

THE REVIEW OF A RESEARCH PROPOSAL TO STUDY
THE EFFECTS OF 130 TORR OXYGEN ON SUBMARINERS

HELD AT THE NAVAL SUBMARINE MEDICAL RESEARCH LABORATORY
4 SEP 1986

Douglas R. Knight and Arthur B. Callahan, editors

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Approved and Released by:

C. A. Harvey

C. A. Harvey, CAPT, MC, USN
Commanding Officer
Naval Submarine Medical Research Laboratory

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EXECUTIVE SUMMARY

Scientists at the Naval Submarine Medical Research Laboratory and the U.S. Army Research Institute of Environmental Medicine have agreed to collaborate in studying the effects of oxygen-lean atmospheres on human performance. The design of that study is critically reviewed in this report.

ACKNOWLEDGEMENT: The editors wish to thank Professor Arthur B. DuBois, of the John B. Pierce Research Foundation, for chairing the scientific review.

PROCEEDINGS

Fleet Applications (LT Upchurch). The extinguishment of fires aboard patrolling submarines relies on crew action and speed of response. Therefore, anything that slows the growth of fires will assist crews in bringing fires under control. Submarines routinely operate with oxygen concentrations close to 19%. This provides crews some protection from fires, since it is believed that 19% O_2 reduces the rate of flame spread by one third when compared to the maximum allowed oxygen level of 21%. Unfortunately, further reductions of O_2 concentration make it difficult to maintain the composition of submarine air within specified limits.

The Officer of the Deck is responsible for maintaining the partial pressure of oxygen (P_{O_2}) at 140-160 torr while the barometric pressure (P_B) is 700-800 torr, provided the oxygen concentration never exceeds 21% (figure 1). He does this by "bleeding" O_2 into the atmosphere from storage banks. Reductions of P_{O_2} occur when there is an increase in crew activity, venting, or operation of the high-pressure air compressors. It is usually possible to maintain the P_{O_2} within ± 5 torr of the desired level, but there are instances when P_{O_2} drops to lower values. It is harder to maintain $P_{O_2} > 140$ torr when $P_B \leq 740$ torr (figure 1). If the lower limit of P_{O_2} were reduced to 130 torr, the Officer of the Deck could maintain 19% oxygen, as an average concentration, without concern for slipping below the current limit of 140 torr.

The other method of reducing O_2 concentration is to raise P_B of the atmosphere by the addition of hyperbaric nitrogen. There are design limitations which preclude the use of this technique on a routine basis. Sufficient high-pressure air must always be available to make an emergency ascent to the surface. Yet the air banks reserved for emergency ascent also support other engineering needs, such as operation of various valves. A gradual rise of P_B results when air-operated equipment leaks into the atmosphere. At some point, air must be compressed from the atmosphere back into the high-pressure tanks. An extra set of air banks would have to be installed in order to maintain a hyperbaric atmosphere. The current practice of snorkeling would preclude the maintenance of hyperbaric pressure, but there are instances when submarines abstain from snorkeling for long periods of time. There may also be a problem with injury to the ears by the excursions of P_B .

The snorkeling procedure is used for training, drills, and emergency procedures. The loss of electrical power requires snorkeling for operation of the diesel engine. The diesel's air intake is fed by atmospheric gas that is ultimately derived from the fan room. Outside air enters the ship's fan room through the snorkel mast. Since the air inlet is of large diameter, flooding of the ship is prevented by the action of solenoid valves in the snorkel head valve. Closure of the head valve allows a significant partial vacuum to develop in the ship, as the diesel engine

does not immediately shut down. There may be a prolonged closure of the head valve during "sink-out", when the ship is trimmed too heavily at periscope depth. The diesel will continue to draw air from the atmosphere until manually shut down, or automatically shuts down at a partial vacuum of about 5 inches mercury (ca. 630 torr). Diesel engines generally shutdown by the time P_B drops to 700 torr; but more data are needed to confirm this impression.

In summary, The SUBMARINE FIRE SAFETY COMMITTEE would like biomedical scientists to validate the use of lower P_{O_2} 's aboard nuclear submarines. To do this, specific information is needed regarding human tolerance for living in the cross hatched area (figure 1) of an expanded oxygen zone. In order to minimize the chances of a fire, the COMMITTEE wishes to encourage submarine commanders to operate with oxygen concentrations below 19% by publishing the idea in the atmosphere control manual.

