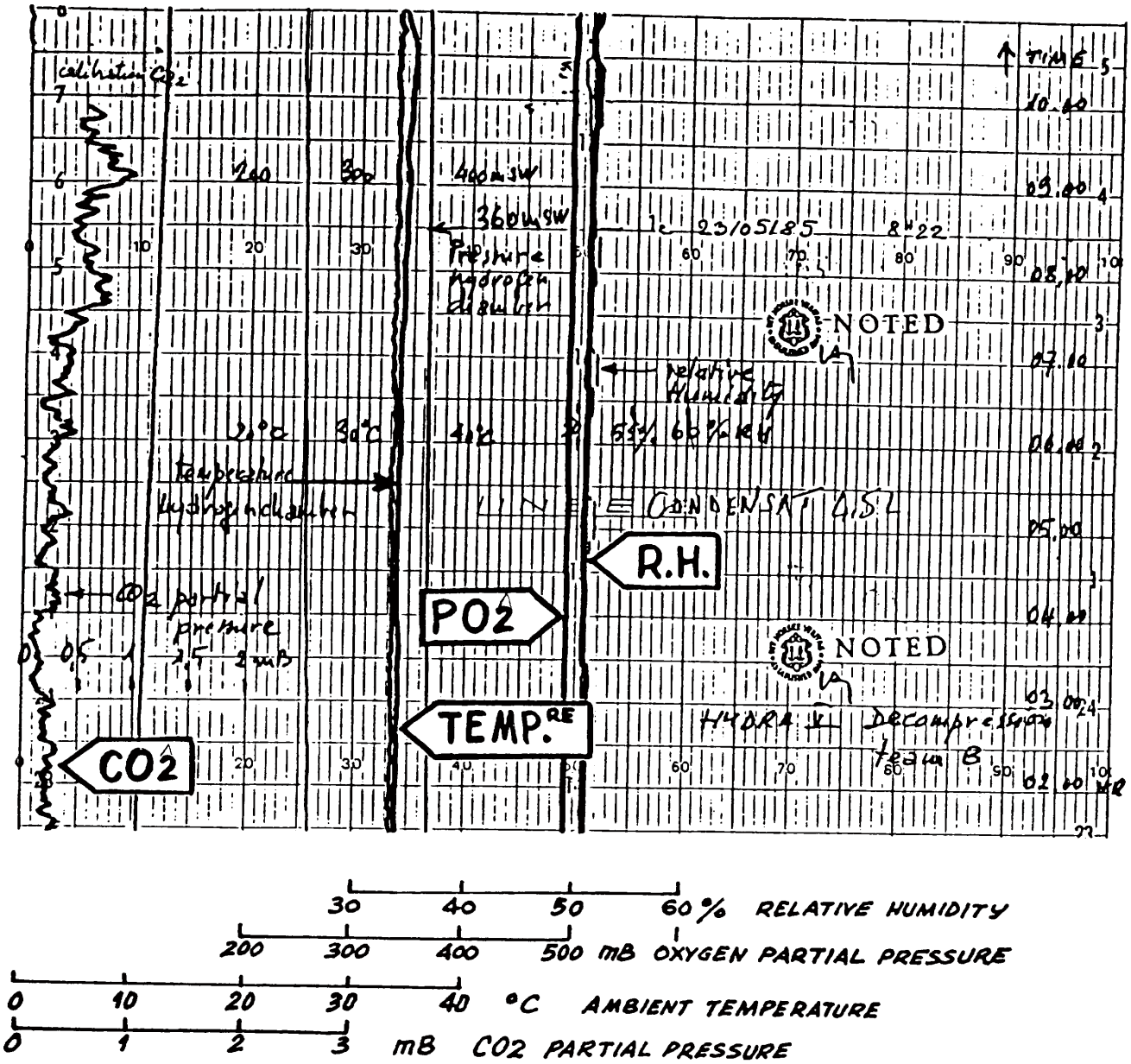


Fig. 9. Ambient Hydrogen Chamber Parameters

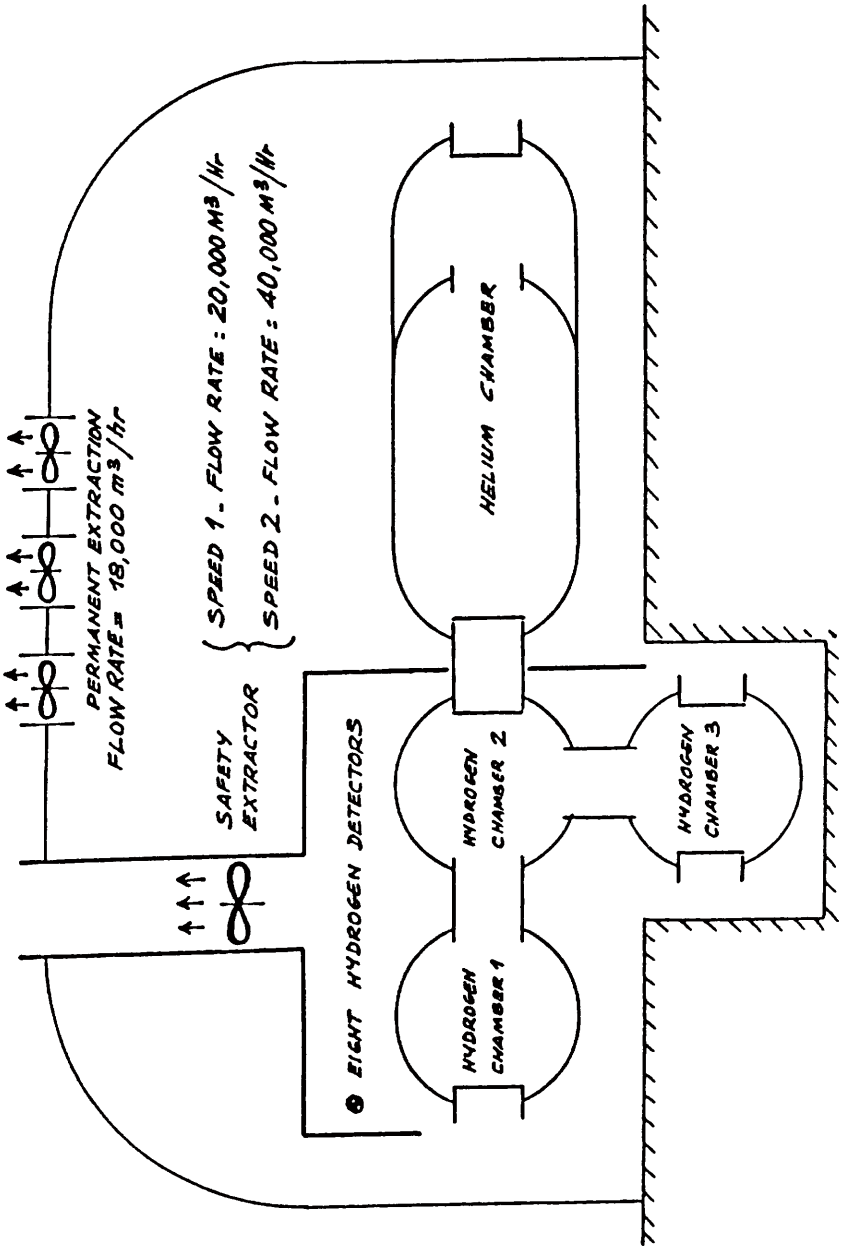


Fig. 10. Lay-Out of the Hydrogen Extraction System

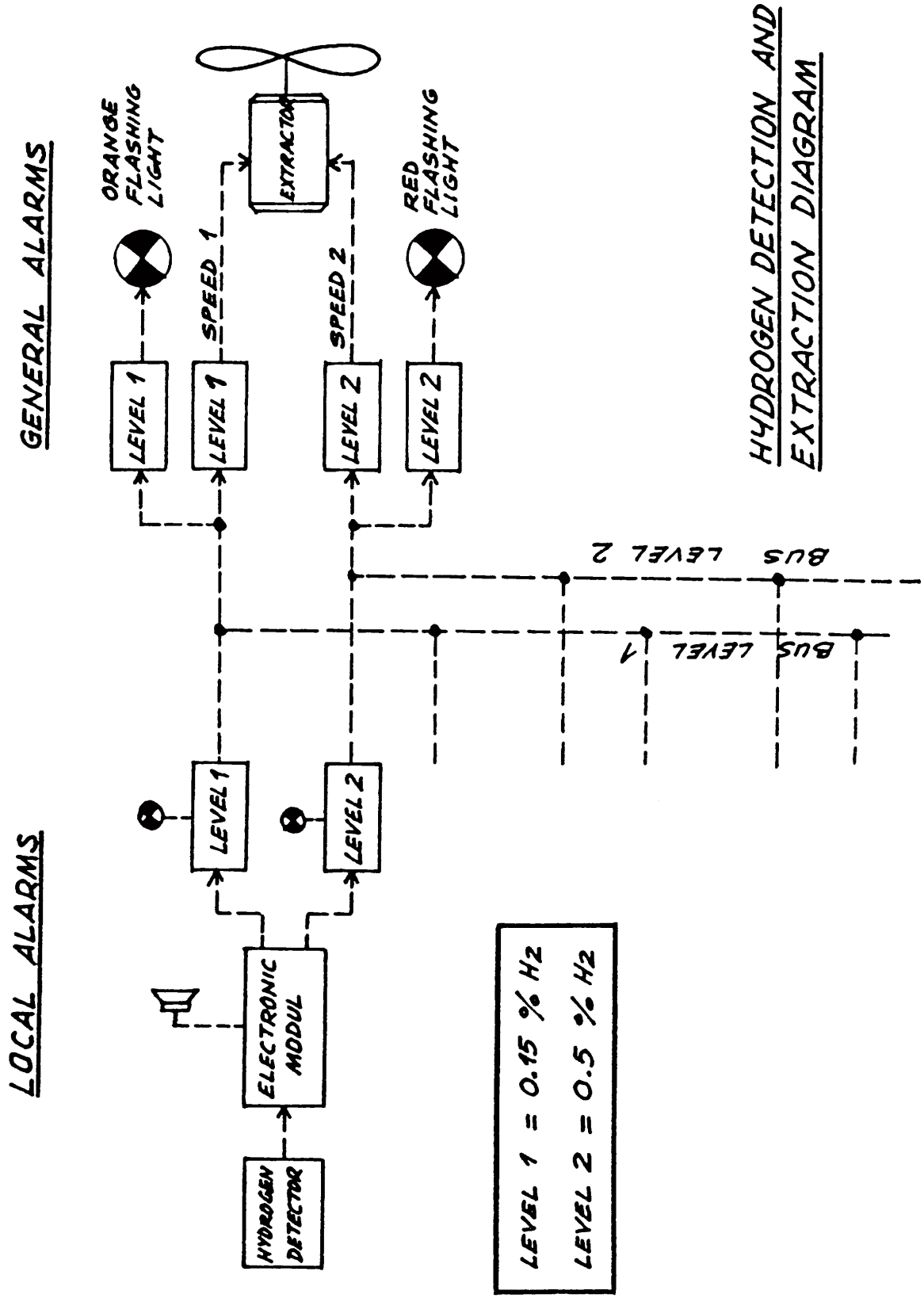


Fig. 11. Hydrogen Detection and Extraction Diagram

DISCUSSION FOLLOWING PRESENTATION BY GORTAN AND DELAUZE

BRAUER: Shall we begin with the H_2 detectors? What kind of detectors are we talking about?

DELAUZE: They are catalytic combustion detectors with two big speakers.

IMBERT: The kind that are used in submarines.

EDEL: Do I understand from the presentation that 4% would be a safe limit of O_2 and H_2 under any conditions?

DELAUZE: Yes, 4% under any conditions, any pressure from 1 to 75 bar, and 20 to 60% of H_2.

LUNDGREN: Did you use the extractor continuously during the experiment or start it up only in case of leakage?

DELAUZE: It was to be used only in case of leakage.

ZALOSH: I notice that your minimum O_2 concentration for addition decreased as pressure increased, about 5%. That seems the opposite trend to some of the data I presented an hour ago. They showed in some cases an increase with pressure, and in some cases a decrease.

DELAUZE: The experiments performed at COMEX did show a decrease in the critical O_2 concentration with pressure.

ZALOSH: I don't question your results. I pointed out in the presentation that the previous results for the minimum are a minor extrapolation but still an extrapolation near the lower limit for low H_2 concentration. In your experiments I know you were mostly concerned with the upper regions but you also run some very low H_2 concentrations.

DELAUZE: Yes, we did.

ZALOSH: Then you have less of an extrapolation than the previous runs.

BRAUER: Would it be fair to ask Henri to tell us what your experience actually was with the total assembly? Did you have H_2 leaks? How were they controlled? How satisfactorily did that system, as you put it on the board, turn out in your experience?

DELAUZE: We never had any detectable H_2 leaks.

BRAUER: A lock which was used spewed out some H_2, activated the whole system, and made a very dramatic performance. But that is the only case I saw.

LUNDGREN: Was that routine when you opened the locks?

IMBERT: Yes, it was.

DELAUZE: Every time we opened the lock, we activated the alarms.

ORNHAGEN: Did you wash your locks with N_2 before opening?

GARDETTE: Yes.

ZALOSH: In concluding an experiment, did you purge the mixture through the ventilation system that you use for emergency?

DELAUZE: No, since we had an exhaust pipe 6-8 m above ground, we could vent directly.

FLYNN: What about the injection of O_2 into the life support system? Was this a straight injection, or was there some mixing device inside?

DELAUZE: The apparatus was a straight injection, one with a safety device that never allowed direct communication between the O_2 supply and the chamber.

SYSTEMS DESIGN SUGGESTIONS FOR LABORATORY EXPERIMENTS WITH HYDROGEN

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The physical properties of hydrogen are described in *Gas Encyclopaedia* (1) and in *Hydrogen and Commodity Specifications for Hydrogen* (2). In general terms, the biggest problem with H_2 is its high tendency to react with O_2. However, any breathing mixture containing H_2 must be nonexplosive. This means an H_2 concentration lower than 5% or an O_2 concentration lower than 3% (3).

MIXTURES WITH LOW HYDROGEN AND HIGH OXYGEN CONTENT

If air, with a low H_2 concentration, passes over a platinum catalyst, the H_2 reacts with some of the O_2 of the air under heat and water production. This principle has been used to provide heated breathing gas to divers. The H_2 concentration used is normally between 0.5 and 1.0% and such a gas mixture will be a hazard only while being prepared. Leaks to ambient air or handling of such a gas mixture will never cause any fire or explosive hazards.

MIXTURES WITH HIGH HYDROGEN AND LOW OXYGEN CONTENT

The properties of H_2 that make it valuable in diving are its low density and low cost. An H_2 content as high as possible is desirable, but because of the narcotic properties of H_2, a partial pressure higher than approximately 2.5 MPa is likely to cause too much narcosis which has to be avoided. Therefore, a breathing mixture for H_2 experiments typically contains 40-98% H_2, depending on the total pressure. Such a gas mixture, although nonexplosive due to a low O_2 content, is a potential fire hazard if it leaks into the environment. A laboratory intended for work with H_2 therefore needs some special features.

- All personnel should be trained to work as if H_2 were actually present in the ambient air.
- The person responsible for the H_2 activities should have full authority and control over other activities in the building.
- The laboratory should be designed to minimize the risk of ignition of leaking or dumped H_2.
- The equipment should be designed in such a way as to minimize the risk of H_2 leaks.
- The laboratory should contain equipment for the detection of H_2 leaks and equipment for fire extinguishing.

- Handling of H_2 and mixing of hydrox has to be performed in such a way as to minimize the risk for ignition.

Training of Personnel

Because of the difficulties in detecting H_2 and the ease with which an H_2 mixture is ignited, the safest way is to always act as though H_2 were present in the ambient air when handling H_2 equipment. Some important steps toward this are:

- Smoking and the use of open fire should never be allowed in the laboratory. This includes also the time between experiments with H_2.

- The risk of static electricity discharge should be mimimized by the use of grounding posts where personnel can discharge static electricity to prevent sparks from hands to valves, locks, and other potential leak sources.

- Avoid the use of nylon or other synthetics in carpets, coveralls, and clothes. Use conductive floor material and conductive shoes.

- Avoid low relative humidity in air

- Always use low sparking tools of copper-beryllium when working on equipment that contains H_2 or is close to H_2-containing equipment

- Always switch off electrical equipment before a power line connector is pulled apart or inserted.

Control Over Activities

The ease with which H_2 spreads makes it important to have control over other activities in any building in which H_2 is handled. If the building is large, instructions regarding how to behave in case of a leak should be posted. An alert should reach everyone in the danger zone in case of a leak.

Laboratory Design

Designing a laboratory where H_2 will never escape to the ambient air is virtually impossible. Therefore, procedures and equipment have to be such that the risk of ignition of H_2 escaping from the system is minimized. An annotated bibliography of U.S. regulation, standards, and guidelines related to the use of H_2 was presented by Hord in 1978 (5).

Procedures

A couple of measures to minimize the risk of ignition of gas by human action are: 1) do not smoke or use open fire; 2) avoid static electricity sparks; 3) use sparkless tools; 4) be careful with electricity, and so on.

Ventilation

Good ventilation in areas where H_2 is handled will reduce the risk for explosion by lowering the H_2 concentration in the ambient atmosphere. The

ventilation should be adjusted to the size of the possible leak. Preferably in low stand-by ventilation and one or two forced ventilation levels should be used. The change of ventilation level should be automatically controlled by H_2 sensors in critical positions. It is important that the ventilation is arranged in such a way that air velocity is high to optimize the "dilution" of the leaking H_2.

Detectors

Detectors for H_2 are a must in indoor H_2 handling. At least one detector should be placed at the highest point in each room. Other detectors could be located above potential sources of H_2, like locks, valves, and penetrators. The alarm set-point could be varied but 0.5 to 1% in air is a practical level to avoid too many false alarms during routine operations. It is recommended that detectors are displayed in such a way that it is also easy to see where a short lasting leak has been. An audible or visual signal, loud or light enough for everyone involved to hear or see, is a necessity for bigger chamber systems and long duration operations.

Electrical Equipment

Electrical equipment in close proximity to the H_2-containing system and equipment like lights or fans that can not be switched off in case of a leak has to be of a type that is approved for use in explosive environments. This is difficult to achieve when working in older laboratories designed for work with nonexplosive gases. However, an explosion-safe emergency system for light, ventilation, chamber support, and so on, is recommended so that main power can be cut in case of a big leak.

Fire-fighting Equipment

Fire in the building is a greater threat to H_2 operation than to other hyperbaric operations because of the consequences if equipment is damaged by the fire. A high standard of fire-fighting equipment and training of personnel is therefore required. Means for cooling down any H_2-containing equipment with water are obligatory.

It is worth mentioning here that burning H_2 from a leak should not be extinguished by any means other than cutting off the H_2 flow because of the great risk of creating an explosive mixture that can be ignited. An explosion usually causes more damage than a fire. Therefore, in case of a H_2 fire, one should cool down surrounding equipment and shut off the H_2 supply.

Equipment Design

Hydrogen is compatible with most gasket and O-ring materials. SS-Steel is recommended. High tension steels can be subject to H_2 embrittlement which must be avoided. However, the risk is lowered if O_2 is present in concentrations above 0.5% as is the case in most systems for diving. (6). Cylinders for storage of H_2 at higher pressure than 15 MPa should be of special quality. Particular attention has to be drawn to the fact that H_2, because of its high diffusivity, can pass through cast metal that does not allow other gases under pressure to pass.

Leak and Fire Handling

Burning H_2 from leaks can be extinguished if the piping involved is pressurized by an inert gas such as He and the H_2 source is shut off.

The valve stem of pressure bottles and other valves is a common place for a H_2 fire. Fire resistant gloves should therefore be available at critical places to allow closure of valves which have a small fire around the valve stem.

For fires in closed areas standard Halon systems should be sufficient.

Building materials should preferably be fire resistant and polycarbonate plastic should be used in windows instead of glass, to prevent splinter accidents.

Preferably a building should have a weak point, acting as a "rupture disk", to prevent total damage of the building in case of explosion. Such a "rupture disk" could be a door, wall, or roof designed to open at a certain overpressure in the building.

Infrared (IR) detectors aiming at the critical points of the gas system may help to get an early indication of the almost invisible H_2 flame at the leak. Only pollution of the flame from surrounding material such as paint, plastic valve handles, brass parts, and so on, give a clearly visible flame. IR detectors can also be used for supervision of outdoor and remote gas supplies.

Handling of Hydrogen and Hydrox

Gas supply

Gas bottles should preferably be stored outdoors. Small units, each protected by a flow fuse, are recommended. Bottles of inert gas (He and N_2) or a vacuum system are recommended to purge all tubing of air or O_2 before it is pressurized with H_2.

Gas mixing

The preparation of an O_2-containing H_2 mixture is one of the difficulties encountered when doing H_2 experiments. To increase safety, only very small volumes at any one time can be allowed within the explosion limits. This is achieved by good and rapid mixing. In our laboratory a mixer for hydrox utilizes two perpendicular high velocity flows.

Turbulence will give a good mixture within a short distance from the mixing point. An automatic shut-off of O_2, when the H_2 flow is below a set value or the FO_2 in the mixture is too high, is required to prevent accidental mixing of hydrox with too much O_2. Capillary inlets for H_2 and O_2 give the necessary gas velocity and also act as flash back arrestors in case of ignition. Good mechanical strength and a heat sink is achieved by making the mixer in a block of stainless steel (Fig. 1)(7).

