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Key Documents of the Biomedical Aspects of Deep-Sea Diving

SELECTED FROM THE WORLD'S LITERATURE
1608–1982

Volume I

CAISSON AND TUNNEL WORK

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CAISSON AND TUNNEL WORK

ALBERT R. BEHNKE, JR., M.D.

In his chapter on High Pressure, Paul Bert (1878) outlines the early history of pressurized tunnel operations beginning with the innovation of the caisson by Triger in 1841, the recognition by Pol and Watelle in 1854 of the etiology of decompression sickness and recompression as a therapeutic modality, and problems encountered in the construction of the Eads bridge across the Mississippi River in St. Louis in 1869. Another account of the St. Louis operation is given by Jarcho (1968) and relates the experience of the physician on the project, Alphonse Jaminet.

The paper by Heller, Mager, and von Schrotter (1895) describes the extensive pathology recorded in caisson operations in Austria at the turn of the century.

Bornstein (1914) records the early German experience during the course of pressurized tunnel operations under the Elbe river.

Early experience and progressive alteration of decompression tables are recapitulated in the excerpts of a report by Behnke (1968). Noteworthy in these excerpts is the extensive report of F. L. Keays (1909) which embodies a description of 3,692 cases of decompression sickness of which 20 were fatal. The phenomenon of habituation to pressure was recognized at this time.

Subsequently, Thorne (1941) reported 300 cases of decompression sickness in the New York Queens Midtown Tunnel project. Kooperstein and Schuman (1957) reported the results of improved decompression tables based on U.S. Navy format. Only 44 cases of decompression sickness occurred during the course of the Lincoln (Third Tube) Tunnel project (1955–1957). In this operation the curtailed periods of work shifts,under pressure commensurate with worker safety, tended to render pressurized tunneling economically prohibitive.

In 1969, Dr. J. L. Sealey, Medical Consultant to the Municipality of Seattle and Metropolitan Engineers, organized a committee to revise decompression tables for compressed air workers directed to safety and economic feasibility. Preliminary results following employment of these tables is outlined in the previously cited Behnke excerpt (1968).

In the United Kingdom, habituation to work in compressed air accompanied by a progressive lowering of the incidence of decompression sickness has been evaluated systematically by Walder (1966). In recent years in the United Kingdom, decompression procedure has been improved by adoption of Hempleman's Blackpool Tables (1973).

Analysis by Walder and McCallum (1974) of the results obtained in usage of Blackpool and Washington State Tables tends to favor the former. However, there is currently no air decompression table governing work in compressed air which will prevent disability when work shifts are greater than four hours at gage pressures above 32–34 pounds per square inch.

New approaches to decompression following work shifts in compressed air (Behnke, 1969), stipulate 1) employment of oxygen and 2) habitat residence in compressed air first proposed in 1942. Prototype decompression tables relative to the above-mentioned approaches are outlined by Jones and Behnke (1978). Earlier, Nashimoto and Mano (1974) made a preliminary assessment of the value of oxygen directed to the safe decompression of Japanese tunnel workers.

CAISSON AND TUNNEL WORK

A. R. BEHNKE

The articles included in this section are reprinted by permission of their original publishers as follows:

Behnke A. R.: *Excerpts, medical aspects of work in pressurized tunnel operations*. From a monograph prepared for Transit Insurance Administrators, Bay Area Transit Project, San Francisco, 1968, 8 pp.

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MEDICAL ASPECTS OF WORK IN PRESSURIZED TUNNEL OPERATIONS

Albert R. Behnke

Excerpt pages 42-47 from a publication prepared for Transit Insurance Administrators in connection with pneumatic tunneling work for the San Francisco Bay Area Rapid Transit District Construction Project (BART), March 1968.

PREVENTION OF DECOMPRESSION SICKNESS

The history of decompression sickness was in the beginning of this Century marred by disability and death. Progressive increase in decompression time following completion of the East River (Pennsylvania Railroad) Tunnels, and chiefly decrease in hours of work have culminated in the elimination of all serious disability with the exception of bone changes as demonstrated by the Third (Lincoln) Tube (1955-1957). This bone pathology was probably inherited from earlier tunnel operations which provided inadequate decompression. During the past three years increased work time and greatly extended decompression time have been tested in the State of Washington. (Sealey, 1969)[1]

It is instructive to review the efforts of the State of New York to cope with this major industrial problem. The physiologic basis for decompression was analyzed mainly in the light of New York tunnel experience. The conclusion reached was that if the State of Washington stipulations, currently adopted by the States of California and New York, fail to prevent bone changes, it becomes mandatory to consider prolonged residence in compressed air. Such exposure for periods of 5 days interspersed with intervals for rest and recreation have been highly successful in the more hazardous diving operations. There is no reason except for the initial adjustment to an altered work-recreation schedule why such regimen should not be highly successful in tunnel operations both as a safeguard to health of the worker and as a means to assure normal work periods in compressed air. (Behnke, 1942)[2]

NEW YORK EXPERIENCE

Early Operations. - In 1909, F. L. Keays,[3] Medical Director for the contractor in charge of the construction of the East River Tunnels for the Pennsylvania Railroad reported on 3,692 cases of decompression sickness arising out of 557,000 decompressions. There were twenty deaths. At gage pressures to 32 psi, the men worked 8 hours out of 24, taking a one-half interval out for lunch either under the working pressure or at a slightly reduced pressure. At pressures higher than 32 psi, the men worked in shifts of 3 hours with 3-hour rest intervals. The working pressure never exceeded 42 psi. Keays preferred a 6-hour continuous shift to two 3-hour shifts "as it exposes the man to the risks of only one decompression instead of two".

Some remarkable feats of work in compressed air were accomplished at the time. Mr. H. Japp,[4] managing engineer for the East River Tunnels reported that in 23,000 decompressions from 40 to 42 psi, there were no serious or fatal cases. Three hundred and thirty men were employed for 36 days in a two-shift daily schedule that called for 3 hours on shift with a three hour rest interval between shifts at normal pressure. The total time for decompression for each shift was 48 minutes, as follows: 1) pressure was lowered from 40 to 29 psi in 5 minutes, the men then walked 1000 feet in 10 minutes to a second lock, 2) pressure was lowered from 29 to 12.5 psi in 8 minutes, the men spent another 10 minutes in walking to a third lock, 3) pressure was lowered from 12.5 to O psi in 12.5 minutes. Japp comments, "Thus a total of 48 minutes was taken for decompression which should have required 90.5 minutes by Haldane's method I and 123 minutes by his method II. Reporting on 8,510 of these decompressions, Keays recorded 1.6 per cent minor cases. Noteworthy is the statement, "Only seasoned men were employed", evidently an acclimatization which has been pointed out in recent years by British medical authorities dealing with tunnel problems.

One of the paradoxes in decompression practice is the fact that decrease in incidence of bends is not proportional to increase in decompression time beyond a minimal requirement. The work period for which Japp prescribed 48 minutes decompression time for a 3 to 3.5 hour work shift at 40 psi, would require 98 minutes (British Tables regulating tunnel work), and 162 minutes (U. S. Navy) for

the same exposure at equivalent diving depth.

Revised Tables 1912. In contrast with the above-mentioned stringent work periods and restricted decompression, were the seemingly liberal Tables formulated about 1912 in connection with the Public Service Commission Tunnels, Dr. Edward Levy, Medical Director. [5]

New York Table, 1912

Pressure psi	Total Hours of Work	Shift Hours ON	OFF	ON
1 to 22	8	4	0.5	4
22 to 30	6	3	1	3
30 to 35	4	2	2	2
35 to 40	3	1.5	3	1.5
40 to 45	2	1.0	4	1.0
45 to 50	1.5	0.75	5	0.75

A comparison of decompression time, 1912 New York Table, with U. S. Navy diving practice is presented in the following table.

Specific Pressures	Depth Equiv.	Duration Shift	Interval between Shifts	Decomp. Time per Shift	Diving Decompression Time for Similar Exposures U. S. Navy	Royal Navy*	USN for 2nd Expos.
psi	feet	hours	hours	minutes			
17.8	40	4	0.5	7	12	20	42
26.7	60	3	1.0	12	57	60	82
31.2	70	2	2.0	19	52	55	99
40.0	90	1	4.0	24	26	30	46
49.0	110	0.75	5.0	28	30	30	50

* Medical Research Council Underwater Physiology Committee Report IX, 1957

U.S. Navy Chamber Tests of the 1912 New York Table. - In 1947, Captain Van Der Aue conducted chamber tests at 26 psi with 3-hour shifts and 3-hour interval (2 hours longer than that stipulated in the N. Y. Table). The subjects were divers in good condition, at rest, and were given a more liberal decompression time than called for in the Table, as follows:

First Shift 26 psi (3 hrs): decompress to 13 psi in 3 minutes,
decompress 13 to 0 psi in 15 minutes,
Total time, 18 minutes.

Interval 3 hours at normal (0 psi)pressure

Second Shift 26 psi (3 hrs): same decompression as for first shift.

The Outcome of These Exposures

Diver	Condition Between 1st and 2nd Shifts	Condition Following 2nd Shift
1	No symptoms	Bends, recompressed
2	Pain, left shoulder after 175 minutes	Bends, recompressed
3	Pain, both knees after 120 minutes	Bends, NO recompression
4	No symptoms	No symptoms
5	Skin, itching	Skin, itching
6	No symptoms	Pain, hand; no recompression
7	No symptoms	Pain, rt. arm; NO recompression
8, 9, 10	No symptoms	(8) Back pain, fatigue (9) No symptoms (10) Stiffness, knee
11	Fleeting pain, shoulders	Bends, NO recompression
12	No symptoms	Bends, NO recompression

Revised Tables, 1922. - The 1912 New York Industrial Code Rules Relating to Work in Compressed Air and Tunnel Construction were amended in accord with Dr. Levy's recommendations.

New York Table, 1922

PRESSURE psi		HOURS			
Minimum	Maximum	Maximum Total	First Shift Maximum	Minimum Interval (Open Air)	Second Shift Maximum
Normal to	18	8	4	0.5	4
18	26	6	3	1	3
26	33	4	2	2	2
33	38	3	1 1/2	3	1 1/2
38	43	2	1	4	1
43	48	1 1/2	3/4	5	3/4
48	50	1	1/2	6	1/2

DECOMPRESSION: FIRST STAGE, REDUCE GAGE PRESSURE TO 1/2, RATE 5 POUNDS/MIN. REMAINING DECOMPRESSION UNIFORM

(a) Rate 3 lb/min. Working pressure, 0 to less than 15 pounds

(b) Rate 2 lb/min. Working pressure, 15 to less than 20 pounds

(c) Rate 3 lb/2 min. Working pressure, 20 to less than 30 pounds

(d) Rate 1 lb/min. Working pressure, 30 pounds or over

It may be stated that no more succinct decompression table was ever formulated.

Inadequacy of the 1922 Tables. - In the Thirties it was difficult to reconcile the striking difference between decompression practice as applied to divers (stage decompression according to Haldane's principles) and to tunnel workers (the split shift, shortened decompression time at a uniform rate following the initial drop). However, there appears to be merit, and this will be discussed later, in halving the gage rather than the absolute pressure. The tunnel practice permits more time to be spent in the early stage of decompression when the maximal quantity of nitrogen is being eliminated from the body. Nevertheless, despite the greatly curtailed hours of work, it was found that the 1922 Table did not prevent serious disability. Thus, Thorne (29) reported 300 cases of decompression sickness (that occurred) in the Queens-Midtown Tunnel Project (1938). In addition to the 300 cases there were 135 cases of mild pain ('niggles', British) located in the joints and along the extremities. The pains were transitory and not severe enough to incapacitate the patient but were aggravated by change in temperature. Poor local circulation resulting from the fatigue of strenuous physical effort, and the damp atmosphere of the tunnel environment were considered to be responsible for these symptoms which, as in England, are not treated by recompression. IF THESE SYMPTOMS ARE DUE TO BUBBLES (PRECURSOR OF 'SILENT' BUBBLES THAT I BELIEVE CAN BE PRESENT IN THE ABSENCE OF SYMPTOMATOLOGY), THEN ONE MUST CONSIDER A POSSIBLE RELATIONSHIP IN THE DEVELOPMENT OF BONE CHANGES.

Of the 300 cases reported by Thorne, there were 25 cases in which the central nervous system was involved: 3 cases of hemiplegia; 2, monoplegia; 2, nystagmus; 2, diplopia; 5, numbness and tingling in both legs; 5, motor weakness, both legs; 2, paralysis; 3, sensory and motor paralysis. Urinary and bowel inconvinence was present in all spinal cord cases (underlined). Recovery was complete with treatment except in one case of paralysis of both legs. The patient regained urinary and bowel control but weakness of both legs persisted. There were an additional 30 cases of vertigo (the 'staggers'): 6, simple vertigo; 10, vertigo, vomiting, staggering nystagmus; 8, vertigo, nausea, and tinnitus. There were 15 cases diagnosed as 'chokes'. In all, there was a total of 70 Type II (Serious) Cases.

New York Table, 1955-1957 Lincoln Tunnel Operation. - - Reference has been made under discussion of Bone Lesions of the steps taken by the New York State Department of Health and the Port Authority following World War II to revise the 1922 Table with consultation from Van Der Aue, Duffner, and Behnke.

PRESSURE psi	HOURS		
	Maximum Total	Maximum/Shift	Minimal Interval
Normal to 22	6	3	2 1/2
over 22 to 30	4	2	3 1/2
over 30 to 35	3	1 1/2	4
over 35 to 40	2	1	4 1/2
over 40 to 45	1 1/2	3/4	4 3/4
over 45 to 50	1	1/2	5

The decompression time for these short work shifts was allocated in stages comparable to U.S. Navy practice. Although Kooperstein and Schuman, as discussed earlier, reported only 44 cases of decompression sickness out of 138,034 decompressions (3.18 cases/10,000), it is not possible to state with complete assurance that there were no bone lesions connected with this specific operation. The anamnestic injuries of the past were brought to light by X-rays which revealed

de facto bone changes in workers with long experience in compressed air but WHO HAD NO RADIOGRAMS AS PART OF THEIR PHYSICAL EXAMINATION FOR EMPLOYMENT IN THE LINCOLN TUNNEL OPERATION.

WASHINGTON STATE TABLES, 1963

In 1961, Dr. J. Leon Sealey,[1] Medical Consultant to the Municipality of Metropolitan Seattle and Metropolitan Engineers, organized a committee to formulate decompression tables regulating work in compressed air in connection with the major sewage tunnel project through Seattle and environs. The additional medical consultants included Drs. Patterson and Robinson of Vancouver, Dr. Frederick of Detroit, Captain Duffner and this author. The objective was to develop decompression tables based on two concepts, 1) a single daily work shift with stage decompression in accord with U. S. Navy experience, and 2) a potential 8-hour work day in compressed air apportioned between work at tunnel pressure and the decompression time required. For example, a 6-hour shift at 22 psi requires 103 minutes for decompression; total time under pressure, 7 hours and 43 minutes. A 5-hour shift at 32 psi requires 178 minutes decompression; total time under pressure, 7 hours and 58 minutes. The extended period of time allotted for decompression for the usual range of tunnel pressures (0 psi to 35 psi) is more than twice the time allotted for the same work shifts in England, and even exceeds the decompression given in U. S. Navy Diving Tables. A comparison of decompression time for pressures in the range of 22 to 49 psi is shown in Table 6 . Noteworthy is the fact that total decompression time for two split shifts according to the conservative U. S. Navy Tables for repetitive dives, is less than that for the single shift as stipulated in the State of Washington Tables.

This innovation in tunnel decompression practice has been employed throughout the Seattle project which was completed in the early part of 1966. There have been 207 cases of bends in approximately 30, 000 decompressions above 14 psi. The incidence of Bends as stated numerically has not been appreciably reduced compared with tunnel operations since 1945 both in England and the United States. However, in Seattle, all cases including 'niggles' (British terminology for minor symptoms) which in other operations evade or escape treatment, were accorded recompression.

The major accomplishment of the single shift-prolonged decompression schedule is the absence to date (May 1967) of disabling bone changes. Additional time will be required (to 1968-1970 or longer) to rule out absence of bone pathology attributable to decompression following work in compressed air, but the outlook is favorable.

The State of Washington Tables formulated mainly by Captain Duffner, have been adopted by Michigan, New York. and California to regulate decompression practice. A criticism this author would apply is that decompression time is spent for the most part at low pressures following a rapid decrease to the first stop. More time, e. g., 15 to 20 minutes could be taken in a relatively slow ascent to the first stop in order that nitrogen in the rapidly desaturating tissues is eliminated, hopefully without bubble formation. The physiologic basis for decompression will be discussed in the following paragraphs.

TABLE 6

TOTAL DECOMPRESSION TIME FOR SPECIFIC PRESSURES AND EQUIVALENT DEPTHS, NAVY DIVING AND BRITISH TUNNEL PRACTICE.

DECOMPRESSION TIME IS ALSO GIVEN FOR SPLIT SHIFT AND SINGLE SHIFT WORK IN COMPRESSED AIR.

E = Exposure Time in Minutes
D = Decompression Time (Min.)

SPECIFIC PRESSURE PSI	EQUIV. DEPTH FEET	ROYAL NAVY		MINISTRY OF LABOR	STATE OF WASHINGTON, CALIFORNIA CODES	AUTHOR'S CALC.***	U.S. NAVY		U.S. NAVY REPETITIVE DIVING TABLE 1ST SHIFT	INTERVAL (Hour)	2ND SHIFT
					(22 psi)						
22.2	50	E 180 D 35	E 360 D 70	E 360 D 35	E 360 D 103	E 360 D 102	E 180 D 30	E 360 D 82	E 180 D 30	2	E 180 D 55
					(28 psi)						
26.7	60	E 120 D 30	E 240 D 90	E 240 D 42	E 240 D 127	E 240 D 102	E 120 D 27	E 240 D 82	E 120 D 27	3	E 120 D 49
					(32 psi)						
31.2	70	E 90 D 30	E 180 D 100	E 180 D 57	E 180 D 126	E 180 D 111	E 90 D 24	E 180 D 112	E 90 D 24	4	E 90 D 56
					(36 psi)						
35.6	80	E 75 D 30	E 150 D 115	E 150 D 68	E 150 D 142	E 150 D 116	E 75 D 29	E 150 D 110	E 75 D 29	4	E 75 D 54
40.0	90	E 60 D 30	E 120 D 110	E 120 D 83	E 120 D 143	E 120 D 108	E 60 D 26	E 120 D 108	E 60 D 26	4	E 60 D 54

* Royal Navy Table from MRC R. N. Personnel Research Committee Report Investigation into Decompression Tables, IX, December 1957.

** Table 3 on page 6 in MRC (Medical Res. Council) Report 281, W.D.M. Paton, D.N. Walder, 1954. (34) These tables are the basis for decompression in British Tunnel Operations. (superseded by Hempleman's Blackpool Tables, 1966)

*** Excess pressure (psi) x 13.5. Excess Pressure = (% saturation 120' tissue x working pressure) - 12.

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New Approaches to Medical Aspects of Work in Compressed Air

ALBERT R. BEHNKE, CAPT. MC, USN (RET.)

The Bay Area Rapid Transit (BART) project is the first large scale, compressed-air tunnel operation in California and the largest industrial enterprise undertaken in the Bay Area. The objective is to provide automated rail service over 75 miles of duo-rail tracks. The special problem is the pressurized construction of six miles of underground tunnels. A noteworthy feature of the entire operation is the non-pressurized laying of the Trans-Bay tube in which sections of tunnel, each weighing 10,000 tons, are lowered into a man-made trench across the bottom of San Francisco Bay with the help of divers. Pressurized tunnel work, contrary to the usual location under a water bed, is essentially in progress in the Bay Area under busy, commercial thoroughfares.

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Also presented in part at the 53rd Annual Meeting of the Industrial Medical Association, San Francisco, Calif., April 22–25, 1968. The author is solely responsible for the statements in this paper.

There are multiple sites of pressurized operation which involve many contractors. It is anticipated that work in the different tunnels will be continuous throughout a 24-hour period, and will engage the services of about 600 workers apportioned to six different tunnels in widely separated areas. In view of the need for specialized knowledge concerning decompression problems, and the requirement for heavy equipment in recompression therapy, it was essential to provide the various contractors with an over-all, unified medical service. The features of this service included a comprehensive physical examination in accord with newly formulated State regulations governing work in compressed air, facilities for recompression therapy and first-aid treatment and disposition of cases of industrial illness and injury. In order to implement these services BART selected Transit Insurance Administrators (TIA), staffed with a highly qualified safety supervisor and other personnel, to deal with problems of medical service and accident control. In addition the services of the chief engineer of the National Surety Corporation were made available to TIA for full-time, on-site safety engineering.

Medical Monitoring of an Industrial Operation

The BART project may be characterized as a huge, multifaceted task force operation (in military terminology) which has been superimposed upon the normal daily activities of several communities. In contrast to military planning, however, one cannot draft medical personnel who are able to devote full time to such project with single-minded purpose. A competent industrial clinic can be selected to provide medical and definitive surgical services of high order, but these services require a temporary staff of additional contract doctors not necessarily qualified or motivated to deal with industrial problems.

Initially, it was an objective to monitor activities of workmen as we did those of military personnel. During the rescue operations, for example, at the time of the sinking of the U.S.S. Squalus and subsequently during the extensive salvage work conducted over a period of three and one-half months, there was not a single day of lost time due to injury.[1] During one phase of the salvage efforts,

heavy chains (each link weighing 50 lb.) were reeved under the sunken submarine, despite the roll and pitch of the salvage ship. Contributing to safety was the exceptional fitness of the divers who had previously been "conditioned" by daily exercise in which baseball was substituted for the customary noon meal. Specific safety measures consisted of rehearsals of each underwater maneuver so that a given diver became proficient in the specific task which he subsequently performed underwater. Further, there was no pressure applied to the divers to accelerate their work rate above optimal efficiency. Finally, a quantitative assessment of physical condition was provided by periodic recording of the pulse rate of each diver in response to a standard step test exercise.

In pressurized tunnel work, lack of communication between doctor and worker precludes systematic on-job surveys, or regular examination of limited numbers of men prior to or following a workshift. There are however, competent safety engineers who conduct the type of on-site surveillance which is routine for a military doctor, notably in submarine and aviation services. Hence, the role of the contract physician tends to be relegated to the dispensary where he "treats" rather than "prevents" such maladies of patients who are adversely affected by heat and humidity, or who incur chemical burns in the handling of grout. It is certain that a number of impediments must be overcome in order to realize the potential of a new approach to an industrial operation, patterned after the rewarding type of medical supervision accorded aviation and submarine service men.

Rationale Underlying Certain Features of the Physical Examination

GENERAL COMMENTS: Tunnel workers may be divided into miners who engage in manual labor during shifts of specified duration, supervisory personnel, and those with special skills who are usually non-shift employees. The miners comprise men who, from history and physical examination, are fit to engage in strenuous labor daily in compressed air. Since manual laborers are always available, there is no difficulty in enforcing stringent criteria with reference to age and weight, and freedom from pulmonary pathology, designed to protect them against decompression sickness and aeroembolism. The difficult problem is the disposition of supervisors over the age of 40. These experienced men, particularly those who are knowledgeable in pressurized tunnel construction, are in short supply. The demand for their services is insistent. However, many of these men harbor the usual physical impediments of an older age group which in younger, robust years was prodigal with respect to health matters. If their sojourn in compressed air was extensive, there is high likelihood of aseptic bone necrosis in the medullary shafts of long bones as well as occasional juxta-articular involvement of the heads of humerus and femur. Further, these lesions may be produced by fat emboli emanating from fatty livers associated with chronic alcoholism. Obstructive pulmonary disease, especially when cysts are present, renders the older supervisors susceptible to aeroembolism. The predominating physical impediments, mitigating against work in compressed air, are associated with age and obesity. It is worthwhile, therefore, to clarify these factors in relation to decompression sickness.