Research Design (CAPT Knight). Sea-level residents are accustomed to working in 21% oxygen (160 torr O_2 -600 torr N_2). Reductions of oxygen concentration interfere with thermal decomposition and aerobic metabolism, resulting in suppression of fires and impairment of human performance. But, human activity need not suffer from hypoxia if physiologically acceptable P_{O_2} 's are maintained by a life-support system. Man could perform quite effectively when breathing 11% oxygen at P_{O_2} 130 torr, if the life-support system used hyperbaric nitrogen to maintain barometric pressure at 1182 torr (equation 1).

$$(1.) \%O_2 = 100(P_{O_2}/P_B)$$

Industrial activities flourish in nitrogen-based atmospheres containing 130 torr oxygen. For example, the residents of Denver are quite productive in performing skilled tasks and sustaining their community. The same is true of Air Force Crews operating at cabin altitudes of 5,000-8,000 ft. Therefore, it's reasonable to suspect that submariners could successfully operate with similar deficiencies of oxygen.

There are instances when the artificial atmosphere of a submarine must be exchanged with Earth's natural atmosphere. If the submarine atmosphere is hyperbaric, sudden reduction of the ship's internal pressure to sea-level will diminish the crew's P_{O_2} . During snorkeling, the diesel engine can create a partial vacuum in the ship during closure of the head valve. In the worst case, P_{O_2} could drop to 95-100 torr.

PROPOSAL. Before the Naval Medical Command sanctions the lowering of P_{O_2} to 130 torr, experiments must demonstrate that crews can effectively perform their duties in the unique environment of a nuclear submarine. Before conducting sea-trials, we wish to document the responses of submariners to an oxygen-deficient environment. The submarine atmosphere will be simulated by contaminating the atmosphere of a hypobaric chamber with 10 ppm carbon monoxide and 0.9% carbon dioxide. According to shipboard practice, the subjects will live an 18-hour day that is divided

into 6 hours of sleep and 12 hours of activity. Different groups of 11 men will be exposed to P_{O_2} 's of 160, 130, and 100 torr at sea-level pressure (figure 2). This means the groups will breathe 21%, 17%, and 13% oxygen. Accidental, prolonged operation of the diesel engine during closure of the head valve will be simulated by superimposing a 6-hour reduction of barometric pressure to 576 torr on the group exposed to 17% oxygen. Five days will be spent in training the subjects for their 8-day exposure. An additional 1.5 days will be used to observe their recovery.

[Discussion. The effects of confinement and changes of circadian rhythms would be controlled by the exposure to 21% oxygen. There is a potential problem with using smokers, since performance may be altered as a function of withdrawal rather than hypoxia. The simulation of a partial vacuum may cause some subjects to develop acute mountain sickness in less than 6 hours.]

USARIEM's Altitude Chamber (Dr. Cymerman). The 12-man altitude chamber has been in operation since 1966 and currently supports 2000 man-hours of experimentation per year. It is designed to maintain a constant environment over a long period of time (eg 7 weeks) and supports test procedures as elaborate as cardiac catheterization. Low pressures are maintained by the Venturi principle. Subjects usually live in the 2200 ft³ room (20 X 30 ft), conduct personal hygiene in the air lock (500 ft³), and perform tests in the 1100 ft³ room (9 X 10 ft). There is one pass-through in each room. Fire extinguishers are located inside the chamber. The climate is controlled within the following limits: 0-50,000 ft simulated altitude; 20-80 $\pm$ 5% rh; and -20-110 °F. The air masks vent to the chamber atmosphere. The chamber is operated by 3 trained technicians that work in 8-hour shifts. A medical aid room is located near the chamber.

A control system is being installed for the purpose of maintaining concentrations of oxygen, carbon dioxide, and carbon monoxide within levels required for this study. The performance of the system will be tested in December, 1986.

There are two problems with exposing 11 subjects for 8 days. First, Army bunks will only permit sleeping accommodations for 8 subjects in the 2200 ft³ room. The use of 11-12 subjects would diminish the floor space per man to unacceptable crowding. Second, frequent entry through the air lock will make it difficult to control the atmosphere's composition. For this reason, it's important to know how many investigators will enter the chamber and how frequently.