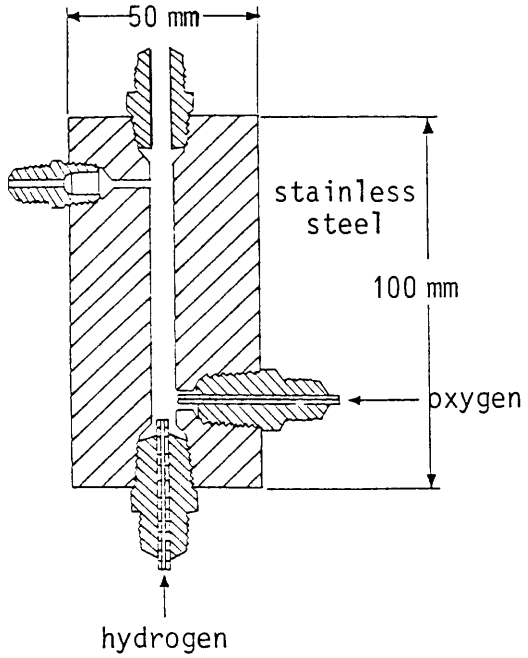

Fig. 1. A schematic drawing of the mixing chamber in the mix maker used in animal experiments (7).

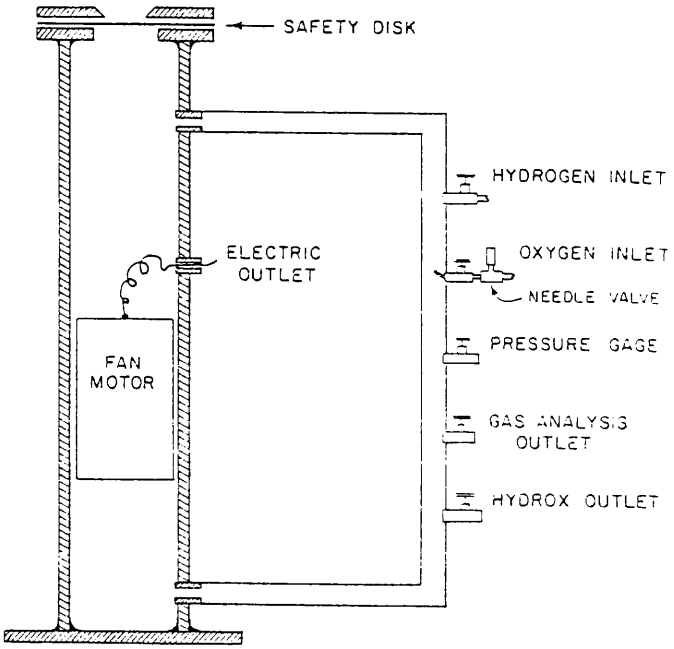

Fig. 2. Schematic drawing of Fife's mix-maker

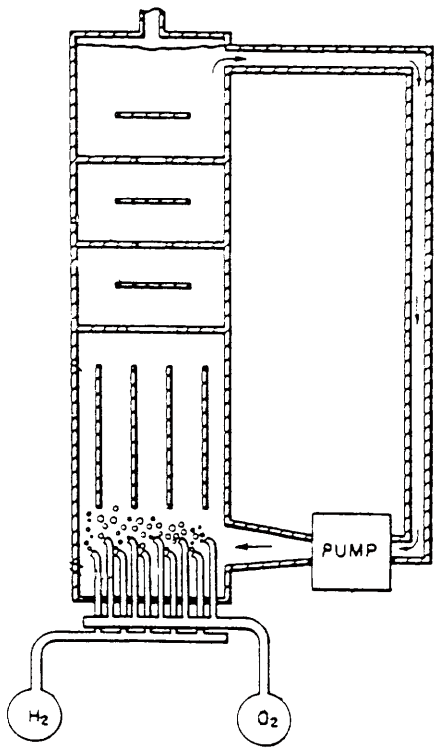

Fig. 3. Schematic drawing of Hill's mix-maker

Other types of mixers have been used or have been recommended, such as the circular flow mixer (Fig. 2) built by Fife (8), and the liquid mixer (Fig. 3) suggested by Hills (9). The most risky way to mix is to let O_2 flow directly into an H_2 cylinder.

Dumping gas

Experiments in large chambers at high pressures mean that large volumes of gas have to be dumped into the atmosphere at the end of the experiment, if the gas is not compressed back into the gas supply. Decompression of animals or humans is usually so slow that dumping into the atmosphere does not cause problems. The light gas diffuses rapidly in the air and creates a nonexplosive mixture.

If large volumes have to be dumped, burning of the gas in a flame ignited by a continuously burning pilot-flame will ensure that no explosive clouds will be formed. To prevent flash back in dump lines, sinter metal or liquid flash back arrestors can be used. The continuous addition of an inert gas like nitrogen, as early as possible into the dump line will prevent the formation of an explosive mixture caused by stagnant H_2 and diffusion of O_2 from the air via the flash back arrestor.

AN EXAMPLE OF A LABORATORY

The system shown in Fig. 4 was actually used in the Hydrox A experiments (7).

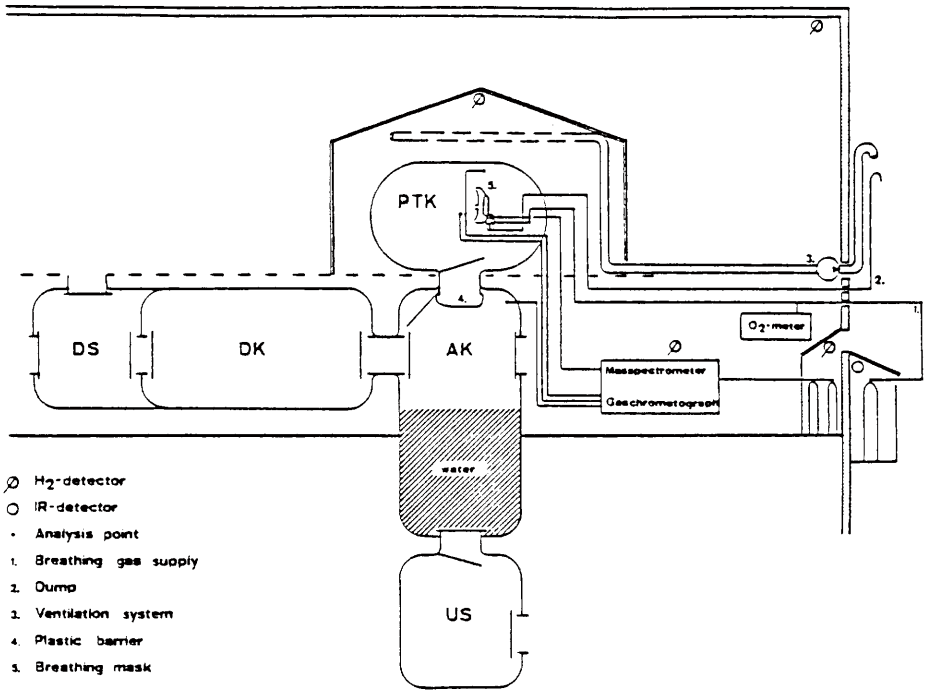

Fig. 4. Schematic drawing of a chamber laboratory for H_2 experiments.

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DISCUSSION FOLLOWING PRESENTATION BY ÖRNHAGEN

YOUNGBLOOD: I noticed on the schematic that your emergency He backflow supply is outside the building. Is it also adjacent to the H_2 storage area?

ÖRNHAGEN: It is there for practical reasons only. You see in real life this whole panel was mounted in a window which we replaced with an aluminum sheet on which we mounted all the valves so we could stand inside and maneuver them while we had all the valve bodies outside.

BRAUER: For those of you who are thinking of doing experiments, one thing Hans has not mentioned is that the need for virtually all of the precautions, not quite all of them, but virtually all of them, disappears the

moment you move your H_2 installation out into the open. So if you come out of the Scandinavian climate into a civilized one you can save yourself an enormous amount of headaches by simply insisting that the H_2 does not enter your main building or that any building where it does enter has a big hole in the roof and that there are no corners where the H_2 can be trapped. I think it's worth adding that the oil industry which has been handling H_2 in laboratories for something like 40 to 50 yr, insists that wherever possible their buildings be constructed with such open roofs and no dead corners. If you have to design a low cost assembly rather than the Cadillac model, that's worth considering.

FIFE: I would like to address the question of embrittlement by H_2. I recall that the French had a hatch that went and I understand that hatch was made out of cast iron. Is that true?

ZALOSH: Cast iron is notorious for H_2 embrittlement.

FIFE: I think there has been one problem with the one the French had. I looked at some old work by Kesterson. He did quite a few studies on H_2 embrittlement related to radiation effects on the metal, for the nuclear industry, I am sure. But if you extrapolated his data, he used several different kinds including stainless steel, but if you extrapolated his data backward, it turned out that O_2 tended to prevent or minimize the embrittlement. If he extrapolated that backward, it turned out that you could reach the point of little or no embrittlement at something like 1/25th of 1% O_2, and by the time you talk about 3% O_2 you're 10 orders of magnitude above the amount you need to reach this point. Have you looked at that? Do you really feel there is a problem in H_2 embrittlement? After all cylinders of H_2 have been sitting around for 25 yr and they haven't leaked or had any problems.

ÖRNHAGEN: We are not that much concerned about H_2 embrittlement just because we have never had to deal with ultra-pure H_2. The H_2 that we purchase is industrial grade electrolytic H_2, and it has O_2 as a contaminant. In fact that's why we buy it so cheaply. There is O_2 in it which doesn't bother us, since in any event we add more O_2 to it.

GIRY: As far as metal is concerned, the advice which has been given by some of our engineers is: Don't take stainless steel. We prefer just plain steel as more efficient because of less cracking and carbon inside. Has anybody heard about that?

ZALOSH: I wanted to mention a couple of practical technical developments that may be of interest. One has to do with visualizing the H_2 flame. You say you are using infrared detectors. What we have used in the last 2 yr in running our experiments are infrared video cameras. These are the same cameras that are used for security purposes in low light conditions. They are commercially available at a very reasonable price and they work very well. You can see any H_2 flame in them and they are made to scan entire rooms. It is a very useful technique that has not been applied in laboratories but I think should be. The second technical point that I want to make is in regard to approved electrical equipment. We have Code division 1

and division 2. There is an important distinction: In one case the equipment is approved for an atmosphere which under normal conditions is flammable or explosive. Therefore the equipment has to be what is called "explosion proof," meaning that it has to be able to contain an explosion; that makes it very expensive, because it has to be very high pressure material. The second category is applicable to experiments: division 2 concerns applications where you have only a flammable mixture under accidental conditions. In this country at least the electrical national code specifies that equipment approved for that kind of application doesn't necessarily have to be explosion proof but rather what we call "intrinsically safe," meaning gas mixtures won't be ignited once you pour them in there. It makes a big difference in the price, so if you can't afford explosion proof equipment you can find some that is approved to be "intrinsically safe."

YOUNGBLOOD: I would like to ask whether anyone has experience with ultrasonic leak detectors? They would give you indications of a leak before any ignition.

ÖRNHAGEN: I have used them but there still is nothing like soap solution when it comes to the real leak detection. I mentioned the fact that H_2 can go through porous and cast metals. We bought some pressure reducers made of cast aluminum for the mixture and we started to pressure test with H_2. The H_2 alarm came on, and when we started out with this ultrasonic detector, we could hear that there was something leaking but we couldn't really detect where it was. Even when we went over all the fittings with it, we still couldn't find anything. Not until I put soap solution on the cast metal of the pressure reducer did I see that in one of them there were two pores bubbling out H_2 right through the metal. The ultrasound detector picked it up all right, but didn't allow us to localize it. Maybe I wasn't too good at using it but the soap solution, when it comes to the detailed point, still functions better.

FIFE: We also rely very heavily on the soap. During compression we stopped every hundred feet and checked every single fitting in the whole facility. When we are down at depth, we make a full check every hour. You have soap all over everywhere, but at least that's safe and has been no problem.

MILLER: The stethoscope is pretty good.

FIFE: Some of these are so small that you will not hear them.

MILLER: Even with a stethoscope?

FIFE: Yes, when just an occasional bubble comes out, you can have a problem. You can't afford to have any whatsoever. I wouldn't touch the stethoscope. I think you have to detect the H_2 sooner.

SECTION VI
Decompression and Counterdiffusion Considerations

ULTRASONIC DETECTION OF CIRCULATION BUBBLES DURING ISOBARIC TRANSIENT COUNTERDIFFUSION AFTER A SWITCH FROM HYDROGENATED ATMOSPHERE TO HELIOX

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INTRODUCTION

In the literature, the use of hydrogen as a respiratory gas goes back to Lavoisier. However, the idea of using H_2 in mixtures breathed during diving is relatively new.

Zetterstrom is the first, who performed real dives at sea (2). We then had to wait until 1966 to observe a growing interest in the use of H_2 stirred by the work of Brauer (3-5) in the United States and of Fructus in France (6). Then, there were the studies of Edel (7-10) in man, and Fife (11) in dogs. In 1984, the Swedish Navy, acting as a forerunner thanks to Zetterstrom, decided to resume experiments on human subjects (12).

All these works are devoted to the study of H_2 in mixtures, especially with respect to:

- its possible toxicity;
- its narcotic power;
- its effects on the divers' ventilatory performances.

In addition, a number of authors have shown an interest in a recently observed phenomenon called "counterdiffusion" by Graves at al. (13). This a phenomenon results in various troubles, such as cutaneous erythema, articular pains, and even nausea and vomiting, connected with the formation of bubbles without any change in pressure. This phenomenon occurs under certain circumstances when a body saturated with gas is suddenly ventilated with another gas of a different kind.

Lambertsen and Idicula have specified the conditions for the occurrence of this counterdiffusion phenomenon in animals. They have shown that in some cases it can result in the animal's death. Later on, they showed the occurrence of the phenomenon in man and specifically stated its effects (14).

We shall not discuss again the theoretical considerations on counterdiffusion which have already been extensively developed by D'Aoust (15,17). So far as we know this author is the only one who has studied and evaluated the counterdiffusion risk in animals by means of the ultrasonic method of detection of circulation bubbles (18-21). Thus, he was able to specify the supersaturation values reached during counterdiffusion (18,19). This enabled him to conclude that it is the difference between the solubilities of different gases that causes counterdiffusion (17), but also that perfusion plays a prevailing part in the development of the phenomenon (20).

Finally, he was one of the first to consider the possibility of switching between other gases and H_2 (16). We know that to use H_2 during deep dives it is necessary, for safety's sake, to compress the divers with heliox before switching to another breathing mixture near 100 msw, and then return to heliox within the same depth limits. Therefore, during compression, as well as during decompression, the diver who is more or less loaded with the gas, if not saturated, will have to switch over to another gas mixture. This raises the question of the possible occurrence of counterdiffusion during gas mixture switch overs. D'Aoust at al. have given a kind of answer: "A switch from H_2 to helium appears relatively safe..." (21).

In 1983 COMEX resumed its H_2 experiments, performing a 90 msw dive at sea during which two divers breathed hydrox without any apparent trouble. A series of experiments was then scheduled at the Hyperbaric Centre of COMEX. A lot of work was necessary as regards final technological adjustments, to comply with safety requirements.

The first human experiment, called Hydra IV, was organized with the purpose, among other things, of estimating the possible counterdiffusion risk upon diver's return to heliox from a short exposure to hydrox. Another experiment, called Hydra V, was then organized to evaluate:

- the possibilities of a progressive return to heliox by stages after a long period of exposure to hydrox;

- the possibilities of decompressing in hydrox.

MATERIALS

Diving Chambers

The Chambers shown in Figs. 1 and 2 are those of COMEX, as used during the Hydra IV Dive. Unit 1.the hydrosphere, a "swimming-pool" chamber, 5 m in diameter, comprising a gas volume (heliox); a circular floor partly covering the "pool"; in the middle, a transparent plastic bubble where comparative tests were performed with heliox and hydrox, in a dry environment and in water and *Unit 2*, an eight-person living compartment communicating with the laboratory chamber. Outside there is a control room for both units. Hydrox mixture supply and exhaust are through a separate system. The installation is in accordance with safety standards for H_2 use.

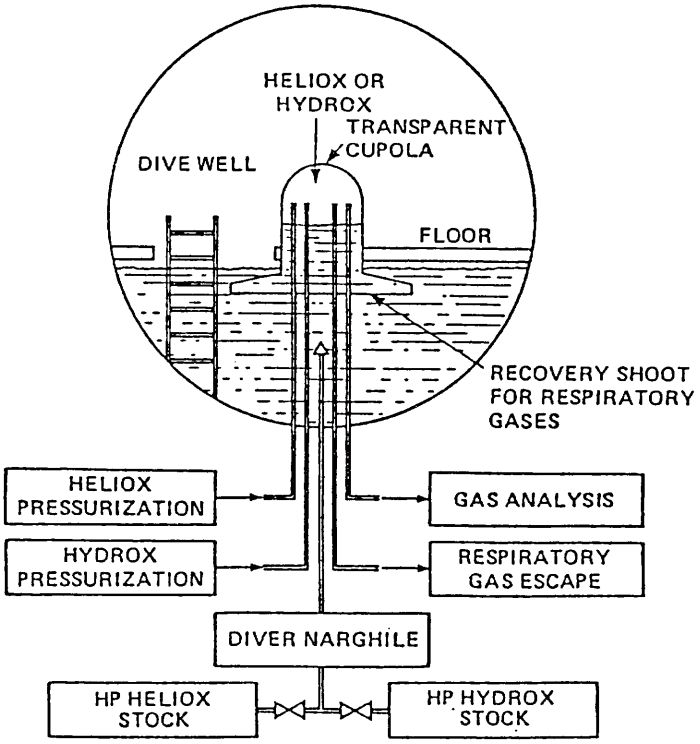

Fig. 1 Hydrospere

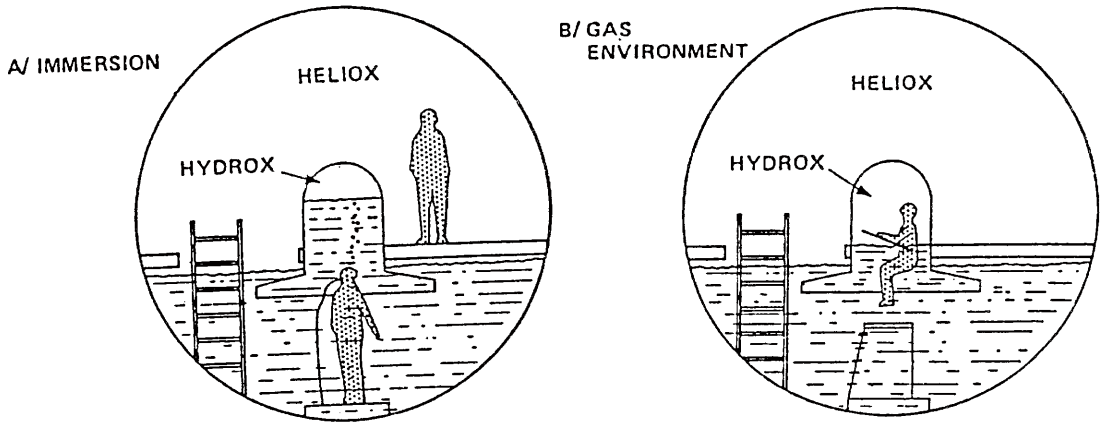

Fig. 2 Hydrosphere

During Hydra V Dive the chambers used were the three spheres of the Experimental Hyperbaric Centre (CEM) of the COMEX to which a large life compartment has been added.

Bubble Detectors

The bubble detectors are those we have already been using for several years. They have been developed, and recently improved, the INSA (Pr. Guillaud and Mr. Lakestani). Doppler signals are systematically recorded on magnetic tapes and cassettes in chronological order, so as to group the results for each diver.

Divers

In the Hydra IV dive six divers, whose biotypological features are summarized in Table 1, were divided into two groups: A and B. Each group included one experienced diver selected for his long professional experience, one physician diving occasionally, and one sporting or occasional diver.

TABLE 1

Divers	Origin	Age	Weight (kg)	Height (m)	Mean skinfold (mm)
A1	COMEX	45	63	1.63	8.4±3.8
A2	COMEX Engineer	27	76	1.89	8.5±2.7
A3	COMEX sporting diver	37	75	1.73	8.0±1.8
B1	COMEX	32	72	1.76	6.8±1.6
B2	U.K.	40	82	1.79	10.9±3.3
B3	U.K. Physician, sport diver	39	72	1.65	13.9±4.9
Mean		36	73	1.75	9.4
S.D.		±6	±6	± 0.08	±3.9

In the Hydra V dive six divers also were divided into two groups: A and B. Their biotypological features are listed in Table 2. The A group was composed of divers selected because they had taken part in a previous experimental dive to 450 msw, the results of which could be used as reference. Among the three divers of the A group, who were all quite experienced divers, the A1 diver had previously participated in Entrex V, the A2 diver in Janus IV, and Entrex IX, and the A3 diver in Janus IV, where he was found prone to produce bubbles.

TABLE 2

Divers	Origin	Age	Weight (kg)	Height (m)	Mean skinfold (mm)
A1	GISMER	40	88	1.89	7.5
A2	COMEX	35	78	1.83	8.3
A3	COMEX	34	74	1.76	7.1
B1	GISMER	32	73	1.76	5.6
B2	COMEX	31	75	1.79	8.8
B3	INPP	33	75	1.73	7.5
Mean		34	77	1.79	7.5
S.D.		$\pm$ 3	$\pm$ 5	$\pm$0.05	$\pm$1.1

The B group comprised three divers of different origin. Diver B1, although he was a deep diver, was performing his first experimental deep dive below 300 msw. Diver B2 had already performed deep dives (Entrex V), while Diver B3 of the INPP was taking part for the first time in an experimental dive.

Dives

The Hydra IV dive was carried out from November through December at the Experimental Hyperbaric Centre of the COMEX in Marseilles, France. It was a conventional 300 msw saturation dive with heliox, during which divers were subjected to sequential exposures to hydrogenated mixtures at different times during compression, bottom stays, and decompression.