ROLE OF AGE AND WEIGHT IN PREDISPOSING TO DECOMPRESSION SICKNESS: Quantitative evaluation of these variables stems from a stimulating analysis of Gray[2] which embraced thousands of simulated altitude decompressions in low pressure chambers during World War II, and involved Air Force Trainees in the age range of 18 to 28 years. The particular value of the altitude decompression for our purpose, is that the tissues of the body are in equilibrium with ambient nitrogen at the time that pressure is reduced. Hence, body fat is "saturated." The limitation of the data is that the results apply primarily to groups and not individuals. Nevertheless, the group information is unequivocal. With respect to age, there was an increase in Relative Susceptibility (R.S.) expressed by the regression relationship, R.S. = 10.8 (age) -- 145. This formulation reveals that R.S. increases by 10.8 percentage points for each year increase in age in the range of 18 to 28 years. Absolute susceptibility of any age group can then be approximated by reference to the incidence of decompression sickness for the 23-year old group. Thus, if a particular flight yields an absolute susceptibility of 50% in the 23 year-old subjects, the absolute susceptibility in the 18 year-olds should be approximately 23% and in the 28 year-olds, approximately 77%.

In regard to overweight, a simple index of weight (lb.) divided by height (in.), designated *linear density*, showed a high correlation (0.91) with Relative Susceptibility, and R.S. = 12.2 (linear density) — 177. This formulation states that R.S. increases by 12.2 percentage points for each increase in linear density of 0.1 unit. If a linear density of 2.3 is taken as the reference index (e.g., weight, 159 lb.; height, 69 in.), and the absolute susceptibility to decompression sickness of the group with this index is 50%, then a group with an index of 2.8 (e.g., weight, 193 lb.; height, 69 in.) will have an absolute susceptibility of about 80%.

Body fat: Fat with an oil/water solubility ratio for nitrogen of 5.2 to 1, serves as a reservoir for storage of molecular nitrogen absorbed during compression. A man whose body weight comprises 30% fat (66 lb.) will have 2,000 ml. more nitrogen in his body fat after saturation at 3 Atm (29.4 psi, gage pressure) than a lean man (154 lb.) whose weight consists of ten percent fat (22 lb.). This difference in nitrogen storage capacity would exclude all obese men from work in compressed air were it not for the fact that at 29.4 psi, work time in the United States is restricted to about four hours. The excess fat (above ten per cent of body weight) is, therefore, only partially saturated (about 37%) with nitrogen. In the lean man (ten per cent fat), body fat is 75% saturated at the end of four hours, i.e., four hours represents two time units (T.U.) on an exponential uptake curve where 1 T.U. represents 50% saturation at the end of two hours, and 6 T.U. represents 98.4% saturation at the end of twelve hours.

In the corpulent man (30% fat), the half-time (= 1 T.U.) required will be six hours (i.e., three times longer than the two-hour half time required by the lean man). At the end of four hours, the fat of the corpulent man will be 37% saturated (4/6ths T.U.). Even with an increase of blood supply of 50% to adipose tissue, the fat in the corpulent man will not be more than 50% saturated at the end of four hours.

Reduction of work time in compressed air greatly decreases the risk of decompression sickness which otherwise would be formidable for the obese man. It is of interest that work hours in the United States are reduced in relation to pressure (psi); (22.2, six hr.; 26.7, four hr.; 31.2, three hr.; 35.6, 2.5 hrs; and 40, two hr.), such that the excess pressure of nitrogen in the 120-minute half-time tissue does not exceed 16.5 psi at the various pressure levels.

Body Weight: According to current height-weight standards derived from insurance data, a large part of the working population, and many of the supervisors, could be physically disqualified as "overweight." It was necessary, therefore, to develop criteria as to what constitutes overweight, particularly in older men, who, in addition to obvious, excess fat, are often muscular and fall into the "large frame" category. Our investigations over a number of years have shown that *relative weights* can be computed from body girths and stature[3] for different regions of the body. Thus, trunk (fat) girths may be compared with those of the relatively lean extremities. The trunk girths (A′) selected are the average of two abdominal perimeters (at the waistline and at the level of the iliac crests and omphalion) and the hip girth around the maximal protrusion of the buttocks. The extremity girths (B′) comprise those of the flexed biceps, maximal forearm (extended) and calf, minimal wrist and ankle, and the knee at mid-patellar level. The contralateral dimensions of the upper and lower extremities are averaged. In lean men, B′ is equal to or exceeds A′; in fat men, the excess of A′ over B′ is a numerical assessment of overweight attributable to fat.

In Table I, the sum of the extremity girths (B′) is tabulated for each inch of stature. The percentage variation of B′ for 1, 2, and 3, respectively, is 5, 10, and 15%, and for the projected weights calculated from B′ and stature, 10.3, 21, and 32.2% from the mean, respectively. The column of mean weights representative of American males in the age group, 20 to 25 years, has been calculated from $0.1166\ h^{1.7}$ where h is stature in inches. Close approximation of these mean weights is also derived from the rounded B′ values substituted in the equation, Mean W (lb.) = $(B'/55.5)^2 \times h^{1.7} \times 0.843$, where h is in inches. Relative weights from trunk girths (A′) may be computed in a similar manner by substitution of A′ for B′ in the equation.

An examinee is not "overweight" if B′ weight is equal to or exceeds A′ weight, or body weight. A football player, for example, six feet tall, may weigh between 203 and 222 lb. and not be overweight in regard to excess fat. The B′ weights provide a far more realistic estimate of appropriate weight for big men, than insurance weights raised to an arbitrary upper limit of 20% above average for age and stature (Table I). Such upper limit will usually not exclude muscular men, but, in the absence of B′ measurements, the amount of excess fat is indeterminate and may be too generous.

If the examinee is obese, then further diagnostic tests are in order to assess carbohydrate tolerance, and serum insulin and triglyceride levels. In contrast to an earlier era, it is now possible to diagnose and control derangements of intermediary metabolism associated with adult obesity. The workman should have the benefit from current dynamic advances which lead to control of angiopathy and coronary heart disease.

Patency of Auditory Tubes and Auditory Acuity

During compression it is necessary to resort to voluntary procedures such as the Valsalva maneuver, swallowing, yawning, and thrusting the jaw forward in the effort to equalize pressure on both sides of the tympanic membrane. During the past 35 years, about 150,000 compressions to 50 psi have been applied to American submarine personnel in connection with submarine escape training. Five to 25%, or more, of trainees at any given time have been unable to accommodate readily to excess pressure, chiefly

TABLE I

PROJECTED NORMAL WEIGHTS DERIVED FROM EXTREMITY GIRTHS AND STATURE FOR LARGE ADULT MALES COMPARED WITH ARBITRARY WEIGHTS WHICH ARE 20% HIGHER THAN AVERAGE WEIGHT FOR STATURE ACCORDING TO EQUITABLE ASSURANCE TABLES, 1940

Multiples of S.D.			Mean	1	2	3	Weights Calculated as 1.2 × Avg Weight for Age and Stature		
			% Deviation from Mean						
Extremity Girths B′			Mean	5	10	15			
Projected Weights*			Mean**	10.3	21	32.2	Age Group years		
K $h^{1.7}$*	h inches	Mean B′ cm					25	35	45 & over
17.91	79	182	196	216	237	259			
17.76	78	181	192	212	232	254			
17.60	77	180	188	207	227	249			
17.44	76	179	184	203	223	243	226	235	240
17.28	75	178	180	199	218	238	221	230	235
17.11	74	176	176	194	213	233	216	226	230
16.95	73	175	172	190	208	227	210	220	226
16.78	72	174	168	185	203	222	204	214	220
16.62	71	173	164	181	198	217	198	208	214
16.46	70	172	160	177	194	212	192	202	208
16.29	69	170	156	172	189	206	187	196	202
16.13	68	169	152	168	184	201	182	191	197
15.96	67	168	148	163	179	196	178	186	192
15.81	66	167	145	160	175	192	173	181	187
15.62	65	165	141	156	171	186	168	176	192
15.46	64	164	137	151	166	181	164	172	178

* *MEAN WEIGHTS (lbs)* = $(B'/55.5)^2 \times h^{1.7} \times 0.843$, *h(stature, inches)* $k = 0.843$

** " " = $0.1166\ h^{1.7}$, *h in inches*

because of infection of the upper part of the respiratory tract. In a specific study,[4] 156 men (or 36.2%) of 432 men developed some degree of aerotitis media. Post-pressure audiograms showed no significant shift below 2,000 cps but there was a significant depression of acuity at 3,000, 4,000, 6,000 and 8,000 cps. All examinees regained baseline values as seen in the 14 to 20 day post-pressure audiogram.

It is a remarkable fact that repeated barotrauma produces so little disturbance of hearing in the speaking range, although some permanent residuum cannot be excluded with certainty. Divers as a group sustain hearing loss in the high cps range but the role of excessive noise constitutes a known cause for this type of impairment. The rarity or absence of proved deafness due to barotrauma stands in contrast to loss of hearing produced by gunfire.

Upper respiratory and nasal allergies predispose to aerotitis. Despite precautions an appreciable number of workers will require decongestants to reduce turgescence of the mucosa. It is important that decongestant drugs have no side-effects which impair ability to perform dexterous and heavy work in a hot atmosphere.

Pulmonary Pathology

Some of the most serious instances associated with work in compressed air have arisen from pulmonary embolism secondary to pulmonary pathology. Congenital cysts, scar tissue vessicles, and emphysematous bullae may function as air-entrapped sacs. Pneumothorax may be a complication. In the screening of examinees, it is important to detect obstructive lung disease early. Individuals may be surprisingly free of symptoms until the disease process has advanced well beyond dangerous limits. Wilson[5] considers that the stethoscope is neither an accurate nor an efficient instrument except to detect all but the grossest changes. For the routine examination it is essential to have a spirogram and a measurement of peak expiratory velocity or equivalent quantitative tests of pulmonary function.

Radiographic Survey of Long Bones

Early lesions indicative of aseptic bone necrosis are difficult to detect. Careful positioning is required to reveal critical areas in the head of the humerus and/or femur which give rise to crippling deformity. At Transit Medical Center, it has been possible to develop a positioning technique which eliminates or minimizes overlapping of the acromion and conflicting shadows of the rims of glenoid and acetabular cavities. Anterior-Posterior (AP) radiographs are taken of each head of the humerus and proximal shaft, and of each femoral head and proximal shaft of the femur. Anterior-Posterior and lateral radiographs are taken of each knee including the distal femur from its midpoint to the midpoint of the proximal tibia and fibula (See Operative Technique chart).

OPERATIVE TECHNIQUE CHART

Equipment:

X-ray 300 M.A. 150 KV	Tube: Dynamax "40" or "46"
125 KV Generator	1.2 mm Focal Spot
12:1 Ratio, 80 Line Grid	RPS 54 Eastman X-ray Film
Hi-speed Screens	90 Sec. Profex-ray Automatic Film Processor

	MA	Time sec	Distance inches	Bucky	KV relative to Body Size		
					Small	Medium	Large
Shoulder (A.P.)	100	1/15	40	yes	90	100	110
Hip (AP)	100	3/20	40	yes	90	100	110
Knee (AP & Lateral)	100	1/30	40	yes	90	100	110

Other Tests

Equilibrium: Disturbances of equilibrium are frequently observed in decompression sickness. Two equilibrium tests based on the extensive experience of Graybiel and Fregley[6] with aviators, possessed high validity and were easy to administer and score. In the *sharpened Romberg*, the subject assumes a standard position upright with arms folded against the chest. He then aligns his feet (shoes on) heel-to-toe and; with eyes closed, he strives to maintain equilibrium for a period of 60 seconds. In the second test (SOLEC), the subject assumes standard position and, standing on one foot, he closes his eyes and strives to maintain equilibrium for 30 seconds.

Cardiovascular Response to Step Test Exercise: The height of the platform is 16 inches. The examinee, holding a ten pound barbell in each hand steps up and down bringing both feet to the floor after each step-up. Six step-ups are performed in 30 seconds. Pulse rate is counted 5-20 seconds at the termination of the 30-second bout of exercise. Successive bouts of exercise can be performed with 30-second rest intervals, or the exercise can be continuous until terminated by fatigue. We routinely use this type of test in the Navy to obtain standard scores daily on divers in lieu of repeated physical examinations. Pulse rates which deviate more than 2-sigma from the mean score for a particular individual, or gross disturbance in neuromuscular coordination, require physical examination by the doctor. The feasibility of the test routine for tunnel workers has not been established.

Decompression Sickness

Etiology: Despite the preponderance of overt evidence that intravascular bubbles are the initiating cause (i.e., bubbles following decompression of animals have been observed to circulate in arteries and veins; complete protection against decompression sickness is afforded by pre-oxygenation to effect nitrogen removal from tissues prior to rapid altitude ascent), there are complicating factors such as fat embolization, liberation of proteolytic enzymes, potassium ions, and peptides. Further changes are vasoconstriction, loss of circulating plasma, hemoconcentration, and development of shock. It is more and more evident that recompression alone needs to be supported in the serious cases by fluid replacement, sedation, and cardiac restorative measures.

Features: The injuries are manifest singly or in combination with pain (bends), pulmonary symptoms leading to frank asphyxia (chokes), paralysis, and chronic bone lesions. Minor effects are a debilitating fatigue, rash, pruritus, and paresthesias. The manifestations of decompression sickness of the tunnel worker, diver, and aviator are similar; the aviator is seldom afflicted by paralysis but he is more prone to develop "chokes." The majority of symptoms arise within one hour after decompression, followed by an exponential decline to only an occasional case during the ensuing 12 to 24 hours.

In Rivera's[7] analysis of 935 cases, the following percentages apply to the relative incidence of signs and symptoms: localized pain (91.8); numbness (paresthesia) (21); muscular weakness (21); rash and pruritus (15); temperature changes, nausea, vomiting (7.9); vertigo (8.5); visual disturbances (6.8); paralysis (6.1); headache (3.9); loss of consciousness (2.7); urinary dysfunction (2.5); dyspnea (chokes) 2.0; fatigue (1.2); convulsions (1.1); and edema (0.5).

Classification: In the United Kingdom, two types of decompression sickness are recognized: *Type* I, simple pain in the region of a joint; and *Type* II, all manifestations of a serious nature. Joint pain, however, may be preceded or followed by *Type* II symptoms. Thus, transient visual disturbances (scintillating scotomasa) may precede joint pain, or respiratory difficulties may supervene, as well as shock, and occasionally paralysis, if "bends" are untreated. A better working definition of *Type* I malady is "*mild*," meaning that there is immediate

response to, and no complications following, recompression. On the other hand, *Type* II is "*serious*;" favorable response to recompression is delayed or uncertain, and there may be residual impairment despite recompression, fluid administration, and other supportive measures.

Decompression Sickness To-date in the BART Project

Incidence: From November 1967 to July 1, 1968, there have been 35,269 man-decompressions at pressures between 9 and 16 psi in shifts of six hours duration, which have been attended by 18 instances of decompression sickness involving 16 men out of a total complement of 284 workers.

Comments on Cases: The unusual feature of the representative cases (Table II) is their occurrence at unusually low pressures of 11.5 to 16 psi for work shifts limited to six hours. Rarely in other projects is decompression sickness reported below 18 psi. Possible contributory factors attending illness following exposures at low pressures are dehydration of workers in a hot atmosphere attending operation of automated machinery at the face of the tunnel, and the disruption of circadian rhythms as a result of continual rotation of work shifts. The difficult problem is to explain the isolated occurrence of illness in the worker exposed repeatedly to the same stresses which induce no ill-effects.

Case Reports

Type II, serious, Foreman 183, age 35, weight (192 lb.), height (70.5 in.). This worker, one-hour following a six hour shift at 13.5 psi (2000–0200 hours) developed dizziness and blurred vision while driving a "pool" car enroute home, a distance of 25 miles from the tunnel. He did not report initial symptoms to the Medical Center but persisted in driving home. Subsequently, he had headache, developed pains in both legs; later, he felt nauseated and vomited. Three hours post-decompression the patient was unable to walk without wall support, his skin was mottled, and he was partially aphasic. Recompression on oxygen (26.7 to 0 psi) for 3.7 hours was attended by full recovery.

Three months later this worker complained of not feeling well; he had transient double vision, and a rash was present over the dorsal trunk area (Table II). Symptoms were relieved by breathing oxygen at normal pressure, but the patient, nevertheless, was accorded routine oxygen pressure therapy (26.7 to 0 psi) for 160 minutes.

Type I, *mild,* Foreman 131, age 42, weight (147 lb.), height (66.8 in.). History: 12 years intermittent exposure in compressed air

TABLE II

DECOMPRESSION SICKNESS (D.S.) AT LOW WORKING PRESSURES (PSI) IN RELATION TO SHIFT, DECOMPRESSION TIME (DC), INTERVAL ELAPSING PRIOR TO RECOMPRESSION (IRC), AND TOTAL RECOMPRESSION TIME (TRT) ON OXYGEN.

Patient	Age yr	Rel. W*	psi	Shift	dc min	Signs and Symptoms	IRC hrs	TRT min
Miner 1360	47	91	11.5	0800–1421	13	Pain, knee and calf	6.5	160
Inspector 601	45	100	13.0	0200–0800	16	Pain, shoulder	6.5	162
Engineer 279	38	120	13.0	2200–0200	16	Pain, knee	12.5	159
Inspector 274	44	106	13.0	1400–2000	16	Pain, knee; scotomata	5.7	165
Electrician 724	36	117	13.0	0800–1220 1330–1400 1430–1700	6 6 5	Extreme fatigue, unsteady gait, slurred speech, (simulated drunkenness)	3.2	155
Miner 440	30	119	13.0	2000–0200	6	Pain, knee	6.0	155
Mole Operator 596	25	122	13.0	0200–0505 0520–0800m	15 6	Fatigue, pruritus, erythema, tenderness, axillary area	3.8	166
Foreman 183	35	113	13.5	2000–0200	6	Dizziness, blurred vision, headache, nausea, vomiting, aphasia, unsteady gait	3.7	229
Second Attack			14.0	0200–0800	16	'not feeling well', transient double vision, rash	2.0	160
Foreman 131	42	93	16.0 16.0 16.0 16.0	2000–0200 2000–0200 2000–0200 2000–0200	33 45 53 33	Pain, knees (No Treatment) Pain, knees** No Symptoms Pain, knees; dizziness	8.0 9.2	162 170

SECOND ATTACK —

**Relative Weight* $= \frac{\text{Scale weight}}{\text{avg W for age}} \times 100$

***A recurrence of pain which was relieved during working shift.*

without decompression sickness. Current: Several hours following a six hour shift (2000–0200 hours), pain was felt in both knees, persisting during the day, and was relieved during the course of his regular (2000–0200) work shift. At the end of this shift, he increased his decompression time from the prescribed 33 minutes to 45 minutes. Nevertheless, two hours post-decompression, knee pain (similar to a toothache) recurred, patient was unable to sleep and he reported for recompression therapy.

Following treatment and some rest, he worked his regular shift (2000–0200) and was given 53 minutes decompression. He remained free from symptoms. However, following his next work shift, he reverted to the usual 33-minute decompression. Subsequently, he experienced transient dizziness and, later, pain in both knees. Recompression therapy was effective. The foreman has continued to work in compressed air without complaints.

Type I, *mild;* complicated by alcoholism. Miner 1360, age 47, weight (170 lb.), height (72.5 in.), former diver. Patient felt pain in his calf and knee during a course of drinking over a period of several hours following an exposure of 6.33 hours (0800–1421 hours) at only 11.5 psi. Decompression time was 13 minutes. During the previous ten days he had experienced pains in calf and buttock musculature but he did not apply for treatment. Since the shift pressure was only 11.5 psi, there was a question of diagnosis; heat cramps could have accounted for previous and current pain. However, during recompression therapy (26.7–0 psi) leg pains were relieved. Subsequently, the worker has continued on his job and he has had no complaints.

These cases demonstrate that isolated instances of decompression sickness can arise following work at relatively low pressures (11.5 to 16 psi). Mention has been made of dehydration and disruption of circadian rhythms as complicating factors. Although some of the patients had been drinking, and harbored excess fat, others were lean, athletic, and apparently in prime physical condition. One patient was a decathlon athlete; another, a long distance (17 mi.) swimmer.

Recompression Therapy

In 18 routine oxygen treatments (26.7 – 0 psi) there was a single recurrence of pain which required additional therapy. The "low-pressure" oxygen therapy is well-tolerated, effective, and easy to administer. Table III incorporates a conservative table both for oxygen therapy and the employment of oxygen during decompression. A unit exposure (U.E.) consists of oxygen inhalation for 20 minutes, followed by inhalation of air for a period of five minutes. At 25 psi, one, two, and three U.E. are administered, depending upon the response of the patient. At 15 psi, the number of U.E. is double the number required at 25 psi.

TABLE III

GUIDE FOR ADMINISTRATION OF HYPERBARIC OXYGEN DURING DECOMPRESSION OF COMPRESSED AIR WORKERS AND FOR RECOMPRESSION THERAPY (FROM CUMULATED EXPERIENCE OF EARLIER AND LATER WORK AT THE EXPERIMENTAL DIVING UNIT AS MODIFIED BY BEHNKE).

Pressure psi	Unit Exposure (U.E.) (Decompression interval)	min	Number of Unit Exposures for Routine Inhalation		
25	Oxygen	20			
	Air	5	1*	2*	3*
25 to 15	(Oxygen)	45			
15	Oxygen	20			
	Air	5	2	4	6
15 to 0	(Oxygen)	45			
	Total Time min		165	240	315

**In recompression therapy, NO SYMPTOMS AT END OF UNIT EXPOSURE. Patient able to walk and exercise*

In the treatment of Type II (serious) cases, it may be necessary to go to 75 psi and breathe a 50% oxygen-nitrogen mixture as outlined by Behnke and Shaw,[8] in 1937. If suitable mixtures are not available, recourse is to follow standard U. S. Navy Treatment Tables for treatment of serious cases.

Prevention of Decompression Sickness and Aseptic Bone Necrosis

Historical Aspects of Decompression Practice and Disability: Work in compressed air at the beginning of this Century was marred by disability and death. In 1909, Keays,[9] Medical Director for the contractor in charge of construction of the East River Tunnels for the Pennsylvania Railroad, reported 3,692 cases of decompression sickness out of 557,000 decompressions. There were 20 deaths. At gauge pressures up to 32 psi, men worked eight hours out of 24, taking one-half hour interval for lunch, either under working or at slightly reduced pressure. At pressures higher than 32 psi, men worked two shifts of three hours with a three hour rest interval.

Some remarkable feats of work in compressed air were accomplished at the time. Three hundred and thirty men, for example, were employed for 36 days in a two-shift daily schedule that called for three hours on shift with a three hour rest interval between shifts, at normal pressure. The total time for decompression following each shift was 48 minutes. Reporting on 8,510 of these decompressions, Keays recorded 1.6% of minor cases. Noteworthy is a statement, "only seasoned men were employed," a recognition of acclimatization to higher pressures which has been confirmed in recent years by British medical authorities[10] concerned with tunnel problems.

Progressive increase in decompression time, and chiefly decrease in hours of work, have culminated in the elimination of all serious disability with the exception of bone changes. A paradox, however, in decompression practice is the fact that decrease in the incidence of Type I and II cases is not proportional to increase in decompression time beyond a minimal period. The work shift at 40 psi, which in Keays' time was accorded 48 minutes decompression, would require 92 minutes (British Ministry of Labour Tables), 162 minutes (U.S. Navy Tables), for the same exposure at equivalent depth, and 183 minutes (Washington State-California Tables) (Table IV). The incidence of decompression sickness, however, is similar, following the three widely divergent time schedules allotted for decompression (Table V).