[Discussions. Three tiered bunks could be used for sleeping accommodations. The number of investigators entering the chamber could be reduced by training the subjects to perform their own testing. The lock's atmosphere could be isolated until it approximates that of the subjects' atmosphere. Also, a barrier could be placed outside of the lock to diminish convective mixing of outside air with that of the chamber atmosphere.]

Army Applications (Dr. Cymerman). USARIEM scientists have never studied normobaric hypoxia. The proposed exposure to P_{O_2} 95-100 torr, by simulated snorkeling (figure 2), should cause headaches² within 4 hours. But "staging", by exposure to normobaric P_{O_2} 130 torr, could protect men from acute mountain sickness resulting from rapid ascent to a simulated altitude of P_{O_2} 95-100 torr.

Proposed Measurements. Group discussion suggested that procedural tests (eg timed performance of memorized tasks) are resistant to hypoxia, but decision making is susceptible to hypoxia. Submariners commonly encounter new problems requiring mathematical solutions during ships' operations.

VISION. Scotopic vision and field-of-vision may change in P_{O_2} 100 torr. Scotopic vision will be measured in a dark room by asking² the subject to report his detection of a low-intensity, pin-point light. The field-of-vision test will be performed in the 0-180° meridian using colored LED's. The LED's will detect visual sensitivity to red, white, and green, since these are the important colors for periscope operators.

MENTAL PERFORMANCE. NSMRL's battery of psychomotor performance tests seem appropriate for use, since they are sensitive to nitrogen narcosis and cannot be memorized. All tests will be administered to resting subjects. Select tests will be administered while the subjects exercise for 20 minutes at 65% of their maximum capacity. Maximum capacity is defined as the peak work load achieved while breathing 160 torr oxygen. Before, during and after exercise, the subjects will rate their perceived level of exertion.

HEALTH AND MENTAL STATUS. Each subject will be questioned periodically about his mood and perception of health. Moods are not expected to change at 130 torr, but may change at P_{O_2} 100 torr. The changes of mood are expected to be transient and could² disappear after 24-36 hours of exposure to hypoxia. An environmental symptoms questionnaire will be used to evaluate any symptoms of mountain sickness reported by the subjects. The questionnaire has been validated by field use at Pike's Peak.

Measurements of serum enzymes have been selected to screen for liver damage. Alveolar and arterial gases will be measured to document changes of oxygen stores in the body.

Discussion of Proposed Tests. The amount of time for experimentation could be a problem since 11 subjects will require at least one hour per investigation. Subject motivation is another factor potentially affecting the test scores.

Would two weeks of exposure uncover symptoms of mountain sickness that might otherwise be missed using shorter exposures to P_{O_2} 130 torr? Probably not since physicians at Denver have reported the effects of altitude to appear in the first few days of exposure.

Measurements of serum enzymes do not test the effect of hypoxia and atmosphere contaminants on the function of cytochrome P-450. This would best be approached by use of experimental animals such as the laboratory rat. The discomfort associated with sampling of arterial blood may cause the subject to hyperventilate. If so, the arterial oxygen content would not be an accurate index of oxygen stores in blood. It would be better to measure oxyhemoglobin saturation non-invasively and assume that alveolar P_{O_2} equals arterial P_{O_2} .

Discussion of Experimental Design. Some people respond differently to hypoxia. If there is wide variation of responses between subjects, eight may be too small a group for testing mental performance. The way to judge adequacy of sample size is to perform a power analysis. An alternative method would be to select subjects predisposed to hypoxia. For example, the Cherniack test requires a candidate to take 3 successive breaths of nitrogen before resuming ventilation with air. Individuals with insensitive carotid bodies, as judged by a weak hyperventilatory response to nitrogen, would be more susceptible to hypoxic deterioration of mental performance.

[Discussion then indicated that three Laboratories have been performing hypoxia sensitivity tests. To date, the results have been non-uniform.]

The double blind protocol will be very difficult to perform. For example, a decision must be made whether air masks will be routinely worn by the investigators. The masks dump air into the atmosphere, making it difficult to control the oxygen concentration. Yet, wearing of the masks during exposure to P_{O_2} 100 torr would be informative to the investigators. Smoking may break the code since P_{O_2} 100 torr is not expected to support flaming combustion.