The characteristics of this heliox saturation dive shown in Fig. 3 were as follows:

- Compression:
    - 0 t0 120 msw, 1st stop reached within 40 min;
    - 120 to 180 msw, 2nd stop within 40 min;
    - 180 to 240 msw, 3rd stop within 2 h and 20 min;
    - 240 to 300 msw, bottom, reached in 2 h 20 min, P_{O_2} 400 mbar.
- Bottom stay:
    - 64 h, P_{O_2} 400 mbar.
- Decompression:
    - Duration without stops at 150 and 80 msw;
    - 9 d 4 h 25 min, that is 220 h and 10 min;
    - P_{O_2} 600 mbar from 300 to 200 msw;
    - 500 mbar from 200 to 15 msw;
    - 24 % between 15 and 10 msw, then return to air.

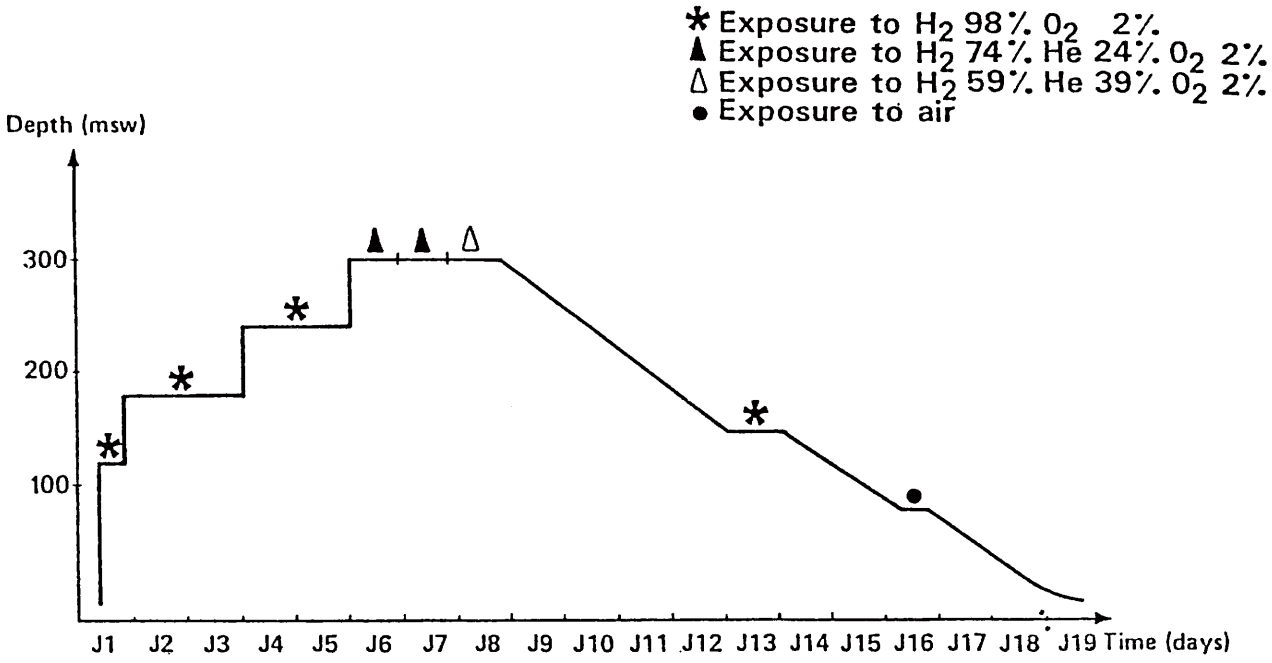

Fig. 3. Profile of the Dive Hydra IV

There were five stops in the following sequence: at 120, 180, and 240 msw during compression, and at 150 and 80 msw during decompression. The H_2-containing mixtures were breathed during such stops and at the bottom.

The Hydra V dive was carried out from May through June at CEM under the care of both COMEX and the French Navy. The various phases of this dive are summarized in Fig. 4.

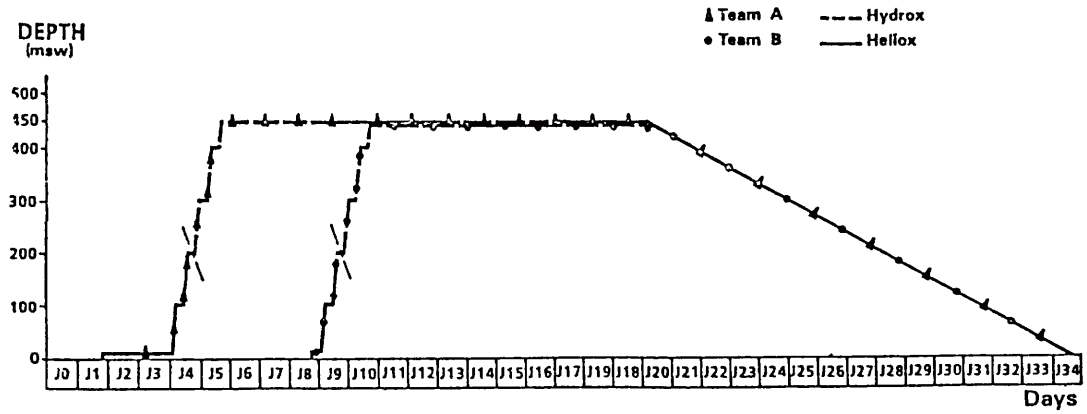

Fig. 4. Hydra V Initial Profile

The particulars of this dive concerning compression and similar to the compression in the Entrex dives were as follows:

- 0 to 100 msw within 3 h;
- 100 to 200 msw within 4 h and 30 min;
- 200 to 300 msw within 5 h and 20 min;
- 300 to 400 msw within 9 h and 20 min;
- 400 to 450 msw within 5 h and 50 min.

From 0 to 200 msw compression was made in He atmosphere, then in H_2 environment from 200 to 450 msw. Pi_{O_2} was kept at 400 mbar. Every 100 msw there were compression stops for 2 h and 30 min. The initial experimental protocol specified that, at the bottom, each diver group was to be exposed to hydrox to perform exercises in a dry environment followed by a return to heliox. Then, they were submitted to a new exposure with exercise in water before joining the others for the decompression. We shall see later how the course of events compelled us to modify this experimental protocol (Fig. 5).

METHODOLOGY

Each circulation bubble measurement sequence included the following: a precordial detection, called detection "at rest" (R), in the standing subject after a few minutes inactivity; then a precordial detection "with movement" during and following each one of three knee-bend movements separated by a 1-min time interval. Bubble grades were estimated according to the KM code (22). The measurements also included bubble detection on each subclavian vein, in the carotid-jugular area on the right and on the left, on each femoral vein and, whenever possible, at the level of the vena cava.

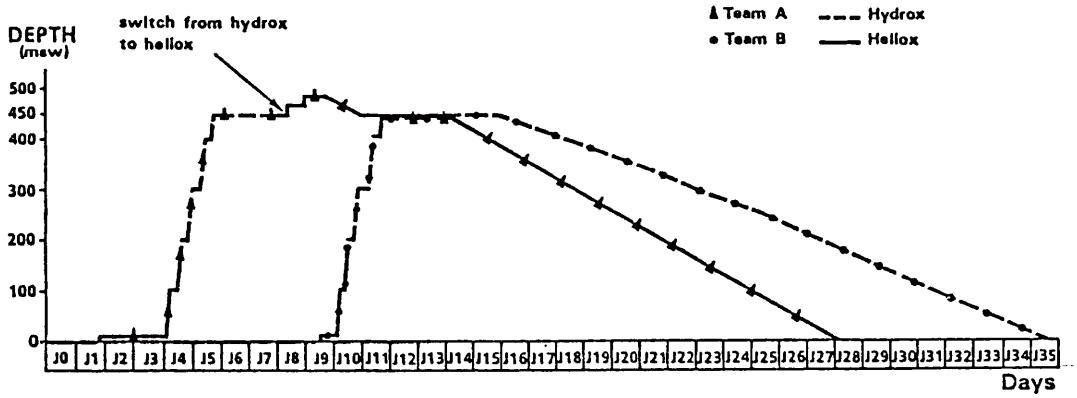

Fig. 5. Hydra V Modified Profile

Hydra IV

Measurements were made at the end of each exposure to hydrox immediately on return to heliox, and then every 0.5 h later, except when bubbles were detected after the 3rd h. In such a case, the bubble detection was carried on sequentially until the bubbles disappeared.

Nature and Conditions of H_2 Exposures

The divers experienced two types of exposures: in a dry environment and in water. Dry exposures were carried out within a bell made of methyl methacrylate and arranged according the Figs. 1 and 2. This bell enabled us to isolate a limited volume of H_2, insufficient to result in an explosive mixture when accidentally exposed in the chamber environment. Moreover, the exposure duration could thus be strictly controlled, since the switch from heliox to hydrox and conversely, was immediate and consequent upon the divers' passage from the chamber to the bell via the swimming pool which was the required interface.

Within the bell the divers remained seated, emerging from the water from the waist up (Fig. 2). The divers had a small shelf at their disposal to perform psychometric tests, and they stayed in direct telephonic and visual contact with the chamber and the outside. The under water exposure was carried out in the pool at room temperature. The divers were dressed in conventional diving suits with an umbilical tube. They remained in a marked out area so that the expired gases could be trapped in the immersed recovery chute surrounding the bell. (Fig. 2). In addition to psychometric tests, the divers had to carry out some ergometer exercises, to evaluate the combined effect of effort together with hydrox breathing on a possible measurement. Time distribution of exposures to hydrox atmospheres is given in Fig. 3.

During Hydra V

Sequential measurements were made during confinement and bottom stay to make sure the probe was operating properly and to keep the divers accustomed to the positions of the probe on each of the relevant sites.

When switching from the 55% H_2 atm to the 30% H_2 mixture, which occurred on Day 8 for the A group, a bubble detection test was performed immediately on arrival of the divers in chamber 2 at 30% from chamber 1 at 55%. Measurements were then made every h over a 5 h period. Likewise, as regards the switch from the 30% mixture in chamber 2 to the 0% mixture in chamber 4, we applied to the A group the experimental protocol requiring a detection on the divers' arrival in the chamber and then every hour for the subsequent 4 h. We shall describe modifications made in the protocol and account for such modifications when discussing test results.

RESULTS AND DISCUSSION

Hydra IV

Results after gas switching of the precordial measurements during hydrox exposures are listed in Table 3. Exposures to 98% H_2 at 120, 180 and 240 msw did not result in a counterdiffusion phenomenon that could be detected on return to a heliox environment, except in divers A1 and A2, who breathed the hydrox mixture during immersion over periods of 30 and 8 min, respectively. The observed bubble grades remained low, that is grade 1 at rest and grade 2 with movement. During exposures at 300 msw, the breathed H_2 percentage was 74%, equivalent to a 98% mixture at 222 msw.

On the first day, only the three divers in group A exposed for 30 min in the dry environment, showed some bubbles, up to grade 2 with movements in diver A2. On the second day, only diver A1 exhibited grade 2 bubbles at rest and during movements, after 30 min exposure under water. On the 3rd d, one of the two divers exposed for 60 min to a 59% H_2 mixture under water (which corresponds to 180 msw with a 98% mixture), namely diver A1, exhibited a few isolated bubbles during movement.

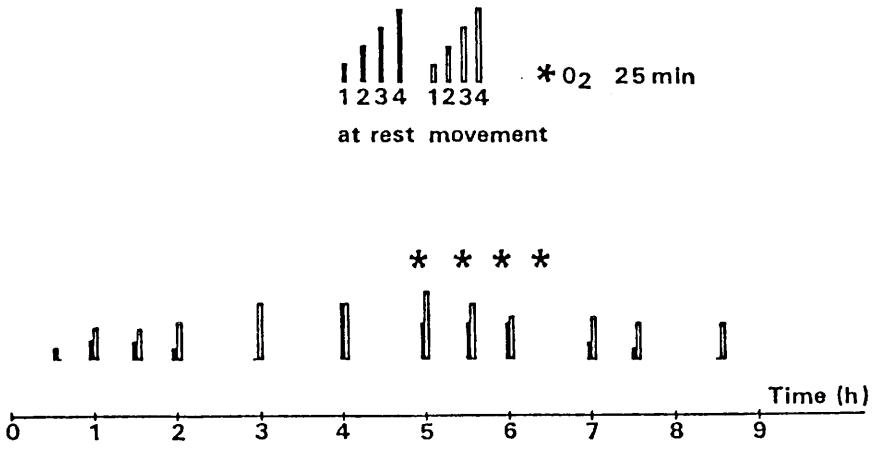

Fig. 6. Bubble detection results after a 240 min H_2 exposure at 150 msw:counterdiffusion effect subject A1 - Hydra IV.

TABLE 3

Stop	Breathing mixture $H_2/He/O_2$	Exposure duration with mixture/ Divers/Bubble grade R/M			
		In dry environment		During diving	
120 m	98/0/2	45 min	A2B1 / A3B2 /		
		60 min	A1B3 /		
189 M	98/0/2	30 min	A1 / A2 / A3 /	30 min 60 min	B1 / B2 / B3 /
	98/0/2	30 min	B1 / B2 / B3 /	60 min	A1 / A2 / A3 /
240 m	98/0/2	30 min	A1 / A2 / A3 /	60 min 30 min	B1 / B2 / B3 /
	98/0/2	30 min	B1 / B2 / B3 /	8 min 30 min	A2 1/2 A1 1/2 A3 /
300 m	74/24/2	30 min	A1 1/ A2 1/2 A3 /1	45 min 30 min	B1 / B3 /
	74/24/2	30 min	B2 / B3 /	30 min 45 min	A1 2/2 B1 /
	59/39/2			60 min	A1 0/1 B1 /
150m	98/0/2	120 min 240 min 360 min	B2 / A1 3/3 B1 /		

A1 A2 A3 Divers team A B1 B2 B3 Divers team B
Bubble grade at rest (R) and with movement (M)

During exposures of 98% H_2 at 150 msw, only A1 (who is known as a particularly "bubble producing" subject in spite of his outstanding professional experience without any noticeable incidents) exhibited bubbles after 4 h of exposure to hydrox in a dry environment. The grade of bubbles exhibited by this diver increased regularly for 4 h, up to grade 3, at rest as well as with movements (Fig. 6). He also exhibited many bubbles on the subclavian veins. This diver was then supplied with O_2 and heliox by turns, through a mask, for 2 h as follows: O_2 for 25 min and hiliox for 5 min. The bubble grade then decreased slowly down to 0 (R) and 2(M) 8 h and 30 min after return to heliox.

Oddly enough diver B1, who is also an experienced diver holding some professional records, exhibited no bubbles after 6 h of exposure to hydrox, even though he was known to be a bubble-producing subject since the Janus IV saturation dives performed on land in December 1976 and at sea in October 1977. Measurements made during exposure to air at 80 msw during decompression have not given many results.

On the whole, a short-duration exposure to H_2 in the form of hydrox resulted in quite moderate bubble grades. However, and curiously enough, diver A2, who certainly is a bubble-producing subject, exhibited a high bubble grade after an 8 min exposure at 240 msw, whereas diver A3 exhibited no bubble after a 30 min exposure under the same conditions. The difference is even greater as regards exposures at 150 msw: after a 4 h exposure A1 exhibited high grade bubbles for a long time, whereas diver B1 exhibited no detectable bubbles after a 6 h exposure at 150 msw. Such a considerable interindividual variation is nevertheless usual as regards the bubble phenomenon. We never observed any clinical symptoms correlated with bubble flow.

At 150 msw we were faced with a problem concerning diver A1. Taking into account his steadily increasing bubble flow, we first treated this diver by means of O_2 supplied through a mask. This did not prove to be particularly effective. Therefore we considered the possibility of recompression treatment. But we could not be sure whether the few meters recompression usually carried out to treat bends occurring during decompression from saturation would have been sufficient. As a matter of fact, the detected bubbles were circulating bubbles. The only possible way to treat them would have been to recompress to such a pressure as to reduce their volume sufficiently for them to be eliminated by the lung filter without induced incidents. We did not know the pressure required to obtain such a reduction.

Hydra V

Results of the measurements made to determine the importance of the counterdiffusion phenomenon are listed in Table 4. As you can see, the counterdiffusion remained quite moderate when switching from a 55% H_2 mixture to a 30% H_2 mixture. On the contrary, switching from the 30% H_2 mixture to heliox resulted in immediate production of circulating bubbles. Within 10 min after the switch over, diver A2 exhibited grade 2+ bubbles at rest and grade 3 bubbles during movements together with some clinical symptoms (Fig. 7) (23).

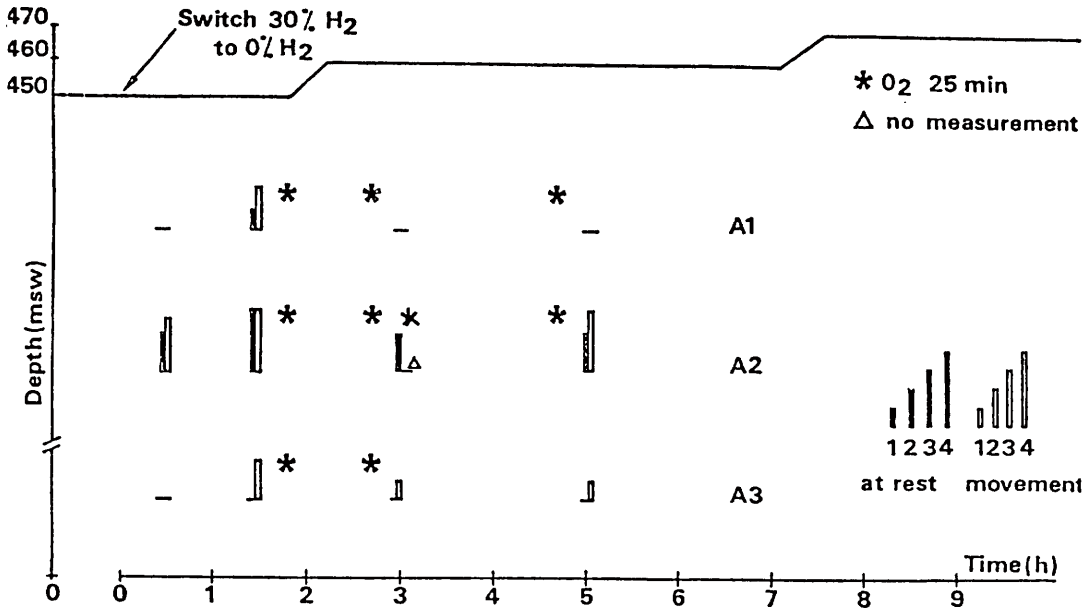

Fig. 7. Bubble Detection Results After A Switch From Hydrox to He: Counterdiffusion Effect Dive Hydra V

TABLE 4

Results of Bubble Detection After Switching from Hydrox to Heliox, Hydra V Dive.

Subjects / Sequence	H	A1 R	A1 M	A2 R	A2 M	A3 R	A3 M
Recording after switching from the 55% to the 30% hydrox mixture	1/2 h	0	0	0	0	0	0
	1 h 40m	0	0	0	0	0	0
	3 h	0	0	0	0	1-	0
	5 h	0	0	1	1	0	0
	7 h	0	0	0	0	0	0
Recording after switching from the 30% to the 0% hydrogenated mixture	10 mn	0	0*	2+	3*	0	0
	1 h 20 m	1	2+	3+	3+	0	2
	3 h	0	0	2	MN	0	1
	5 h 14 m	0	0	2	3	0	1

*Divers exhausted and nauseated. MN : No measurement : diver exhausted (lying down).

Compression { to 460 msw at the beginning of the 5th h / to 470 msw at the beginning of the 7th h } after return to heliox

Diver A1 produced bubbles only once; that was 1 h and 20 min after his return to heliox atmosphere. He produced grade 1 bubbles at rest, and grade 2 bubbles during movements. His clinical symptoms were also more moderate. As for diver A3, he exhibited an even lower bubble grade and felt only some itching, even though he was known to be a sensitive bubble-producing subject during decompressions from saturation. After his return to a heliox, 1 h and 30 min later, the pressure was increased by 10 msw and Pi_{O_2} was set at 600 mbar on account of persistent symptoms. After return to heliox atmosphere 6 h later, as the situation had not changed very much, it was decided to recompress the divers to 470 msw, and to break off the program for the moment until the situation would be clarified.

The program was then modified as shown in Fig. 5 with suppression of gas switching for the B group.

After return to the heliox mixture chamber and compression the 470 msw, the divers were allowed to rest 12 h at 470 msw. Afterwards they were decompressed to 450 msw within 40 h. Return to H_2 was cancelled and it was decided to put off decompression until complete recovery of the divers.

CONCLUSION

The results obtained show that even comparatively brief periods of H_2 breathing at depth in subjects saturated on heliox and returning to heliox at 240 and 300 msw can entail a hazard of isobaric formation of some bubbles in the blood stream. More serious counterdiffusion problems associated with symptoms of skin bends and grade 3 or 4 bubble concentration recorded by the Doppler technique were observed on isobaric switching from 30 to 0% H_2 in heliox following saturation in 55% H_2 in heliox at 450 msw and 8 h in 30% hydrox-heliox at the same pressure. Gradual reduction of the relative concentration of H_2 during decompression after saturation in 55% hydrox in heliox can apparently be accomplished safely.

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DISCUSSION FOLLOWING PRESENTATION BY MASUREL

FLYNN: Do you have any idea of the magnitude of a shift over from H_2 to He that might be safe at a constant total pressure, say 450 m for example, from 10 atm H_2 to 0 H_2, or from 5 atm to 0 holding total pressure constant?

MASUREL: This is difficult to say. Many animal experiments would be needed to determine a meaningful value.

FIFE: My question is almost the same. What would you expect to have in the way of counterdiffusion problems if you make the decompression on H_2 until you get say 7 ATA partial pressure and then shift over to He. Would you expect a problem there?

MASUREL: Probably yes, but we really lack all the needed experience.