Aseptic Bone Necrosis

The serious, large-scale medical problem arising from work in pressurized tunnels has been infarction of bone, and death of cells in the absence of infection. Aseptic bone necrosis as visualized by x-ray has been reported in as many as three out of four old-time workmen. In a classical paper by Bell, Edson, and Hornick,[11], a radiologic survey was reported on 32 compressed air workers in New York, none of whom had symptoms or gross signs indicative of bone lesions. The men had worked from three to 33 years, intermittently in compressed air. The shortest continuous employment was ten months, the longest 36 months. Fourteen men gave a history of bends. Of the 32 patients only eight failed to show bone changes considered to be typical of aseptic bone necrosis.

The radiographic findings are revealed strikingly in overt cases as areas of increased density in the head, neck, and medullary shaft of long bones which have a high content of fatty marrow.[12] The irregular, serpentine metadiaphyseal lesions are entirely confined within the medullary cavity of the shaft as linear strands of calcification in areas of infarction

TABLE IV

COMPARISON OF TOTAL DECOMPRESSION TIMES (MINUTES) FOR VARIOUS PRESSURES AND WORK PERIODS ACCORDING TO BRITISH MINISTRY OF LABOUR, U.S. NAVY, STATE OF WASHINGTON, AND AUTHOR'S CALCULATION.

psi	ft equiv.	Duration hr.	British	USN	Washington State (psi)		Author*
22.2	50	6	35	82	103	(22)	100
26.7	60	5	50	—	126	(26)	135
		4	42	82	104	(26)	108
31.2	70	4	61	—	163	(32)	154
		3	57	112	126	(32)	111
35.6	80	4	87	179	198	(36)	199
		3	82	121	170	(36)	149
40.0	90	4	102	—	213		243
		3	92	—	183		186
		2	83	108	143		108

**Excess Pressure* × 13.5 = *Total Time (min.)* *Excess P = % sat. 120' tissue* × *gauge P* — 12

TABLE V

DECOMPRESSION SICKNESS IN GREAT BRITAIN FOR EXPOSURES OVER 18 PSI, AND IN THE UNITED STATES DURING THE COURSE OF TUNNEL OPERATIONS

Tunnel	Compressions × 1000	Decomp. Sickness percentage		Ratio	Over-all %
		I*	II*	I : II	
Dartford 1957–1959	400	0.64	0.0330	19:1	0.67
Blackwall 1960–1964	807	1.02	0.0421	24:1	1.06
Clyde 1958–1963	1610	0.25	0.0441	6:1	0.29
East River 1909–1912 (Keays)	557	0.59	0.07	8:1	0.66
	Twenty Deaths				
	Working Pressure psi	Man-Shifts		Decompression Sickness cases	%
Lake City (Seattle) 1964–1967	18–20	4000		19	0.47
	21–25	7000		37	0.53
	26–29	1600		22	1.37
	30–34	1400		15	1.17
East River 1909–1912 (Keays-Japp)	40	8510		136	1.6
	(330 men worked two 3-hour shifts daily with an interval of 3 hrs between shifts)**				

**Type I* (*pain in and around joints, i.e., bends*), *British*

**Type II* (*other involvement, serious cases*), *British*

***Decompression time:* 48 *minutes per 3-hr shift*

At pressures up to 32 psi, men worked 24-hr shifts daily; decompression time was 33 min per shift (32 psi).

and fibrous marrow replacement. A prime consideration is that these lesions are not disabling and there is no evidence that extension of the preexisting intramedullary infarctions will cause arthritic involvement.

On the other hand, if the lesions are juxta-articular, the normally smooth cartilaginous surfaces of joints may be disrupted to produce crippling. Remarkably, only shoulder and hip joints (humeral, femoral heads) are disabled; by contrast, the knee which is the most frequent site of bends in compressed air workers, has remained singularly free from disabling deformity.

An impediment in diagnosis is the latent period of a year or more before radiographic changes are seen. The subsequent functional impairment arising from irregularity of, or breakdown of, joint cartilaginous surface may not become overt for many years. In an authoritative report by McCallum et al.,[13] juxta-articular (and potentially disabling) bone lesions were observed in ten per cent or more of workers who engaged in construction of tunnels under the River Clyde. The lesions were related to the number of times a man was decompressed, to the pressure at which he had worked, and to the number of attacks of decompression sickness (bends). The conclusion reached by British authority was that currently accepted decompression procedures (in England), and treatment of bends in civil engineering practice do not prevent necrosis of bone.

Despite this bleak picture, there is empirical evidence that greatly shortened decompression time and the manner of decompression (i.e., relatively short, uniform decompression of tunnel workers following an initial, abrupt reduction of pressure, compared with extended decompression by the Haldane method as employed by divers) may be responsible for the pathologic changes. In 1961, Dr. Sealey, Medical Consultant to the Municipality of Seattle and Metropolitan engineers, organized a committee to revise decompression tables for compressed air workers. Objectives were to formulate tables based on two concepts: (1) a single (rather than split) work shift followed by stage decompression in accord with U.S. Navy experience; and (2) a potential eight hour work day in compressed air apportioned between work at tunnel pressure and decompression time. The Washington State

Tables as formulated by Captain Duffner, MC, USN provided, for example, 103 minutes decompression following a work shift of six hours at 22 psi. The extended period of time allotted for decompression over the usual range of tunnel pressures (0 psi to 40 psi)) is almost always more than twice the time accorded the same work shifts in England, and even exceeds U.S. Navy decompression time (Table IV).

The experience with these Tables, which have been adopted by New York, California, and other states, after two and one-half years trial in Seattle (Fall, 1964 — Spring, 1967), is that effective work can be accomplished in compressed air, not only without crippling bone disability, but also without appreciable (innocuous) medullary involvement.

Alternatives to the prolonged, daily decompression in air afforded by the Washington State Tables relate to: (1) inhalation of oxygen during decompression; or (2) residence in compressed air (saturation exposures) followed by prolonged decompression at weekly or fortnightly intervals. The rationale underlying these newer approaches to work regimen in compressed air and decompression practice will be outlined.

Oxygen Decompression Of Compressed Air Workers

PHYSIOLOGICAL PRINCIPLES: In a remarkable manner the body tolerates an abrupt reduction of pressure following short exposures in compressed air at relatively high pressure (45 psi), or following long saturation exposures at low pressure (15 psi). It would appear, and this is a basic tenet of Haldane's postulates, that gas in a state of supersaturation can be transported in blood circulating from tissues to lungs. In the early Nineteen-Thirties, considerable doubt arose as to the validity of the "ratio" principle. At that time it was observed that decompression, according to Haldane's stage method following chamber exposures in compressed air of three to four hours duration, was frequently complicated by *bends*. As a result of accumulated experience, it was considered probable that, in decompression, gas bubbles form as soon as a state of supersaturation is initiated. What appears, then, to be a condition of supersaturation is, in reality, a reflection of the body's tolerance for "silent" gas bubbles.

The Isobaric (Oxygen Window) Principle of Decompression: It remained for present-day saturation diving with a gas such as helium, which is relatively insoluble and highly diffusible, to dispel credibility of "supersaturation" as the modality of inert gas transport from tissues. Thus, many hours, often running into days, are required for decompression of divers after prolonged sojourn at deep depths. Rates of decompression are far slower than those applicable to caisson workers, and consume as much time as ten to 15 minutes per foot or 23 to 34 minutes per pound decrement. This slow ascent is consistent with the existence of a very small driving force or pressure head (Δ P) for diffusion of inert gas from tissues and subsequent transport in blood. What is the physiologic basis for this driving force?

Essentially, during the course of blood flow through capillaries, oxygen is unloaded in varying amounts to diverse tissues. The result of this transfer creates a *space* or "Oxygen Window" through which inert gas can be transported from tissues to lungs. At normal pressure during inhalation of air there is a pO_2 in arterial blood of about 100 mm. Hg, and this is reduced to about 40 mm. Hg in the venous end of capillaries. The small "Oxygen Window" (60mm. Hg) can be greatly enlarged by inhalation of pure oxygen at elevated pressures. Noteworthy is the fact that if oxygen pressure is raised to two atmospheres (15 psi), then an arterial pO_2 of some 1,500 mm. Hg will fall to 500 mm. Hg or less in the venous end of capillaries.

The great advantage conferred by the "Oxygen Window" principle is that, during the course of decompression from hyperbaric atmospheres, inert gas can be eliminated from tissues via the "window," at a pressure *isobaric* with ambient pressure. The limitation to employment of oxygen (apart from *fire hazard*) is restriction of pressure level of inhalation relative to time, if toxic reactions are to be avoided. This matter will now be dealt with in our outline of some applications which have been made to incorporate oxygen into diving and chamber decompression practice.

Experience With Oxygen In Decompression Practice

The effectiveness of oxygen in shortening decompression time has been employed routinely in the U.S. Navy. During the Squalus salvage operations divers were brought rapidly to the surface and then recompressed on oxygen in a dry chamber at pressures of 26.7 psi (60 feet) to 17.8 psi (40 feet). At high pressures (usually at or above 4 Atm, 44.1 psi; occasionally, as low as 3 Atm, 29.4 psi), the convulsive seizures associated with oxygen inhalation interdict its use. Exercise notably augments oxygen toxicity and seizures in SCUBA divers have been reported at depths as shallow as 30 feet (13.4 psi). *At rest*, however, in the dry chamber, oxygen can be breathed without untoward reactions at pressures up to 30 psi (by phlegmatic men) for a period of two hours. Interruption of oxygen breathing by short intervals on air, greatly extends tolerance time. In the notable experiments of Van Der Aue et al.,[14] 993

dives were performed to test surface decompression. Minor symptoms of nausea and irritability were experienced by four of the first 28 divers who inhaled oxygen during recompression to the 50-foot level (22.3 psi). When recompression was limited to 17.8 psi (40 feet), only nine divers in the group of 30, who made 993 dives, reported nausea or irritability. Objectively, oxygen-induced vasoconstriction is reflected in a rise of both diastolic and systolic blood pressure.

Oxygen has not been routinely employed for decompression of tunnel workers, chiefly because a regimen has not been developed which would eliminate the *fire hazard*. Experience in hyperbaric chambers has demonstrated that effective control measures can be enforced to render oxygen inhalation safe. The employment of oxygen for decompression of tunnel workers would not only reduce decompression time (Washington State-California Tables) by one-half, but this measure would, in all probability, eliminate decompression sickness and aseptic bone necrosis. Some confirmatory data as to the usefulness of oxygen under exacting conditions will now be outlined.

Oxygen Recompression Following Surface Decompression: Bringing a diver rapidly to the surface for subsequent immediate recompression, or *surface decompression* (*decanting*, British) as the practice is usually designated, was forced upon diving personnel during the salvage of the submarine, S-51, in 1925, because cold water and tides rendered decompression in the open sea impractical. The procedure permits the elimination of excess inert gas from body tissues under ideal conditions, that is, with the diver breathing oxygen, warm, at rest, and under observation. The danger lies in the formation of extensive gas embolism during the interval between bottom depth and recompression.

The surface decompression dives of Van Der Aue et al., constitute rigorous trial of the effectiveness of oxygen recompression. During their stay on the bottom either in the sea or in cold water in the wet tank of the Experimental Diving Unit, divers breathing air engaged in heavy work. They were then brought to the surface at the rate of 25 feet per minute, and removed to the chamber during a time interval maintained constant at 3.5 minutes for removal of encumbering diving gear. Recompression followed immediately (0.5 min.) to 17.8 psi (40 feet).

The data in Table VI relate to these procedures. It was safe for the divers to work 150 minutes at depth (70 feet, 31.2 psi) provided 40 minutes of oxygen recompression was given in the chamber. Borderline recompressions are 44 minutes following 150 minutes at 80 feet (35.6 psi), and 43 minutes following a work dive at 90 feet (40.1 psi). Noteworthy are the symptoms of fatigue, itching, and Bends, when chamber recompression time was inadequate. It is apparent that somewhat more than 50 minutes of oxygen inhalation is required following a heavy work dive of 120 minutes at a depth of 100 feet (44.1 psi).

Oxygen Decompression Following Air Exposures in Chamber Tests: Under less stringent conditions but longer exposures in compressed air, it is observed (Table VII A) that oxygen inhalation normal pressure (1 Atm, 0 psi), compared with air breathing, is effective in preventing decompression sickness following abrupt release (1.5 min) of pressure from 16.9 psi (38 feet). However, the time on oxygen of six hours is too long for routine employment. Tests were not made to determine if oxygen inhalation could be shortened. Likewise, in Table VII B, oxygen decompression following prolonged (saturation) exposures of twelve hours in compressed air is not only lengthy but favorable outcome is uncertain. In tests not shown in the Table, it was found that reduction of exposure time in compressed air to six hours reduced decompression time by a factor of three to four. Although the quantity of nitrogen taken up by tissues after six hours may be small, it certainly gives rise to Bends unless many hours are taken for decompression. Oxygen decompression is most effective when stay in compressed air is not sufficiently prolonged so as to saturate fatty tissue, e.g., four hours at 30 psi; two hours at 40 psi.

In Table VII C, the data were recorded in tests of a "worst possible" case to demonstrate safety and effectiveness of oxygen decompression as it would be employed (with possible modification in regard to pressure level) in tunnel work. The test subject was over-age (65 yr.), overweight (by about 10 lb.), and, earlier in life, susceptible both to diving and altitude decompression sickness. He was subjected to bouts of heavy work in an unventilated chamber in which relative humidity was above 90% (Effective Temperative Index, 81). Despite dehydration and fatigue resulting from work, he did not develop prodromal or actual symptoms of decompression sickness. Prior to each test, usually on successive days, he was in good condition.

The decompression times (Table VII, C) probably incorporate an appreciable safety factor which may be reduced for younger men. However, the levels at which oxygen was inhaled (30 psi for ten minutes, and 20 psi for two hours) without interruption might give rise in less phlegmatic persons to nausea and irritability to which apprehensive individuals are prone. Workman[15] has set forth an oxygen decompression Table for decompression of personnel in

TABLE VI

A. OXYGEN (CHAMBER) RECOMPRESSION FOLLOWING SURFACE* DECOMPRESSION FROM AIR DIVES IN THE OPEN SEA AND AT THE EXPERIMENTAL DIVING UNIT (E.D.U.), VAN DER AUE ET AL.[14]

B. REACTIONS FOLLOWING PROGRAMMED SHORTENING OF OXYGEN RECOMPRESSION TIME OF DIVERS WHO ENGAGED IN HEAVY WORK AT A DEPTH OF 100 FEET (44.1 PSI) AND BROUGHT RAPIDLY TO THE SURFACE* (E.D.U. WET TANK DIVES FROM VAN DER AUE ET AL.[14]

A. Depth feet	Pressure psi	Bottom Time min	Time on Oxygen in Chamber min	Elapsed time from depth to recompression in chamber min	Number of Dives and Bends (—) Key West	E.D.U.
70	31.2	52	0	3	—	4(0)
		90	24	9	8(0)	—
		120	32	9	—	4(0)
		150	40	9	8(0)	—
80	35.6	40	0	3	—	4(0)
		85	20	9	8(0)	—
		115	31	9	—	4(0)
		150	44	9	6(2)	—
90	40.1	60	14	10	—	5(0)
		80	25	10	8(0)	—
		120	43	10	7(1)	4(0)

B. Number of dives	Time at Depth min	Water Stops	Time in Chamber on Oxygen at 17.8 psi	Reactions None	Fatigue	Itch	F & I**	Bends
4	26	0	0	4				
4	28	0	0	1	3			
4	30	0	0	2	2			
4	40	0	0	1	1	1	1	
4	50	0	10	4				
8	60	0	33	5	3			
4	60	0	15	4				
4	60	0	5	1		1		2
8	75	0	19	6	1	1		
4	75	0	11	1				3
8	85	0	51	8				
4	85	0	16	1				3
4	120	3' 30 ft	50	3	1			
4	120	3' 30 ft	41	1				3

**Rate of ascent to surface (25 ft/min); at surface 3.5' before recomp.*
***F & I, fatigue and itch.*

hyperbaric chambers which prescribes the inhalation of oxygen at pressures of 13.4, 8.9, and 4.45 psi (30, 20, 10 feet, respectively). The total time for decompression following residence in compressed air (three hr.) at 31.2 psi is 58 minutes and 78 minutes following a four hour exposure. These periods of oxygen inhalation are about the same as those in Table VII C.

Periodic Sojourn in Compressed Air

It has been apparent for many years that prolonged residence in compressed air (and habitation pressures need not exceed 14 psi) would solve most of the medical problems outlined in this paper. The practicality of the more difficult "saturation" exposures in diving operations oriented partly toward work objectives has been demonstrated. In a past era, patients have even been maintained comfortably for more than a week in a pressurized sphere. Any proposal, however, such as prolonged residence in compressed air must have "worker acceptance" and Union-Management sponsorship. Heretofore, extended residence in compressed air for periods of ten to 14 days at a stretch, although entirely feasible, has had little appeal to highly paid men accustomed to an eight hour day, 40-hour week routine. To implement this new approach would require test demonstrations which could be conducted at modest cost.

Specifically, a *Holding Facility*, at no time pressurized higher than 12.0 psi (27 feet equivalent) would permit workmen to leave (if a personal

TABLE VII

A. VALUE OF OXYGEN INHALATION AT ONE ATMOSPHERE FOLLOWING RAPID DECOMPRESSION (1.5 MIN.) FROM 16.9 PSI.

B. A COMPARISON OF DECOMPRESSION WITH OXYGEN AND WITH AIR FOLLOWING 12 HOURS EXPOSURE IN AIR AT 26.7 PSI.

C. OXYGEN DECOMPRESSION FOLLOWING AIR EXPOSURES

A. E.D.U. Tests, 1939-1940, Behnke			
psi	*Equiv. Depth*	No. Tests	Type of Decompression — Remarks
16.9	38	15	1.5' from 16.9 to 0 psi — 14 Tests- No Symptoms
Duration: 4 to 24 hrs.			Oxygen Inhaled for 6 hrs at 0 psi (1 Atm) — 1 Test — Bends
16.9	38	8	1.5' from 16.9 to 0 psi — 2 Tests — No Symptoms
Duration: 5 to 12 hrs.			Continued on Air at 0 psi
Composite Signs and Symptoms			6 Tests
rash, dizziness, muscular soreness, Bends			

B. E.D.U. Tests, 1939-1940	Chamber Tests, 12 Hours Exposure in Air
psi *Depth*	Duration of Inhalation of Oxygen at 22.3 to 17.8 psi for Each Exposure and the Results of the Oxygen Decompression
26.7 60	minutes
10 Tests:	63 69 80 82 84 92 154 (*Bends — Knee pains in all tests foll. decompression*)
	92 93 (Bends — Pains in the upper extremities)
	102 (spinal cord involvement)
7 Tests:	Duration of Oxygen Inhalation at 22.3 to 17.8 psi + Oxygen Inhalation Continued at 1 Atm (hrs)
	81 81 93 102 154 161 161
	\+ \+ \+ \+ \+ — No Symptoms
	4 2.2 4 3.2 1.8
	Air Decompression, Duration of Each Exposure (min) + Oxygen Inhalation in Some Tests at 0 psi
	237 237 237 237 275 275 311 — Underlined
	\+ \+ \+ \+ — decompressions
	4 4.3 2.5 5 — *followed by Bends*

C. Oxygen Decompression Following Chamber Exposures of Worst Possible Case* (Transit Medical Center Tests, Behnke, 1968)					
Heavy work Pressure 30 psi	Exposure Time (hrs)	1	2	3	4
Heavy work	Oxygen, 30 to 20 psi (min)**	—	40	60	80
Pressure 40 psi	Oxygen, 30 to 20 psi (min)**	30	60	90	120

**Subject overage (65 yrs), overweight (10 lbs). Subject remained in good condition following all tests.*

***The inhalation period for oxygen included 5 minutes decompression from 20 psi to 0 psi (normal pressure).*

emergency arose) at any time, if safeguarded by minimal decompression. Effective work at pressures higher than 12.0 psi could be conducted also, with minimal decompression based on the "excursion principle" which has rendered deep sea diving safe and practical.

Larsen and Mazzone[16] have provided test data which support the feasibility of NO-decompression excursions from a "storage" exposure in compressed air equivalent to 35 feet diving depth (15.6 psi), Table VIII. All excursions were made in a dry chamber following a 24-hour saturation period at 35 feet equivalent (15.6 psi). After completion of the excursion dives, the divers were held at *15.6 psi* for six hours in order to detect any effects of decompression. Decompression from 15.6 to 0 psi then followed a schedule formulated by Capt. Workman, MC, USN. Thus, after an excursion of four hours to 44.5 psi (100 feet), followed by stay of six hours at *15.6 psi, decompression* embraced a reduction of pressure to 8.9 psi (20 feet) in five minutes; stay of 40 minutes breathing air at this pressure; reduction of pressure to 4.45 psi (ten feet) in five minutes; stay of two hours at this pressure breathing air, followed by oxygen inhalation for one hour, then to 0 psi in five minutes. Total time required for decompression from 15.6 psi to 0 psi: three hours, 55 minutes.

The essential proposal applicable to tunnel workers remains to be developed in detail during the course of experimental work exposures. One of the hard lessons learned from use of diving decom-

TABLE VIII

A. TEST DATA IN A DRY CHAMBER WHICH SUPPORT THE FEASIBILITY OF "NO-DECOMPRESSION" EXCURSIONS TO HIGHER PRESSURES FROM A SATURATION (STORAGE) PRESSURE OF 15.6 PSI (FROM LARSEN AND MAZZONE).[16]

B. CONSERVATIVE APPLICATION OF THESE DATA TO TUNNEL WORK AS A SCHEDULE SUBJECT TO PROGRAMMED TRIALS.

A. Saturation Pressure psi	Equivalent feet	Excursion to Higher Pressure psi	feet	Time of Exposure min.	
15.6	35	44.5	100	240	(25)*
15.6	35	48.6	109	120	(20)*
15.6	35	52.1	117	90	(15)*
15.6	35	60.1	135	60	(10)*
15.6	35	73.5	165	30	(5)*

**Permissible time for NO-Decompression excursions from one atmosphere (0 psi) to higher pressures (U.S. Navy Tables)*

B. NO-DECOMPRESSION WORK SHIFTS AT HIGHER PRESSURES*

Pressure in Holding Facility	Pressure for Work Shift	Work Time*
psi	psi	hr.
15	25	6
15	30	4
15	35	3
15	40	2

**At the higher pressures men could work two shifts daily, i.e., 'split-shift' with suitable rest intervals*

pression tables, as Van Der Aue et al. have convincingly demonstrated, is that *extrapolation is dangerous.*

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BAROMETRIC PRESSURE

Researches In Experimental Physiology

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Chapter I

HIGH PRESSURE

1. Diving bells.

At the beginning of the sixteenth century Sturmius invented the diving bell, which was to render such great services. It was simply a bell heavily weighted, which, full of air, was allowed to sink vertically in the water until it touched the bottom. The water penetrated the apparatus to a height which increased with the depth of the immersion: at ten meters, there was under the bell, in volume, half air and half water; at twenty meters, two-thirds water and one third air, etc.; the workmen, who were ensconced up to that point on seats like shelves, got down from them to work under the worst conditions.

The inventor considered the harmful effect which the air compressed by the descent might exert upon them; to prevent it, says Panthot,[1] he advised that air should be taken along in bottles which would afterwards be broken under the bell.

This procedure, which could not alter at all the tension of the air, was improved upon by Halley, with a purpose in greater harmony with the laws of physics. The English physician planned to drive out the water which encroached upon the workman and to renew the air which had been made foul by his respiration; he did so by letting down under the bell small barrels full of air, which the diver received and opened at will; the warm and foul air escaped from the top of the bell by means of a valve. Halley even found the means of permitting a diver to leave the bell, keeping in communication with the compressed air contained in it by mean of a tube and a helmet covering the head. (Brizé-Fradin, 2nd. S., pl. I.). This was the first idea of the diving suit.

Spalding made improvements of a purely mechanical type in Halley's apparatus; these improvements did not prevent him from meeting death in his own apparatus in 1785.