Should different groups of subjects be used for each P_{O_2} (between-subjects design), or should the same group be used for all P_{O_2} 's (within-subjects design)?

FOR DIFFERENT GROUPS- Each person could serve as his own control by performing all tests during the baseline (training) period. In that case, it would seem advisable to conduct training in the chamber.

AGAINST DIFFERENT GROUPS- There may not be enough statistical power in the tests to show a statistical difference between small groups.

FOR SAME GROUP- A repeated-exposure design increases the statistical power of the tests, since the comparison is within subjects.

AGAINST SAME GROUP- Hypoxia may stimulate physiological responses which remain for some time after the subjects return to 160 torr oxygen. For example, 100 torr oxygen can stimulate erythropoiesis. This presents the problem of determining when de-adaptation is complete. Repetition of exposure provides the subject a learning experience that improves performance.

An alternative is to perform a severity study, in which P_{O_2} is dropped until the subjects show decrements of performance.

Do the subjects need to be submariners? Submariners are the target population for this research. They are a homogenous subpopulation of Naval personnel who share the attributes of good health, motivated service, and tolerance of confined spaces. On the other hand, it is not absolutely necessary to use submariners since divers and soldiers have successfully performed the proposed battery of psychological tests.

SUMMARY

There are good reasons for doing the collaborative study. The Navy would like to operate submarines with crews exposed to 19% oxygen. It is therefore desirable to reduce the permissible limit of P_{O_2} from 140 to 130 torr. Snorkeling rarely drops a ship's internal pressure below 700 torr, but accidental circumstances could create a partial vacuum of -5 inches mercury. The effects of reduced oxygen concentration and partial vacuums can be studied in an altitude chamber.

The selection of physiological and psychological tests is appropriate, except for collecting blood samples which attempt to measure arterial oxygen content and detect damage to organs such as the liver. The exposure time of 8 days is appropriate in the absence of data showing that longer exposures at 5,000 ft altitude cause delayed onset of mountain sickness.

Discussions uncovered the problem of using a within-subject versus between-subject design. Repetitive exposures of the same men to all conditions would increase the investigators' chances for observing changes of performance in relationship to ambient P_{O_2} . But improvement with practice might disguise an effect of hypoxia. The use of different men for each P_{O_2} would introduce the possibility that subject variability prevents observation of statistically significant effects.

It is difficult to design a field study until results of the chamber studies are known.

ADDENDUM- A FOLLOWUP TO THE MEETING

Power analyses of within-subject designs were made of the proposed psychological tests. Dr. Banderet analyzed the results of an altitude chamber exposure to 4,200 m (13,800 ft) and 15°C. Measurements were taken at 1 and 4 hours after ascent. The subjects' scores at altitude were compared with their performance at sea-level. The order of presentation to both pressures was counterbalanced. The most sensitive data for each test were used in the power analysis calculations (generally the 4 hour measurements).

<u>TEST</u>	<u>POWER ANALYSIS</u>
CLYDE MOOD SCALE	11 SUBJECTS
MULTIPLE ADJECTIVE AFFECT CHECKLIST	12 SUBJECTS
ENVIRONMENTAL SYMPTOMS QUESTIONNAIRE	7 SUBJECTS
ADDITION	12 SUBJECTS
CODING	6 SUBJECTS
MAP-COMPASS	20 SUBJECTS
NUMBER COMPARISON	6 SUBJECTS
PATTERN RECOGNITION	15 SUBJECTS
TOWER	50 SUBJECTS (index A)
	7 SUBJECTS (index B)

Dr. Rogers determined that ≥ 14 subjects were needed to achieve significant results ($P < .05$, 2-tailed test) from a MATH TEST, if the subjects were tested under conditions of hypoxia or nitrogen narcosis. His analysis was based on a power level of 0.8 and the standard deviation was ± 5.5 . He assumed a correlation of 0.6 and a mean difference of 3. More subjects would be needed to achieve significant results if a between-subjects design were used.