FIFE: I have switched, but not from saturation, and for only a short time, with no problem. Of course, I wonder about the saturation effect. I only went to 330 ft, 10 ATA and then came back to 7 and shifted, so it wasn't the same thing. I worry about the effect of saturation.

FLYNN: Was there enough time so that a problem that might have developed during the first step maybe showed up only after the second step? Could it be that the first shift somehow prepared the ground to cause bubbles in the second shift?

MASUREL: Maybe, but I think the time between the first and the second shift should have been long enough to get rid of any bubbles that formed after the first step. The time was 5 h and there were no bubbles.

LUNDGREN: But the question remains: Has something happened that you can't detect in the bloodstream? Could it still be that somehow there are more nuclei generated or are there stationary bubbles that are large enough to show the second shift?

MASUREL: This is a hypothesis but we do not have the ability to answer with the present state of the art.

BRAUER: Is not one of our problems that we don't in fact know what the H_2 burden is that those people carry at that time? Until we know that, any calculations we could make will remain largely hypothetical. Yet with H_2 much more nicely than with other gases, one should be able to measure unloading directly as a function of time. The next time one has to discuss this, one might evaluate any observations against actual figures of the H_2 burden carried by the subjects.

MILLER: Claes' point is that you can still have microbubbles hanging around.

BRAUER: I am totally aware of that possibility, but at the moment everybody is wholly ignorant of how much H_2 is left in those people after any given time and hence what the consequences of any microbubbles might be. That

uncertainty at least can be removed readily. There was surely a striking contrast between the lack of clinical problems on the first step, lowering H_2 partial pressure isobarically, and the appearance of significant problems on the second step. We cannot explain this now, and that, I think, isn't going to be changed by any discussion at this time. Regardless of the question of microbubbles or micro-nuclei, it is the burden of H_2 and the diffusion potential of He that will determine whether or not there will be counterdiffusion problems in any given situation.

FRUCTUS: Clinically, in fact the only valid symptom that was observed was itching, the cutaneous effect due to direct counterdiffusion between skin and ambient atmosphere. Any other symptoms of bends, including articular symptoms that would normally be associated with circulation bubbles, were not proved. In particular, the vestibular syndrome, which I was afraid might show up, didn't do so. So for the moment, you are looking at a clinically very mild bends situation in which the only bubbles documented are expressing themselves in relation to the cutaneous effects rather than to other more general effects.

FLYNN: Can we get a clarification of this? Were the joint pains in these divers felt to be decompression sickness or some kind of phenomenon associated with compression? Was the feeling that of decompression sickness?

FRUCTUS: Clinically the bends pains can be readily differentiated from the "no joint juice" pains which occur only in motion, and in the present case the pains clearly were "no joint juice" type pains and not the bends type.

LUNDGREN: Yet we know that 8 h is a relatively short time in terms of the life of free gas in the body. On the one hand we have some speculation as to what might be going on, and on the other hand we have your method of detection which is highly refined as the Doppler method goes. But yet, we are painfully aware that the Doppler is not necessarily as sharp a tool as we would like to have to predict or even trace relevant decompression complications.

YOUNGBLOOD: I would like to make an observation which this paper certainly emphasizes. In the early days of Doppler use we only listened immediately after a dive, and if we heard nothing, we supposed that there was nothing there and didn't listen further. I think that this was a mistake. As Dr. Masurel showed, we need to have an organized plan where we listen for at least 8 h or perhaps even longer on a regular, planned basis.

PROJECT HYDROX

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Since hydrogen is the lightest of all gases, we might expect it to offer the lowest resistance in a laminar flow system which should promote more rapid diffusion of O_2 and CO_2 within the gas exchange units of the lungs at depth. On the basis of solubility and diffusion co-efficients, one would expect the uptake and elimination rates in bodily tissues to be more rapid for H_2 as compared with N_2 and possibly, as suggested by Keller, even more rapid than He.

In spite of the potential advantages of H_2-O_2 as a breathing mixture for deep diving exposures, early investigators were discouraged from experimenting with Hydrox in view of the explosive and flammability characteristics of this mixture, for a broad range of H_2:O_2 ratios (2). However, work done by the Bureau of Mines (1), and by Dorr of Ocean Systems (2), have demonstrated that O_2 percentages as high as 3 or 4% in H_2 are completely safe with respect to explosive and flammability hazards. A mixture of 3% O_2:97% H_2 could be utilized as shallow as 7 ATA where the O_2 partial pressure in the mixture at that depth would be equal to the O_2 partial pressure in air at sea level.

Brauer's work where mice were exposed to mixtures of O_2 with N_2, He, and H_2 at elevated pressures indicated that the narcotic potency of H_2 was less than that for N_2 but greater than that for He. Convulsive seizures occurred at significantly higher pressures with H_2 as opposed to He (3).

Prior to hydrox, the only human experimentation, aside from a brief dry chamber exposure by Case and Haldane (4) in 1941, was conducted by the Royal Swedish Navy. In the early 40s Zetterstrom designed a cracking plant for shipboard use to produce a mixture of 72% H_2:24% N_2:4% O_2 which was used in a series of open water dives to a maximum depth of 12 ATA (5). Mixtures of 96% H_2:4% O_2 were used for subsequent deeper dives by Zetterstrom. In his final dive he reached a maximum depth of 520 ft where he was apparently free from any symptoms of narcosis (6). This dive most regrettably resulted in his death due to the inattentiveness of the crew member in charge of the forward winch attached to the diver's stage which permitted the diving stage to be raised to the surface from the maximum depth of 17 ATA without halting for any of the required decompression stops.

In 1957, two successful manned exposures were made to a depth of 7 ATA for 10 and 20 min in a single lock chamber 1 m in diameter and 2.5 m in length. The small size of the chamber permitted very rapid changes in the chamber atmosphere which was used to provide data on atmospheric control in later experiments (7).

In these tests, the chamber, initially containing air, was pressurized with pure N_2 to provide an atmosphere of 97% N_2:3% O_2 upon reaching 7 ATA. This mixture should be safe in the event of any accidental contamination

resulting from a leakage into the chamber from the H_2 system. The H_2 system was completely independent of the main breathing mixture supply and included an overboard dump system terminating in a flashback arrester outside the building.

The initial exposure pressurization to 7 ATA required 2 min. The diver breathed 80% He:20% O_2 during compression in 3.5 ATA. At that point he shifted to 97% He:3% O_2 and, upon arrival at 7 ATA, switched to the H_2:O_2 breathing system. The diver lifted an 18-kg weight half a meter 200 times during the exposure period at maximum pressure in this test. At the end of the exposure period, the chamber was rapidly purged, first with N_2 and then with air to provide a physiologically safe breathing medium in the event of failure of the BIB system during decompression.

In this dive as in the subsequent exposure to the same pressure for 20 min, the diver was switched to a 96% He:4% O_2 mixture as the ascent commenced. After 1 min, the diver was then shifted to an 80% He - 20% O_2 mixture which was used during decompression until arrival at about 20 m. At that point the diver was shifted to pure O_2 which was used for the remainder of the decompression. Pain was felt in the elbow at the 13-m level. Decompression, however, was continued as programmed to the surface. Pain recurred during each subsequent pressure reduction and diminished rapidly during the time spent at each decompression level.

Further manned experiments at this pressure for exposure times of up to 2 h were made in a larger chamber between September 1970 and April 1971. These tests were made to obtain biomedical data and determine the decompression obligation resulting from longer exposures with H_2-O_2 where the tissues with longer half-saturation times would limit or control decompression (8). Both Edel and Fife experienced problems related to the faster tissue compartments. In some cases the decompression requirement for H_2 in the faster tissue compartments seemed to be unusually restrictive, in consideration of an anticipated range of half-times and M-values, when compared with the decompression requirements for the same compartments for N_2 and He. An accurate knowledge of the decompression requirements for such tissue compartments would be essential for the development of decompression tables for use with H_2-O_2 mixtures in a bounce diving mode. Fife (9) carried out a number of additional experiments with dogs, rats, and mice at pressures of up to 305 m. Additional experiments were made for short durations with humans breathing H_2-O_2 to depths of 300 fsh. Some decompression problems resulted from these exposures which involved fast tissue compartments. Interestingly enough, only Edel (7,8,10) and Fife (9) have made studies in which decompression was a primary interest. In other studies decompression requirements were assumed to be within certain limits and in general the studies utilized tables which were believed to be within safe limits. The lack of symptomatic response to decompression in recent French and Swedish H_2-O_2 experiments (11,12)and X. Fructus, personal communication, in which the slowest tissue compartment was controlling from total saturation exposures attests to the safety of the procedures followed.

The practice of linearization for convenient control in saturation decompression, lack of DCS problems, and the lack of knowledge of the

individual base susceptibility to decompression sickness of the divers precludes a meaningful evaluation of the decompression profiles in terms of the decompression obligation in the slowest tissues from the most recent saturation exposures.

With respect to the slowest tissue compartments, in the results of Project Hydrox II, Edel (10) appears to provide the most definitive information with respect to decompression obligation. In this study the same subjects were exposed to 2 h exposures at 200 fsw with normoxic mixtures of N_2, He, and H_2 in separate dives spaced 1 wk apart to avoid influence from acclimatization. Analysis of the data (which involved a 50% incidence of sickness for each mixture used) indicated that the decompression requirements for H_2 were almost exactly midway between those for He and N_2 for the slowest tissue compartments.

In terms of H_2-O_2 saturation decompression requirements, the problem is somewhat academic. Saturation decompression utilizing linearized ascents is a much simpler problem than that for "bounce" dives in which many tissue half-time compartments are involved and the staging must be optimized for a decompression procedure which is both rapid and safe. In a saturation decompression profile only one compartment is involved and a lengthening of decompression time by 10 to 20%, after weeks of exposure at the working level is of little consequence, and in the event of minor problems for a more susceptible individual, it is always possible to reduce the rate of ascent in a specific instance.

The practical results from the recent Swedish and French experiments indicate the ability to provide for safe decompression from such saturation exposures.

The recent French and Swedish saturation type exposures had no significant involvement with the faster tissue half-time compartments. In this area few available data exist. Some information is included in studies by Edel (7,8) and Fife (9) but is insufficient to provide verification of a decompression model for H_2. On the positive side many of the profiles were successful with the limited number of subjects utilized in the programs. In Project Hydrox II the only incidence of decompression sickness occurred in the slower tissue compartments which were being studied and as a result of reductions of the anticipated decompression requirements for those tissue compartments. In this study, however, most of the faster tissue compartments were not involved in the decompression requirements and care was taken to ensure that the early portion of the decompression, where faster tissue components were involved, was overly conservative so as not to influence the results of the study of slowest tissue compartments.

Project Hydrox II was initiated in 1974 to assess the potential use of H_2-O_2 as a breathing mixture in deep diving operations (10). The project was conducted at the Research Division of Michel LeCler, Inc, near New Orleans, Louisiana, with funds provided by the Office of Naval Research and Bureau of Medicine and Surgery. In addition, a scientific team from the Naval Submarine Medical Research Laboratory participated in the program to increase the spectrum of data developed in this 24 manned test-dive series.

Four test subjects were involved in this experimental series in which each subject was exposed for a 2 h period a 7 ATA--six times during the program. Each subject was exposed twice on each of three breathing mixtures which were 97% N_2:3% O_2, 97% He:3% O_2, and 97% H_2:3% O_2.

The basic operation (with respect to chamber atmospheric control and use of breathing mixtures) was the same in this series as the Project Hydrox I. The pressure profiles were made as identical as possible except for some changes in the time distribution of the decompression obligations of the three inerts involved. This was done to provide a basis for direct comparison between the inerts involved and derived ratios of tissue half-times for H_2 as compared with He and N_2.

Analyses of the results were made by computer cross matching of all possible relationships of tissue half-time and M-values which would apply to the decompression incidence experienced in this series. As a result the only applicable combination for H_2-O_2 indicated a half-time compartment 1.5 times that for He and 0.75 times that for N_2. The indicated value for H_2 with respect to both the slowest half-time compartment and its corresponding M-value was approximately midway between He and N_2 values.

Although an interpretation of these values indicates potential problems with inert gas shifting from H_2 to He after a prolonged H_2 exposure with the derived 1.5:1 inert gas exchange ratio, this is less than would result with a similar shift from N_2 to He with an assumed ratio of 2:1.

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DISCUSSION FOLLOWING PRESENTATION BY EDEL

YOUNGBLOOD: What do you think might have happened if you had switched to nitrox instead of heliox on the way up?

EDEL: If I switched to nitrox instead of heliox? I think it would have worked. You might even have gotten some advantage out of it in the hydrox situation.

HOUSTON: When you say the divers at the end of the test preferred a particular mixture, on what basis would they say they preferred it? Easier breathing medium, something psychological or what?

EDEL: I think it was primarily the easier breathing. The initial choice of the divers was in all four cases He-O_2 first, N_2-O_2 second, and H_2-O_2 last. And this was, I think, psychological again. The *Hindenburg* phenomenon all over again. But after they had experienced this, and the presumed hazard didn't materialize, it didn't seem important anymore, and they then chose on the basis of respiratory resistance.

HYDRA V DIVE

ULTRASONIC BUBBLE DETECTION AND DECOMPRESSION

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From the first day on the bottom at 450 msw, the behavior of divers exposed to 55% hydrox mixture was quite remarkable. They were so pleased with the dive conditions that it seemed advisable to take advantage of these experimental conditions to decompress the second group in hydrox, thus getting a greater mass of information.

Subsequently, the difficulties encountered by the first diver group, when switching from one gas to another, strengthened us in our choice. This paper presents the results of both decompressions.

MEANS AND METHODS

Let us remind you that the device used was the same as the equipment already mentioned. The conditions for the use of this equipment as well as for expressing and processing the results were also the same. Detection frequency was most often three sessions/d as follows: one measurement in the morning on the subject's waking, one at 2 pm, and one in the evening at 8 pm; only during five decompression days of the A group, did we limit ourselves to one measurement in the morning and one in the evening, so as to reduce the demands on the divers.

As already mentioned in our paper, and as Mr. Gardette has just described in detail, each diver in group A and B was decompressed according to a different protocol.

DECOMPRESSION WITH HELIOX MIXTURE

Following the counterdiffusion incidents observed during the switch-over from hydrox to heliox, the divers of the A group had been compressed from 450 to 470 msw where they rested for 12 h, a very slow decompression rate not very likely to result in physiological stress.

After resting an additional 3 days at 450 msw, the divers were decompressed after having been exposed for 1 h to a 600 mbar O_2 mixture, supplied through a mask. Decompression was performed at a rate of 45 min/m, up to 15 msw from the surface and 60 min/m from 15 msw until surfacing with a Pi_{O_2} as follows:

- 600 mbar from 450 to 350 msw;
- 500 mbar from 350 to 120 msw;
- 600 mbar from 120 to 15 msw;
- 24% between 15 and 0 msw.

Results of circulating ultrasonic bubbles detection are given in Fig. 1. The first bubbles occurred in subject A2. This subject also produced the greatest number of bubbles during the switch from hydrox to heliox. On the whole, the bubble production rate remained very low up to 280 msw. With one exception in diver A1 at 184 msw, the bubble grades at rest were never higher than grade 1, which is quite low, even though the divers exhibited grade 3 bubbles during movements on several occasions between 295 and 38 msw. Afterwards diver A1 exhibited a slight bend at 1.3 m from the surface.

Taking into account the average value of bubble grades in the three divers of the group, and for each detection both at rest and during movements (Fig. 2), one can notice an early occurrence of bubbles during movement together with a steady increase up to near 280 msw where the bubbles at rest become regular in two out of three divers.

Figure 2 shows that the maximum bubble flow appears at 180 msw and that, in practice, this bubble flow remains roughly constant between 280 and 100 msw. The bubble flow decreased only during the last part of the curve and it fell virtually down to 0 upon the divers' arrival at the surface.

As regards bubble flow development, the decompression results are not very different from what could be observed during the Entex IX dive, with an identical decompression profile. The bubble grades measured during the present dive were slightly higher. In the aggregate, it is difficult to think that events occurring before decompression had an aggravating effect on decompression.

DECOMPRESSION WITH HYDROX

Even before counterdiffusion incidents occurred among the divers of the A group, it had been decided to decompress the divers of the B group in a hydrox atmosphere, because their behavior was apparently free from any trouble in the hydrox environment. Subsequently, the advantage of decompressing the 2nd group in the hydrox environment was confirmed by results obtained with the A group.

At that point we had to choose between two alternatives: either decompressing the divers and gradually removing H_2 so as to return by 200 msw to a heliox atmosphere, or decompressing normally in the hydrox atmosphere to 200 and then switching gases according to the same method as at 450 msw. It seemed to us that it would then be difficult to determine the respective roles of counterdiffusion and supersaturation in the possible formation of bubbles. Therefore, we selected the first solution as the least hazardous, although decompression methods to be used in the hydrox environment are not well known yet.

Everything considered, we chose to decompress in 2 msw decompression steps, immediately followed by 1 msw recompression step in the He environment, so as to gradually enrich the mixture with He, and to reduce the H_2 percentage. The divers were thus gradually returned to 200 msw with only 2% H_2. Decompression was started at a rate of 70 min/m, but in the absence of bubbles this rate was gradually increased:

- up to 65 min/m from 350 msw;
- up to 60 min/m from 300 msw;
- up to 55 min/m from 250 msw to 15 msw.

For convenience's sake only, the decompression rate was then reduced to 90 and 120 min/m between 15 msw and the surface. The Pi_{O_2} was kept at 500 mbar between 450 and 100 msw, at 600 mbar from 100 to 15 msw, and then at 24% up to the surface. Results of circulating bubble detection carried out during decompression are listed in Figs. 3 and 4.

It appears that bubbles occurred later in the B group than in the A group, that is at 282 msw. Afterward, a regular bubble flow was observed from 271 msw in B3 who never exhibited bubble grades higher than one at rest and three during movement.

On the whole, the decompression of the B team was tolerated better, and it might have been possible to increase its rate sooner. It seems that a decompression rate of 50 min/m would be a good compromise likely to ensure safe decompression with both gas mixtures. It would also have prevented A3 from suffering bends.

It is worth noticing that H_2 decompression rates do not appear to be radically different from those of He. A decompression rate of the same order for two gases as different as He and H_2 (Table 1) would be a factor in favor of perfusion as a decompression limiting element.

TABLE 1

Solubility of inert gases in biological fluids and tissues: a review.
Weathersby PK, Homer LD
Undersea Biomedical Research 7 (4) 277-256 (1980).

Note: We choose for each case mean value from the references.

Gas	Atomic weight	Oswald' Solubility coeggicient at 37° C in ml/liter			
		Water	Oil	Blood	Muscle
H_2	2	18	49	18	17
He	4	10	17	10	12
N_2	28	14	73	18	