Brizé-Fradin, from whose work [3] I have borrowed most of the preceding information, summarizes in the following words the disadvantages of the diving bell:

> 1. Keen and unendurable pain in the ear, due to the compression of the tympanic membrane;
> 2. Deterioration of the air by the breathing of the workmen, with asphyxia as the result;
> 3. Most physicists have found a third disadvantage; they believe that the elasticity of the air, acting in all directions and at all depths, compresses the blood vessels, and the arteries, and causes hemorrhages.
>
> We may oppose to this statement unvarying data and direct experiments; let us listen to M. Halley:
>
> "I myself was one of the five persons who dived to the depth of 18 meters, without being inconvenienced by it; we remained for an hour and a half; I could even have staid there longer, for there was nothing to prevent it."
>
> This testimony of M. Halley could be seconded by that of all the divers. The pressure of the air under water, at a depth of 18 meters, does not cause blood-spitting; if one dived deeper, of course, he would find the limit where the compressed air could not be breathed. (P. 171)

And yet, adds Brizé-Fradin:

> Noting the equal value of the water pressure and the compression of the air, it seems that the diver placed under the bell at a depth of 18 meters should be in a state of general collapse. (P. 173)

The Court Councilor of the Emperor of Russia, whose fatal ascent of Mont Blanc we have already reported, Dr. Hamel,[4] descended in a diving bell installed by Rennie in the port of Howth, near Dublin; the depth of the water was about 30 feet. He felt no other inconvenience than violent pains in his ears, "as if some one were forcibly inserting a stick," which he checked by swallowing his saliva. From that the idea came to Hamel "that the divers' bell might serve as a remedy in cases of deafness resulting from the obstruction of the Eustachian tube."

In regard to the rest he merely says:

> I expected to experience some painful effect upon respiration, resulting from the pressure of the air increased by the weight of almost a whole atmosphere; and yet I did not feel the least inconvenience in this respect.

The same year, Dr. Colladon [5] descended in the same bell and to the same depth. He is a little more explicit:

> We descended so silently that we did not perceive any movement of the bell; but as soon as it was immersed in the water, we felt in our ears and on our foreheads a sensation of pressure which kept

> increasing for several minutes. However, I did not experience any pains in the ears; but my companion was in such pain that we had to stop the descent for a few minutes. To remedy this distress, the workmen advised us to swallow our saliva, after closing the nostrils and the mouth tightly, and to hold our breath for a few instants, so that, by this exercise, the inner air might act upon the Eustachian tube. My companion got little relief from this procedure. When we began to move again, he was in great pain, he was pale, his lips had lost their color, one would have thought him nauseated. His prostration was due, no doubt, to the violence of the pain, added to a fear which he could not overcome. This experience produced the opposite effect upon me: I was in a state of excitement, as if I had drunk some alcoholic liquor, I had no pain, I merely experienced a strong pressure around my head, as if an iron ring had been fastened tightly about it. While I was talking with the workmen, I had some difficulty in hearing them; this difficulty in hearing became so great that for three or four minutes I did not hear them speaking; I did not even hear myself, although I was talking as loud as I could, and soon the noise caused by the violence of the current against the walls of the bell no longer reached my ear. (P. 6) . . . .
>
> At last we reached the bottom of the sea, where every disagreeable sensation ceased almost entirely . . . .
>
> We breathed very easily during our whole visit under water . . . . Our pulse rate showed no change . . . . .
>
> As we rose again, our sensations were very different from those we had experienced as we descended; it seemed to us as if our heads were becoming much larger; that all our bones were on the point of separating. This discomfort did not last long. (P. 8.)

To these almost negative observations, Colladon adds two facts which are most interesting and which were the point of departure of important therapeutic applications:

> None of the workmen become deaf; it would rather seem that in certain cases, the effect of the bell on the ears might serve as a remedy for deafness. One of the workmen, who had habitually breathed with great difficulty, was completely cured shortly after undertaking work in the bell. (P. 14.)

The diving bell today is completely abandoned. It has been replaced by caissons filled with compressed air by the Triger method.

Interesting attempts have been made repeatedly to invent submarine boats in which men would live either in compressed air or in air at normal pressure. These attempts began in the seventeenth century; Father Mersenne, the friend of Descartes, did not scorn to apply himself to the subject; more recently R. Fulton in the port of Brest made attempts which perhaps should have been encouraged; then came Payerne, whose *submarine hydrostat* operated with some success. In our own time, M. Villeroi,

then Rear-Admiral Bourgeois invented *cigar-boats* which might be used in case of war. But since no observation of a physiological nature has been made with the help of these contrivances, and since I have no desire to write a history, no matter how short, of the industrial applications of compressed air, I now come without other transition to the numerous data relating to the digging of mine shafts and to the sinking of bridge piers by the Triger method.

2. Apparatuses Constructed by the Triger Method.

It is, in fact, to M. Triger, a French engineer, that we owe the valuable invention of the use of air compressed to high pressures for boring mine shafts and sinking bridge piers. It was a question of working in the grant of Haye-Longue (Maine-et-Loire) coal-bearing strata covered with alluvial deposits over which flowed the waters of the Loire. It was impossible to drain off the water which seeped through and prevented them from extending the galleries: M. Triger conceived the simple but brilliant idea of driving it back and holding it by pumping compressed air in through the upper part of the shaft; protected by the drainage thus secured, workmen could stop the leaks by vaults of masonry.

M. Trouessart, whose report on this wonderful discovery we shall quote later, comments that Denis Papin had already had an idea of this sort, in 1691, and he quotes the following passage, which is indeed very noteworthy:

> Fresh air could be injected constantly into the diving bell by means of a strong leather bellows furnished with valves, by a tube passing under the bell and opening into its upper part. And so, since the bell would always remain empty and rest entirely on the ground, the bottom in this place would be almost dry and one could work there just as if he were out of the water, and I have no doubt that it would save much expense when construction must be carried on under water. Moreover, in case the leather bellows were not strong enough to compress the air as much as would be necessary at great depths, one could always meet this difficulty by using pumps to compress the air.

But from this idea to the complete invention of M. Triger is a long way; in 1839, he solved the problem from a practical standpoint, and listed the numerous applications which would later be made of it.

The complete explanation of this invention is in a Memoir [8] presented to the Academy of Sciences in 1841.

We naturally omit all details of the construction of the appara-

tuses and come to the mention of physiological phenomena, not much considered, as we shall see, by the celebrated engineer.

An interesting fact appears at once; M. Triger wished to try upon himself the effect of compressed air. Now:

> At the moment when the manometer had hardly risen to the height of 40 inches (total pressure), there was a report, and we were struck with icy cold and plunged into the most complete darkness, because of the instantaneous formation of a thick mist: a windowpane of the apparatus had burst.
>
> This explosion had no other result that to cause us a great surprise.

M. Triger next mentions, ascribing them quite accurately to their cause, the pains in the ears that accompany compression and decompression. Then he adds, and this is all his Memoir contains on the subject which interests us:

> At the pressure of three atmospheres, it is not possible to whistle in compressed air: but the power is lost only when one reaches this pressure.
>
> In compressed air, everyone talks through his nose, and this becomes increasingly noticeable with increase in pressure.
>
> The workmen have noticed that while they were climbing the ladders, they were less out of breath in compressed air than in free air.
>
> I shall end with a rather interesting observation, which I was in a position to note personally: namely, that a miner, named Floc, who had been deaf since the siege of Antwerp, invariably heard more distinctly in compressed air than any of his comrades. (P. 892.)

Professor Trouessart,[7] commissioned by the Industrial Society of Angers to investigate the practical results of the apparatus of M. Triger, gave an account of his researches in an interesting Memoir.

There is very little mention of physiology in it; however, we do find in it a few observations which deserve to be reported here, particularly because they were the first made on man at pressures of 3 atmospheres above the normal atmosphere:

> It is with a certain apprehension, we admit, that one goes down for the first time into the apparatus to be subjected to a pressure of three atmospheres there. These 32,000 kilograms above the former pressure which you will have to endure are enough to terrify the stoutest shoulders.

First comes the description of the pains in the ears, which are thoroughly studied and explained:

> A phenomenon which is more difficult to understand is that deaf persons not only hear better in compressed air than in free air, but that they hear better than persons whose ears are normal . . . .

One of the strangest results is that one suddenly loses the power of whistling under the pressure of 2¾ to 3 atmospheres.

The functions of nutrition, respiration and circulation do not seem perceptibly altered in compressed air. At the time of our first visit, we thought that we found an increase in the pulse rate of every one subjected to the experiment; but on our second visit, the result of a more accurate observation, made by a member with much experience in taking the pulse, was completely negative . . . .

The respiration is neither slower nor faster. It seems that it is not more active and that the animal heat is not increased. The blood too gushes out under normal conditions. In a word, the most surprising thing is that there are very few changes in the vital functions. The workmen assert that they climb the ladder more easily and are less out of breath when they reach the top. This cannot result from the rather slight loss in their weight. Is it possible that they can hold their breath longer because of the greater density of the gas inhaled at each respiration? On the other hand, they maintain that they become much more tired when working in compressed air than in open air. We think that this is the result of the very great humidity of the atmosphere of the shafts, which hampers the insensible perspiration and promotes the more rapid secretion of sweat in those who have to exert their muscular powers in such a medium. Perhaps this humidity would also explain the somewhat severe pains in the articulations experienced by some workmen a few hours after leaving the shaft . . . .

We may conclude that there is no serious danger in staying several consecutive hours for several successive days in air compressed to 3 atmospheres.

Our author says nothing of the duration of the decompression; he seems, moreover, to pay more attention to "the passing from a ow to a high pressure": he only says that they opened the cock gradually.

In a second communication to the Academy of Sciences, M. Triger[8] repeats his former observations. He adds to them the following data:

Everyone talks through his nose and loses the power to whistle at 3 atmospheres. To ascertain the effect of compressed air on a stringed instrument, I had a violin taken down into the shaft and it was found that at the above pressure the sound lost at least half of its intensity.

Then comes the first suggestion of the rather serious symptoms of decompression:

I should say here that two workmen, after passing 7 consecutive hours in compressed air, experienced rather keen pains in the articulations, half an hour after leaving the shaft. The first complained of a very sharp pain in his left arm, and the second experienced a similar pain in his knees and left shoulder; rubbing with spirits of

wine soon relieved this pain in both men; they kept on working the following days.

In 1846, M. de la Gournerie,[9] getting his idea, he said, from an apparatus suggested in 1778 and approved by the Academy of Sciences in 1779, used for the extraction of rocks in the channel of the port of Croisic a boat with a metal chamber open at the bottom, from which the water was expelled by compressed air.

He submerged it only 3 or 4 meters; it is not surprising then that

> The workmen never found that the air pressure inconvenienced them. It merely gave them a slight discomfort in the ears for a few seconds.
>
> The pulse rate is not noticeably increased. (P. 308.)

In the mines of Douchy (Nord) the method used by M. Triger on the banks of the Loire was first imitated. The difficulties were greater, because here it was not a matter of penetrating permeable sands with a sheet-iron tube 1.50 meters in diameter, but of digging a shaft 3 meters in diameter through limestone.

We shall shortly quote the important Memoir which the physicians Pol and Watelle devoted to the study of the symptoms which attacked numerous workmen in this undertaking. The first account of them was given by a report of the engineer Blavier,[10] sent to examine this new invention.

He first mentions the pains in the ears and the inability to whistle. A certain effort must be made in speaking:

> It seemed to us also that in the diatonic scale the voice lost a tone or a tone and a half in the upper notes without gaining in the lower ones.

He found no difference in the pulse rate before entering the apparatus and while within it:

> If the effects of compressed air upon the animal organism do not appear during the whole time that one is subjected to it, at least during one shift of workmen, the same thing is not quite true if we try to consider subsequent effects . . . . Most of the workmen, although selected from the most robust and healthy, have frequently felt heaviness in the head or pains in the legs a few hours after leaving the caisson. Only one of them experienced complete paralysis of arms and legs for 12 hours. The superintendent of the mine assured us that the effects felt almost always coincided with some excess committed between shifts. (P. 361.)

However, Blavier himself, after being subjected to the total pressure of 2.6 to 3 atmospheres, was attacked by a fairly severe symptom:

> The day after our visit of December 5, keen pains appeared in the left side, and we felt a rather severe painful discomfort for several days afterwards. Since a chill or some other cause not connected with the compressed air might have been acting, after we were quite free from these pains, December 28, we were anxious to try the experiment again, and when we left the shaft, we took the greatest precautions to protect ourself from any chill. In spite of these precautions, the next day, very noticeably at the same hour, that is, 20 hours after our exit from the medium of compressed air, we felt in the right side pains just like the former ones, which kept us numb for four or five days. (P. 362.)

We now come to the important Memoir, the first written by physicians about these symptoms, in which MM. Pol and Watelle [11] recount the effects of compressed air upon the miners during the excavating at Avaleresse-la-Naville, at Lourches, in the grant of Douchy (Nord).

The authors took care to warn the reader that since their notes were made without any intention of publication, they made their observations without plan, without program, and consequently without system. But they thought, and with good reason, that their work would nevertheless present some interest and some utility.

During the exploitation, the total pressure rose to 4¼ atmospheres. The compression was made in a quarter of an hour, the decompression in a half-hour; 64 workmen took part in the work; they usually stayed four hours consecutively in the apparatus, twice a day.

The authors described separately the physiological effects which they observed in themselves and the pathological effects experienced by the workmen:

1. *Physiological effects*: Pains in the tympanic membranes; slowing of the respiration and particularly a decrease in the amplitude of the thoracic expansion, which became hardly perceptible; slowing of the pulse, (from 70 to 55); increase of urinary secretion.

The authors also mention a "muscular sensation of a resistance to be overcome, as if the unusual density of the ambient atmosphere hindered movement; the inability to whistle, experienced above 3 atmospheres, is also attributed to an unexpected resistance, experienced by the muscles of the tongue in compressed air.

On the return and during the decompression, they experienced a keen sensation of cold, a kind of panting; the pulse rose to 85.

Pathological effects. Taking the observations as a whole, we

see that out of 64 men, 47 withstood the work fairly well; 25 had to be discharged; 2 died. Taking them in detail, we see that 14 felt slight symptoms, 16 more or less severe symptoms, sometimes even threatening life; 2 died.

On the other hand, 2 benefited by a certain improvement. One (First category, obs. I) was asthmatic, and breathed better in the shaft; the other (Third category, obs. 3) chloro-anemic, having had frequent blood-spitting, found that his oppression disappeared and his mucous membranes became redder:

> We see dawning, (MM. Pol and Watelle said in this connection) without concealing the difficulties of application, a new resource of palliative therapeutics in the treatment of most dyspneas.

The universal rule without exceptions was that the symptoms appeared at the time of decompression:

> The danger does not lie in entering a shaft containing compressed air; nor in remaining there a longer or shorter time; decompression alone is dangerous: *pay only when leaving.*

Let us see now what these more or less serious symptoms are. They are, first, pains in the eardrum, more or less severe and lasting, and M. Pol states that they can be checked much more quickly by blowing one's nose than by going through the motion of swallowing.

As for the other symptoms, as MM. Pol and Watelle had the good sense to give the complete observations, I think I cannot do better than to summarize each in a few words, following the order in which they presented them:

First Category. *Workmen on the Job from the Beginning.*

Observations. I. Asthmatic, breathes better in the shaft. On decompression, violent oppression with exaggerated circulatory reaction. Discharged.

II. Went up to 4½ atmospheres. Respiration hampered, decrease of appetite, indigestion, pains in the limbs. Stools dark. Lost much weight.

III. Same effects.

IV. Same.

V. Did well up to 3 atmospheres. After that, dizziness, muscular pains, cramps or general numbness, vomiting of dark matter. All this on the return to open air.

One day, an hour after leaving the shaft, having eaten, he complained of distress; when placed in bed, *he lost consciousness.* Pulse full and rapid, face congested, respiration short and stertorous; obscure sound everywhere, bronchial murmur, mucous râle; muscular resolution. Bled, purged, plastered. After four hours, return to consciousness. In three days, cured. Discharged.

VI. Taken to 4¼ atmospheres without accident. One evening, after going to bed apparently well, at 11 o'clock seized by muscular pains accompanied by contractions like tetanus spasms.

Skin cold, pulse small and slow, urine abundant and clear. Respiration uneasy; same results of auscultation as V.

Baths at 32° so aggravated the pains that the patient could not remain in them. Friction, strong sudation, quiet. Recovered next day, back at work.

VII. At a pressure of 3.3; cerebral disturbances, like intoxication with coma, hebetude, stuttering. Respiration accelerated, pulse rapid. Pupils dilated.

Two similar attacks, cured one in nine days, the other in fifteen. Continuance of double vision and vertigo, with deafness on one side. Discharged.

VIII. Presented an excessive form of two common phenomena: 1. suppression of the functions of the skin and increase of the urinary secretion during the compression: 2. increased rapidity of the heart beats after decompression; his pulse rate rose from 58 to 130.

IX to XVII. Nothing important to be noted.

XVIII. Healthy and vigorous. Experienced repeatedly keen pains in the limbs and chest. Respiratory disturbances increasing with the pressure, as well as the muscular pains which were very acute.

Was discharged. During the last days went down into the shaft without permission. Worked there without complaining; went out with his companions, washed himself like them, immediately fell unconscious and died in a quarter of an hour. Autopsy shows only obstruction of the lungs, congestion of the liver, the spleen and the kidneys; nothing in the brain except gritty congestion.

XIX. Violent oppression with dullness on percussion and bronchophony; rapid pulse, cold skin, continual cough; clonic contractions of the limbs; more sensitive after five hours of treatment.

Then, at another time, to these symptoms are added: dilation of the pupil, relaxing of the limbs, *subdilerium, coma.* Three bleedings in rapid succession; blood bright red on leaving the vein; cured. Discharged.

XX. Same symptoms as VII. Also remained deaf on one side, with vision much weakened. Discharged.

XXI. One day, sight affected and double, hearing gone; respiration hampered, cough frequent, pulse hard and galloping. Blood red, recovered.

XXIV and XXV. Nothing important.

XXVI. Usual thoracic and cerebral symptoms; recovered after profuse sweatings. (P. 250 to 259.)

Special Category of men who worked only one day and without preparation at 2.8 atmospheres.

Nine men left the shaft without making any complaint. But shortly afterwards, eight experienced very severe muscular pains, which disappeared during the night, except in one, in whom they persisted several days.

Second Category. *Workmen who worked only above 2.9 atmospheres.*

I. No effect.

II. Only muscular pains in the left thigh, which yielded to cold water.

III, IV. Nothing.

V. Moderate muscular pains, but persisting from one shift to the next; recompression relieved them immediately.

VI. Nothing.

VII. 28 years old. Athletic. Pressure of 3.8 at the beginning. After 10 days, loss of consciousness, violent lockjaw. Rapid pulse.

Reddish bleeding eight hours afterwards, purging, blisters.

Two days after, *consciousness suddenly returned:* the patient opened his eyes, seemed to awaken from a dream, said a few astonished words.

Recovers, but remains extremely deaf.

Third Category. *Workmen who began at 4.154 atmospheres.*

I, II. Nothing.

III. Had previous hemoptysis. Improvement.

IV, V, VI. Nothing, except rather severe muscular pains.

VII. 40 years old. Very robust. Went down into the shaft only once. On coming out (decompression in twenty minutes) *died* almost immediately.

Autopsy held 36 hours after death: generalized subcutaneous emphysema (existed before putrefaction began, the authors note); nothing in the meninges, in the brain, or the cerebellum; *congestion of the lungs with generalized darkish tint* (underlined by the authors); blood fluid and dark in the heart; liver, spleen, and kidneys congested.

VIII. Nothing.

IX. Moderate muscular pains.

X. At his first trial, very severe muscular pains, persisting for several days. Discharged.

XI. Same.

XII to XIX. Nothing, except insignificant muscular pains. However, they sustained the pressure of 4¼ atmospheres for three months.

XX. At his first trial, too rapid decompression. A few minutes after his leaving the *lock-chamber, looked like a corpse:* face pallid, icy cold, eyes dull, pupils enormously dilated, respiration uneasy; on listening to the heart, heard only a vague quivering; pulse imperceptible; perception gone; involuntary urination; dark vomit; complete loss of muscular power.

Warm bath, blankets, friction. After a half-hour, the pulse begins to be perceptible, the respiration is deeper, a little warmth appears in the body; the patient stammers disconnected words. During the night, hardly has warmth been reestablished when acute pains appear in the muscles; keen pains in the head, blindness and deafness; wretched pulse, 50.

Evident improvement two days afterwards; the patient sees vaguely. Vision remains weak and pupils are abnormally dilated.

XXI. At his first trial, too rapid decompression. Severe muscular pains persisting for six days.

XXII. At his first trial, too rapid decompression. *Loss of consciousness*, resolution of limbs; respiration embarrassed, pulse full, hard, 130.

Bleeding blood red, blistering; after four hours, consciousness returns. During the night, cramps and muscular pains of terrible violence.

Survives, but with great weakness of vision and extreme deafness. (P. 265-275.)

I shall now quote the description of the complication which attacked M. Pol himself, because it contains the account of a very strange symptom, upon the importance of which we shall dwell later. The pressure undergone had been 3.48 atmospheres:

At 11 o'clock, he reached his lodging; he felt keen pains in his left arm and shoulder; the walls of the thorax were also painful. It seemed to him that emphysema existed in these regions . . . . About midnight, he had a few chills, followed by vomiting. He took a cup of tea and went to sleep; soon abundant sweat broke out. The next day, he was in his usual condition. (P. 250.)

In summary, the symptoms noted, *at the time of decompression*, are as follows:

Respiratory difficulties, which may go as far as anxiety;

Acceleration and hardness of the pulse;

Muscular pains which are often very severe: "none of the effects of decompression appeared so general; sole symptom in many cases, it is the initial symptom in almost all . . . . It is the first and the largest link in a chain which includes successively, by ascending order of severity and descending order of frequency, non-permanent or clonic spasm, resolution, and finally sideration" (P. 227);

Cerebral symptoms, dullness of intellect, loss of sensitivity and consciousness, coma. Deafness, blindness, very often permanent;

Finally, sudden death.

The reading of the observations abstracted above shows what a variety of form and intensity is presented by the symptoms, even for the same pressures, in different individuals, and sometimes in the same individual.

MM. Pol and Watelle noted that young men from 18 to 26 resisted much better than mature men; out of the 25 who were discharged, 19 were more than 40 years old, and 5 were more than 30; the other was 28 years old.

These symptoms are attributed by the physicians of Douchy exclusively to pulmonary, hepatic, renal, or cerebral congestions. In the special chapter devoted to the enumeration of theoretical explanations, we shall see what theories of these pathological phenomena were given by MM. Pol and Watelle.

I have wished to review at length their important Memoir, the first study of high pressures to appear, not only because of the numerous interesting observations reported in it, but also because truths of great importance are clearly revealed by it:

1. "Compression, up to 4¼ atmospheres, is not dangerous in itself; it is endured very well and infinitely better than a rarefaction which is proportionately much less." Only the return to normal pressure is dangerous; its danger is proportional both to the amount of the compression and the speed of the decompression: the decompression must therefore be very gradual;

2. In compressed air, the venous blood becomes bright red. This effect lasts a short time after return to normal pressure;

3. We are "justified in hoping" that a sure and prompt means of relief would be to recompress immediately, then decompress very carefully;

4. Chlorotic or anemic persons and those who have respiratory difficulty will be benefited by a stay in air compressed to a variable degree.

During the work at Douchy, an explosion occurred at a time when the total pressure was 3.20 atmospheres. It was the subject of a report by M. Comte,[12] chief engineer of the mines. Eight men were in the apparatus at the time; four were crushed to death; two others, after beginning to climb the ladder to leave the cylinder, let go of it, without anyone ever being able to find out why or how; a seventh workman felt no ill effects; the eighth, who was overtaken by the water, also managed to escape. In regard to him, M. Comte suggests a strange and interesting hypothesis, interesting because it shows how easily the best minds go astray in these questions:

> Perhaps he found some help in rising above the water . . . . in the specific lightness given him by the compressed air with which certain parts of his body were still more or less filled. (P. 130.)