The power analyses suggested that at least 12 subjects be exposed to all levels of hypoxia by a within-subject design. Figure 3 depicts a mixed-design which exposes ≥ 16 subjects to 160, 130, and 100 torr oxygen. The design permits evaluation of the effect of a partial vacuum on crew performance. After 5-6 days of training (T), the subjects will live inside the altitude chamber for the entire period of time shown on the graph. Performance at P_{O_2} 160 torr will be measured during the baseline (B), first-recovery (R_1) and second-recovery (R_2) periods. The durations of these periods equal the length of exposure periods (E_1, E_2). Symptoms of hypoxia (ie, acute mountain sickness) should develop within 72 hours of oxygen deficiency; therefore, the times of exposure (E_1, E_2) will be 72 hours plus time for breathe-down. Illness from hypoxia should disappear

within 1-3 days of returning to 160 torr oxygen. A partial vacuum will be imposed on the subjects at the end of exposure to 130 torr oxygen, which corresponds to event S_2 for group A and S_3 for group B (figure 3). The tests of tolerance for partial vacuum will be administered during events S_1 , S_2 , S_3 , and S_4 (figure 3).

The breathe-down time to 13% oxygen is estimated to be 33 hours aboard an SSN-578 class submarine, compared to 9 hours in USARIEM's hypobaric chamber.

There are 2 problems with using the mixed-design: First, the development of acute mountain sickness during one level of hypoxia may degrade performance in the next level of oxygen. Second, performance may improve as a function of experience at the task; yet there is no control exposure for the effect of experience. These problems seem to be manageable. First, recovery from the symptoms of acute mountain sickness should be accompanied by return of baseline mental function. Second, the effect of experience is assumed to be resistant to the levels of hypoxia imposed on the subjects.

A problem could arise from using the 18-hour day (see page 2), since the probable shift in circadian rhythm of body temperature could degrade human performance. Unless the effect of circadian rhythm is specifically controlled, a circadian effect could not be distinguished from a hypoxic effect.

PARTICIPANTS

CHAIRMAN

Dr. Arthur B. DuBois, MD
Professor and Director
John B. Pierce Research Foundation
290 Congress Avenue
New Haven, CT 06519
(203)-562-9901

SPEAKERS

LT Jeff Upchurch, USN
Chmn, NAVSEA Submarine Fire Protection Committee
Code 92D
Naval Sea Systems Command
Washington, DC 20362
autovon 222-1566
(202)-692-1566

Dr. Al Cymerman, Ph.D.
Director, Altitude Research Division
U.S. Army Research Institute of Environmental Medicine
Natick, MA 01760
(617) 651-4852
autovon 256-4852

CAPT Douglas R. Knight, MC USN
Dept of Biological Sciences
Naval Submarine Medical Research Laboratory
Submarine Base, New London
Groton, CT 06349-5900
(203)-449-2508
autovon 241-2508

DISCUSSANTS

Paul B. Rock, D.O., Ph.D.
Major, Medical Corps, US Army
Altitude Research Division
U.S. Army Research Institute of Environmental Medicine
Natick, MA 01760
(617) 651-4802
autovon 256-4802

Louis E. Banderet, Ph.D.
Health and Performance Division
U.S. Army Research Institute of Environmental Medicine
Natick, MA 01760
(617) 651-4850
autovon 256-4850

Mr. James Devine
Altitude Research Division
U.S. Army Research Institute of Environmental Medicine
Natick, MA 01760
(617) 651-4820

Dr. Arthur B. Callahan, Ph.D.
Director, Dept of Biological Sciences
Naval Submarine Medical Research Laboratory
Submarine Base, New London
Groton, CT 06349-5900
(203)-449-2539
autovon 241-2539

Dr. Saul Luria, Ph.D.
Director, Vision Dept
Naval Submarine Medical Research Laboratory
Submarine Base, New London
Groton, CT 06349-5900
(203)-449-2527
autovon 241-2527

Dr. William Rogers, Ph.D.
Behavioral Science Dept
Naval Submarine Medical Research Laboratory
Submarine Base, New London
Groton, CT 06349-5900
(203)-449-2521
autovon 241-2521

Dr. Donald V. Tappan, Ph.D.
Dept of Biological Sciences
Naval Submarine Medical Research Laboratory
Submarine Base, New London
Groton, CT 06349-5900
(203)-449-2515

LCDR Jeffry Bowman, MSC USN
Dept of Biological Sciences
Naval Submarine Medical Research Laboratory
Submarine Base, New London
Groton, CT 06349-5900
(203)-449-3419