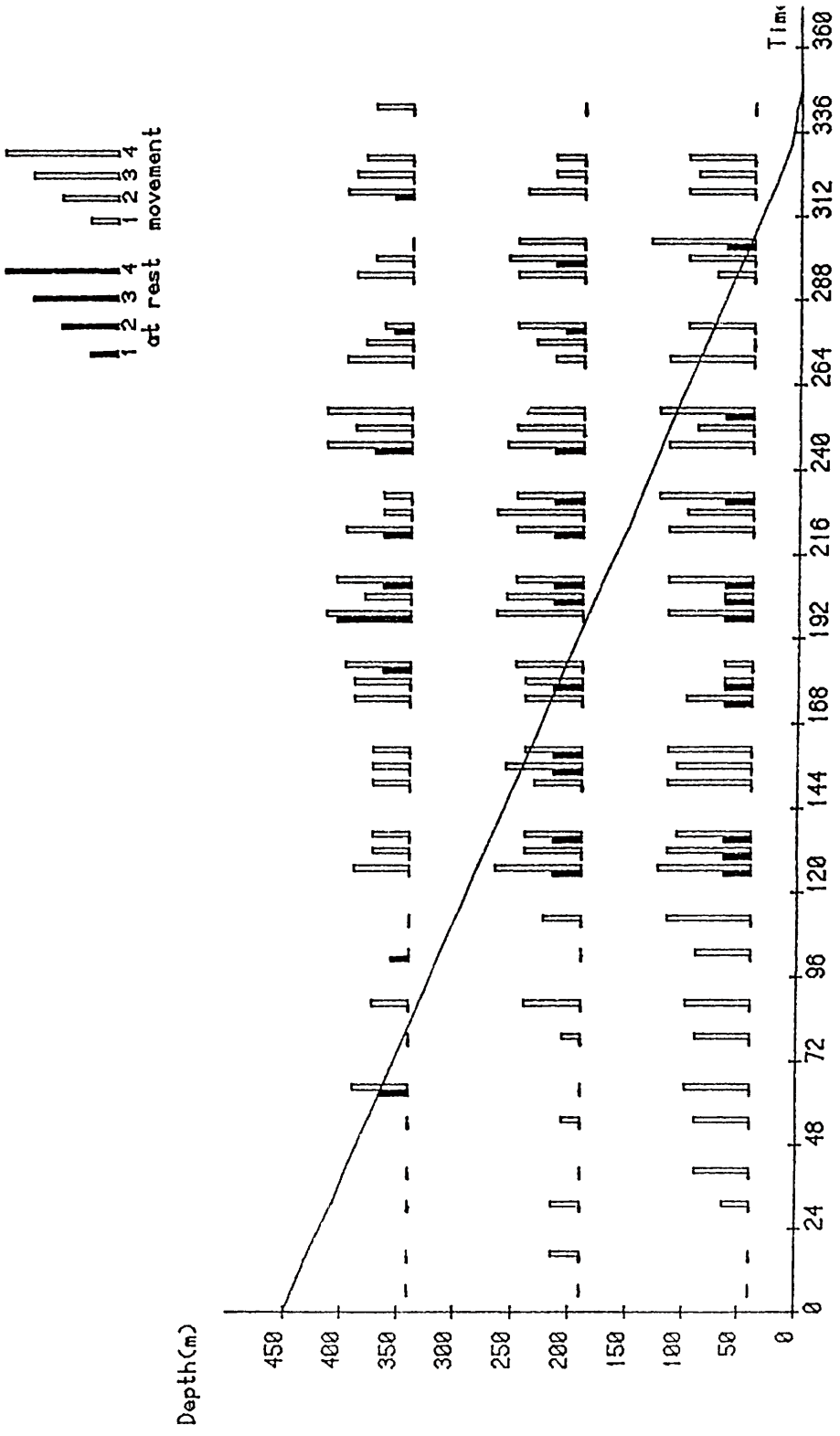

Fig. 1. Bubble Detection: Individual Results
Dive Hydra V

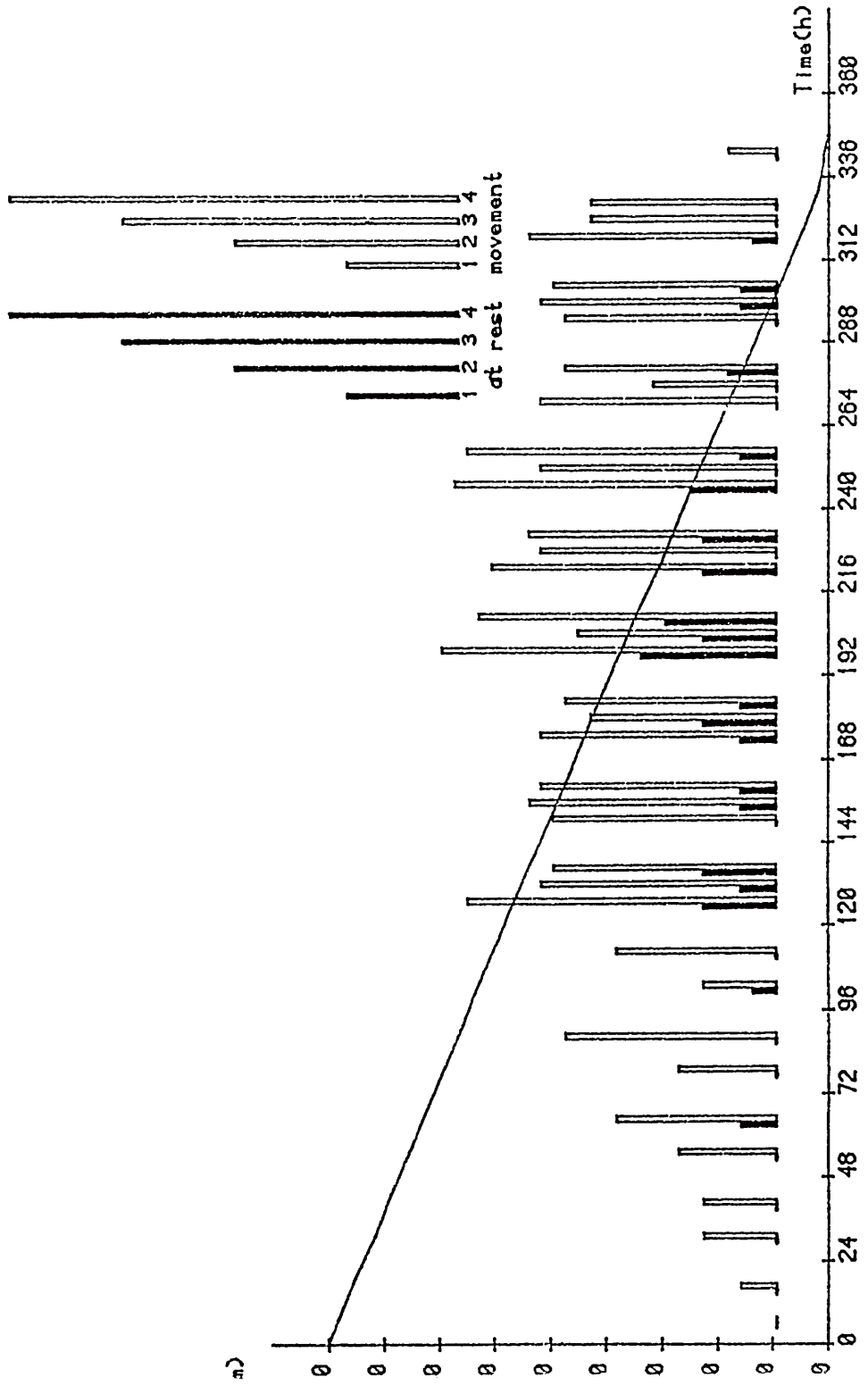

Fig. 2. Mean Bubble Grade For Every Detection
Dive Hydra V
Team A

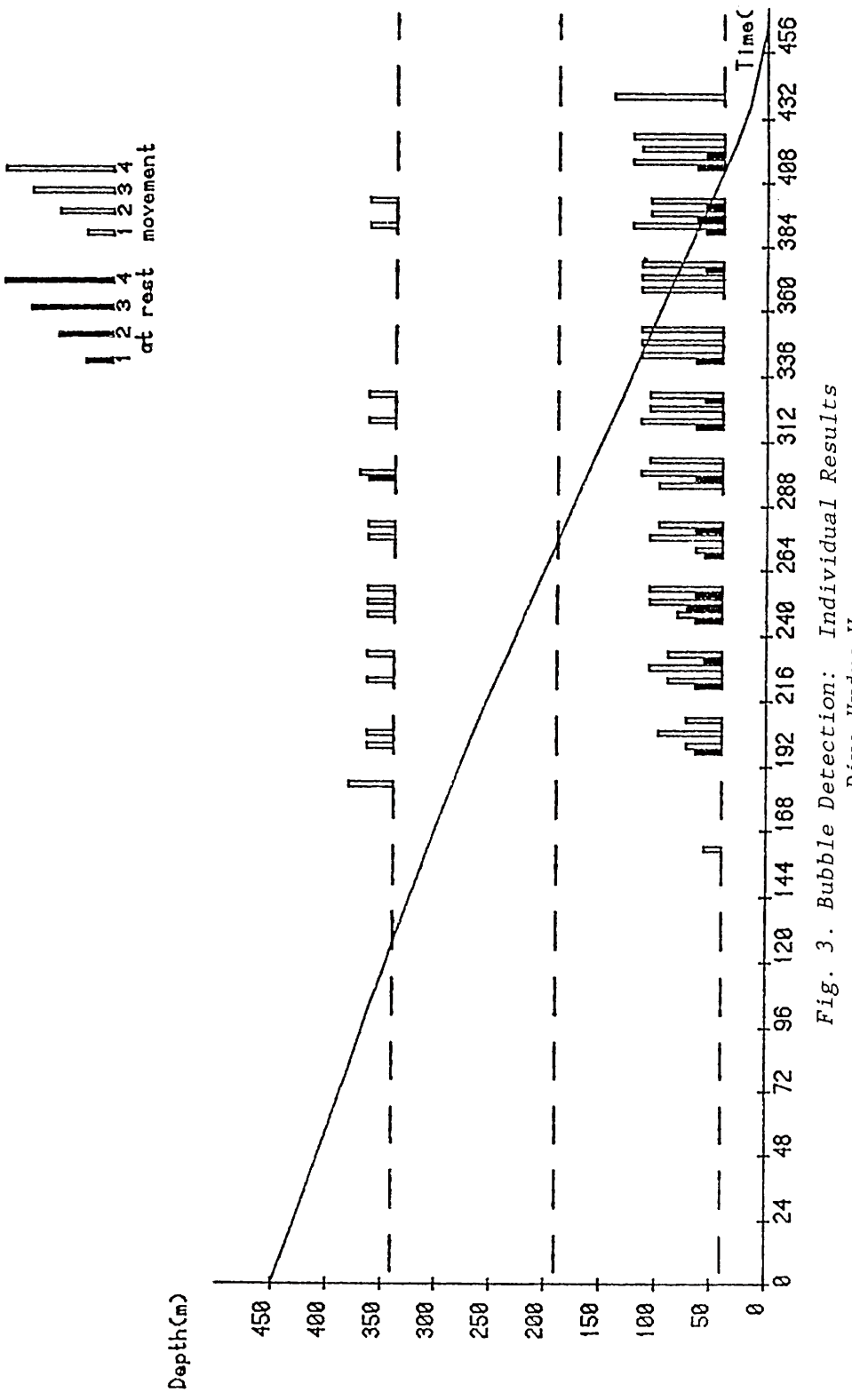

Fig. 3. Bubble Detection: Individual Results
Dive Hydra V

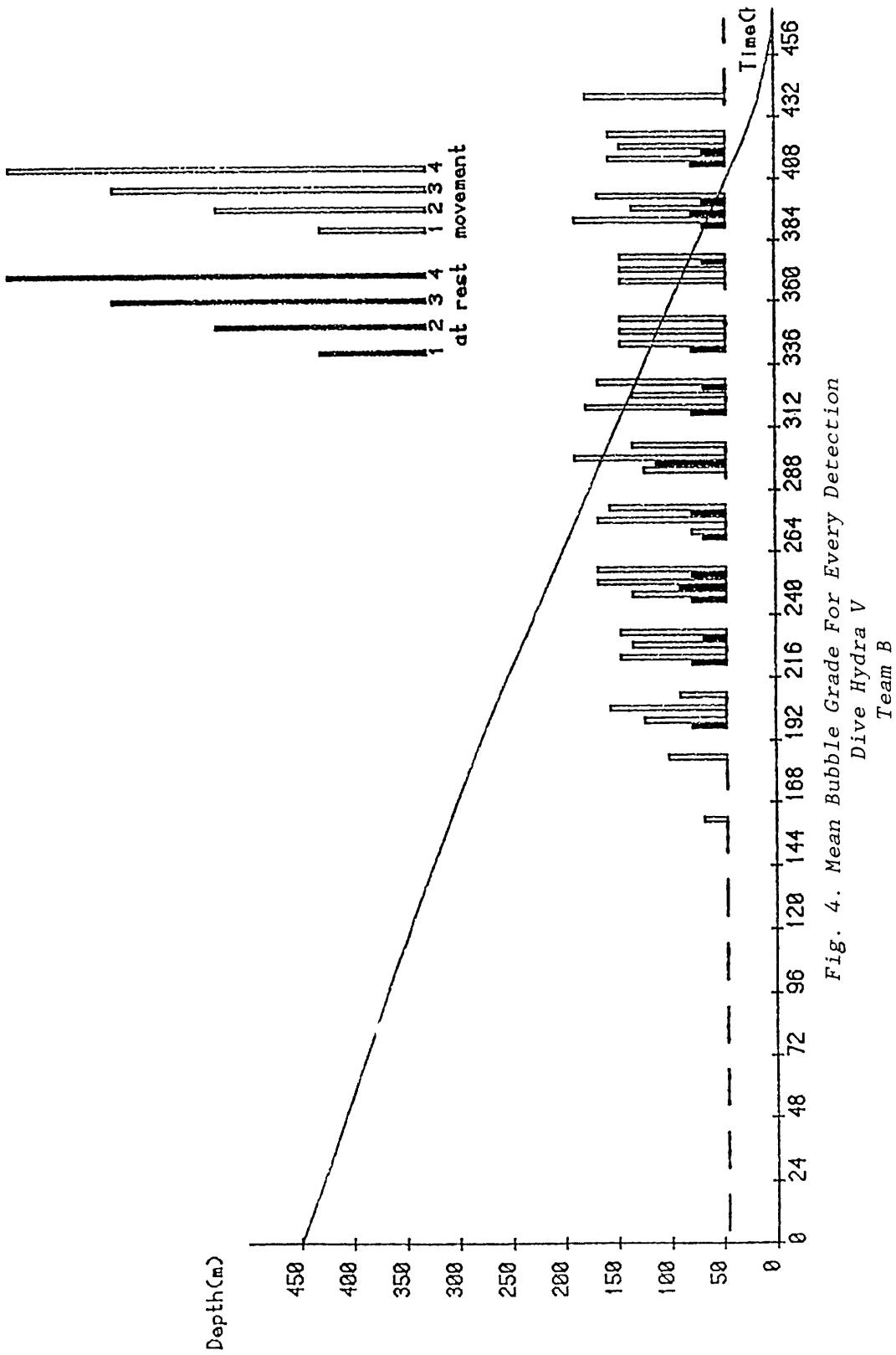

Fig. 4. Mean Bubble Grade For Every Detection
Dive Hydra V
Team B

DISCUSSION FOLLOWING PRESENTATION BY MASUREL

EDEL: I notice in your slides that few bubbles or none at all were detected in the first portions of the profile while you did see them in the latter part. Doesn't this suggest a possible asymmetry in the decompression characteristics as opposed to the true decompression obligation throughout?

MASUREL: In fact for the decompression with hydrox the initial rate of ascent was very low to prevent bubble formation and as the decompression was quite safe the rate of ascent was modified continuously, increasing as the decompression progressed until 55 min/m at about 250 msw.

DELAUZE: You note we have absolutely no bubbles in any of the subjects at the start. I think taking about 1 m/h as the ascent rate might prove a good compromise between the two gases. In any event even when we detected bubbles, the rate was very low so we can't really decide what the true situation might be with H_2.

YOUNGBLOOD: I would still like some clarification about the isobaric tests with the divers who breathed the He/O_2 during the second phase of the isobaric counterdiffusion tests. Have they all undergone the therapeutic compression to 470 m and then the decompression prior to the second counter-diffusion experiment? Were these substantially the same divers who developed the bubble manifestations during decompression?

MASUREL: Yes, the divers who had many bubbles during the counterdiffusion were also the ones with many bubbles during the decompression.

YOUNGBLOOD: And the one diver who had no bubbles was he also compressed to 470 m?

DELAUZE: Yes, all of them who were in the chamber at the time were of course carried down to 470 m.

ÖRNHAGEN: You mentioned the two choices you had, either to gradually take away H_2 or to decompress in hydrox to 200 m and then make the switch at 200 m. Is that 200 m figure based on the fact that you didn't want to be above 2% O_2 and you didn't want to go below 0.5 atm O_2 during the decompression?

DELAUZE: The decision was made that we would not go above 2% O_2. In the future we might well extract some of the H_2, but we didn't want to attack all of the problems at the same time.

BRAUER: I think that in fact a rule that is becoming increasingly clear is that the multifunctional experiment that at one time was viewed so very favorably has shown itself to be a relatively inefficient and dull tool. I think perhaps you would agree, and I believe Dr. Doucet would be in accord with that, that increasingly as we progress, each diving experiment should be formulated around one or two major questions that can be answered conclusively rather than around 20 questions which would stay indefinitely.

DELAUZE: I quite agree. On such a first saturation experiment we compromised quite deliberately to assure the safety of our divers.

BRAUER: I think it might be worthwhile reminding this group that those of us who have been involved with decompressing animals somewhere in the 1, 2, or 3 kg range are pretty well convinced that the parameters we are using now for such decompressions for H_2 are nearing the critical level. We have accidents if we go past them. Those parameters are very distinctly slower for H_2 than they are for He. I'm intrigued to see that in man so far we are not seeing that. I still think it is worth remembering, because our curves, and I think Dr. Örnhagen's also fitted that, follow the old Barnard pattern: You draw white circles for accidents, black circles for clean decompressions, and you draw the line between them. The difference between the gases seems quite real.

SMITH: If you decompress mice following saturation exposures to determine maximal depth from which a no-stop return is possible, then N_2 and He are surprisingly close, something like 10 and 12 atm, whereas the relevant physical properties, diffusion rate, and solubility differ by factors of 2. So I think there is a paradox in the animal experiments. I think this means we don't really understand decompression sickness.

BRAUER: I couldn't concur more. I have listened for 20 yr to papers dealing with decompression theory and giving elaborate theories, but always at the end everybody had to shrug their shoulders and say, "Those theories look very beautiful but they don't really work as usable predictive devices. We don't really understand what is going on, and we are back to the trial and error techniques." Indeed, those are what has guided literally every step to greater depth, and every extension of bottom time since the turn of the century.

SMITH: Could I add one final comment? You talk about the diffusion rate. The diffusion rate, in liquids, of He and H_2 differ by a factor of two, He being the faster of the two, paradoxically. So regardless of whether you look at the solubility, or the perfusion ratios, or fat/water distribution, you would expect He to be faster than H_2 by a factor of two. I was a bit surprised, Dr. Masurel, that you thought your results confirmed a perfusion mechanism.

MASUREL: You have just reminded us that the diffusion rate and the solubility rate of He and H_2 are different but vary in opposite directions. He is more diffusible than H_2, and conversely H_2 is more soluble than He, which perfectly accounts for the counter diffusion phenomena.

What I intended to say was that the possibility of using a similar decompression rate for both gases shows that solubility and diffusion are not the limiting factors unless they are compensating for each other in the present case.

The perfusion rate is the only common point in the gas washout. The possibility of using close decompression rates suggests that the washout rate of both gases is almost the same. This could be an argument to say

that perfusion is a limiting factor.

EDEL: We were looking into that question as well. In the initial diving tables used in the Zetterstrom dives the diffusion factor dominated, and to everybody interested in decompression, this seemed extremely attractive. In the final analysis we found that our results didn't fit either the diffusion or the perfusion by itself, but in tissue there seems to be a roughly equal contribution from both sides. Our animal experiments, I might add, confirm Dr. Brauer's statement, and probably Dr. Fife has had similar experience. We tried to decompress dogs on a linear profile with He and with H_2. While we had very good results establishing the He profile, when we tried to use it on H_2 we had very dramatic, early decompression sickness. I stress "very early," because we used a linear profile, whereas the actual response to the decompression loading is believed by most people to be curvilinear. So we had the curvilinear one intersected with the linear profile at a very deep level, and this again I think tends to suggest a caution about too rapid decompression with a pure H_2 saturation dive.

BRAUER: Do we in fact have any data on H_2 and He diffusion rates in tissue? I would expect them to be very different from those in homogeneous fluids, especially water.

FLYNN: There is one theoretical situation in which rapid diffusion would make things worse rather than better. You can think of a tissue cylinder with arterial blood coming in at one end, let's say carrying no inert gas species, and then trying to pick up gas from that cylinder. The amount that is picked up from the tissue then is the blood flow times the partial pressure at the venous end. If you have a gas with very low diffusibility, the partial pressure in the blood will increase as you go down that cylinder, and the venous end would be high. If you have a highly diffusible gas, some of what has piled up at the venous end can diffuse back rapidly to the arterial end and destroy the gradient. It is entirely possible that in a perfusion type situation a highly diffusible gas may wash out more slowly. I think that maybe if you could look at the mean residence time of a gas molecule in tissues with various sorts of capillary architectures, you might see how this works.

ÖRNHAGEN: I want to make a comment regarding the problems of a linear decompression. I would like to remind you of a slide I showed yesterday where we ourselves at 30 atm always started with a step before we went over into linear decompression. Contradicting what Dr. Edel showed us, we had no problems with this first initial step. Such a step ought to provide bubble formation and later problems, should it not?

EDEL: I have never objected to a step use. You use the step to establish a gradient. As a matter of fact, if you recall the TEKTITE profile, I departed from the traditional method of starting a linear decompression from a saturation point and I made an initial step precisely to generate a gradient to accelerate the decompression rate. I was comparing the linear to the best model that we have for a saturation decompression requirement which is curvilinear. Now, you still have to establish a gradient, regardless of whether you ignore the fact that you can do that by allowing a gradient to develop as you start up, or whether you make a step at first and

then follow the present linear pattern. But there is a difference between what we believe to be the correct response to decompression following curvilinear and linear profiles, in that you may not get the equivalent decompression stress in the beginning with a linear profile, but only toward the end, while with a curvilinear one you maintain the same decompression thrust throughout the entire profile.

FIFE: In practice we found when we were working with dogs that you have to increase the decompression time by about one third between the heliox and the hydrox in order to have a safe dive. All other things being equal, including the first step, the decompression still took about one-third longer on H_2 if we wanted to avoid bends.

FLYNN: I would like to ask in regard to the switch over from H_2 to He with the creation of this "no joint juice" (NJJ) problem, is there any thought about what the mechanism is that created this particular problem?

FRUCTUS: All these divers had experience with NJJ syndrome during previous heliox/N_2 trimix dives to 450 m. During Hydra V, none of them experienced this kind of pain while on the bottom on hydrox trimix, though one of them in particular had suffered the NJJ pains during previous heliox dives. When they were switched to heliox, the joint pains appeared, so rapidly in fact, that at first we thought they might be pains similar to those of decompression pains. In fact, however, they didn't respond to the recompression but gradually went away during the final decompression.

GIRY: And by the way, these pains in diver A3 did not prevent him form performing the exercise studies.

FRUCTUS: And finally, in the second team who didn't make the switch at depth, nobody suffered from joint pains. At the moment there is no more explanation for the NJJ syndrome under these conditions than for the presence of the plugged-up-nose syndrome under heliox and its absence under hydrox.

FIFE: Brian Hills suggested the possibility that the different gases create a different osmotic pressure and that this is the result that can cause NJJ syndrome. Did you actually have a fluid shift?

BRAUER: The problem with Brian Hills calculation was that he lost a zero in that calculation. Otherwise it is fine.

LUNDGREN: Given that we have no solid theory to explain the NJJ syndrome by itself, still there was this difference between H_2 and He. What would be your suggestion to explain the difference? Is it simply a matter of H_2 narcosis?

FRUCTUS: I don't believe so. Whatever narcosis there was, was really very weak. The pains occur during movement characteristically, and I feel sure the divers would have perceived them if anything of the sort had been present during the hydrox phases. We have evidence that they remained sensitive to pain.