The new method quickly became general. Other shafts were sunk, and data similar to those reported by MM. Pol and Watelle were observed.

That happened, for instance, according to the report of Bouhy [13] in the mine of Strépy-Bracquegnies (Belgium):

> At Strépy-Bracquegnies, all the laborers, except one, who worked in air compressed to 3.70 atmospheres, and from 4 to 5 hours consecutively, were attacked, after leaving the apparatus, by more or less acute pains . . . . These pains, the seat of which was chiefly in the articulations, such as the knees, the shoulders, and the joints of the arms, appeared in certain persons so severely that they sometimes went more than forty-eight hours without being able to sleep . . . .
>
> It was noted that some laborers who had had rather severe attacks and who had gone down to work were completely relieved of pain as soon as they were in compressed air, but that the pains came on again some time after they had left the apparatus.
>
> Besides these effects, the author again mentions unpleasant stinging over the whole surface of the body and especially on the extremities.

But compressed air is used chiefly on the foundation of bridge piers, and it is under these conditions that hundreds of workmen are exposed to its effects every year. It is therefore of interest for us to explain briefly the mode of application of the Triger method in this particular case.

Figure 6 will permit us to be very brief in our explanations; it is a cross-section which we borrow from the memoir of Dr. Foley, which will be reviewed later.

A cast-iron tube MM composed of concentric rings fastened together by bolts *m*, and ending at the bottom of a widened chamber or "crinoline," is let down upon the bed of the river in the spot which the bridge pier is to occupy. It is topped at its upper end by a room with 3 compartments; the one in the middle, F, is in constant communication with the cast-iron tube; a blowing machine, through a tube G, constantly pumps into it air which is sufficiently compressed to drive all the water out of the cast-iron cylinder, and escape constantly bubbling all around; the bottom then becomes dry, as happens in a glass tube into which a child blows after immersing it in water.

Under these conditions, the workman who is coming to work opens the door of one of the lateral chambers, E, and closes it behind him, and by a cock communicating with the central chamber F, equalizes the pressure of the air about him with that of the air in the cylinder. When this has been done, he easily opens the inner door, hitherto held shut by the pressure, and goes down to the bottom of the shaft by a ladder. There he works and fills with the earth which he digs out buckets which are hauled up and emptied outside. Does he wish to leave? He goes to the other lateral chamber C in which the air has remained under pressure, goes in, closes the door, and by a cock communicating with the

exterior allows the excess of compressed air to escape. He can then easily open the outer door and leave the apparatus.

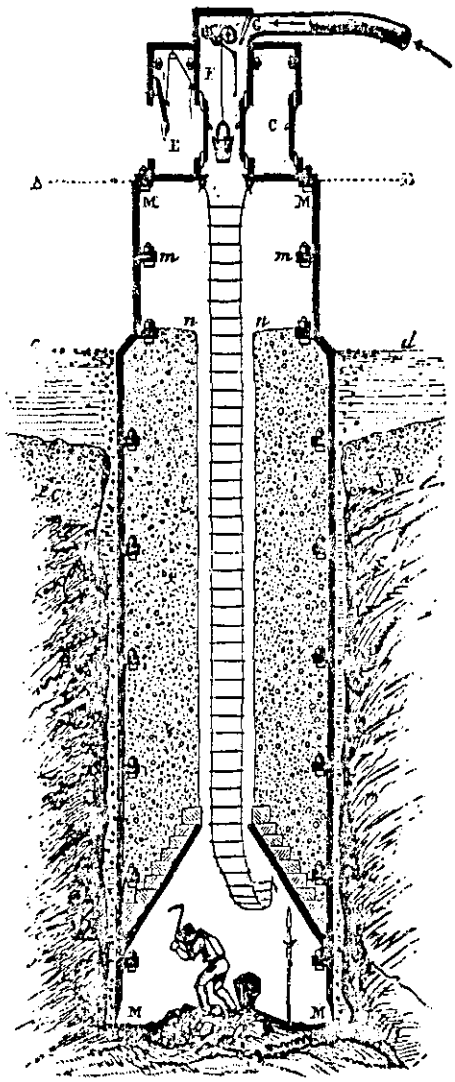

Fig. 6—(borrowed from the thesis of M. Foley). Diagram representing the construction of a bridge pier by caissons with compressed air.

As the work progresses and the excavation becomes deeper, the cast-iron tube sinks of its own weight and that of the masonry *nn* in which it is loaded; then more cast-iron rings are superposed

until the digging is finished; then there is nothing more to do but fill the whole cylinder with masonry and the pier is finished.

It is by this method, which is so simple and yet which is much more complicated in practice than the preceding description seems to indicate, that a great many bridges have been constructed since 1851.

The idea of this application of his system of drainage to the foundation of bridge piers belongs to M. Triger [14] himself. But this idea was not put into execution until 1851, by an English engineer Hughes, in the construction of the Rochester bridge over the Medway in the county of Kent.

An engineer of French descent, Brunel, constructed by this system the bridge of Chepstow, over the Wye (1849-1851) and that of Saltash (1854-1859); for the latter, the maximum depth reached was 26.68 meters below high water. Only in connection with this one did a fatal accident occur; a man died on leaving the cylinder in which he had remained a very short time. I could not get detailed information on these facts, however.

In 1856, M. Cézanne [15] was charged with the construction of a bridge at Szegedin (Hungary), to permit the Austrian railroad from the south-east to cross the Theiss, a tributary of the Danube.

He used the system of caissons with compressed air. The work of excavating was "stopped at about 20 meters below high water, so as not to expose the men to the pressure of 3 atmospheres, beyond which work is very difficult." (P. 355)

A special section of the memoir of my regretted colleague is devoted to the study of the physiological effects of compressed air:

> There are three phases to be distinguished: the entrance, the stay, and the exit.
>
> When the cock admitting the air is opened, the ears are immediately attacked by a violent buzzing accompanied by pains the intensity of which varies with the individuals . . . .
>
> The stay at the bottom of the caisson, in a pressure of three atmospheres, may be prolonged for several hours without ill consequences; the tone of the voice is somewhat impaired, and the respiration hastened as if by rapid walking; if a cigarette is waved about, it burns with a flame; candles burn rapidly, but with smoky flame. . . . . .
>
> The time of exit, though not very painful for the great majority of individuals, is the most dangerous for the workmen . . . . Sometimes there is an issue of blood from the nose and the throat; some persons experience violent, but brief neuralgia; others have headaches and toothaches for several days . . . . .
>
> Laborers who usually work in the caissons look ill; however, they resist the ill effects very well. (P. 369.)

December 12, 1859, there was an explosion at a bridge pier at Bordeaux, and consequent instantaneous decompression; seven of the laborers working there felt no ill effects. Two were killed, but by purely mechanical causes.

M. P. Regnauld,[16] who gave a report of the work, does not say at what pressure this accident took place, but we conclude from his Memoir that the caisson at that time had certainly been sunk more than 12.90 meters. (p. 82)

In 1859, the bridge of Kaffre-Azzyat was built over the Nile: the piers were excavated to a depth of 26 meters below the water. Five Arabs died from the effects of the pressure: one in the cage, as he was leaving, but before he had reached the open air; the pressure was 36 English pounds per square inch.[17] The others felt ill in the caisson and died during the decompression; the pressure then was more than 30 pounds. Blood issued from their mouths, noses, and ears.

The Memoir of Babington and Cuthbert,[18] from which I have borrowed the preceding data, is particularly devoted to the medical study of symptoms observed during the laying of the foundation of the bridge of Londonderry, in October, 1861.

The depth reached was 75 feet below water level:

> The pressure sustained by the laborers was, at the maximum, 43 pounds per square inch, in all. They suffered from pains in the ears, headaches, pains in the legs, nosebleeds, and general distress. These symptoms increased greatly when the cocks were opened wide and the change in pressure was therefore too rapid . . . . These symptoms appeared first when the men entered the compressed air; but they were much worse when the change was made from the caissons to the open air: serious, even fatal, symptoms appeared then.

I am copying in abridged form the six observations of the authors:

> I. October 3, 1861. Man 28 years old, who had worked four hours under a pressure of 23 pounds; when he came out, he fell unconscious. Cold and livid; total insensibility, facial paralysis on the right side; strabismus of the right eye; pupils almost motionless; pulse 150, small and irregular; heart sounds hardly perceptible; respirations very irregular, 24 to 44 per minute; inspiration abrupt, expiration prolonged.
>
> Bleeding: blood dark, viscous and sticky . . . . Died 24 hours after leaving the cylinder.
>
> II. Case absolutely similar, occurred at the same time . . . . Died also in 24 hours.
>
> III. 23 years old. When we visited him, he was completely prostrated, but was conscious, and complained of pains in his legs and thighs. Unable to walk, hands and feet cold and without sensation.

Was seated with his feet *in the fire*, so that several of his toes were burned without his feeling the heat.

He had not become sick immediately, and as he had had pains in his legs for days before, he had not called the doctor until several hours after leaving the cylinder.

Two days afterwards he was cured except for his burns.

IV. Similar case. Hemoptysis. Cured.

V. 18 years old, October 3. Four hours under pressure; fell unconscious while being decompressed . . . . In a semi-comatose state, responded when stimulated and fell back into unconsciousness. The symptoms of coma passed in 18 hours; he was then totally paralyzed from the fourth rib. Retention of urine, loss of sensation, and other symptoms of diseases of the cervical medullary region.

Died in the hospital 162 days afterwards; never regained sensibility or movement.

VI. 30 years old. Identical symptoms; except that the paralysis began only with the eighth dorsal vertebra. Lived 30 days.

Many other cases of slight paralysis, muscular pains, and other nervous affections were also observed.

Unfortunately no autopsy could be made.

We shall see later the explanation which the two English physicians gave of these data.

In 1859, a work of the greatest importance, the bed of the piers of the bridge from Strassburg to Kehl, was carried out with the use of compressed air. Two interesting Memoirs, one more particularly pathological, the other more physiological, reported to us the sensations felt, the phenomena observed, and the symptoms which appeared. The first in date is that of Dr. Francois; [19] we shall discuss that one first.

The author begins by describing briefly the apparatuses used in the construction of the bridge. One shift lasted four hours, and there were eight hours of rest between shifts. The total pressure rose to 3½ atmospheres. According to the rules, the decompression should have taken from 6 to 8 minutes up to 2 atmospheres; from 12 to 15 minutes up to 3 atmospheres; but the carelessness of the laborers almost always prevented strict carrying out of this rule.

Physiological effects. Easier, less frequent respiration; greater expansion of the chest, "which explains itself;" circulation accelerated during the compression, then slowing at the time of the return to open air; perceptible loss of weight, even in the workmen who had no pains.

The author does not give much time to these data, and says that they will be discussed in the work of M. Bucquoy which we shall review presently.

Pathological effects. These are first *earaches and inflammations of the ear,* after which the hearing often remains much impaired.

Then pains in the muscles or the joints: there were 133 cases of this sort. They disappeared after a few days. Sometimes there was a rather evident local swelling, but without crepitation. In one of the cases, the left breast of one of the workmen suddenly swelled so as "to resemble the well-formed breast of a woman;" this painful swelling quickly yielded to the application of cupping-glasses with scarification. (P. 307.) In another case, the patient was left unable to use his left leg.

M. François also mentions as frequent the itching of the skin, *fleas,* as the workmen call it; it yields, he says, to washing with cool water.

He explains, by congestions about the lungs, the heart, the liver, and the spleen, some rather vague symptoms, in which suffocations, palpitations, etc. are involved; one of the patients, who was, moreover, subject to hemoptysis, died a few months afterwards.

Finally, the violent headache and the loss of consciousness are attributed to a cerebral congestion; these congestions began only after a quarter or a half an hour. In one of these cases, the workman, who left the caissons (3 atmospheres) without experiencing anything but a very uncomfortable prickling over the whole body, walked to the citadel with a nimble step; when he reached there, he fell as if struck by lightning: repeated bleedings, purgings, etc.; he recovered, except for a considerable weakness of the lower limbs for a rather long time.

This brings us to the description of some functional lesions of the spinal cord: retention of the urine, violent pains in the limbs, and, for one patient, paraplegia persisting on the left side; the pressure was 3 atmospheres.

Let us finally say that slight nasal and even pulmonary hemorrhages have sometimes been noted.

I mention only for the record a work of M. Willemin,[20] which is only a simple report of that of M. François, all of whose conclusions the author seems to accept, for he does not give any attention to the theoretical explanations.

The thesis of M. Bucquoy [21] is, on the contrary, an original work of real importance. His observations, as I have said, were made at the time of the construction of the bridge of Kehl.

At the beginning of his exposition we find a bit of information from which we shall perhaps later derive some profit, namely, that the air in the caissons in which the laborers were working

contained on the average (six analyses at different periods) 2.37% of carbonic acid.

Reaching the study of the physiological phenomena, M. Bucquoy first describes the pains in the ears.

In regard to the circulation, he gives the following table:

Number of Observations	Pulse in the open air	Pulse during the different periods of the compression		Increase
10	77.85	While the air was entering	100.05	22.20
9	77.08	After a quarter hour stay	90.12	13.04
7	75.39	After 25 minutes	86.80	11.41
28	76.05	After a half-hour	81.57	5.32
11	76.59	After 1 hour	83.58	6.99
3	76.50	After 2 hours	83.30	7.00

So, in compressed air, the pulse rate is higher than in open air, and that is true for all degrees of pressure and especially up to 2½ atmospheres. M. Bucquoy, who states here that he disagrees with the authors who observed the patients, adds:

> I have, nevertheless, one observation which seems to confirm what M. Pravaz says as to the sedative effect of compressed air. One of my friends, M. Ritter, who went down into the caissons with me in spite of a very high fever, found that his pulse fell from 95 to 75 after an hour's stay. (P. 24.)

The respiratory capacity also increases, as Pravaz had already said (see the following chapter); the following summarizing table gives the average measurement of this modification:

Number of Observations	Time when they were made	Respiratory capacity in cubic centimeters
103	10 minutes before entering the lockchamber	2950
103	After a halfhour stay in compressed air	3224
103	A quarterhour after return to open air	3075
10	After three quarters of an hour	3004
10	After 2 hours	3000
10	After 10 hours	2980
10	After 15 hours	2950

So the increase, which is constant, and which, as other tables show, keeps growing up to 2 atmospheres, persists for a fairly long time after the decompression.

So M. Bucquoy adds with reason:

> Showing that this effect is not passing, that it does not cease with the compression, my experiments make us anticipate the efficacy of treatments of compressed air for patients whose vital capacity is too small. (P. 29.)

In regard to the general phenomena of metabolism, M. Bucquoy, after analysing all works preceding his and showing their contradictions, at least apparent, declares that he:

> Is inclined to believe that in compressed air the respiratory combustions increase; but the bases on which they have tried to establish this idea lack solidity, and the question must be re-examined.

Dr. Foley [22] has written an odd pamphlet on our subject, which is often quoted and praised. He had observed the symptoms of the caisson-workers at the time of the construction of the bridge of Argenteuil over the Seine in 1861; the maximum pressure had not gone above 3½ atmospheres. I shall begin by quoting a few of the most characteristic passages in which M. Foley describes and at the same time explains the phenomena experienced in compressed air:

> In the caissons all sounds have a metallic tone which shakes your brain; and when one speaks, he makes the base of his skull vibrate as a trumpet would do.
>
> Let us explain these phenomena. By flattening all of our mucous membrane which is exposed to the air, the compressed air makes our pharyngo-laryngial and bucco-nasal cavities larger and more sonorous through the bones.
>
> Moreover, for the vibration, it gives to the edges of the larynx, the tongue, the lips, the soft palate, and even the nostrils, tensions which are greater in proportion to the increase in its density. We must therefore not be surprised that all these organs raise the pitch of the sounds which they produce . . . . Because of the weakness of our lips, we all lose the power to whistle in compressed air.
>
> Some persons feel that taste and the sense of smell are weakened or entirely lost in compressed air.
>
> The flattening of the mucous membrane which is exposed to the air, which makes impossible any hemorrhage of the respiratory tracts and cures suddenly (though not without pain) coryza and hoarseness, explains all these data perfectly. How could a withered, shrivelled organ collect any savors?
>
> Our skin is more substantial than our mucous membrane; in spite of that the caissons affect it. Its papillae, like those of the nose and tongue, become less sensitive, and many workmen, whose hands, however, are very callous, find their sense of touch less sure in compressed air . . . .
>
> In this same medium, our pulse soon becomes filiform and even imperceptible. The venous pressure soon fails, our circulation flags, but our tissues do not become livid; the contrary is more likely to take place.
>
> That is because the great tension of the air, favoring the combination of the oxygen with the blood, as with all the other combustibles, makes it so rich that it comes out of our veins as ruddy as out of our arteries. What loss of color would be possible with such a liquid?

In compressed air, our pulmonary capacity increases, and the movements of our ribs lessen. The excessive pressure which dissolves the oxygen in our finest vasculo-sanguine ramifications makes the action of the thorax unnecessary, and for this reason, our coordinating nervous center reduces it to its minimum of amplitude.

Economy of strength and time, such is the law which the human spirit follows in the numerous combinations which it makes to keep us in harmony with the world, even when it is a matter of our vegetative life.

The laborers, when they are working in the caissons, feel fatigue less than in the open air, and do not become so breathless. Hunger seizes them quickly; they sweat a great deal and yet are never thirsty.

This is the reason for all these phenomena, which are contradictory only in appearance.

The absence of thirst, in spite of enormous loss by sweat, is the result of the great quantity of water which the compressed air holds in solution and forces into the organism.

The sweat is due to the assistance which our outer tegument never refuses to the lungs, especially in a warm atmosphere, when it is a matter of throwing off much of the muscular materials broken down by work.

Hunger results from the enormous consumption of our various tissues by the excess of oxygen which penetrates them and by the more energetic contractions of some of them.

The lessened breathlessness is caused by the circulatory slackening which brings back (towards the lungs, the liver, and the spleen) only a very little venous blood, since there is hardly any, to tell the truth.

Finally, the absence of fatigue results precisely from the richness of this same nourishing liquid, which unceasingly repairs our muscles at the same time that their own contractions destroy them.

In compressed air, our secretions are modified; those of the lungs and the skin increase considerably. Those of the alimentary canal, the kidneys and the liver, their converse in many circumstances, do not change, or rather, generally diminish. (P. 12 and 13.)

When leaving the compressed air, when no illness is to follow, one immediately has a feeling of comfort. It seems as if one breathes as if in spite of himself, that one's chest is full of air, and that one is lighter. That is because there is no longer the heavy weight upon you. (P. 17.)

Such are the effects produced by the passing action of compressed air. According to M. Foley, the workmen who are frequently subjected to it experience phenomena of another sort:

Any too long period of work within the caisson is divided into two stages: one of benefit, the other of organic loss . . . .

As long as the first lasts, the caisson worker has an increased appetite, leaves his work without fatigue, and returns to the open air more alert, more lively, and more eager than usual. He feels stronger and boasts of it with reason, for then the richness of his blood profits him.

> As soon as the second begins, the contrary takes place. The workman loses appetite, and, more and more, reaches his work as he leaves it, melancholy and tired. His skin becomes flabby, loses color, becomes almost clay-colored. The conjunctiva takes on a wine-colored hue. His gaze is dull. His face and body grow thin. Indecision, distaste for movement, stupor almost, appear in all his motions, and gradually the time comes when, outside the caisson, he seems to have lost strength; when the normal atmosphere is no longer sufficient to aerate his blood.
>
> In the compressed air, all these painful symptoms disappear; unfortunately they reappear as soon as he goes out, and more and more quickly too. Soon even the excess pressure fails to revive him. He is then on the point of being able to regain the strength he loses, every time he works, only by the intervention of morbid phenomena. (P. 18.)

So much for the purely physiological phenomena. As for the symptoms, the *fleas*, or excruciating itching of the skin, hardly ever begin to appear before the pressure of 2.5 atmospheres; beyond 3 atmospheres, "everyone has them;" the muscular swellings (*sheep*) are frequent at about 3 atmospheres, as are the "synovial swellings;" but the joints themselves are attacked only later and more rarely. The muscle symptoms affect particularly those which have been tired by repeated contractions.

The number of days during which the laborers have worked in the caissons seems to M. Foley a very important consideration; under an almost equal pressure, the symptoms would become more and more frequent and severe the longer one worked.

No fatal ending or paralysis, however, has been observed at Argenteuil. The most serious symptoms are muscular pains, which, judging by the details of the observations, seem to have been of extreme violence.

M. Foley disagrees with all the other authors on two main points, which are of the highest practical importance. According to him, in the first place, when the workmen prolong their stay in the caissons beyond 12 hours, they come out without harm: that results, he says, from the fact that "the nervososanguine reaction is general" (p. 49); but this so-called explanation is of little importance.

In the second place, curiously enough, he considers that the speed of the decompression is of little importance. One minute per atmosphere of compression seems to him long enough:

> For pressures above 3½ atmospheres (decompression in 2 minutes 30 seconds), would it be necessary to follow the same progression? I do not think so; two and a half minutes are a long while in an icy lock-chamber. (P. 56.)

If one is to use these high pressures, M. Foley advises that the men be decompressed in "three minutes." Furthermore, he is so far from the idea that a rapid decompression can be dangerous, and so persuaded that it is merely a matter of chilling, that he summarizes his thought by this precept:

> If the thick and icy mist which is sure to appear seems too penetrating to you, make haste! (P. 53.)

Constructing foundations by the use of compressed air was used in 1862 on the viaduct over the Scorff, at Lorient, and in 1864, on the bridge over which the railroad of Napoléon-Vendée crosses the Loire at Nantes.. The chief engineer Croizette-Desnoyers,[23] who gives the most minute details about the construction and the operation of the apparatuses set up by the Gouin Company, does not mention the condition of the workmen; he is satisfied with admitting that "at great depths, the system of laying foundations by the use of compressed air may injure the health of the workmen." (P. 392)

And yet serious accidents had occurred at the bridge over the Scorff.

The list of sick workmen, drawn up by Dr. Nail, contains 16 names; the accidents, all due to the compressed air, include: 1 case of deafness, 6 cases of pains in the joints, 1 of muscular pains, 6 cerebral congestions, 2 deaths.

The two deaths were not simultaneous. The first occurred March 17, 1862; the workman died "of asphyxia on leaving the caisson;" the second, June 3, in another pier; the medical note says: "died after four hours of cerebral congestion and asphyxia."

I could get no details about either the symptoms which preceded death or the results of the autopsies, if there were any, or even the pressure reached. I know only that the decompression was made regularly in 10 seconds and that the maximum excavation for the first pier was 18 meters, for the second only 12 meters.

There were, therefore, 8042 shifts of workmen, among whom there were only 16 accidents serious enough to be noted. Other workmen who were in the lock-chamber with the two victims experienced no symptoms.

This double disaster was the cause of a court summons against the company officials, accused of homicide by carelessness; they were acquitted by the court of Lorient (September 30, 1862) and by the court of Rennes (December 11, 1862). The preambles of of the judgment and the decree are very interesting, because they

reveal the vague ideas of the doctors about the real cause of the accidents, and these uncertainties inspired the acquittals given.

Another accident, followed by another court instance, took place at the bridge over the Scorff. M. Gallois, civil engineer, an agent of the company, who went down into the caissons May 12, 1862, on his return to open air was attacked by symptoms of paralysis "as a result of cerebro-spinal congestions, spells of dizziness, and nervous shocks," so that he had to be sent to a watering-place; he died two years afterwards.

His request for damages was refused by the tribunal of the Seine (August 18, 1861); the Orleans company produced an opinion of M. Dufaure, which reveals, like the legal documents which I mentioned a moment ago, the uncertainties of medical science. The celebrated lawyer combats the opinion of Pol and Watelle about the necessity of making the decompression very slowly with that of M. Foley. The tribunal gave no decision as to the scientific question, but declared that Gallois had not received an order to go down into the caisson, and that consequently the company could not be held responsible.