Mr. Arthur Messier, MS
Dept of Biological Sciences
Naval Submarine Medical Research Laboratory
Submarine Base, New London
Groton, CT 06349-5900
(203)-449-2537

Mr. James Dougherty, MS
Dept of Biological Sciences
Naval Submarine Medical Research Laboratory
Submarine Base, New London
Groton, CT 06349-5900
(203)-449-4680

Ms. Elly Heyder, MS
Dept of Biological Sciences
Naval Submarine Medical Research Laboratory
Submarine Base, New London
Groton, CT 06349-5900
(203)-449-2511

HM1 Daniel Francis, USN
Dept of Biological Sciences
Naval Submarine Medical Research Laboratory
Submarine Base, New London
Groton, CT 06349-5900

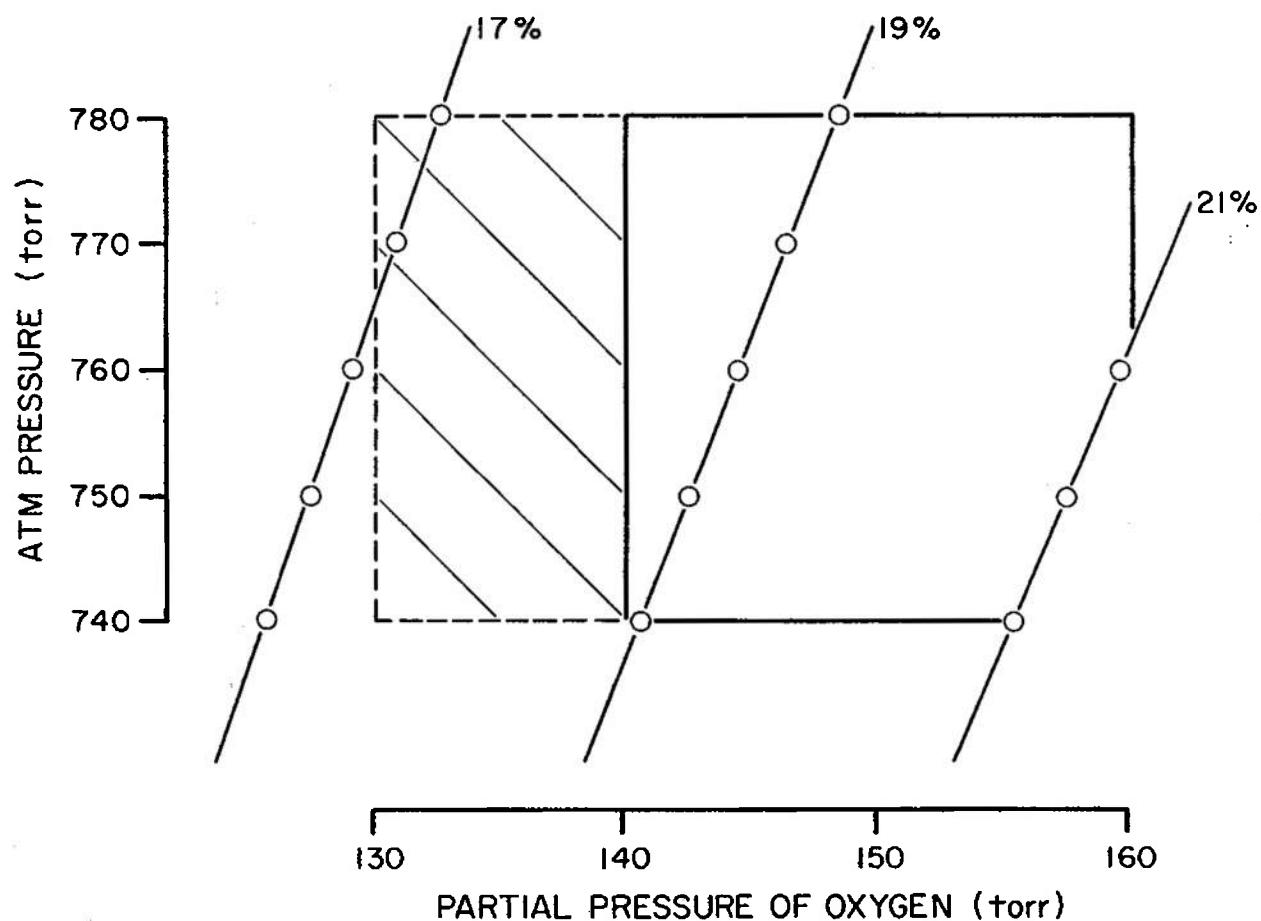


FIGURE 1. THE OXYGEN ZONE ABOARD SUBMARINES. Submarines currently operate with P_{O_2} 's of 140-160 torr (clear area of the figure). The objective of research is to determine if crews can operate effectively at P_{O_2} 's 130-140 torr (cross-hatched area of the figure).

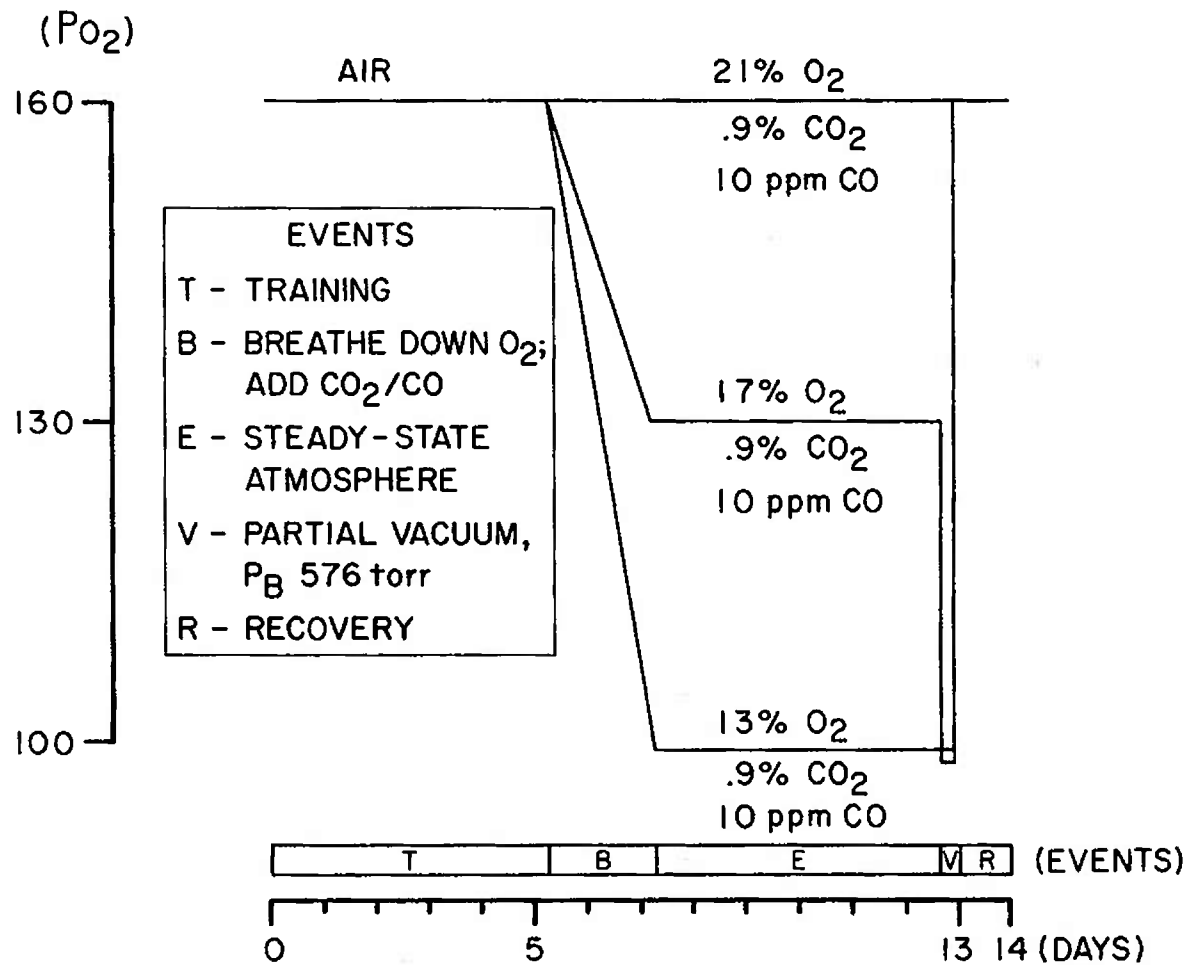


FIGURE 2. PROPOSED DESIGN FOR CHAMBER STUDIES. A different group of subjects would be exposed to each percentage of oxygen. The CO_2 and CO routinely contaminate submarine atmospheres at the indicated concentrations.