DELAUZE: There are in fact three ways to analyze narcosis: One is you look at the people and you decide there is some narcosis. You can talk to the people and confirm that. The second one is to use psychological tests. The third one, and this is the one that concerns me as employer who is legally and morally responsible for the divers in the water at great depth, is the overall picture of your observations and the divers' impressions. These are not monkeys. They also have their brains, and are capable of analyzing their overall impression of their situation. They are very susceptible to what's happening. All of these have talked to me and to Dr. Fructus and commented on the new experiences they had, but none of them indicated that they might have been insensitive to heavy pain because they were drunk, and that matches everything else we know about them. After all, what we are looking for at the end is an answer to the question: Is H_2 a curiosity or is it an industrially promising approach to deep diving? If it is the latter, there can be no question of sending people into deep water when they are in a narcotic situation. So my answer to your question in a categorical, "No."

LUNDGREN: I see no reason why our traditional definition of narcotic levels and anesthesia should not be looked upon with caution when it involves a completely new situation where there may well be interference of high pressure. I think it is in order to repeat the question: Is there any possibility that the anesthetic action of H_2, given these very special circumstances with a very high pressure interacting with it, would somehow help to cover those particular symptoms?

DELAUZE: No, there is not.

FRUCTUS: Biological experiments which were being conducted by the CERB team during the Hydra V dive failed to evidence any cellular damage during the dive. So , perhaps there is hypoesthesia, I wouldn't contest that point. What I can say is that there has been no major syndrome of NJJ.

BRAUER: But that, of course, would not answer the question of either anesthesia or narcosis because all pharmacologists' definitions of this insist on the reversibility of it, and it is only when you are seeing other effects beyond the narcosis that you begin to expect any kind of histopathology. Perhaps the one point that might apply to the question that Dr. Lundgren is asking and that might come out of the animal experiments is that they show acclimation at least to some aspects of the narcosis. You might very well expect that symptoms that might have been masked at the beginning of such an exposure might come to the fore as this effect came into play, especially in view of the really different time courses of pressure accommodation and of habituation to inert gas narcosis. I haven't heard anything of this in our discussions, but it is worth watching for. If I understand what our friends at COMEX for instance will want to do, they will not want to go for deeper levels of narcosis but rather for slightly lighter ones. But there remains this very tricky business of titrating the diver. You know perfectly well that all N_2 diving to more than 50 ft is in fact done with people under light narcosis, and we select people for their ability to function under these conditions. I'm sure this applies here and makes

evaluation very difficult. It is in fact the one objection that I think could be raised to the use of professional divers as subjects in such studies: They are selected to be resistant to that aspect of underwater work, and perhaps one might want to do some experiments in which one uses other more "naive" subjects to explore that particular aspect.

FIFE: During the induction of anesthesia one will sometimes see hyperactivity just before full anesthesia development. When we are seeing H_2 anesthesia, as I think I heard the term used, is there a preanesthetic stage where there is hyperactivity?

BRAUER: The answer is an unqualified, "yes," in the animal experiments. You see the typical excitement stage.

FIFE: But how about in the human work?

SMITH: It has been seen there.

BRAUER: You have seen euphoria. In the Hydra IV experiment, when the levels were high enough, they did see euphoria, but its extent was rather mild, I think. And note that Giry's and Örnhagen's descriptions of their very comfortable and cheerful divers seem pretty close to euphoria.

SECTION VII
Perspectives and Reviews

USE OF HYDROGEN FROM THE PERSPECTIVE OF THE DIVING INDUSTRY AND ITS FUTURE

H.G. DeLauze

I think it was a very good idea to have all of us from different organizations and with different opinions together and I must say I found our meeting and our discussions quite refreshing. You realize of course that I do not come here as a scientist but rather as a manager of the diving community to try to give you some philosophy and my candid prophecy about deep diving. Some of these things probably are aspects you do not know about simply because we as managers are unfortunately today more involved in making the rounds of the banks and of our clients than enjoying technology and strategy with our R and D company team. Then I think it is good from time to time to do some cross-breeding. Of course you understand that what I am going to say are my own thoughts and they may not be what you believe and certainly should not hurt your pride as distinguished scientists or professors or your own philosophy, for the ones among you who are contractors in our deep diving community.

The first thing we would probably ask this morning is, why use H_2 in the diving industry? I do not believe that this is for purely scientific reasons. The industry just is not that affluent these days. The volume of work performed by divers in the worldwide offshore subsea business--and I am speaking of diving jobs from very routine assistance to highly specialized jobs like welding in deep water--represents about $500-700 million per year. You can see, therefore, that you cannot in any way compare us with NASA. When you propose to develop a new technology, the volume of business to which this technology might be applied worldwide is an extremely important consideration. From 1972 to 1982 the cash flow generated by this industry was in the range of 15-20%. Thus diving contractors had about $100 million for buying equipment--new caissons, new saturation systems and the like--for getting dividends to their shareholders and for making investments in physiology and research. I can tell you the dividends received by shareholders across the industry have never been high! The only company that should normally be obliged to give dividends to their shareholders is Oceaneering, because they are public, unlike COMEX, which is a private company.

But today the amount of available market is poor, and all over the world probably as much as 40% of all bounce and saturation diving systems stand unoccupied and our industry is dramatically starving. The result is a mad competition where many of our colleagues are skimping on training of their divers. Besides I believe that today, if you were strictly to enforce the worldwide qualification rules for diving equipment, 50% of the diving systems in standby would be scrapped immediately. COMEX would be less touched by this because, unlike some of our competitors, we have always been very reluctant to take shortcuts, and maybe because we have amassed money and technology more than anybody during the "golden years" of the offshore industry. To try to develop a new technology like hydrogen diving today is quite a challenge. To extend the limits of diving requires a lot of money,

time, and talent. When you compare the diving industry with outer space--and not only NASA--we see that we really are a very, very poor industry.

An additional problem is that in most of our countries there is a great fragmentation of effort. In France we did manage today (thanks largely to Dr. Doucet) to have the French Navy and COMEX working together and as a result we saved a lot of money. Here in this country there clearly is still a lot of fragmentation. The United Kingdom is probably in a better situation than it was three years ago but in Scandinavia, Swedes and Norwegians are each going their own way. Thus at present we really have a situation where diving research teams are working in their own corners and where commonality of goals and strategies has not been achieved. Some of the companies in diving today are just making enough money to pay their bills and personnel, and do not invest any more in scientific research.

In the United States you do have a helpful Navy. On the other hand in France, while we have good cooperation with the French Navy, we never get one cent out of them in terms of jobs. When they have something to do in deep water they use their own divers, their own ships, and their own diving systems, whereas in America, the U.S. Navy would have hired a diving company.

I do not see much change in this overall situation over the next 5 yr. Even though the offshore oil industry, as we said this morning, could not actually survive for a single week without the diving industry to back it up, the same oil industry has a curious sort of indifference or even resentment toward the diving industry. This is attributable to many things, most particularly perhaps to the fact that at the very beginning of offshore development, divers have often been associated with trouble in the minds of oil engineers. When a catastrophic situation suddenly develops on an offshore drilling project, the oil company needs to call in the diving company services to correct the situation. It is then tempting to resent those divers' who are often associated with problems. Furthermore, our industry had a lot of accidents, especially in the North Sea, in the 1972-80 period.

Diving mishaps are immediately considered by the oil industry as evidence of bad management or carelessness or bad performance. I for one do not believe that this is so. A lot of the accidents that I remember in the profession at large probably could not have been avoided. Anyway there has been big change. Every year between 1972 and 1975, five to eight divers died in North Sea accidents. In 1984 I believe there was no accident and while we have not yet finished with 1985, so far again there has been none. In the meantime there were many helicopter crashes and three major catastrophes with platforms collapsing in heavy seas. Thus while we may not be among the best we are certainly no longer the scapegoat. We have achieved a certain level of security accepted by the oil company managers and by the divers themselves. As far as the divers are concerned, a lot of them are reluctant to accept correct working methods, coming as they do from a community whose members see themselves as supermen.

As far as the economic situation of the diving community is concerned, the worldwide diving business has leveled off. The oil industry has not got rid of us, yet. At the same time, we cannot produce enough money to support the continuation of a good diving technology. As the oil companies' decision makers believe that diving is already a "pioneer store," they see no particular need to support our industry, which they feel in any event will not be there much longer.

Should we sit on a bench in the park and wait for a better day or should we do something to improve our situation? I do not believe in being passive, and so we decided at COMEX to see what we could do. The oil companies want to have deep water production in the 300-600 m range in the Gulf of Mexico and California (recent discoveries),in the United Kingdom, Norway, Brazil, and India. It is my firm belief that what I would call a true robotic situation for subsea production is a long way off. Offshore industry has not reached what I would call a true, reliable, and safe use of robots and remote control vehicles (ROVs) that will be able to perform all the tasks necessary underwater. I believe that we shall have to come to terms with the oil companies and become part of this robotization effort. We have a lot of experience underwater; it must not be wasted. Divers should be able to work in maximum water depth. Being involved in dives such as Hydra V proves that COMEX certainly is interesting itself in that connection. Furthermore, it is also challenging to see if we can do something better than the competition; and beyond that, we believe it is nice for our country as well as for COMEX to be among the leaders in this field.

So what we do with H_2 is in fact part of our industrial strategy to determine whether this gas can be used on an industrial basis and if so will it strengthen the COMEX position? We cannot say today, after having placed six divers at 450 m and after having had a bit of anguish in doing our first transfer from H_2 to He, that we are ready tomorrow to go deep diving in the open sea with H_2. We have a number of things to do before that.

In the first place we must see what our limits are and after we have discussed our programs with our partners and friends, we will try to perform an experimental dive that will be either an open sea experiment or another simulation test of the effects of H_2 in the 500-700 m range. We plan to see what the amount of H_2 in the mix needs to be. Dr. Fructus is for 300 msw; I am for 400 msw. We might find something in between, or we might gradually increase the amount of H_2 in the mix according to the degree of narcosis during the first few days of exposure. We will do this sometime in the fall of 1986. But the ultimate proof is of course a series of dives at sea, something between 400-500 m, provided we can raise sufficient financing and a DSV for the 3-4 wk it will take to prepare the piping and everything else to handle H_2 mixes, and another 4 wk for operations at sea.

With regard to this project we are still hesitating between two possible strategies. One would be to use one of our COMEX 300-ft barges in Marseilles and put aboard it our 600-m saturation system and related gear we built for Hydra V, and then to tow it to a suitable place near Marseilles, for instance off Cassis, where we can find 600 m of water only about 5 miles

from shore. There it will be exposed to the Mistral and to the east wind, but it is close enough to call our divers back in case of trouble or bring the whole system back to shore if bad sea conditions arise. That is probably the cheaper way to do it but it will still run between $5-6 million if I include the cost of mobilizing a hull system for only one operation.

Another way would be to employ a large lockout submarine (500 ton displacement) we are developing today, the *Saga*. We started on *Saga* 2 yr ago in cooperation with IFREMER, the French Institute for Ocean Technology. The *Saga* pressure hull was originally built by Cousteau in 1972 under the name of Argyonète with government money, so that French taxpayers have already paid in part for this development. We acquired the *Saga* hull in 1983 and are now about a year away from launching. This project will run about $22 million total budget in France for its first Stirling configuration. She will then be powered using two closed-circuit Stirling cycle engines that we acquired from Subpower in Sweden. This is a development we are in fact doing in conjunction with the Swedish Navy. (We ordered four engines, two for *Saga* and two for the Swedish Navy.)

The first engine will be ready in December 1985 and the second one in May 1986 after performing approximately 1000 h of tests in a pilot plant in Malmö. We should have our submarine in the water in September or early October 1986 in Marseilles where we have the *Saga's* shop and offices and a lifting system to put the submarine in and out of the water. We will then of course not yet be ready to use it in connection with H_2 diving as we will have a year of tests to perform in the beginning. We expect to be looking for an experienced submarine captain in the first 3 or 4 mo of 1986, and we ill then begin to gather a crew. Then, probably beginning in 1987, we will start our heliox lock-out dives.

What I would really like to do are long dives. With our submarine we have up to 1 mo capability for staying underwater. We shall have with us approximately 12,000 kilowatt h of available energy, and since the engines use a thermal bypass recovery system we should produce sufficient hot water to heat the divers. For the beginning we think in terms of missions of 150-200 miles back and forth with divers locked out of the pressurized hull section every day or twice a day for 5-10 d of operations in depths of water somewhere between 100-200 m, in other words under classical easy diving conditions. Then it is my intention that, if we can find some way whereby COMEX will pay only 50% of the bill, we will try to do a H_2 dive in the 400-600 m range. That will be more likely in late 1987, so early because we are designing lockout chambers, regeneration, gas storage and circuits, piping, and conditions for diving aboard the *Saga* for H_2 utilization.

If these tests are successful, then I think we will conduct a crusade to convince our clients that H_2 is not all that bad. After all, the stuff the oil companies handle every day in production units may be worse than the H_2 which we should have to use. Certainly the oil industry has plenty of experience handling explosive situations and we will try to convince them that after all, we too, should be able to use H_2 on their rigs and platforms where they might reserve a little place in their explosive area for their subsea workers. I believe that with our technology we should be able to

produce piping and valves and controls to use H_2 safely. After all in the United States you distribute methane gas in cities into the kitchens of people with piping of a quality which is surely inferior to what we can produce and what we will use with H_2. Thus we believe that we should be able to handle it much more safely than the household gas which is a matter of everyday experience. The question is how can we convince the oil companies many of whom now are emotionally against H_2. They certainly believe that if they allow us to use H_2 something bad is inevitably bound to happen.

Of course, some countries are probably more ready than others to use H_2. I was talking recently with top executives of Petrobras in Brazil where they have the same problem as many countries with commercial balance in buying He in hard currency. They are buying their He outside Brazil and it costs around $ 15 million a year. If we can improve their trade balance by substituting H_2 , which they know how to make in Brazil, for He they must buy, they will like that very much. Furthermore, in some oil-producing countries you do not have the sense of strict regulations you might meet for example in Norway. In those countries they say, "Why not try H_2?" I do not forecast the common use of H_2 before 1989-90. By that time we shall have gone through design and construction of new equipment specifically intended for H_2 utilization. In any event at COMEX from now on, especially after Hydra V, all our equipment will be designed to be H_2 compatible.

What will be the future of deep diving in terms of what depths we will reach, what will be the equipment of divers--I think all these questions can be answered only from a crystal ball. You of course know that in parallel with the diving industry a large fleet of ROVs are being built. There has been an explosion of ROVs built in the last 5 yr. I think every university dealing with oceanography dreams to have its own "toy" and plays around with a more or less successful ROV prototype. We ourselves probably developed our own first ROV far too early. That was in 1970 and we called it TOM 300. I would say this was at least 10 yr or so too early, as even in 1980 a ROV was still a curiosity for many users. Whereas today, you have a whole collection of series-produced ROVs, in other words ROVs of which there are more than 10 units out in use.

EDEL: Excuse me, could you say why it may have been too early?

DELAUZE: In 1970, the oil company strategy makers were screaming for remote control help. They wanted to use robots for everyday simple tasks already well in hands of the professional diver and they were just not ready for it. And when we talked about what we could develop with their money, or course, the answer was, "Oh, for that job why do you need all this stuff?" You need to realize that the oil industry is by instinct a very conservative industry, except when they are faced with something they cannot reach at all. It is a fact that the oil industry will use tools that are appropriate for their immediate purposes with, except for a few examples, very little foresight and imagination. They have certainly kept up with the diving technology; all you need to look at is the dives they have sponsored over the last few years in the 400-500 m range. I am convinced that the economists in the oil companies are presently looking at their plans and discov-

ering that to go to truly robotic installations will require an enormous amount of time and money. At this point they may come back to us and say, "Look, let us try to combine our strategies, even if we've been far apart for the last 10 years." I believe that a constructive association between man in the water and the man on deck watching a ROV performance in a TV monitor is presently the only way to operate in the ocean. I simply do not believe that one can perform without the other. I think the steps we are discussing here of introducing H_2 into the subsea industry are in the right direction and I feel convinced that in the near future, extending the range of the diver in good working conditions is an important strategy.

DISCUSSION FOLLOWING PRESENTATION BY DELAUZE

BRAUER: Thank you, Henri, for a magnificent summary of the kind of thing that was in the background of many of our discussions but falls largely outside the range of knowledge or experience of those of us who are primarily scientists and technological people. I might, in passing, tell you that even as our conference is going on I gather that our good friends at the Shell Oil Company are dispersing a very sizable amount of money for the purpose of discovering a "new" diving gas while at the same time they have been unwilling to send anybody to this particular meeting. Presumably this is a nice illustration of the very kind of point on which Henri has just been commenting.

I think that perhaps as we enter upon this final round of discussions and round tables designed to pull together the judgments and conclusions to which we have listened for a few days, it might be useful to have in mind the curve of working depths as they have developed over the years. In the early 1930s surely effective diving depth was little deeper than 40 m. During the late 1930s the *Squalus* salvage was accomplished at a depth of roughly 100 m, and the jump in depth reflects directly the impact of the introduction of He into diving technology in the mid-1930s. From then on until the late 1950s and even into the early 1960s the figure changed very little. In 1962, 40-50 m still was the depth at which commercial diving was effective, and greater depths, to 100-150 m, remained very much the exception. A major burst came again during the mid- and late 1960s with the introduction of saturation techniques that got us in fairly short order to the 300 m level as something realistically and commercially feasible by the early 1970s, and a very slow creep to effective diving depths toward 400, or as you have just heard, 450 m by the early 1980s. One of the questions I think we should discuss before we break up is whether, in what remains of the 1980s, the introduction of H_2 will give us another jump in the curve of practicable depths, and if so, whether it is possible to anticipate the limits which this might make realistically attainable.

DELAUZE: Let me make a practical comment. Let's take as an example the situation in Brazil. With the best techniques on hand we are today able to undertake reasonably and safely work at 450 m. In fact, only three diving companies in the world have this capability and of them only COMEX has actually had divers in the sea at that depth; the others haven't been there

yet. In Brazil where they accept bids from anybody as long as it is the cheaper bid, there is now a tender for a job at 450 m. If we except the three above contractors, two companies that never have gone any deeper than 150 m have answered that bid and declared themselves able to work at 450 m tomorrow!!

I would like to add something to what I said earlier, namely to inform you that the *Saga* I after its steering tests starting at the end of 1986, will probably be used in 1987 in some kind of test contract, just to demonstrate this new strategy in deep diving services. Beyond this we signed an agreement last year with ISE and ICS in Canada and have formed a new company, ISTS, the new owner of Saga I. After its commercial demonstration in European waters, the Saga will be transferred to Canada. She'll be moved there in mid-1988 where our Canadian associates are developing a nuclear plant and its energy conversion system. The unit is being developed around a 1.5 MW microreactor with a beryllium reflector and will produce warm water, no steam, at about 95°C. The efficiency of the Carnot cycle under those conditions is very low, only about 5-6%, so that from our 1.5 MW we will produce only about 100 kiloWatt electric power. This whole operation is being done in an international quadruple partnership with COMEX contributing 25% of the costs. The nuclear section and its reactor will be assembled and commissioned in Nova Scotia. This will enlarge the *Saga I* by about 10 m and *Saga I* will become *Saga N*. Integration of the nuclear system will take about 18 mo. In 1989 or 1990 then, depending upon licensing for the site for the submarine ISTS will operate the first civilian nuclear submarine. At that time the *Saga N*, which today displaces about 500 tons of water, will have a displacement of 700 tons. Then the only limitation to our stay on the sea floor will be fatigue of the crew, as the nuclear charge will be good for at least 3 or 4 y. By that time we should be able with reasonable care to go under the ice pack since we will keep steering and navigation capabilities intact. This is a sort of dream for me that I have been thinking of for many years.

Today the development of large diving support vessels could be in the age of dinosaurs. The price of a 100-m modern DSV is in the range of $30-40 million just to support a couple of divers on the bottom. Besides, if we send the divers 400 m down, it takes about half an hour for the bell to go down and as long for it to come up. Divers are then very far away from the surface habitat which is their ultimate refuge. I believe that the long-range, large lock-out submarine solution is very attractive financially as it competes on equal terms, at least, with the big support vessels. And, furthermore, I strongly believe that a diver 10-15 m from his friendly mother submarine and under direct vision from the team in the submarine will be much safer and much more useful in the water, and hence will yield more performance than one that comes from a ship that is 450 m away and from a diving bell to which he is tethered by a long umbilical. So the strategy at COMEX now is that the submarine option can be expected to be a very good solution in deep diving for the next 20 yr.

LUNDGREN: What will be the depth limit of *Saga*?

DELAUZE: At the moment, the design is for 600 m for the hull and 450 m for the diving system. But finally we expect to go to 600 m in all the components.

LUNDGREN: What will be the dimensions of the pressurized living quarters?

DELAUZE: The main caisson is 2.5 m in diameter and about 6 m long.

WELLS: There must certainly be some economic advantages to the use of H_2. Could you give us some feeling for how important, how large they might be?

DELAUZE: If we try to convince the people that the savings in terms of the gases are important we are in fact being a bit hypocritical. If one does a good job with the He recovery and uses modern diving equipment, then the difference in gas costs is really proportionately quite small, except of course for very short jobs where recovery equipment and gas storage gear is too heavy and difficult to handle and may not be so economical. But in any event, the He that is in the caisson most of the time is lost in the end. So I believe that there is a significant economy left. Besides, if one produces it in quantity, H_2 is really far, far less costly than He. Still, whatever savings one makes, they are not really big money in comparison with the total cost of diving. What is costing money in diving is the depreciation of equipment and the cost of financing equipment.

You take a DSV of $30 million, financing costs may be as much as $3 million a year. The depreciation is another $3 million so that means $6 million a year to work perhaps 200 d (and that is already a fantastic commercial achievement). Therefore, merely the costs of money and depreciation represent something like $30,000/d, so that before spending one dollar on consumables or on divers' wages or on overhead and maintenance, it costs $30,000/d just to put in 20 h of diver's bottom time. That is of course why oil companies are very nervous when they have a diver in the water and are delayed by anything, such as bad communications (and the divers' communications today are still in a prehistoric stage). A DSV meter is ticking away at a rate of $1,000/h of bottom time.