Here is the condition in which Dr. Hermel,[24] a homeopathic physician living in Paris, found M. Gallois, who had him called in consultation a few days after the accident:

> May 21, 1862, we were called in Paris in the case of M. Gallois, a civil engineer, aged 24. We found the patient suffering from incomplete paralysis of the lower limbs, permitting him neither to stand upright nor to walk without support; he could advance only in a very awkward manner, placing both hands on all the surrounding objects; the movements of his limbs were irregular, jerky, trembling; he dragged his feet; if he tried to stand upright, a violent trembling immediately shook his legs and forced him to sit down. After three or four steps, the same convulsive trembling stopped him, because it kept increasing and would have made him fall. Over his whole body cutaneous sensitivity was exaggerated, it was hyperesthesia, the skin was the seat of an annoying pruritus, without any trace of an eruption. The movements of the tongue were so difficult that the patient could not pronounce all the words distinctly. Both memory and ideas were confused. As a result of the suffocation, a frequent cough tired him when he talked and produced a profuse expectoration of mucus with the appearance of the white of an egg. Auscultation of the chest and percussion showed that the lungs, though permeable to air in their whole extent during deep inspirations, did not possess their full elasticity; one could hear, especially on the left side, the expansion of the pulmonary vesicles beginning and stopping suddenly before the movement of inspiration was finished. This expansion of the pulmonary vesicles was therefore incomplete, which hampered normal respiration. The abdominal functions were interrupted; the

constipation could be overcome only by enemas; there was paralysis of the rectum. The bladder was also paralyzed; urination could take place only by use of the catheter. He had lost appetite, and the cough often caused vomiting.

Knowing the perfectly regular life of this young man, we asked him about the date and the mode of onset of this disease.

He told us that while he was employed at the railroad works at Lorient, he had gone down into a caisson under a pressure of three atmospheres (including the outer pressure), where he had remained three hours to check the progress of the work in the foundation of a pier. Three or four minutes after his exit, he felt an icy cold, sudden and penetrating, as a result of the enormous rarefaction of the air in proportion to the inner pressure. When he tried to wash his hands, he perceived that movements of the arms were impossible, he could not put his hands into the tub because he could not lift them higher than his waist.

Taken home by two men who supported him under the arms and placed his feet on the steps he had to descend, he went to bed; after four or five hours he wished to get up, but he was completely paralyzed. An energetic treatment was given him and made him able to come to Paris after a fashion. On the tenth day he was in the condition which we described above.

For ten days we gave belladonna (twelfth) and *bryonia*, which checked the cough a little. June 2, we began to apply every other day the rheophores of an electro-galvanic machine over the hypogastrium, to overcome the paralysis of the bladder. After the third treatment, he began to urinate without the catheter, but the next day, he was forced to have recourse to it again. After the fourth treatment, he urinated voluntarily only during the day. After the fifth, the urine resumed its natural course. The constipation persisted. We electrified the walls of the abdomen and the anus. Defecation, although sometimes difficult, was reestablished about the eighth treatment. After the tenth treatment, the abdominal organs had gained strength and activity, especially on the left. The right leg was still dragging, and in certain positions it was still affected by convulsive trembling; he could not have stood up on one leg; he used a cane in walking.

In July, he went to the baths of Balaruc, from which he returned August 1. His condition was improved, but there was still a faltering in the right leg. The cough persisted, although not so bad; respiration was still incomplete. Soundness of speech, ideas, and memory was reestablished. He no longer experienced pruritus or hyperesthesia of the skin. Six more applications of electricity caused a great improvement in the movements; he could walk without support.

Today, January 12, that is, after eight months of treatment, he has at times tiring fits of coughing; his respiration is almost normal, he becomes breathless if he walks too far or too quickly. He walks without support, but there is still stiffness in the right leg, and we cannot say when he will be completely cured. (Vol. XVII, p. 198-200.)

Also in 1862, a bridge was constructed over the Adour, in Bayonne, in the construction of which the pressure had to be

raised to more than 4 atmospheres. The civil engineer who supervised the work, M. Counord, twenty years old, who up to that time had felt no symptom, on December 31, a few minutes after leaving the lock-chamber, in which the decompression had been made in 4 or 5 minutes, was attacked by vertigo, dizziness, and complete loss of consciousness. The pressure was 4 atmospheres, the length of the stay in compressed air was one hour; the day before, he had remained in the caisson for two hours. Three hours afterwards, when he regained consciousness, he was completely paralyzed in both sensation and movement in the lower limbs, with loss of sensation in the arms.

The detailed observation of the beginning of this strange case was given by Dr. Limousin,[25] of Bergerac, who does not hesitate to attribute the symptoms to a hemorrhage of the spinal cord:

> I called upon M. C., who had been brought from Bayonne to Bergerac, on January 12, 1863: complete paralysis of the lower limbs, involuntary excretion of the feces and urine, normal sensitivity everywhere, a little exaggerated in the lower limbs; if they were struck suddenly, or touched with a cold body, a sudden extension was produced. Intelligence normal. In the epigastrium and the hypochondria, pains which were checked by the application of morphine on the bare skin. Up to January 20, two doses of cathartic were given; nothing new appeared except very painful convulsive movements of the abdomen.
>
> January 28. Excruciating pains appeared yesterday in the belly; it is flaccid, pressure does not change it. The patient's condition is terrible: constant moaning, voice faint, cold sweat, face cadaverous, pulse imperceptible, 48. Dry cuppings, enemas with laudanum have no effect. I then prescribed 20 centigrams of extract of opium in four pills, one every hour.
>
> On January 29, with the second pill, the pains stopped; the patient fell into a profound sleep; he awoke quite free from pain. In the first few days, a small erosion had formed on the sacrum, today there was a huge scab; the buttocks, and the lumbar region were dull red; the patient could lie only on his back.
>
> *February 20.* The sore on the sacrum, sprinkled with gray cinchona bark, has shrunk to the size of a 5 franc piece; it is pink and granulated; painful contractions have yielded to the application of metallic armatures. Movements can be made by the paralyzed limbs; they are executed more freely on the right side; on the contrary, sensitivity is very dull on the right, and keener on the left side in the same parts; there are formications over the whole body; one day sight was entirely gone for a few instants; erections, rare at first, have become more frequent. Finally defecation and urination are voluntary.
>
> It is hard to find a better example of medullary apoplexy: sudden attack, lesions of contractability, sensation, a special sense, and the eye; reflex movements caused by the slightest stimulus; great lowering of the vitality of the tissues, manifested by the rapid mortification of

the regions sustaining the weight of the body; finally, erections not accompanied by any stimulus of the genital impulse. There was never any considerable sensitivity along the spine.

The improvement did not make very rapid progress. In May, 1870, M. Counord took several steps without support; he still had very unusual reflex movements when his lower limbs were pinched; the sensitivity of the left leg was much diminished. I saw him again in May, 1876; he could climb one flight of stairs with great difficulty and with the aid of an arm; formications in the upper limbs seemed to indicate a morbid action in the upper regions of the spinal cord; the functions of urination and defecation had become normal again.

A few days later, a terrible accident, in which three men died, saddened the Bayonne works; the caisson had burst, as happened at Douchy, and later at Chalonnes. The suggestion [26] was made that the death of the workmen had been caused by the decompression; that is probably a mistake, as is shown by the following extract from a letter written me by the engineer Bayssellance, who was kind enough to make a little investigation of the matter, at my request:

The pier, being deeply imbedded in the sand, measured in all more than 30 meters from base to the water level. The inner pressure, therefore, was about 4¼ atmospheres. The upper surface, not being constructed with a view to such a high pressure, buckled perceptibly: this buckling caused a deformation of the cast-iron cylinder of the equilibrium chamber. One of the bolts having yielded to the uneven tension, a shock was produced which made the whole upper part of the equilibrium chamber fly to pieces. The decompression in this small portion of the apparatus was therefore sudden; in the interior of the pier, the capacity of which was 200 to 300 cubic meters, it must have been more gradual, and brought a violent current of air upwards from below, bringing with it the planks and the sand of the resting stages.

According to the foreman, the results were quite different from what was reported. *No man was killed by the change of pressure.* Since the wet sand from the bottom was no longer restrained, it rose rapidly, reached and passed over one of the men who was climbing the ladder; he was found seventeen days afterwards when the caisson was being cleared out, clinging to the ladder rungs in the position of climbing. Another was carried away by the air current and found himself at the top without really knowing what had happened to him. Two others who were on the intermediary stages were carried up and crowded against the under side of the floor of the equilibrium chamber, and were almost suffocated, with their mouths full of sand; they were taken to the hospital, and died the next day, I think. Finally, five men who were in the equilibrium chamber itself

were covered with sand, which even penetrated the skin, and remained for a few moments as if stupefied, but none of them was seriously ill.

This result does not agree with what had been told me; but M. Wolff was on his rounds at the moment of the accident; and M. Counord was ill; it seems more certain to trust the version of a witness though it is almost the opposite. Moreover, this man was present at a similar accident, at the time of the construction of the bridge of Bordeaux; there too, no death was caused by the sudden decompression; two men only were killed by fragments of iron.

But if a sudden decompression of more than three atmospheres was not fatal, this change, though moderated by a stay of 4 or 5 minutes in the equilibrium chamber, was none the less dangerous in the long run. According to M. Counord, 90% of the workmen were ill, all attacked by violent pains in the joints, oppression, disturbance of vision, etc. The foreman whom I saw was attacked three times, and suffered greatly, but never more than a day. One morning, out of eleven men who were leaving, nine were seized with pains after a few moments.

Certainly it is not impossible that the decompression had something to do with the death of the two workmen who were buried in the wet sand; but that is not proved. The strangest thing in this observation is to see men experiencing almost no symptom after an instantaneous decompression from at least 4 atmospheres.

In 1865, there was a similar foundation under the Louet, at Chalonnes (Maine-et-Loire), for the bridge of the line from Angers to Niort. A catastrophe as yet unexplained killed two workmen:

February 20, 1865, when pier number 2 had reached bed rock, at a depth of 14 meters below the low-water mark, when everything seemed finished, when the work-chamber was already filled with concrete, and when the caisson, like a chimney, was also filled up to a depth of 5 meters, suddenly a violent explosion occurred and half of the metal roof of the equilibrium chamber [1] was hurled about 30 meters away. Two laborers, who were in the work-room, were crushed. No explanation for this terrible accident has yet been found. (Lectures on Bridges by M. Morandière)

It is probable that in this case, for some unknown reason, the tension of the compressed air had risen far above that required by the depth reached; the force of the explosion proves that.

I am endebted to Dr. Gallard for some interesting details about this distressing accident:

The death of the two workmen (this learned colleague writes me) was almost instantaneous, like a thunderbolt for one of them, a little slower for the second, who still breathed for a few seconds, but had already lost consciousness.

The autopsy (made by M. Gallard under bad conditions, after exhumation and previous autopsy by the physician of Chalonnes)

showed numerous patches of interlobar and vesicular emphysema on the lungs of the two victims. There were besides numerous ecchymoses in spots under the pleura and the pericardium . . . . I seem to remember that the blood . . . . contained a few bubbles of gas . . . . The notes of the autopsy were lost by the physician of Angers to whom I had dictated them.

Should we attribute the death to the decompression? It is hard to decide, in view of an unsatisfactory autopsy and especially the fact which we reported above in discussing the bridge of Bayonne.

M. Triger was disturbed by the accidents caused by the application of his method, and sent to the Minister of Public Works a Memoir on this subject, which was submitted to the examination of MM. Combes, Hennezel, and Féline-Romany.

The report [28] of these engineers, after briefly reviewing the works carried out by the Compagnie du Midi over the Tech, at Bordeaux and Bayonne; by the Compagnie de l'Ouest at Argenteuil, at Elbeuf and at Orival over the Seine, at Briollay over the Loire; by the Compagnie d'Orléans over the Scorff at Lorient, over the Louet at Chalonnes, and over the Loire at Nantes, states that:

The accidents to which laborers working in compressed air are exposed rarely endanger their lives, cause only rather short interruptions of work, and, especially, are very few, compared to the number of men passing through the lock-chambers in each job.

The diseases caused by these accidents can be prevented by the use of the means specified in the course of this report.

These means are the use of woolen garments in the lock-chamber and a decompression for which no uniform rule could be given:

There is no rule to be observed other than the one which common sense indicates, namely, not to open the cock too quickly, for compression as well as for decompression, so as to give the organism time to place itself in equilibrium with the medium in which it is immersed.

M. Triger requires that the decompression last 7 minutes, and states that then the symptoms disappear completely. It seems to us that this time should vary with the constitution of the workman. (P. 125.)

The excavation of the shaft of a coal mine at Trazegnies, in Belgium, at about this same time, was the subject of a very interesting work by M. Barella.[29]

The total maximum pressure was 3½ atmospheres. The decompression was made in about 20 minutes.

According to M. Barella, in addition to pains in the ears one experiences:

Dryness of the pharynx, a considerable decrease of the urinary secretion, a sensation of respiratory improvement, for it seemed to me that I had never breathed so freely, and so easily.

As for the pulse, we did not obtain a very definite result; however, in most of our workmen, it seemed to us that the rate had decreased by a few beats. (P. 598.)

The symptoms observed were:

1. In seven workmen, epistaxis, not serious;
2. In eleven workmen, pains in the thoracic and abdominal members, sometimes *crushing, lancinating, excruciating.*
3. Severe itching on the legs, unaccompanied by pain, a very frequent symptom. (P. 605.)

M. Barella calls attention to the fact that none of these symptoms occurred during the stay in compressed air; they were observed only when the workmen were leaving the apparatuses. Moreover, they began to appear only above 2.8 atmospheres.

M. Barella says that the little wounds which the laborers inflicted on themselves while at work did not bleed, "which is explained by the pressure on the cutaneous teguments."

A student at the School of Mines of Liége, who went down into the shaft April 15, experienced on his exit very serious symptoms, which he describes himself in the following words:

During the decompression, I felt a discomfort which I attributed to the cold.

After I had come out, when I wished to raise my right arm, I could not make it reach a definite point without making the effort two or three times. My sight was affected, and I saw my arm moving much as one perceives objects after he has whirled about several times.

The paralysis grew worse and it became impossible for me to move my arm which hung inert, I could not even make motions with my hand. The phenomenon was rather like that of an arm which has gone to sleep. It appeared progressively and in the same manner in my right leg.

They placed me on a bed, for I could not walk, I sank down. They rubbed me. I was dazzled and my eyes refused to serve me at all. I saw only at long intervals, and for a second at the most, then everything disappeared to reappear only after a few moments in the same way. My eyes were dull and glassy, they told me, and perceived only a white, vaporous light.

I recovered the use first of my leg, then of my arm; the instants during which I could see grew closer together, and I saw distinctly for longer periods.

Finally no symptom was left except a violent headache and the usual signs of a fit of indigestion. I threw up my food. My headache disappeared in the open air, and I went home, having nothing but fatigue to remind me of my former experiences.

> The friend who accompanied me, who had eaten the same meal as I, had no unusual sensation. (P. 612.)

Among the conclusions of M. Barella, we shall quote two:

1. It is best not to go beyond a pressure of three and a half atmospheres above normal pressure.
2. We may take as a standard of the duration of the decompression 10 minutes per atmosphere.

The others have only a purely medical interest: lymphatism, heart ailments, etc.

In America, the first bridge constructed by compressed air was over the Great Peedee River, for the railroad from Wilmington to Columbia and Augusta. I have found in my reading no information about this work from the point of view which interests us here.

In 1869, a truly gigantic work was undertaken at Saint Louis (United States). A bridge with two piers was built over the Mississippi. On the east pier, the depth reached was 33.70 meters below the usual water mark; it was a depth without precedent in the applications of the method, which was to be increased by the occasional floods of the river. The total pressure rose to 4.45 atmospheres. The total number of workmen employed there was 352; about 30 were seriously affected: 12 of these died.

Here is an extract from the report made by the chief engineer of the work, M. Eads:[30]

> When the depth of 60 feet was reached, some of the workmen were affected by muscular paralysis of the lower limbs. It was rarely painful, and went away in two or three days. As the caisson sank deeper, the paralysis went away more slowly. In some cases, the arms were affected, and more rarely the sphincters and the intestines. The patients also had much pain in the joints when the symptoms were very severe. Nine tenths of the patients felt no pain and got well very quickly.
>
> The duration of the stay in the air chamber was gradually shortened from 4 hours to 3, to 2, and finally to 1 hour. The use of galvanic plates or rings seemed, in the opinion of the director of construction and the workmen, to give a remarkable immunity against attacks. Finally, they all had them. They were made of alternate rings of zinc and silver, and placed on the chest, the arms, the elbows, the waist, and under the soles of the feet. The acidity of the perspiration was sufficient to establish a galvanic current, and the opinion of those with the greatest experience in these matters was quite favorable to this remedy. Captain Eads is strongly inclined to believe it to be valuable . . . . .
>
> The engineers of the port, who very often visited the caisson, have never been ill.
>
> Physicians have differed greatly about the cause of the symptoms.

Some maintained that a slower return to normal pressure would have been less dangerous; others blamed too rapid compression for all the trouble. The fact that the workmen employed to operate the doors were never affected, although during the two hours of their work they were very frequently in extreme and alternating conditions of pressure — one moment at normal pressure, and 5 minutes afterwards sustaining a weight of 50 pounds per square inch of the surface of their bodies — would seem to prove that these two theories are wrong, and makes us believe that the real cause of danger lies in the long duration of the stay in this air where the body endures so great a pressure, and not in the rapid changes to which it is exposed . . . . . .

The transitions lasted from 3 to 4 minutes . . . . . .

Considering that thousands of persons, even delicate ladies, had visited the air chambers for a short time without harm, after the caisson had reached bed rock too, and that no serious symptom attacked the workmen after the reduction of the working time to 1 hour, M. Eads concluded that the real cause lay in the prolonged labor . . . . Too long a stay was invariably followed by paralysis. Dr. Jaminet, physician at the job, after staying one day for 2¾ hours when the depth was 90 feet, was severely affected after returning home.

Dr. Bauer,[31] surgeon at the City Hospital, to which were taken the 25 workmen affected during the laying of the foundation of the Saint Louis bridge, presenting what he calls "Bridge cases," gave some interesting information about the symptoms observed in these patients:

Respiration becomes more laborious, and the pulse more rapid at the beginning of the compression, which passes off rather quickly in persons who are in good health. The voice takes on a nasal tone which it retains even after leaving the compressed air.

When they leave, all the workmen are very pale and extremely weary, even to the point of stretching out on the ground. In others, one sees involuntary, choreic muscular contractions with bleeding from the nose and lungs.

In serious cases, there is paralysis in different degrees, from slight paresis to a complete loss of movement and sensation.

Very often, urination is rendered difficult or wholly impossible, so that the urine must be drawn with a catheter: it is often bloody. Respiration is not affected; fever rarely appears and then it brings on a fatal ending. Death occurs in a state of coma, with delirium, hiccuping, stertorous respiration, and muscular cramps; the pupils are dilated towards the end . . . . .

Among the patients observed, only a few were cured in the course of the first week; others remained under treatment for a month; four died. In the paralytics, there are found congestions of the cerebral and medullary meninges, edema of the arachnoid, softenings of the brain and the spinal cord without definite localization. In one case, the softening covered the anterior horns and lateral column the whole

length of the spinal cord. Baumgarten found in this focus abundant cells of the neuroglia attacked by fatty degeneration.

The same facts were told by the chief engineer of bridges and highways, Malézieux,[32] in his fine report on the public works of the United States of America in 1870. He copies verbatim (p. 91-93) the passage from the report of the engineer Eads which we quoted above.

M. Malézieux has also given details about the foundation of the bridge which was to connect New York to Brooklyn. At the time of his visit, they were only at the beginning of this work. But the plans were gigantic; the foundation caisson was 52.46 meters long by 31.11 meters wide, that is, more than 16 ares in area.

In the second Memoir,[33] M. Malézieux gives the depth actually reached. The Brooklyn pier had a foundation 15 meters deep; the New York pier, 24 meters.

For the latter, steam-heating was installed in each of the air-locks, so as to prevent the chill produced by the sudden escape of the compressed air (p. 385.)

As to the physiological effects, M. Malézieux states:

> That he has little to add to what he reported previously about the Saint Louis bridge. M. Roebling (that is the engineer and constructor), however, notes this fact, that the action of the lungs is changed involuntarily in compressed air; the number of times one breathes in a given time is reduced 30 to 50 per cent; which would indicate that the organism reacts against the introduction of oxygen in a proportion two or three times greater than in normal atmosphere.
>
> The natural conclusion to be drawn from this observation is the one which M. Eads had made at Saint Louis; to shorten the duration of work in compressed air as the pressure increases. (P. 395.)

I shall quote in conclusion some information which I owe to the kindness of the managers of a great industrial company, which does a great deal of work on the foundations of bridges with the use of compressed air. These documents refer to works executed very recently outside France; a discretion the motives of which everyone will understand prevents me from giving more definitely the details of date and place.

First, here are general specifications about the manner in which the works were carried on, and which resulted in the accidents; these specifications come from the superintendent of the job himself:

> 1. At a depth of 20 to 22 meters, the shifts still lasted 8 hours, and our men were not too tired, none of them felt any ill effects from the pressure, they were merely inconvenienced by the evil odor of the mud and by the hot air, which, however, we took care to

renew frequently through the hoisting-shaft; under this pressure of two atmospheres, the workmen underwent decompression in 4 or 5 minutes.

2. From 22 to 25 meters, the shifts lasted 4 hours; under this pressure, the men began to feel rather severe symptoms; the decompression took 10 minutes, the opening of the discharge cock was only 25 millimeters, then afterwards 18 millimeters.

3. From 25 to 28 meters, the workmen relieved each other every 3 hours, and were decompressed by means of a cock, the opening of which was reduced to 10 mm.; it took 16 to 17 minutes, and it was while working under this pressure, that our men were most fatigued; very often it happened that 4 out of 7 were affected by the pressure in their legs, heads, and stomachs; in others, the decompression caused paralysis of the bladder or of vision; some of these workmen experienced horrible sufferings for two or three days and then three or four days of convalescence before being able to go back to work; these were the ones most seriously affected; as for those who had lighter attacks, they also experienced great pain for twenty-four hours and then 1 or 2 days of inability to work. (July 22, 1875)

As a sequel to my letter of the 22nd, I wish you to know that in the last four days we have had only two workmen affected by the pressure; only slightly, but enough to keep them from working; we still have in the hospital 2 workmen seriously affected by the pressure since the 21st on coming off duty at 6 o'clock in the evening; they are paralyzed in the lower parts of their bodies, and their urine must be drawn by the catheter.

The decompression lasts on the average 18 minutes; the shifts work 3 hours. (July 28)

To continue my letter of the 28th of this month, I wish to inform you that a man named R, one of the two working in the excavation who were hospitalized as a result of the pressure, died today at half past twelve. The second workman is out of danger, the doctors think; he has recovered except that his legs are paralyzed, and they hope that this trouble will soon clear up.

The doctors claim that the death of R. is due to the pressure, which probably affected the spinal cord; this man had worked before in excavations with compressed air, but had never gone beyond 2.1 or 2.2 atmospheres. (July 30.)

The first of the two workmen who were seriously affected and whom we have just discussed returned to his home; we have had no further information about him.

As to the said R., his autopsy was performed. It resulted in noteworthy findings which Dr. L. describes in a letter addressed the company, and a translation of which follows:

After opening the spinal canal, I found that at the height of the thoracic vertebrae the spinal cord was very soft; for some inches it was transformed into a soft, flowing mass, yellowish gray in color, which above and below merged into the healthy part.

> The cord in general was much congested, as was the brain, but I saw nothing else abnormal, there or in the other organs.

3. Diving Suits.

As we said when we began this chapter, the diving bell has been entirely abandoned for the diving suit, an apparatus which is infinitely simpler and less costly, and which allows each man to work by himself with a certain liberty.