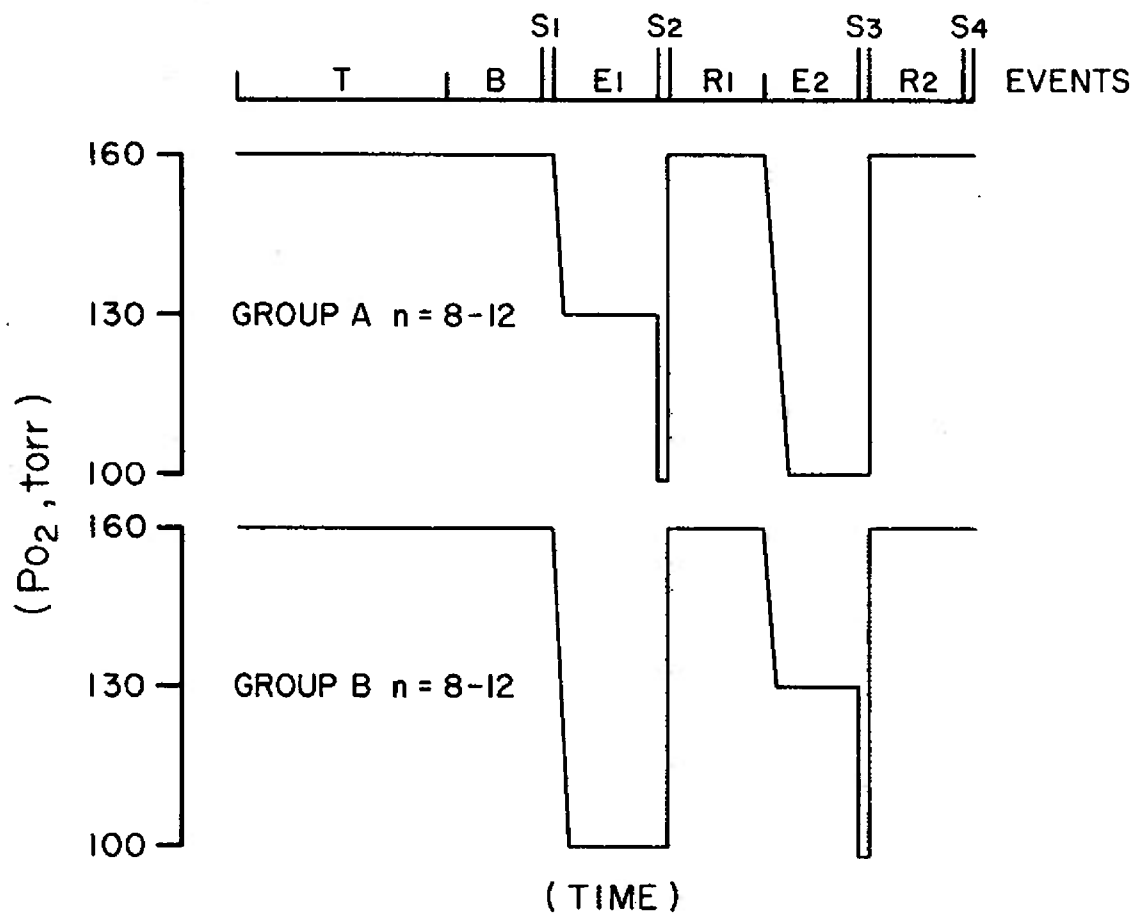


FIGURE 3. MODIFIED DESIGN FOR CHAMBER STUDIES. Two different groups of subjects would be exposed to the same partial pressures of oxygen. The same levels of CO and CO₂ contaminants would be used as indicated in figure 2. SYMBOLS for the events: T, training; B, baseline period; S, simulated partial vacuum; E, exposure; R, recovery.

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