ÖRNHAGEN: We have a tendency always to discuss the very great depths, 300-450 m. What is your opinion on the possibility of using H_2 as a lock-out gas in the 100-180 m range? With today's equipment you can use it in an open system, where technical problems are much less, and still get better performance, and where you are so shallow that you can handle any temperature problems that the diver may encounter. Is there an possibility of using H_2 there?

DELAUZE: Sure, H_2 will come back to the 150-m range, or even 100 m, but the problem is in the equipment. The equipment of today is not ready to handle H_2. When we have built new equipment with the capability of interfacing safely with H_2, H_2 will be used most of the time. But this will take time and money.

ÖRNHAGEN: It would surely be interesting to use the hydrox as a lock-out gas only, and have the divers saturated in heliox. The interwater perfor-

mance for each diver is about 3.5-4 h maximum, and according to the Hydra IV dive, it seems possible to do that type of exercise and still safely come back without any counterdiffusion problems. I think that could prove to be a possibility even with today's equipment, because most equipment today could be used with H_2 as well as He. It should be possible to give a diver a better performance in the water today using H_2 as a lock-out gas.

DELAUZE: Certainly.

ROUNDTABLE DISCUSSION I: PHYSIOLOGIC ASPECTS
DOCTORS LUNDGREN, MILLER, AND DAHLBÄCK

BRAUER: When we first started this discussion, we pointed out that we really have are communities that we are talking to: One is the pharmacologist/biologist community and the other is the diving community. As you have just heard, a third important community enters into consideration--the commercial community, which in the last analysis furnishes the money that allows work to go on. Obviously, these interact. As you have heard in these discussions, a number of the observations that have been made bear on such things as theories of anesthesia, or concepts of respiratory mechanics, that are of interest from the pure science point of view. On the other hand we have colleagues like Dr. Fructus or Dr. Giry who have watched men undergoing simulated dives from the points of view of the clinician and the clinical physiologist, and these observations should allow us to test the validity or the usefulness of the conclusions drawn from the theoretical and purely experimental work as well as to point up new paths of inquiry opened up by work with perceptive subjects. Finally, all of us share a concern as to how we may reach the best judgments and the most effective projections to ensure the safety of the men who work underwater and the peace of mind and the satisfaction of commercial needs of those who take on the responsibilities for bringing the technology into the market place. These then are the general constituents under which we should consider our two roundtable discussions. We shall start with the discussions taking off from the role of the physiologists and pharmacologists.

LUNDGREN: Could I start out on a topic which hasn't attracted much comment here. I have been thinking of why that is so and I would be willing to speculate, and perhaps to get some discussion on it. That is the question of H_2's role in relation to thermal balance. From a simple calculation I made, if you go by the heat capacity of H_2 you would say that it should be somewhere in the order of 40% more effective than He in terms of carrying heat away at comparable pressures. In a way it seems lately that thermal physiology in relation to He diving has lost some of its interest, (or rather there hasn't been terribly much produced lately), but perhaps that comes from the feeling that we know how it happens, why it happens, and to what extent it happens, and the problem is not one of physiology any more but of technology. Perhaps one could take the same attitude with regard to the potential effects of H_2, except of course that it's important to remember that if our technical arrangements break down, as they tend to do at times, then you certainly are faced with the consequences of not being able to cope with the tremendous heat losses that could occur in a situation where the diver is in the sea breathing H_2 and suddenly loses his heat source. I referred in my formal presentation to the observation by Dr. Flynn and coworkers of very severe mucus production in the respiratory airways of subjects breathing very cold He at depth; such mucus production could conceivably be life threatening by choking the diver. I believe you indicated, Ed, that you retain an interest in looking further at that problem of cooling of the airway, both with regard to this new phenomenon that you observed and also to cold-induced bronchospasm. While the engineers can help us prevent many problems, there are times when they won't be

around to help us out when the need suddenly arises, and then we have to know more about the physiology and ways to modify physiology to save the patient.

BRAUER: If you look at the thermodynamic equations that govern pressure effects, it becomes obvious that all of these equations written in terms of temperature have exact analogues written in terms of pressure, although the molecular properties governing the variations of the thermodynamic quantities are different in the two series. Thus, to me it has been something of a miracle over these many years that the interaction of temperature and pressure has not found more expression in terms of comfort temperatures, or chosen temperatures in high pressure environments. We are now accumulating information to show that crustaceans and fish do exactly what they ought to be doing: An increase in pressure of 100 atm will entail as much as a 8-10° C increase in preferred temperature. If anything like this were to happen in mammals, this would be a catastrophe. Fortunately the mammal data we have indicate that the effects there go in the opposite direction--at higher pressures the chosen temperatures decrease-- and the magnitude of the change is much smaller, about -1°C/100atm. In the long run, as you go toward higher pressures, if that's what we will do, this could still become a factor worth taking into account. Of course, while this enters the thermal equation it does not answer the question that Claes raised regarding heat losses in H_2.

LUNDGREN: I'm sure that, to the extent that the H_2-breathing situation arises by accident, this would enforce the cooling and you would have a substantial reduction in body temperature before preventative or curative measures can be taken. At that point the question come in: How does it interact with high pressure and narcosis?

DAHLBÄCK: Let us look at the heat loss via the ventilation. There is a proposed standard for minimum inhaled gas temperatures as a function of increasing depth. At 150 m it is around 20° C, and the question is: Is this lower limit as proposed for He any different for H_2. Another point regarding your calculations, you calculated the heat loss from the heating of the gas from 4° C to about 37° C. It has been shown that in He at 300 m the expired temperature is something like 25°C, when the inspired temperature is around 4° C. So the heat exchange process of the airways during He breathing and probably also during H_2 breathing will modify your figures.

LUNDGREN: You may recall I said that "this is assuming, for the sake of simplicity, thermal equilibrium."

DAHLBÄCK: I assume that, too, but you will regain a lot of heat when you exhale. One thing we do not know is the heat exchange, i.e., the relationship between inhaled and exhaled gas temperature when the divers breathes H_2 at depth. This depends on both heat conductivity and specific heat. But I would guess it is similar to the heat exchange when breathing He as I mentioned before.

MILLER: There are some data for mice. Halsey published the chamber temperatures required to keep the mouse rectal probe at 37° C at high pres-

sures--70 to 80 ATA at least. He did this for He-O_2, H_2-O_2, and neon-O_2, providing at least a comparative set of data for the mouse.

BRAUER: He found that he needed chamber temperatures about 1° C higher in hydrox than in heliox.

DAHLBÄCK: If you look at the bail-out situation (emergency situation, when the umbilical is cut off and no warm water or gas can be supplied to the diver), the endurance is specified to be around 15 min for an operational dive. It has been shown during simulated dives at 500 m at NUTEC in Bergen that if the warm water supply to the gas heater is shut off, the diver will be cooled down within 1 min so he cannot move back to the bell.

FLYNN: What were the inspired temperatures in Hydra V? Divers were in the water breathing for quite long periods of time, and as I recall they didn't suffer.

BRAUER: And skin temperatures?

GARDETTE: They were not measured.

DAHLBÄCK: But you have to take into consideration both the respiratory loss and the heat loss via the suit, which will mount up to the total heat loss.

GIRY: The only solution to all you ask is to try to reclaim exhaled gas heat by using a closed circuit or semi-closed circuit apparatus.

FIFE: Does anybody know, on these cold dives that Ed is doing, what is the temperature of the blood that leaves the lungs? Is this significantly lower, and what are the consequences of that?

FLYNN: We don't have any idea what pulmonary venous temperature might be. What we did have was divers complaining of epigastric discomfort. The deeper we went the more penetration of discomfort there was, and it was in the epigastrium by 1000 ft. In terms of body temperature measured rectally they lost heat on the order of 2° C.

ÖRNHAGEN: A fair guess, I would say, is that the blood temperature is only one or maybe a degree and a half lower, otherwise you will encounter cardiac problems because the cardiac circulation comes right out of that blood from the lungs.

BRAUER: You have that portal circulation around the nasal sinuses in some of the species we are working with. I am fairly sure this was not a negligible factor, for instance, in some of the ruminant experiments. It is worth bearing in mind that not only the heart but also the brain can see some pretty improbable temperatures as a result of the very high heat capacity of any low temperature gases reaching the nasal passages in high pressure heliox or hydrox.

DAHLBÄCK: There are really two different situations: The diver in the water represents one situation, because we have mainly the respiratory heat

problem if he uses a hot water suit with a good distribution of water over the body. In the chamber he is going to be surrounded by a hydrox environment. Hydrox has a much higher heat conductivity than He, so the temperature control of the chamber will be more critical. The temperature limits are likely to be narrower than in heliox.

FLYNN: I think that as a first cut you would not have to consider thermal conductivity in the respiratory heat loss problem. One could adjust the He respiratory thermal limit curve for H_2 diving using the ratio of the specific heats of the two gases. I believe that would be a very close approximation. In terms of blood cooling, you can make some gross estimate of the magnitude from the ratio of specific heats for blood and gas and the relative flows of each, the gas flow being the alveolar ventilation and the blood flow being the cardiac output. You could then calculate the amount of heat that is transferred, and see what the temperature of the blood would be. I suspect that the blood has a very much higher heat capacity than the gas, even at high pressure, and that the blood temperature would not drop that much.

BRAUER: I would like to elicit one statement before we close this discussion: Are we all agreed that in fact, on the basis of what we have been able to hear or see so far, special thermal problems in H_2 haven't been encountered in human experiments? In the animal experiments we have only Halsey's group of mice that need a little higher temperature.

LUNDGREN: If that is to be the concluding remark in the proceedings, we have to caution the reader by saying that we have been able to control it so well only under experimental conditions, so that no one will be left with the idea that we don't foresee any problems.

IMBERT: During deep heliox dives to 100 bar the heat loss that cats are able to withstand without drop in body temperature, as shown by the work of Naraki in Marseille, is approximately 20% of the total heat produced. I think this result may apply to man. With H_2 we have to take into account a 40% increase in the heat capacity in comparison to He experiments in hydrox at 1000 m.

FLYNN: May I make just one more comment about respiratory limit curves based on heat loss. There is no guarantee that these limit curves are going to protect against pulmonary consequences. It may well be that different limit curves in terms of bronchospasm and effects on small airways are needed. To my knowledge those have not been defined previously in any situation.

BRAUER: We perhaps should try for a change of pace and ask Dr. Miller to take over the discussion.

MILLER: Well, one thing we have all agreed on is that man, mice, and tadpoles--but not newts--can be narcotized or anesthetized by H_2. This means that while we have been worrying about how H_2 will differ from He, we really ought to be worrying about how different a H_2-He mixture should be from pure He. The question then is how much H_2 are you going to add to your

He. I think someone said up to 200 m, H_2 is okay. Beyond this you would start adding He. I found it interesting that in the He-N_2 trimix dives, people were obviously trying to keep their N_2 partial pressure as low as possible because of density considerations, whereas in He-H_2-O_2 divers, we are trying to keep the narcotic status as high as possible, again perhaps because of density considerations. Whereas in the Bennett trimix they titrated to the edge of the high pressure neurologic syndrome (HPNS), in the COMEX trimix they titrated to the edge of narcosis. With He at a given pressure we will get HPNS. We can increase the percentage of either N_2 or H_2 in the He until we get narcosis. In between, we will have "safe" mixtures. However, animal studies show that the range of safe mixtures decreases as pressure increases. Indeed, at some pressures there will cease to be a safe mixture. If we could extract from the COMEX data the percent of H_2 in He just sufficient to induce, say, grade one narcosis as a function of total pressure, then we would be in a position to extrapolate to higher pressures. The theoretical basis for making these extrapolations is available and works well in mice.

BRAUER: This works well for anesthesia, but as I showed you before is worthless for HPNS antagonism until you have the data that allow you to plot the appropriate (and usually nonlinear) curve for the species you are dealing with--man in this case. And these and the pressure data we still lack.

IMBERT: May I propose a graph that would allow us to reason upon all the interesting variables that we have to consider for selecting the correct mixtures for future diving: H_2 pressure, He pressure, depth, gas density, and balance between HPNS and narcosis. The graph is obtained by plotting absolute density as a function of H_2 pressure. On such a diagram heliox binary mixtures are plotted on a vertical scale, at the abscissa origin (zero H_2 pressure), parallel to the density axis. Scale steps correspond to increments in depth and density. Hydrox binary mixtures at increasing depths produce a slanting line further to the right. With reference to heliox depth equivalents, and if H_2 and He had the same density, then the slope of the binary hydrox line would equal 1. But as H_2 is twice as light as He, then the slope is roughly 0.5. By connecting the dots that correspond to equal depths on the hydrox and on the heliox lines, we obtain a network of parallel lines, each corresponding to all the possible ternary H_2-He-O_2 mixtures that can be proposed at that depth. The ideal one would correspond to a correct balance between HPNS and narcosis. Hydra IV and Hydra V experiments allow us to plot dots for depths ranging from 240 to 450 m. According to Dr. Fructus, the optimal H_2 pressure increase slightly with total pressure owing to the pressure reversal effect. Assuming that this linear relationship is still valid for depths greater than 450 m, we have plotted values for depths up to 700 m. We can read the corresponding densities on the vertical axis, as well as the heliox depth equivalents. The line connecting all the plotted values separates the diagram into two broad areas: on the left the HPNS area, and on the right the H_2 narcosis area. In fact, the precise course will only be determined by future experiments, but at 700 m--the goal set by Mr. Delauze--a predictable H_2 pressure would be about 28 bar, with a gas density equivalent to about 74 m of seawater. With this figure in hand, Dr. Lundgren can estimate for us

what maximum respiratory exchange is possible, how much CO_2 retention to expect, and so forth. Note also, that the diagram at bottom englobes binary hydrox diving at moderate depths, from 80 to 180 m as proposed by Dr. Örnhagen.

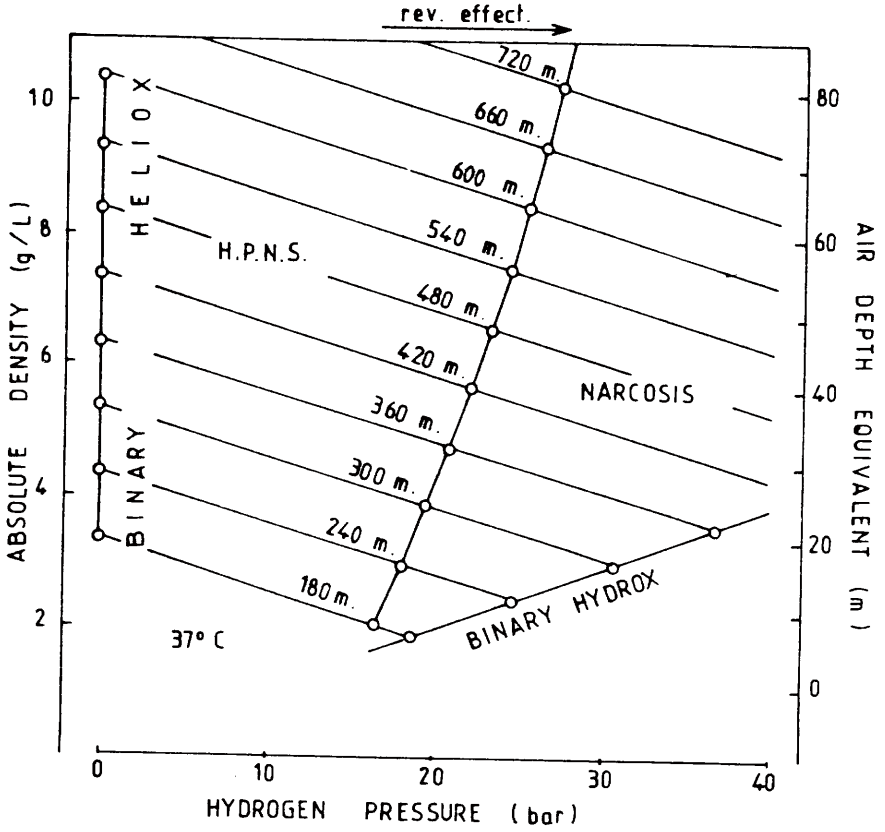

Fig. 1. Hydrogen Pressure (bar)

MILLER: Those circles through which your narcotic limit line is drawn are not experimental points, or are they?

IMBERT: Those circles were obtained from the Hydra experiments up to 450 m and represent predictions at greater depths.

ÖRNHAGEN: Okay, what you say is that you can predict at what point narcosis of a certain degree, degree one, comes on.

IMBERT: Degree two in the Hydra dives.

ÖRNHAGEN: Not even one in Hydra V.

IMBERT: I think we can draw lines for grade zero, one, two, and so forth. Again you have some estimate of HPNS, for instance increase in Rostain's tremor measurements, to give us some idea about the limits for binary heliox diving and enter that in such a graph.

MILLER: The important point I think is that as you go deeper you need to go carefully. My graph is slightly different. It plots percent H_2 in He against pressure. As depth is increased, we have one curve for onset of narcosis, and another for onset of HPNS. As we go deeper, three curves converge and the range of "safe" mixtures becomes narrower. Both approaches seem valid and should be used. Then we can see whether they will agree.

BRAUER: I am quite content with the anesthesia side of Imbert's projection. All the figures match about what we in fact predicted on the basis of the animal work. On the HPNS side, I think once again we must remember that by and large HPNS development and HPNS protection are not linearly related. You cannot draw a straight line and expect to follow it, and in the case of man we do not know yet whether those curves look like those I showed you for the squirrel monkey which bend very sharply toward the inert gas axis, or like one of the mice that goes the other way around. Until we know that, I think you need to be aware of the fact that drawing straight lines on a diagram like this is to be taken not just with a grain of salt but with a whole salt factory.

MILLER: Well, I would agree with that.

DOUCET: Schemata, like Dr. Imbert's, superimpose two totally different concepts: Physical ones, depth and H_2 content, and measurable quantities are all right. But one now superimposes in a similarly precise manner clinical phenomena which are multiparameter in their essence. Your scheme, therefore, is interesting but it does not allow you to resolve the problem or to respond to the question you have posed. The schema does not evoke any new hypothesis which would allow you to progress either with regard to the HPNS or the narcosis.

BRAUER: I totally agree, and frankly I would like to extend the comment to that other diagram of Dr. Miller which seems to me to be open to the same kind of reservation.

DOUCET: Yes, I quite intended to see that included in my comment!

MILLER: The important point is that in this treatment which is very empirical you do not assume that you understand narcosis. What you assume is that you can take one reproducible clinical piece of behavior, and that whatever the mechanisms which operate, if you have some data to begin with, and only then, can you make valid predictions. I agree with you, Dr. Doucet, the method does not help you to predict whether you are in one, two, or three, or whatever. If you tell me at which mixtures and pressure you have grade two, then I can estimate what the mixture should be for some other conditions. It does not help you understand the syndrome, that is correct.

DOUCET: I regret that the interindividual variation is of such magnitude that what you have marked as the safe zone can vary to such a degree that one has no notion at all of where to go.

FRUCTUS: One should not discard too readily diagrams combining physical and clinical data. As an example, a graph showing survival times of men exposed to the sea as a function of water temperature is useful, although to make precise predictions it will need to show interindividual differences. One hears much the same criticism every time one attempts a first approximation of this type. Admitting that a single experiment hardly constitutes proof, nevertheless, some time ago I made the prediction that for H_2 2 bar increase for every 10 bar would be about right. That figure certainly seems to have been near correct!

GIRY: I would now like to go on to a more practical point. What are the criteria telling us whether this or that level of narcosis is usable, or that level of HPNS is tolerable or not? As far as I can see, so many tests have been used to determine the degree of narcosis--some positive and some negative. We have to select one for future experiments in order to know what really happened. Has anybody an idea about that?

BRAUER: From the pharmacologist's point of view, we have learned long ago that comparisons of that type tend to be reproducible and valid only provided you use the same endpoint, and to the extent to which you can relate your results to a standard reference drug. I would argue that the comparison of gases among each other can be put on a very sound basis, and I suspect that you will find that that basis will not vary very widely among tests using a fairly wide range of endpoints so long as they are related to a general change in behavior. I think that is borne out by the experience with H_2. The operational question unfortunately is the equivalent of the old pigeon vomiting test for determining how much digitalis you have in a particular leaf infusion by seeing how much of a given infusion you have to give to make your pigeon vomit. That depended upon the breakfast the pigeon has, the mood he was in, and a lot of other things. That test became useful only when one designated a standard tincture of digitalis and used the biological test only to compare that with one's unknown. In a sense we have that same problem here: While the comparison between gases is quite sound and statistically valid, the operational definition is a much subtler and less reproducible one and so far as I know has never really been achieved except by holding a specific subject repeatedly against a specific task or a specific performance and assessing the effects.

MILLER: The important thing in reproducibly measuring behavior effects in animals is that you sharply distinguish two components that you must keep separate: You must have a stimulus and you must have a response. In some of these measures of HPNS we have heard about here, there is not necessarily a stimulus. You have then to ask yourself whether the situation which does give reproducible results in a defined test is what you want operationally. Do you want your diver to be alert in the absence of a stimulus? Then you can't construct the tests I have been talking about, and you are right: things become very difficult.

BRAUER: The whole question of alertness is one which is not readily accessible to conventional pharmacological techniques. I think electrophysiologically, in terms of reticular substance, it could perhaps be gotten at but hasn't.

ÖRNHAGEN: If you want to look for narcosis, as I pointed out earlier, you must use a test where you know the alertness of the subject, otherwise you are completely at sea. You have to have a paced test. But then, I think it is also very important to measure the vigilance or the alertness as such in a subject exposed to a narcotic gas mixture. If we want to take these gases and use them in operational dives in the sea, the diver is very often in a sort of sensory deprived situation. He is very often deprived of vision; he experiences greatly reduced gravitational stress; he is there waiting for something to happen, for example, some tools to come down; and he is at best warm and comfortable. He could thus be in a largely sensory deprived situation, yet he still needs to remain alert. Thus, you have to measure the effect of H_2 on the vigilance behavior, too, and that is distinct from narcosis.