I have no intention of going back to the origin of this invention although it is very recent; the French word itself scaphandre (σκάφος, boat, ἀνδρός, man) dates from the end of the last century, and was given to a simple life preserver. It is only during the last fifty years that Siebe of London, then M. Cabirol, and finally MM. Rouquayrol and Denayrouze have made a practical apparatus of it, easy to use in fishing for oysters, coral, pearls and sponges, in saving sunken objects, in cleaning and inspecting the hulls of ships, etc.

However, I cannot keep from mentioning a strange invention of Borelli, which had some connection with the diving suit and is interesting in the history of the theories of respiration; I borrow the description of this apparatus, very poorly planned because it did not provide for renewing the air for the diver, from Brizé-Fradin who quotes it without telling where the celebrated doctor-mathematician described his apparatus. He expresses himself in these words:

> Borelli, inventor of the machine called *diver's bladder*, prefers it, for some reason or other, to Halley's bell. It is a globe of brass or copper about two feet in diameter, placed over the head of the diver; it is fastened to a goat-skin garment made to fit the diver. In this globe are the tubes by which the circulation of the air is maintained; at his side the diver carries an air-pump, by means of which he can make himself heavier or lighter, as fishes do, compressing or expanding their air-bladder: in this way he thinks he can meet all the objections made in regard to other machines, and especially the objection in regard to lack of air, since the air which has been breathed is, according to him, deprived of its harmful qualities by circulation in the tubes. (P. 44.)

Let us recall that in Halley's diving bell a man could take several steps outside the bell and continue to breathe by means of a sort of helmet and a tube which ended in the air of the bell; he was therefore almost in the conditions of the modern diving suit. The principal part of the present apparatus (Fig. 7) consists of a heavy metal helmet, with glass portholes, which the diver places over his head; a tube which communicates with a compressing

Aus der physiologischen Abteilung am Allgemeinen Krankenhause St. Georg in Hamburg.

Physiologie und Pathologie des Lebens in verdichteter Luft.[6])

Von

Dr. A. Bornstein, Vorsteher der Abteilung.

M. H.! Im Laufe des 19. Jahrhunderts hat die Technik der Tiefwasserunternehmungen einen gewaltigen Aufschwung erlebt. Einerseits ist die Technik des Tauchens in einer Weise vervollkommnet worden, dass unsere Taucher nicht, wie früher, einige Minuten, sondern nicht selten viele Stunden unter Wasser zubringen; andererseits ist, namentlich seit den Konstruktionen des französischen Ingenieurs Triger im Jahre 1830, das Arbeiten unter Wasser im sogenannten „Caisson" zu einer bemerkenswerten Höhe ausgebildet worden. Man bemerkte aber auch bald, dass das Arbeiten unter Druck in diesen Apparaten durchaus nicht gefahrlos ist, wenn natürlich auch die Gefahren der Arbeit von mancher Seite aus leicht begreiflichen Gründen überhaupt bis in die jüngste Zeit hinein geleugnet worden sind. Doch sind die Widerstände, auf die wir stossen, seit der grossen Monographie von Heller, Mager und v. Schrötter sehr viel geringer geworden.

Das Wesen der anfangs dunkel erscheinenden Krankheit ist seit dem Jahre 1857 durch die Arbeiten der Physiologen Hoppe-Seyler und Paul Bert immer mehr geklärt worden; in neuerer Zeit sind durch die Arbeiten von Schrötter, Zuntz, Haldane und anderen Autoren die Verhältnisse noch weiter erforscht worden, so dass wir jetzt die pathologische Physiologie der Druckluft in ausserordentlich klarer Weise zu übersehen vermögen. Ausser der technischen Bedeutung der Frage und dem Umstande, dass wir in der Druckluft ein interessantes Pendant zu der verdünnten Luft und zu den Untersuchungen über das Höhenklima besitzen, scheint mir gerade dieser Punkt von einiger Bedeutung zu sein: Dass wir ein Krankheitsbild vor uns haben, das in allen seinen Erscheinungen uns mit unseren heutigen physiologischen und physikalischen Methoden fast restlos fassbar ist, in dem keine Krankheitserscheinung nicht einer physiologischen Deutung fähig wäre, und das, wie kaum ein anderes Krankheitsbild, eine rein physiologische Beschreibung gestattet. Wir können so ein Gebiet der sozialen Medizin, der Hygiene der Arbeit mit fast mathematischer Strenge behandeln, und wir können den physikalischen und experimentellen Deduktionen die Zahlen der Morbiditätsstatistik als Bestätigung gegenüberstellen.

Ich möchte nun, ohne längere Einleitung, zuerst die physiologischen Erscheinungen beim Aufenthalt in komprimierter Luft besprechen, um im zweiten Teil meines Vortrags näher auf die krankhaften Erscheinungen einzugehen, die sich im wesentlichen an das Verlassen der Drucklufträume anschliessen.

Um mit der Atmung zu beginnen, so finden sich im Mechanismus der Atmung keine Besonderheiten, wie schon Schrötter angegeben hat, und wie auch ich bestätigen kann. Der respiratorische Stoffwechsel ist bei geringen Ueberdrucken (von $^1/_2$ Atmospäre etwa) insbesondere von A. Löwy untersucht worden, er erwies sich als normal. Ebenso in meinen Versuchen am Menschen und Hunde, die bei höherem Druck (etwa 3 Atmosphären) angestellt waren; sie waren, ebenso wie diejenigen Löwy's, nach der Zuntz'schen Methode angestellt. Den O_2-Verbrauch habe ich ferner noch bei O_2-Atmung in der Druckluftschleuse bei 3 Atmosphären Druck während der ersten $^3/_4$ Stunden der Sauerstoffatmung gemessen; er war auch noch unter diesen Verhältnissen normal. Was Sauerstofftension anbelangt, so entspräche eine solche Versuchsanordnung einem Druck von 15 Atmosphären atmosphärischer Luft, d. h. einem Drucke, der in praxi nie vorkommt. Die höchsten Drucke, die von Tauchern je erreicht worden sind, betragen etwa 7—8 Atmosphären; der Aufenthalt in solchen Tiefen wird aber, der grossen Dekompressionsgefahr halber, nie auf mehr als einige Minuten ausgedehnt.

Ebensowenig wie in der Ruhe wird der respiratorische Stoffwechsel während Körperarbeit durch die Druckluft verändert. Eine bestimmte Arbeit — am Gärtner-Zuntz'schen Bremsergometer geleistet — bewirkt in Druckluft die gleiche Erhöhung der Oxydationen, wie in gewöhnlicher Luft.

Unter allen diesen Verhältnissen wird also der respiratorische Stoffwechsel nicht beeinflusst, wohl aber, wenn bei Atmung von reinem Sauerstoff in Druckluft die Erscheinungen der gefürchteten Sauerstoffvergiftung eintreten. Es findet sich Gelegenheit, auf die dabei eintretenden merkwürdigen Erscheinungen noch näher einzugehen, wenn ich das Symptombild der O_2-Vergiftung im ganzen bespreche.

Die Zusammensetzung des Blutes ist von verschiedenen Autoren untersucht worden. Bei kurzdauerndem Aufenthalt in Druckluft finden sich keine Veränderungen im Hämoglobingehaltes des Blutes; wenn man z. B. Arbeiter vor und nach einer 6—8stündigen Druckluftarbeit untersucht — man nimmt am besten dazu Aufsichtspersonal — so sind die Schwankungen sehr gering. Aron hat im pneumatischen Kabinett bei einem kleinen Ueberdruck und ganz kurzem Aufenthalt sehr kleine Abweichungen gefunden, und zwar im Sinne eines vermehrten Hämoglobingehaltes, doch sind die Abweichungen sehr gering, so dass sie sich möglicherweise aus einer veränderten Weite der Gefässe erklären lassen: in Druckluft ist es nämlich im allgemeinen wärmer als in atmosphärischer Luft, und dementsprechend erweitern sich die Gefässe des Kopfes und der Extremitäten. In systematischer Weise wurde die Wirkung eines längeren Aufenthaltes in Druckluft von meiner verstorbenen Frau untersucht, und zwar an Tieren, die wochenlang in den Drucklufträumen gehalten wurden.

Es zeigte sich dabei, dass sowohl bei Hunden als bei Affen die Ueberführung in Pressluft einen erheblichen Einfluss auf die Zusammensetzung des Blutes ausübt, und zwar sinkt sowohl die Zahl der roten Blutkörperchen im Kubikcentimeter, als auch die Färbekraft des Blutes.

Bei der Interpretation drängt sich natürlich der Befund im Hochgebirge auf, wie er von Löwy, Zuntz, Abderhalden u. a. erhoben worden war, und der eine starke Vermehrung der Blutzellen und des

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1) Lurz, Arch. f. Schiffs u. Trop. Hbyg., 1913, Bd. 17.

2) R. Mouchet et A. Dubois, Arch. f. Schiffs u. Trop. Hbyg., 1914, Beiheft 3.

3) Siehe bei Theiler, Zschr. f. Infekt.Krkh. d. Haustiere, 1912, Bd. 11.

4) Evers, Berl. tierärztl. Wschr., 1913, Nr. 24.

5) Bergschicker, Berl. tierärztl. Wschr., 1913, Nr. 28.

6) Referat, gehalten vor der Berliner physiologischen Gesellschaft am 7. November 1913.

Hämoglobins ergeben hatte. So ergab sich auch sofort die weitere Fragestellung, ob die Verminderung des Hämoglobins in Pressluft eine relative oder eine absolute sei; und zur Beantwortung dieser Frage wurde die Blutmenge der Tiere nach einer für den Pressluftbetrieb besonders modifizierten Welker'schen Methode bestimmt[1]).

Die Versuche wurden an wachsenden Tieren vom gleichen Wurfe angestellt. Der auffallendste Befund war das Zurückbleiben des Körpergewichts. Dadurch wird die Beurteilung der Verhältnisse etwas erschwert. Die Färbekraft des Blutes ist auch hier bei den Druckluftiieren etwas geringer als bei den Kontrolltieren. Die Gesamthämoglobinmenge ist, *auf das Kilo Körpergewicht* berechnet, deutlich höher, jedenfalls nicht gesunken. Noch beträchtlicher ist die Zunahme der Blutmenge bis auf über 11 pCt. des Körpergewichts, und wir können hier direkt von einer Plethora sprechen.

Es scheint diese Feststellung einer experimentellen Plethora von einiger Bedeutung zu sein. Bekanntlich ist über ihre Möglichkeit viel gestritten worden. In der älteren medizinischen Literatur spielte der Begriff eine grosse Rolle, während späterhin das Vorkommen einer Plethora überhaupt bestritten wurde. So waren alle Versuche Ludwig's und seiner Schüler, eine Plethora experimentell zu erzeugen, fehlgeschlagen. Ludwig, Worm-Müller, Cohnheim und Lichtheim suchten namentlich durch Bluttransfusion eine Plethora zu erzeugen; es zeigte sich jedoch, dass die intravenös injizierte Flüssigkeit ausserordentlich schnell den Körper wieder verliess, so dass es nicht gelang, eine länger dauernde Ueberfüllung des Gefässsystems zu erzielen. Cohnheim, der diese Versuche in seiner „Allgemeinen Pathologie" besprach, meinte dann, dass es überhaupt keine Plethora vera gäbe, eine Meinung, der besonders Recklinghausen widersprach. Jedenfalls war es aber bis jetzt niemals gelungen, eine reine Plethora — d. h. eine nicht-*nephritische* — hervorzurufen und darum mögen diese Versuche, in denen es gelang, ein allgemeines, von der Frage der Druckluftwirkung unabhängiges Interesse besitzen.

Einen Einfluss auf die Circulation besitzt die Druckluft nicht. Auch der Blutdruck ist, wie sowohl aus Schrötter's Versuchen, wie auch aus meinen eigenen hervorgeht, so gut wie unverändert, und zwar auch bei sehr raschem Wechsel des äusseren Drucks. Es folgt also das Innere des Körpers augenblicklich den Schwankungen des auf der Haut lastenden Druckes, — eine Tatsache, die eigentlich selbstverständlich ist, die aber doch erwähnt werden muss, weil man früher der Ansicht war, dass diese Schwankungen des Druckes auf die Gewebe die Druckluftkrankheit hervorriefen. Dass die Druckschwankungen aber absolut harmlos sind, kann man leicht im Selbstversuch demonstrieren; ich habe es oft Kollegen gezeigt, die mich besuchten. *Man kann mehrere Male schnell* hintereinander sich in der Druckluftschleuse auf 3—4 Atmosphären komprimieren und sofort so schnell wie möglich dekomprimieren; man kann so in 5 Sekunden Druckdifferenzen hervorrufen, die denen zwischen Berlin und dem Monte Rosa entsprechen, ohne irgendwelche Beschwerden zu spüren; ich habe oft solche Druckdifferenzen bei mir selbst in Zeiten hervorgerufen, die hundertmal schneller waren als die offiziellen Schleusungszeiten. Die Schwankungen des Luftdruckes sind es also nicht, die die typische Druckluftkrankheit hervorrufen, sondern es müssen andere Faktoren im Spiele sein; dieselben hängen mit der Absorption der Pressluftgase durch die Körperflüssigkeiten zusammen.

Nur eine Gruppe von Krankheitserscheinungen hängt mit *dem Luftdruck als solchem* zusammen. Das sind die Ohrerkrankungen. Ist durch angeborene Enge der Tuba Eustachi oder, was sehr viel häufiger ist, durch eine Schwellung der Schleimhaut der Tube[2]), der Luftausgleich mit dem Mittelohr verhindert, so wird es natürlich zu starken Druckwirkungen auf das Trommelfell usw. kommen, es stellen sich Hyperämie, Ecchymosen und andere *Erscheinungen von seiten des Ohres ein, die sehr schmerz*haft und auch gefährlich sein können, die aber leicht vermeidbar sind und daher ein relativ geringes Interesse haben. Ebenso können wir die Erscheinungen übergehen, die bei Verstopfung des Einganges der Frontalsinus entstehen; sie beruhen ebenfalls auf den Druckschwankungen beim Betreten der Drucklufträume; man fasst diese Erscheinungen wohl auch unter dem Namen „*Kom*pressionserkrankungen" zusammen, im Gegensatz zu der eigentlichen Druckluftkrankheit, der „Dekompressionskrankheit, die bei der Dekompression, beim Verlassen der Drucklufträume auftritt.

Ehe wir auf die Druckluftkrankheit eingehen, müssen wir erst noch *die Verhältnisse* analysieren, unter denen sich bei Erhöhung des Atmosphärendruckes der Körper mit der umgebenden Luft ins Gleichgewicht setzt. Die Ueberlegungen sind im Prinzip zuerst von Zuntz angegeben und später von Haldane und von mir erweitert worden; auch Plesch hat, einige Jahre nach Haldane, einmal Betrachtungen in der gleichen Richtung angestellt, die allerdings in manchen Punkten nicht sehr glücklich waren. Ich habe bei meinen weiteren Rechnungen die Ueberlegungen von Zuntz und Haldane *weiterzuführen und experimentell* zu begründen versucht.

1) Cf. Olga Adele Bornstein, Pflüger's Arch., 1911.

2) Auch durch Traumen scheint nach einer Beobachtung, die ich kürzlich machte, eine solche Enge der Tube entstehen zu können.

Wird der Körper eines Tieres in Luft von erhöhtem Druck gesetzt, so wird das Tier allmählich Gas physikalisch zu absorbieren versuchen, und zwar so viel, bis das Tier nach dem Henri-Dalton'schen Absorptionsgesetz mit dem Gase sich im Gleichgewicht befindet. Würde nun das Gas nur durch die Oberfläche durch Diffusion in den Körper eindringen, so würde es viele Tage dauern, bis der Körper wirklich gesättigt ist; in Wirklichkeit jedoch dringt das Gas sehr viel schneller ein und sättigt den Körper in sehr viel kürzerer Zeit, und zwar geschieht dies durch den Kreislauf. Das bei der Atmung in die Lungen geworfene Blut sättigt sich in den Lungen so gut wie völlig mit dem Gase, was man schon aus alten Versuchen Pflüger's mit Sauerstoffatmung schliessen muss. Insbesondere *verdient* von den Gasen *der Stickstoff* — aus später zu erörternden Gründen — Beachtung. Kommt nun das mit N gesättigte Blut in die Organe, so wird es den grössten Teil seines N dort abgeben, bis das Gleichgewicht erreicht ist, dann wieder nach den Lungen zurückkehren, wo es wieder mit N gesättigt wird, von diesem N wieder einen grossen Teil in den Organen abgeben usw., *bis völlige Sättigung* des Körpers *mit* der dem Partialdruck der Atemluft entsprechenden Stickstoffmenge erreicht ist. So wird der Körper wohl hundertmal schneller mit N gesättigt, als es bei der Aufnahme allein durch die Haut der Fall sein würde. Wird nach der Sättigung der Luftdruck herabgesetzt, so wird natürlich der N in umgekehrter Weise durch Blut und Lungen wieder aus dem Körper herausgeschafft — und das ist dann das Gefährliche.

Die Aufnahme und Ausscheidung des N aus den Organen lässt sich rechnerisch leicht verfolgen. Es sei

m g Organ vom Absorptionskoeffizienten α
mit n „ Blut „ „ β

in Berührung, die sich ins Gleichgewicht in bezug auf ein gelöstes Gas setzen sollen, und zwar sei die Gasmenge A, *die entweder im Blut* gelöst sei und auf die Organe übergehen solle — wie es bei Erhöhung des Luftdrucks der Fall ist — oder die im Organ gelöst ist und ins Blut übergehen soll, wie es bei Herabsetzung des Luftdrucks, bei der Dekompression realisiert ist. Es ist nun Gleichgewicht vorhanden, wenn die in der Einheit Organ vorhandene Gasmenge zu der in der Bluteinheit sich befindlichen verhält wie das Verhältnis der Absorptionskoeffizienten, also

$$\left.\begin{aligned} \frac{\text{Organgas}}{m} : \frac{\text{Blutgas}}{n} &= \alpha : \beta \\ \text{Organgas} + \text{Blutgas} &= A \end{aligned}\right\}$$

Daraus berechnet sich:

$$\text{Organgas} = \frac{A\,\alpha\,m}{\alpha\,m + \beta\,n}$$

$$\text{Blutgas} = \frac{A\,\beta\,n}{\alpha\,m + \beta\,n}.$$

Nun nehmen wir an, der Körper sei bei einem bestimmten Druck mit Stickstoff gesättigt und wir erniedrigen den Partialdruck des Stickstoffs, der über dem Körper lagert, entweder durch Luftverdünnung — Dekompression — oder durch Sauerstoffatmung. Dann wird zuerst das im Blute enthaltene überschüssige Gas durch die Lungen ausgeschieden und das Blut kehrt, frei von N, nach den Organen zurück, wo es von den Organen N aufnimmt. Die in den Organen enthaltene N-Menge A verteilt sich dann nach der eben besprochenen Formel *zwischen Blut* und Organen, so dass ins Blut gelangt die Gasmenge:

$$A\,\frac{\beta\,n}{\alpha\,m + \beta\,n}$$

und im Organ bleibt: $A\,\frac{\alpha\,m}{\alpha\,m + \beta\,n}$.

So stellt sich dann das Verhältnis am Ende des ersten Kreislaufs. Während des zweiten Kreislaufs wird dann das Gas

$$A\,\frac{\beta\,n}{\alpha\,m + \beta\,n}$$

nach den Lungen geschafft und ausgeschieden; das gasfreie, nach *den* Organen zurückkehrende Blut nimmt jetzt wieder N auf, aber diesmal etwas weniger, da ja schon etwas abgegeben ist, und zwar ist die bei der zweiten Kreislaufsrunde ins Blut übergehende N-Menge, wie eine kleine Rechnung zeigt.

$$A\,\frac{\alpha\,m\,\beta\,n}{(\alpha\,m + \beta\,n)^2} \text{ usw.}$$

Addiert man diese Glieder, so ergibt sich als die in r Kreislaufsrunden ausgeschiedene N-Menge:

$$A\left[1 - \left(\frac{\alpha\,m}{\alpha\,m + \beta\,n}\right)^r\right].$$

Diese Gleichung ist der experimentellen Prüfung zugänglich. Wir wollen sie zuerst noch vereinfachen, indem wir setzen:

$$\left(\frac{\alpha\,m}{\alpha\,m + \beta\,n}\right)^r = \xi;$$

ann ist $a = A(1-\xi)$, die in einer gewissen Zeit durch die Lungen sgeschiedene N-Menge, wie wir sie experimentell messen können. achen wir nun einen Versuch von der doppelten Zeitdauer, in dem ir ebenfalls die Menge des ausgeschiedenen N messen; dieselbe sei b. ann ist die doppelte Anzahl von Kreislaufsrunden gemacht, statt r uss also 2 r stehen und statt ξ kommt ξ^2, und wir haben analog

$$b = A(1-\xi^2)$$
$$a = A(1-\xi).$$

Dividieren wir diese beiden Gleichungen durcheinander, so erlten wir:

$$\frac{b}{a} = \frac{1-\xi^2}{1-\xi} = 1+\xi;\ \xi = \frac{b}{a} - 1.$$

Machen wir nun einen Versuch, der noch einmal doppelt so lang t, der uns c ccm N liefert, so müsste nach einer analogen Rechng sein:

$$\frac{c}{b} = 1+\xi^2;\ \xi^2 = \frac{c}{b} - 1 \text{ usw.}$$

Wir haben also eine Anzahl Gleichungen, aus denen wir ξ berechnen nnen, und, falls sich die Verhältnisse wirklich so einfach verhielten, üssten wir beim Experiment aus allen die gleichen Werte für ξ bechnen können.

In dieser Rechnung ist der Körper als ein einheitliches Organ annommen. Die Versuche, die ich zur Bestätigung angestellt habe, zeigten, ass dies nicht zulässig ist. Wir können also für unsere Zwecke den örper nicht als ein Organ mit einem einheitlichen Absorptionsoeffizienten und einer gleichmässigen Durchblutung ansehen, sondern ir müssen annehmen, dass mindestens zwei Arten von Organen mit hr ungleichen Absorptionskoeffizienten vorhanden sind. Die darufrichteten Versuche haben gezeigt, dass dies in der Tat der Fall ist. chon vor vielen Jahren hat Exner[1]) nachgewiesen, dass Fette einen öheren Absorptionskoeffizienten für Gase, insbesondere O_2, haben als Wasser. Neuerdings haben Vernon und Quincke die gleiche Tatsache iedergefunden, und ersterer hat speziell den Absorptionskoeffizienten ir N im Fett etwa 6 mal so gross gefunden wie im Wasser und im lute. Daraus ergibt sich, dass das Fettgewebe und überhaupt die poiden Substanzen, also auch das Nervensystem, eine besondere Fähigit haben, den N aufzuspeichern. Ausserdem ist aber die Blutcirculation im Fettgewebe bedeutend geringer als im übrigen Körper. Infgedessen wird zwar, absolut genommen, sehr viel N im Fett absorbiert, dauert aber, wie sich leicht aus unserer Formel berechnen lässt, sserordentlich lange, bis ein Gleichgewicht eingetreten ist. Nach aldane dauert es etwa 5 Stunden beim Menschen, nach meinen eigenen ersuchen und Erfahrungen 8—10 Stunden. Die Rechnung wird dann so komplizierter, man muss für jeden der beiden Kreisläufe eine beondere Gleichung aufstellen, aber die Schwierigkeiten der Rechnung sind icht unüberwindlich, und die Resultate der Versuche stehen in genügend uter Uebereinstimmung, um im allgemeinen diese Vereinfachung der eberlegung zu rechtfertigen: zwei Kreisläufe, der eine im Fettewebe, der andere im übrigen Körper.