BRAUER: I think a special problem coming up here, is implicit in all this; assuming that the effects of the two gases you are comparing were qualitatively alike, you could use the sort of determination that one can make pharmacologically to make a statement to the effect that a diver that can tolerate so many percent N_2 at a given depth could be expected to tolerate such and such a pressure of H_2 at the same, or maybe some other depth. The big question before us, however, is whether in fact the assumption that "narcosis is narcosis is narcosis" is correct. I think this was implicit in some of the questions Dr. Fructus and Dr. Giry have been asking. If the answer here is negative, then all of the present discussion collapses because the two gases to be compared are not in fact qualitatively alike. I think that we must consider whether those differences are important enough to be focused on as a major research target, or whether they are merely within that noise level of miscellaneous testing procedures and as such are likely to be devoid of practical significance.

MILLER: You really need to define what you want, because narcosis is not just one thing; it is many things. You will want to know about vigilance, about various performance factors, and of course there is no reason to assume that every one of those will necessarily behave the same way with changes in pressure or gas mixture.

SMITH: Surely we are in a position now where we can properly assume that narcosis is the same with all the gases we are considering? The observations of differences in effect would seem more likely attributable to differences in the pressures at which they were studied.

MILLER: Behavioral effects have been reported where He appeared to act as a narcotic, for example, which is not what the average diver would expect.

SMITH: Can I make another point? We are assuming that with H_2 we have to tackle both the narcosis and the HPNS. I believe it very likely that drugs like those Halsey is working with will eventually provide a better attack on HPNS than any gases that we presently have: They come in forms that are not easily handled, they are short acting. I think that it quite possible that in the future we will be able to look at a single effect at a time rather than having to define one single substance that will cure every problem in

divers. In a few years I don't doubt that the narcosis will still be with us, but I do believe HPNS will be amenable to attack from different directions.

DAHLBÄCK: The question I would like to raise to this forum is: How does hydrox breathing influence the physical performance of the diver? The main factors to be considered are metabolism, muscular fatigue, circulation, and respiration. I would like to start with the last factor because it is my own area. We have shown that flow resistance will be reduced, which is a positive factor when looking at the performance. I hope we can continue to measure these resistance parameters during more dives to see whether it is true that they are linearly related to density. The dynamic compliance in our dive changed with changes in density, which I cannot explain. There was an increase in compliance with increasing density and that increase would reduce the elastic work of breathing. If this minute change is true it would favor heliox breathing compared to hydrox breathing. The question about reduced CO_2 sensitivity has been raised. Dr. Giry has shown that there is definitely an influence on the respiratory center.

GIRY: It is "likely."

DAHLBÄCK: "Likely," okay. So that remains a question mark to be studied within the area of respiration. Dr. Flynn discussed circulation.

FLYNN: There was no major disruption of any kind. Everything seemed to be just fine. That's no problem.

DAHLBÄCK: Muscular fatigue and metabolism could be discussed at the same time. Is there really truth to the subjective feeling of the divers of increased strength, of a superman feeling? Is there really an influence on the muscular function or the metabolism? I know that Dr. Örnhagen has been doing the Onset of Blood Lactate Accumulation (OBLA) test. It is measured by having a man working on a bicycle where the load is increased in steps. Before the workload is increased, a blood sample is taken and the lactate content is checked. When that passes 4 mmol/liter you say that is the OBLA level of activity and that can be correlated to the fitness of the subject. So far they have not seen any change in the OBLA level. So to summarize, the only real question mark in this area of physical fitness if the reduced CO_2 sensitivity that could be a negative factor. That is my conclusion.

GIRY: There is one paper in the literature (Friess SL, Hudack NN, Boyer RD. Toxicology and Hydrogen-containing Environments - Toxicol Appl Pharmacol 46:717-720.1978) showing decreased sensitivity to CO_2 in H_2. But, remember, in the first slide I presented, I guessed that H_2 may act on any part of the brain, and through this channel interfere with the respiration. That is to say it may be also a question of lessened perception of muscular fatigue or something like that. I am not sure it's CO_2. I have seen decreased response at high CO_2 levels; but that doesn't mean for sure that CO_2 is the stimulus concerned. Perhaps the feeling of fatigue or the information coming from other parts of the body are less stressful for the respiratory centers.

BRAUER: Do we have any experimental data on muscular fatigue to test the divers' perception of that?

GIRY: When we asked our divers some weeks past the dive, "What was the most difficult exercise?" the answer was "On heliox." You can also note that the highest work loads achieved in fact all were on hydrox. So I guess the feeling, the subjective feeling, of fatigue is modified. I know nothing about what really is fatigue, and I feel that nobody knows exactly what it is. So you can't answer that question.

BRAUER: Does anybody here know anything about the relation of the spindle reflexes to the appearance of exercise fatigue? I do not, but certainly there is evidence of change in spindle function, at high pressures.

DAHLBÄCK: There are several methods with which you can measure muscular fatigue. One is the EMG method. The power spectrum of the EMG signal depends on the traveling speed of the action potential along the muscle fibers. This speed has been shown to decrease during fatigue, thus causing a shift of the center frequency of the EMG spectrum to lower frequencies.

GENNSER: You can either stimulate a muscle through its motor nerve or by applying electrodes on the skin over the muscle. Such measurements have been made by Harris and Bennett during the Duke dives and by us during a 350 m heliox dive at NUTECH in 1983 (Bolstad et al - IXth EUBS Proceedings 1983, 91-100). We found that there is a change in the actual force developed by the muscle but the static endurance and recovery didn't seem to change.

DAHLBÄCK: It is possible to look at other muscles than the respiratory, muscles where we might be able to take biopsies and look at the glycogen deposits and other metabolites. That will give us an idea of the metabolism and perhaps muscular fatigue.

FIFE: What is the tonus of the muscles you are talking about? Are there other methods that have been used where you stimulate muscles?

GENNSER: You can either stimulate a muscle through its motor nerve or by applying electrodes on the skin over the muscle; such measurements have been made by Harris and Bennett during the Duke dives and by us in a 350 m heliox dive as stated before. We found that there is a change in the actual force developed by the muscle but the static endurance and recovery did not seem to change.

DAHLBÄCK: There is a possibility that we could look at muscles where it is possible to take biopsies to look at the glycogen deposits. That will give you an idea of one type of fatigue and of metabolism, too.

FIFE: What is the tonus of the muscles you are talking about? Are you having reduced muscle tonus? You get a sense of fatigue if you have reduced muscle tonus, and I am wondering whether that is what we are seeing, not build-up of lactic acid, for example.

LUNDGREN: Did you really mean that? By definition, if you are doing your work tests on a bicycle ergometer, you cannot have a reduced muscle tone and still be doing the same work.

FIFE: Oh, I thought they were talking about subsequent to the work?

DAHLBÄCK: No, this was a feeling of fatigue while working.

GIRY: All the tests of fatigue describe tests of an exhausted person, and the subjective feeling of fatigue is quite different. I have run exercises on the bicycle, began to be tired because I am not very fit, and then switched over to nitrous oxide. Once on the exercise I didn't care if I was tired or not. So the question has been asked not only from the muscular side but also from the CNS side, and I don't know how to measure that. We know what is an exhausted muscle and we know what is an exhausted synapse, but we don't know what is implied when they say, "I am tired."

ÖRNHAGEN: I think there are two ways to measure that other type of fatigue. The one most normally used is called the Borg scale in Scandinavia. It is a subjective scale of fatigue. The other test is called the Cope test in which you are asked to perform a certain amount of work, and you have to make a choice whether you want to go a short time with a high load, or a longer time with a low load. According to experience there are patterns that are more often found in fatigued people. The Cope test has been used before, in combat, for example, for soldiers.

FLYNN: I would like to add just one small point concerning a test that we have used in the laboratory for muscle exhaustion. It is the Wingate Power Test which I think has been used in a number of laboratories as well. This is a supermaximal exercise test lasting 30-60 s. The individual quickly fatigues, causing the pedaling rate and the work load to fall. You fit the fall in time of the work rate to what is essentially a double exponential representing the fatigue value of the two types of muscle fibers. We modified this test to a certain extent so that when the subjects are just about exhausted we suddenly drop the work load and allow recovery to take place. The threshold work load for recovery can be determined. We plan to use the Wingate Power Test in our chamber on the new dive tests. This test is easy to do because you need only a simple ergometer and a stopwatch.

BRAUER: Some of this would clearly lend itself to animal experiments, using for instance a mouse on the treadmill, and for this there is a precedent. We do have genetically specialized strains of mice with different mixes of anaerobic and aerobic fibers in their muscles, and we also have quite acceptable devices for testing the level of motivation at which exhaustion is registered after a given amount of exercise. I think these techniques are worth exploring because they allow various ways of framing one's question, are readily adapted to high pressure environments and do not cost $2 million a piece. You might be able to get the information to answer some of the questions concerning human work.

ROUNDTABLE DISCUSSION II:
CLINICAL AND OPERATIONAL CONSIDERATIONS
DOCTORS FRUCTUS, GIRY, AND ÖRNHAGEN

FRUCTUS: I would like to begin with a question already touched upon by Dr. Brauer: Does H_2 provide a mere masking of the high pressure nervous syndrome (HPNS)? Does it, for example, provide a sort of general narcosis which prevents us from perceiving the HPNS? At the very least there is one important symptom which has been seen so widely, the tremors, which the divers have not perceived during Hydra V while on H_2. As for the EEG data, I don't pretend to understand those. At extreme pressures, the animal data--mice, monkeys, even sheep--leave little doubt that the HPNS becomes a controlling factor. The animals simply will not come back up. It seems very clear that that limit is pushed deeper by H_2. Those are the questions I'd like to pose.

GIRY: I would like to try to bring some answers to one of Dr. Fructus' questions, which is, What is the limit to HPNS, and to what extent can it be the cause of death of animals? We performed in our laboratory experiments to 120 ATA using pure heliox on rats, waiting for them to die and find out why they died. It appeared to us that they died of exhaustion, just because there was no food or water. I would like to emphasize that point: If we want to go to very deep diving, it has to be in reasonable comfort, meaning that we must give our divers as normal a life as possible. During Hydra as well as Entex IX dives, on heliox the subjects had nothing to eat beyond 500 m, and that could be a limiting factor. So I find that the improvement given by hydrox on this aspect of feeding, smelling, and tasting is important. The second factor I can see would be increased work of breathing, which would lead to respiratory muscle exhaustion. But there is evidence in Bennett's data that there is some problem with long-duration exposure at very great depths with modification of muscular ventilation and in that case it seems that N_2 helps.

BRAUER: I think you have brought up at least two phenomena that I have been trying to write off as pressure effects, but that so far haven't been proven definitively to me to be so because they get tangled up with other gas effects--anorexia and dyspnea. With regard to the latter, it seems to me the observations on trimix effects during the *Atlantis* dives make a strong case linking this to a pressure effect on some excitable tissues. Anorexia, at least in animals--and I think the same is suggested by some of the human data--is a matter of appetite changes in high pressure atmospheres, at least partly relieved by inert gas narcosis regardless of gas density. So for survival, 120 ATA is not lethal in the rat. Mice show pressure effects well below 100 ATA. We carry mice to 80 ATA and hold them there for a couple of days. This process will raise their convulsion thresholds to 120-130 ATA and allow you readily to take them up to 100 ATA without HPNS seizures. If, however, you maintain them at 100 ATA for a couple of days, they will die. For the moment I tend to write this off to HPNS or anyway to a high pressure effect on something that is lethal. Still, the possibility of gas density being critical rather than the pressure cannot be excluded, and redoing this

to compare at the same total pressure H_2 with equinarcotic He mixtures, I think, would be very much worth doing.

SMITH: In terms of gas density, of course, we are now looking at lighter gases. But some interesting animal experiments have been done breathing very heavy gases, such as carbontetrafluoride. Even dogs can breathe that at 20 ATA pressure. It does look as though whatever morbid state lends to death is HPNS. While I agree with Giry that you would think that respiratory difficulty related to gas density could be an explanation, I, too, don't think it is. Animals will breathe enormously denser gases than we meet in the heliox dives.

LUNDGREN: They can even be made to breathe liquids for many hours!

SMITH: They breathe liquid, and my dogs were breathing 20 ATA of gaseous carbontetrafluoride which has a molecular weight of 90. That is an enormously dense substance.

ÖRNHAGEN: I would like to stay on the same topic and discuss the breathing, but another side of breathing. It's possible, of course, to keep on breathing at very high densities; that's been proven. But in the every day life of our divers over many days, we have to look at minor changes, and I would like to stress the fact that the quality of sleep is very dependent on gas density. The fact that divers can keep on breathing through the nose in the lighter gas is of great importance for their ability to sleep and keep on doing work for many days during saturation diving. That is what our goal is, after all, and so I think there is good reason to try to keep the gas density as low as possible.

GIRY: To come back for a moment to the anorexia problem in our experiments, the divers could choose what they wanted.

BRAUER: Yes, and they didn't want anything except liquids.

GIRY: As soon as the chamber pressure is higher than 500 m, they wouldn't eat. Furthermore, when they see the food through the porthole, it's okay. As soon as it is in the chamber, it is rejected. So, that's not a cafeteria problem.

BRAUER: That whole problem surely remains one that deserves further work.

ÖRNHAGEN: I can maybe add here that I think we should look upon the gastrointestinal symptoms as being part of the HPNS complex maybe, and things like lost appetite and very slight nausea, could very well be the result of a compression sickness or syndrome.

GIRY: But not with these very slow compressions.

BRAUER: And besides, if the problem were a "compression syndrome," would it not disappear with time?

ÖRNHAGEN: When I used the word "compression syndrome," I meant the high pressure part of HPNS.

GIRY: I should like next to raise a problem which has puzzled me since the beginning of this meeting, which I have already formulated in different ways, and which is practical and very important. How much can we rely on the divers' self-estimation? In H_2 diving a lot of the information gained from the divers is significant for all matters concerned with comfort, but this "superman syndrome" appears to me central for any practical use of H_2 for diving. It raises the question: Can we, at any rate right now, tell that a particular diver is endangering his life and doesn't notice it? There is a call for very careful check of divers under these conditions. This is my main concern.

BRAUER: I think the "superman syndrome" is distinctly a problem. It is surely composed of several entities and one of them is the anesthesia which makes the divers less aware of the effort; the other one may be the special effect of H_2 on the higher centers, that leaves the divers more cheerful or perhaps more euphoric then they would be on He or on $He\text{-}N_2\text{-}O_2$ at the same depth. The longest H_2 exposures we have seen are 5 d so far, are they not? I think the careful monitoring of various aspects of behavior and mood--especially if, as time passes we see longer experiments--might help us understand these phenomena. Many of the higher nervous symptoms may well adapt or acclimate in the course of time in man as they do in the mouse or the monkey, and this may take place at different rates for different symptoms. We certainly have evidence for this in regard to less subtle endpoints, and if those observations could be extended to problems of mood and self-evaluation in man, this might give us a hint as to what we are looking at. How about pain perception, incidentally? Has anyone measured that? After all, there are methods of doing this that should be readily adaptable to the chamber situation.

FLYNN: What about their blood drawing? They had blood drawn several times. How about the pain associated with that?

GIRY: They had a duty to give blood by whatever means it was wanted, but so far as I know they did not complain about it.

ÖRNHAGEN: The reason could be that venipuncture with a good needle does not hurt at all. If there were any capillary blood samples drawn, that might have given a little pain. Going back to the duration of the H_2 exposures--5 d was the exposure to the maximum H_2 pressure, but there were also a number of days during the decompression at slowly decreasing H_2 partial pressures.

BRAUER: True, but of course, the trouble for this kind of thing is that, as several people including yourself, I believe, have pointed out earlier, these things are relatively subtle and depend greatly upon the conditions. To make that kind of comparison between a subject at bottom pressure, and even the same subject on his way out isn't going to tell you very much. It's going to have to be done under rigidly identical conditions, even with a boredom control included, I am afraid.

ÖRNHAGEN: I would like to go back to what I mentioned earlier: We have a tendency here to focus exclusively toward the very deep dives, and we have discussed the problems with loss of appetite and nose breathing, and so on. It was shown clearly in the Hydra V dive that you cannot switch easily at depth from saturation in H_2 to heliox. But I wonder if there is still the possibility to use H_2 as a lockout mix at shallower depth. There are of course difficulties and we shall have to look into these in detail before we try to design any operational methods. For example, in regard to the effect of repetitive exposure to isobaric gas switching: Is that the same as a repetitive decompression, and between which gases can we switch? What has been done so far on humans, except for the Zetterstom dive in which they switched from nitrox to hydrox? Brian D'Aoust has shown that for goats it's possible to go from nitrox to hydrox. That would open up possibilities for the smaller diving companies to perhaps operate in shallower waters with good efficiency, using nitrox down to 50 m, and air for lockout down to 70 m, and then, maybe for the depth range from 70 down to 90 m, use the hydrox as the lockout gas. I think that that could be a possibility, and we should not forget about that depth range.

EDEL: Well, the classical excursion practice is to take a saturation depth, as in your suggestion on nitrox, and then switch for the excursion to a different atmosphere--usually heliox. But now you are suggesting hydrox.

ÖRNHAGEN: It is more a question whether it is realistic.

EDEL: According to the model used, and we think it works fairly well in a dive within limits that we can test, it suggests that if you are making a shift at the same pressure and then you come back to hydrox, the risk is mainly a function of the pressure and duration of the exposure, and there seems to be a fair amount of latitude. But if you increase the depth of the excursion, you are increasing the gas loading and on return you will have a much higher H_2 load because of the increased gradient. Therefore you window can decrease very rapidly and under certain conditions more than others. I am sure it is possible, but I think one would have to study the shift window character very carefully because an incorrect procedure in any shift could create bad problems.

LUNDGREN: Am I right to presume that doing the shift from nitrox to hydrox would be more favorable in combination with an excursion, than with He?

EDEL: Yes, I think that is correct. But now you have to come back again. You are going on an excursion.

LUNDGREN: There is a common pattern for hydrox excursion and back to nitrox saturation that could perhaps be looked at as being a way of doing operational diving.

EDEL: I think you could maybe do it both ways with some variation. You may have certain options that you can follow to increase you window, for example, coming back and going on to an intermediate mixture for a while before going on to the nitrox, or a slight increase in depth when trans-

ferring back to your habitat. There are a number of options, but I think they would have to be very carefully looked at.

FIFE: In 1977 I tried going to 200 ft, or 7 ATA absolute, on air, then increased the partial pressure of N_2 in two stages so I had 97% N_2:3% O_2, and then shifted to hydrox and went on to a depth of 300 ft, sat there for 30 min, then came back to 200 ft, and shifted back in a reverse manner. So I know it can be done. Of course, now this matter counterdiffusion may be a whole different story. However I picked up a lot of narcosis on the way back. It was worse coming back than it was going down, in terms of narcosis.

EDEL: Was this in saturation?

FIFE: No.

EDEL: Was this the same thing entirely?

FIFE: No, I realize that. But my point is that you can make the shift; I don't think that's going to be a big problem.

EDEL: You can make the shift very easily in almost any way you want from a short duration dive as long as you don't increase too greatly the loading on the slow, and possibly the intermediate, tissues. As a matter of fact, in commercial diving it has been a practice to go down on air to your bottom depth whenever that is shallow enough, and then shift over to He-O_2, and this gets extended under some conditions, and sometimes it has been 20 and almost 30 min before the divers actually went on to heliox. But when you look at the gas loading characteristics, even if they have been down there 30 min, only the fastest tissues have been loaded, so you don't really get into a counterdiffusion problem. Coming back you are reversing the process but that is the favorable direction. If you try it by exposing tissues that are saturated, or partly or heavily loaded, then it is quite another thing.

FRUCTUS: Saturation dives with excursions of the Ludion type have been experienced. We have for instance performed Nereid I with saturation to 10 or 15 m in air and air excursions to 40-75 m. First observation--and M. Gardette who was one of those divers, can confirm this--the narcosis was not reduced. A second observation is: Even though the decompressions followed carefully calculated tables and went off without evidence of circulating bubbles by Doppler, yet among the six divers after every excursion there was tachycardia, and at the end of the sequence a significant platelet drop occurred in all six divers. So, the decompressions are not fully adequate. And in any event, we have not seen any adaptation to N_2 narcosis.

REY: I would like to come back to one of the remarks made by Dr. Örnhagen. I am really surprised to see how little emphasis has been placed during the meeting on the effect of the gas mixtures on sleep, not only on its duration but also on its quality. If the effects of H_2 are in fact on the central nervous system, it is possible that we can find a different ratio between paradoxic sleep and deep sleep under hydrox as compared to heliox?

ROSTAIN: I don't know yet the results of the sleep study performed during Hydra V experiments. But on the basis of the results of 10 preceding dives with $He-O_2$ mixtures and $He-N_2-O_2$ mixtures, I think that the things are complex and it is not possible to decide what are the factors involved in the sleep disturbances. I think that practically with the tracings obtained during Hydra V comparing sleep in hydrox, in heliox, and in $He-N_2-O_2$ at the depth of 450 msw, no difference in paradoxical sleep was seen. More generally, data on sleep rhythm obtained in hyperbaric environments are complex, and I don't think at this time that we can say anything about differences between hydrox and the other mixtures before more investigations.

LUNDGREN: May I ask whether there is anything solid and useful in terms of divers' subjective impression of those evaluations?

ROSTAIN: There are few relations between the answers of the divers about their evaluations of sleep and the EEG data of sleep.

FRUCTUS: Dr. Lamy and I have followed that, and the data are really not usable. Every so often there was noise disturbing the divers and also the cots used by the divers were not terribly comfortable.

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