Die Versuchsanordnung zur Messung der aus dem Körper bei Herbsetzung des Luftdrucks ausgeschiedenen N-Menge ist im wesentlichen ie gleiche, wie ich sie zu anderen Zwecken[2]) beschrieben habe. In Verchen von kurzer Dauer (3—4 Minuten) überwiegt, wie sich aus unseren leichungen ableiten lässt, der Einfluss der von den Organen in die ungen getriebenen Blutmenge alle anderen, als da sind: Körpergewicht, ettmenge usw. Es lässt sich daher aus den ausgeschiedenen N-Mengen ie in der Zeiteinheit durch die Lungen getriebene Blutmenge, d. h. das inutenvolumen des Herzens gut berechnen; ich habe diese Frage systemasch weiterverfolgt, indem ich so eine Methode zur Bestimmung des inutenvolumens entwickelte, die ich als die Methode der indifferenten ase bezeichnet habe. Diese Methode ist später von Zuntz und Franz üller sowie von Krogh und Lindhart modifiziert worden, indem sie N_2O stat N benutzten, was manche Vorteile und wohl auch einige Nachile hat. Der Fortschritt dieser Methoden beruht darauf, dass die Einände von Bohr, Haldane und anderen vermieden werden, die den lethoden der Messung durch O_2-Transport gemacht wurden. Doch will ch darauf jetzt nicht näher eingehen, sondern es nur deshalb erwähnen, a sehr viele der Werte, die ich in N angegeben habe, sich auch als inutenvolumen berechnet anführen lassen — und umgekehrt.

Auf diese Art lässt sich also die Sättigung und Entgasung es Körpers bei Kompression und Dekompression darstellen. Dieser 'organg ist bei der Kompression der einzige, der in Frage kommt, icht jedoch bei der Dekompression.

Bei der Dekompression kommt als zweites Moment noch die Bildung von Luftbläschen im Blut und den Geweben hinzu, als in besonders wichtiges Moment, denn in der Bildung von Bläschen m Körper und der dadurch bedingten Schädigung lebenswichtiger Organe beruht die grösste Schädlichkeit der Druckluft und die Gefahr der Dekompression. Auf der Kombination der beiden Faktoren: einerseits der Entgasung durch den Kreislauf und Diffusion der Gase durch die Lungen, andererseits der Blasenbildung durch die Dekompression beruht das Wesen der Druckluftkrankheit. Es seien daher noch einige Worte über das Wesen der Blasenbildung gesagt.

Wird eine mit einem Gase gesättigte Flüssigkeit unter einen verminderten Luftdruck gebracht in der Art, dass der Druck langsam sinkt, so sieht man zuerst keine Blasen entstehen. Es bleibt also in der Flüssigkeit zunächst mehr Gas enthalten, als dem Absorptionskoeffizienten entspricht; die Lösung ist übersättigt, es hat sich ein metastabiler Zustand ausgebildet. Erst wenn man den Druck immer weiter sinken lässt, beginnen Blasen aufzusteigen, und zwar ist der Druck der Blasenbildung ceteris paribus bei sorgfältigem Arbeiten recht konstant, es existiert also für eine bei bestimmter Temperatur und Druck mit einem bestimmten Gase gesättigte Flüssigkeit ein „kritischer Druck", oberhalb dessen die Flüssigkeit übersättigt bleibt, unterhalb dessen sie sich durch Blasenbildung mit dem neuen Druck ins Gleichgewicht setzt. Ostwald hat versucht, die Blasenbildung mit dem Druck in Beziehung zu bringen, indem er zuerst den inneren Druck einer Blase nach Art des Druckes in der Seifenblase berechnete; es ergab sich $p = \frac{2\gamma}{r}$, wo p der Druck in der Blase, γ die Oberflächenspannung der Flüssigkeit und r der Radius der Blase ist. Nimmt man an, dass sich Blasen von der Grösse eines Moleküls bildeten, so wäre $r = 10^{-8}$, $\gamma = 0{,}076$ = Oberflächenspannung des Wassers. Der Druck, bei dem Blasenbildung eintreten könnte — bei einem unter Atmosphärendruck gesättigten Gase — würde dann $\frac{1}{p} = 0{,}0008$ Atmosphären sein.

Ich glaube bewiesen zu haben, dass die Ostwald'sche Auffassung den Tatsachen nicht völlig gerecht wird. Ostwald selbst hat darauf hingewiesen, dass bei sehr kleinen Blasen die Verhältnisse vielleicht etwas anders liegen werden. So sieht man in der Tat schon beim 100—1000fachen Druck deutliche Blasen entstehen. Also die Grössenordnung der Gleichung stimmt durchaus nicht, ausserdem ist nicht berücksichtigt, dass Gase mit hohem Absorptionskoeffizienten sehr viel leichter Blasen bilden als solche mit niederem.

Diese Schwierigkeiten lassen sich sehr wohl überwinden, wenn man vom Standpunkte der kinetischen Gastheorie ausgeht. Wir stellen uns ja die Gase in der lösenden Flüssigkeit nicht ruhend, sondern bewegt vor, eine Auffassung, die besonders Bohr durch Einführung der Invasions- und Evasionskoeffizienten in anschaulicher Weise ausgebaut hat. Die sich bewegenden Gasmoleküle werden in der Flüssigkeit öfters aufeinanderstossen und so den Radius vergrössern und dadurch, nach der Gleichung der Seifenblase, schon bei einem sehr viel geringeren Drucke Blasenform annehmen, als es das einzelne Molekül imstande ist. Man kann sogar, wie es Boltzmann z. B. getan hat, die Zahl dieser Zusammenstösse berechnen, sie ist gleich Konst. $\times \frac{n^2}{\sqrt{m}}$, wo n die Anzahl der Moleküle, m die Masse eines Moleküls ist. An einer Stelle, an der zwei Moleküle zusammenstossen, ist also der Radius in der Ostwaldschen Gleichung sehr viel grösser, die zur Entstehung von Blasen nötige Druckdifferenz also kleiner, so dass wir schon durch den Zusammenstoss von nur 2 Molekülen den tatsächlichen Verhältnissen näher kommen; es können sich aber natürlich auch mehr als 2 Moleküle gleichzeitig treffen. Es ist nämlich eine grosse Anzahl Moleküle, die in der Zeiteinheit im Kubikzentimer zusammenstösst; geringer wird schon die Anzahl der Begegnungen sein, bei denen 3 Moleküle gleichzeitig sich treffen; es lassen sich Begegnungen aber auch von 4, 5, 6 und noch mehr Molekülen denken, die dann allerdings sehr selten sein werden. In der einfachsten Formel der Zusammenstösse ist das Vorkommen von n, der Zahl der Moleküle, wichtig; wir sehen, wie schon bei 2 Molekülen die Zahl der in der Raumeinheit enthaltenen Moleküle, d. h. in unserem Falle der Absorptionskoeffizient der Gase eine Rolle spielt, so dass wir durch Kombination der Seifenblasenformel mit der Formel der Zusammenstösse der Moleküle die tatsächlichen Verhältnisse sehr viel besser beschreiben können, als es Ostwald gelungen ist.

Noch eins ist wichtig. Wir sahen die Anzahl der Moleküle nicht in der einfachen Proportionalität, sondern in einer Potenz. Auch bei mehr Zusammenstössen finden sich immer Potenzen der Molekülzahl; mit anderen Worten: das Henri-Dalton'sche Gesetz gilt nicht für die Gasblasenbildung.

Um es nochmals zu rekapitulieren: Die Möglichkeit, bei der Dekompression druckluftkrank zu werden, hängt einmal ab von der Saturation und Desaturation des gefährdeten Organismus mit Sticktoff, zweitens von der Fähigkeit des Organs, Gasblasen in sich entstehen zu lassen. Die Gassättigung wiederum hängt im Wesentlichen ab vom Minutenvolumen des Herzens, ferner von der Durchblutung des in Frage stehenden Organs im Verhältnis zur Gesamtdurchblutung des Körpers und schliesslich vom Absorptionskoeffizienten des betreffenden Organs, der seinerseits im wesentlichen vom grösseren oder geringeren Fettreichtum des Organs bedingt ist. Von diesem Standpunkt aus lassen sich alle

1) Wiener Akad., 106.
2) Zschr. f. exp. Pathol., 1913.

Symptome der Krankheit erklären und wir können sie von ihm aus besprechen.

Um eine Vorstellung vom Wesen der mannigfachen Erscheinungen zu geben, möchte ich sie, etwas schematisch, für den Augenblick, in zwei Gruppen teilen. Die Symptome der einen Gruppe beruhen auf einer *kleinblasigen, parenchymatösen* Gasinfiltration der Gewebe, die der zweiten auf einer Gasentwickelung im Blute. Die ersten Symptome überwiegen bei der „Caissonkrankheit", die letzten nehmen an Häufigkeit zu bei der „Taucherkrankheit". Zwischen beiden Gruppen stehen diejenigen Fälle, *in denen* Gas in den Geweben und den Lymphspalten frei wird und von dort durch die Capillaren in die Blutbahn getrieben wird. Doch lassen sich die Erscheinungen dieser Art der Erkrankung nicht von einer *Kombination der Erkrankung* beider Gruppen unterscheiden, da dabei sowohl Symptome der Gasblasenbildung im Gewebe wie in der Blutbahn vorhanden sein werden.

Von allen Presslufterkrankungen sind glücklicherweise, wenigstens bei den Caissonarbeitern, diejenigen am häufigsten, die relativ am harmlosesten *sind: es sind dies die* Gliederschmerzen, von den Engländern „Bends" genannt. So waren von 694 Fällen von Druckluftkrankheit, die ich beobachtete, 615 Fälle von „Bends", d. h. fast 90 pCt. Die Leute erkranken unter heftigen Schmerzen in den Extremitäten, die man früher auf eine Blasenbildung im *Centralnervensystem*, und zwar in den Centren oder Bahnen der sensiblen Nerven zurückführen wollte. Ich glaube demgegenüber, dass genügend Beweise für die Ansicht vorhanden sind, dass die „Bends" auf peripherer, *nicht auf centraler Gasblasenbildung* beruhen, ausser den peripheren Symptomen, den Marmorierungen der Haut, Venenanschwellungen, Oedemen, war es namentlich der gelegentliche Befund von Gasblasen im Unterhautfettgewebe des Bauches und der Extremitäten, die mich zu dieser Ansicht führten.

Diese Erkrankungen *sind im allgemeinen* harmlos und gehen bei geeigneter Behandlung bald in Heilung über; doch kommen auch gelegentlich Fälle vor, in denen chronische Veränderungen der Knochen und Gelenke mit Invalidität als Folge der „Bends" auftreten. Ich habe solche Fälle gemeinsam mit Plate zuerst beschrieben, und wir haben auch Röntgenbilder beigebracht, die die Veränderungen der erkrankten Gelenke deutlich zeigten.

Aus zwei Gründen ist der Knochen die Prädilektionsstelle solcher Drucklufterkrankungen. Einmal ist, wie schon *Quincke hervorhob*, die Synovialflüssigkeit sehr eiweissarm und neigt daher besonders leicht zur Gasblasenbildung, andererseits ist die Blutdurchströmung des Knochens sehr schlecht, wie aus besonders angestellten Versuchen *hervorging*.

Sehr bemerkenswert ist in der Statistik das starke Ueberwiegen der Erkrankungen der unteren Extremität. (372 Erkrankungen der unteren, gegenüber 103 Erkrankungen der oberen Extremität.) *Dies ist darauf* zurückzuführen, dass die Circulation, wie wir aus vielen Beobachtungen wissen, in der unteren Extremität sehr viel schlechter ist als in der oberen; so sind die unteren Gliedmaassen ja auch die *Prädilektionsstellen* für das Auftreten venöser und ödematöser Stauung.

Nach den Erkrankungen der Extremitäten folgen an Häufigkeit Erscheinungen, die als Zeichen einer allgemeinen Ergriffenheit des Centralnervensystems anzusehen sind, sie betragen etwa 10 pCt. aller Erkrankungen. Schon *normalerweise fühlt* sich der Pressluftarbeiter nach dem Verlassen der Pressluft nicht ganz wohl, er wird von einer ausserordentlichen Müdigkeit geplagt und schläft durchschnittlich mehr als zu normalen Zeiten. Munter fühlten sich manche überhaupt nur in der Pressluft. Ich habe *diese Klagen oft von den* Pressluftarbeitern gehört und habe selbst darunter zu leiden gehabt.

Der N ist, wie oben schon erwähnt, ein ausserordentlich lipotropes Gas. Dennoch wirkt die N-Sättigung der Lipoide *des Gehirns an sich* nicht schlafmachend, wohl jedoch wirkt schlafmachend, wenn nach der Dekompression kleinste Bläschen im Gehirn entstehen. Es liegt nahe, Betrachtungen im Sinne der Meyer-Overton'schen *Narkosetheorie* anzustellen. Es genügt nämlich die Sättigung der Lipoide mit einem Gase an und für sich nicht, um schlaferzeugend zu wirken, sondern es muss erst eine Schädigung der Lipoide durch das Gas (*hier durch Bläschen*bildung in den Lipoiden) entstehen, um Schlaf hervorzurufen; ich möchte diesen Punkt jedoch jetzt nur kurz streifen, ohne näher auf ihn einzugehen.

In den ausgesprochenen Fällen kommen die Arbeiter taumelnd, meist von *anderen Arbeitern* gestützt, zur Sanitätsschleuse, sie klagen über Kopfschmerzen, Uebelkeit und Erbrechen stellen sich ein. Die Kranken machen auf ihre Arbeitsgefährten oder die sie transportierenden Schutzleute *öfters den Eindruck schwerer* Betrunkenheit. Die Aehnlichkeit mit dem Rausch wird auch dadurch noch grösser, dass das Sensorium nicht selten stark benommen ist. Die Kranken reagieren dann nicht auf Anruf. In *anderen Fällen wieder steht* eine psychomotorische Unruhe im Vordergrund. Die Kranken sind nicht zu halten und schlagen wie wild gegen die Wände der Sanitätsschleuse. Die Erscheinungen sind wohl auf eine *ausserordentlich kleinblasige* Gasentwickelung in den Lipoiden des Gehirns zurückzuführen, die auch die Aehnlichkeit mit dem Bilde der Alkoholvergiftung erklärt. Es kommen auch gelegentlich Fälle von dauernder Invalidität vor, so ist mir besonders ein Kranker in Erinnerung, der *nach Ueberstehen einer* solchen Erkrankung langsam verblödete.

Noch seltener hatte ich Gelegenheit, andere Formen der Druckluftkrankheit zu beobachten, sie machen weniger als 1 pCt. meines Materials aus. Darunter *ist nur eine einzige Apoplexie* — eine Erkrankungform, die bei Tauchern so ausserordentlich häufig ist. Dann mehrere Fälle von Dyspnöe. Diese Dyspnöe führt man im allgemeinen auf Lungeninfarkte, bedingt durch Gasblasen in einem Aste der Pulmonararterie zurück.

Fast immer jedoch *fehlten die physikalischen Zeichen eines* solchen Lungeninfarktes und ich möchte da noch auf folgende Möglichkeit hinweisen: Sättigt man Blutserum bei höherem Druck mit N und dekomprimiert dann, so kommt es vor, *dass man makroskopisch keine* Luftblasen sieht. Bestimmt man dann die Viscosität dieses Serums — ich benutzte das Viscosimeter von Beck und Hirsch — so findet man trotzdem, dass die Viscosität schon *zugenommen hat; mit andern Worten*: es hat schon eine sehr kleinblasige Gasblasenbildung stattgefunden, nur ist sie so gering, dass sie unserem Auge entgeht. Schon eine solche Viscositätsänderung kann erheblich grössere *Ansprüche an das Herz* stellen. Ich möchte so auch einige bedauernswerte Todesfälle erklären, die unter den Erscheinungen der Dyspnöe zugrunde gingen; bei diesen waren, bei der Sektion weder Luftblasen *im Herzen noch in* den Lungengefässen sichtbar. Dagegen fanden sich accessorische Erkrankungen, in einem Falle eine subakute Bronchitis, im anderen eine chronische Myocarditis, es mag so die überhaupt *nicht sichtbare Gasblasen*entwickelung durch Vermehrung der Reibung genügt haben, um bei den schon erschwerten Kreislaufverhältnissen tödlich zu wirken.

Wir kommen nun zu denjenigen Momenten, die die Entstehung der Druckluftkrankheit begünstigen. Es war natürlich *schon frühzeitig* aufgefallen, dass gewisse Individuen sehr leicht druckluftkrank wurden, während andere unter scheinbar den gleichen Arbeitsbedingungen nie erkrankten. Es handelt sich in praxi dann darum, *diese Leute zu erkennen*, bevor sie sich der Gefahr der Druckluft ausgesetzt haben.

Jedenfalls werden Personen, die ein starkes Fettpolster besitzen, sehr viel leichter erkranken als magere. Wie namentlich englische Forscher, Haldane und Hill, betont haben, liegt dies *an dem hohen* Absorptionskoeffizienten des Fettes für Stickstoff. Die Druckluftgesetze aller Staaten schreiben deshalb vor, dass fette Leute von der Arbeit in Druckluft auszuschliessen sind. Trotzdem ich also aufs *strengste fette Leute von der* Arbeit in Druckluft ausschloss, ist der Einfluss der N-Absorption durch das Fett auf die Zahl der Erkrankungen doch noch deutlich bemerkbar gewesen, wie unsere Statistik zeigt, nach der von mitteldicken Leuten 20,7 pCt., von dicken 36,2 pCt. erkrankten.

Ebenso stark prädisponierend wie die N-Absorption der Gewebe sind Kreislaufstörungen. Einmal solche, die den Kreislauf im ganzen stören, sei es den grossen Kreislauf, wie Erkrankungen des Herzens oder der Nieren, *sei es solche, die den* Widerstand im kleinen Kreislauf erhöhen, wie Erkrankungen der Lungen. So kann, wie schon oben erwähnt, eine einfache akute Bronchitis bei einem Arbeiter, der monatelang ohne nennenswerte Beschwerden in Druckluft gearbeitet hat, eine tödliche Druckluftkrankheit hervorrufen. Aber auch lokale Ursachen können den Kreislauf eines Organs verringern und dort eine Druckluftkrankheit hervorrufen. Ein besonders typischer und durchaus nicht seltener Fall ist der, dass ein Arbeiter, stundenlang *mit einem Bein in kaltem* Wasser stehend, arbeiten musste und gerade an diesem Beine mit Bends erkrankte. Hier hat die Vasokonstriktion an der befallenen Extremität die Gasdiffusion in dem Maasse behindert, *dass Blasen* im Gewebe auftreten konnten.

Eine *andere Ursache der Pressluftkrankheit* müsste eigentlich eine vermehrte Fähigkeit der Gewebe zur Gasblasenbildung sein. Individuen, deren Blut bzw. Gewebsflüssigkeit geringe Oberflächenspannung besitzt, müssten *deshalb leichter zu Erkrankungen* neigen, als solche mit einer hohen Oberflächenspannung. Systematische Untersuchungen über diesen Punkt liegen noch nicht vor; vielleicht würden sie für eine weitere Gruppe von *Krankheitsfällen Klarheit über* das prädisponierende Moment schaffen.

Ich möchte hier noch eine Frage kurz streifen, das ist die Gewöhnung an Pressluft. Man war früher der Ansicht, dass es eine Gewöhnung nicht gebe. Man nahm an, dass die einmal *für* die Krankheit Disponierten auch bei jedem weiteren Aufenthalt *in Pressluft erkranken würden*. Meine Statistik zeigt, dass diese

Ansicht irrig ist, wenigstens soweit es sich um sonst gesunde und nicht zu dicke Leute handelt. Es ergab sich, dass $^3/_4$ derjenigen Leute, die in den ersten Schichten an „Bends" erkrankten und trotzdem den Mut zur Weiterarbeit nicht verloren, von der Krankheit verschont blieben, und nur etwa $^1/_4$ wiederholt erkrankte. Es hat offenbar eine Gewöhnung an die Pressluft stattgefunden.

Ich möchte mir vorstellen, dass dabei natürlich nicht eine Gewöhnung der Gewebe an die Gasblasen stattgefunden hatte, sondern dass eine Gewöhnung der nervösen Regulation der Blutverteilung und ein gewisses Training der Wärmeregulation, die ja mit der Blutverteilung aufs innigste verknüpft ist, stattgefunden hat. Solche Erscheinungen sind ja auch sonst bekannt. So fand Mosso bei Soldaten, die zum ersten Male den Monte Rosa bestiegen, beträchtliches Fieber, nach wenigen Wochen bei den gleichen Individuen nur geringe Temperatursteigerungen. In ähnlicher Art wird auch eine Gewöhnung an die ausserordentlich starken Temperaturschwankungen eintreten, denen die Leute ausgesetzt sind. Diese Schwankungen der Aussentemperatur entstehen folgendermaassen: Erst wird bei hohen Temperaturen (30—40° C) mit 90—100 proz. Luftfeuchtigkeit gearbeitet, starkes Schwitzen stellt sich dabei ein, dann plötzliche Abkühlung während der Dekompression infolge der Luftverdünnung. Dadurch entsteht eine starke Vasokonstriktion der peripheren Gefässe, die sich leicht nachweisen lässt. Ich habe einige Versuche an Aufsichtsbeamten gemacht, die zum ersten Male in Druckluft arbeiteten, um wenigstens ein Maass für die Stärke des Schwitzens zu haben, es zeigte sich, dass ziemlich regelmässig die Perspiratio insensibilis sank, und also in der Tat eine gewisse Einstellung des Körpers nicht auf die Pressluft, sondern auf die Faktoren eingetreten war, die prädisponierend für die Pressluftkrankheit wirken.

Was nun schliesslich die Verhütung der Krankheit anbelangt, so haben sich naturgemäss die Versuche der meisten Autoren gerade diesem Gebiete mit Vorliebe zugewandt. Die grundlegende Forderung ist dabei, dass der Uebergang von erhöhtem zu normalem Atmosphärendruck nicht plötzlich, sondern so langsam vor sich geht, dass ein genügend grosser Teil des Gases Gelegenheit hat; von den Organen nach den Lungen transportiert und dort ausgeschieden zu werden, ohne dass es zu Gasblasenbildung kommt. Es ist namentlich das Verdienst Hermann v. Schrötters, auf diesen Punkt immer und immer hingewiesen zu haben, so dass die Notwendigkeit dieses Verfahrens jetzt ausserhalb jeder Diskussion steht. Die Zeit, die zur Dekompression nötig ist, hängt im wesentlichen von zwei Faktoren ab: 1. von der Höhe des Luftdruckes, unter dem gearbeitet wurde, 2. von der Dauer des Aufenthaltes in Druckluft.

Ich habe schon vorhin erwähnt, dass man sich in wenigen Sekunden von einem beliebig hohen Luftdruck ohne Gefahr dekomprimieren kann, wenn man sich nur genügend kurze Zeit unter dem Drucke aufgehalten hat. Es hängt dies davon ab, dass der Körper erst bis zu einem gewissen Grade mit N gesättigt sein muss, ehe Blasen bei der Dekompression entstehen können. Die Sättigung geht sehr langsam vor sich. Nach einer halben Stunde ist der Körper kaum zur Hälfte gesättigt, und die vollständige Sättigung ist beim Fett- und Nervengewebe erst in 7 bis 10 Stunden erreicht. Dies lässt sich leicht aus den vorhin entwickelten Formeln ableiten; ich habe auch eine Reihe praktischer Erfahrungen gesammelt, die das gleiche beweisen. So fiel in einem holländischen Caisson die Morbidität auf etwa die Hälfte, als die Schichtdauer unter sonst identischen Arbeitsbedingungen von 8 auf 4 Stunden verkürzt wurde, — ein Beweiss, dass nach 4 Stunden die volle Sättigung noch nicht erreicht war. Auch am Elbtunnel habe ich Erfahrungen gemacht, die das Gleiche beweisen, namentlich auch an mir selbst. — Ich habe daher in die Hamburger Druckluftverordnung eine Abstufung der Dekompressionszeit nach der Aufenthaltsdauer in verdichteter Luft vornehmen lassen; und auch in anderen Verordnungen — z. B. in der Haldaneschen — finden sich ähnliche Bestimmungen.

An diesem Prinzip der langsamen Dekompression sind verschiedene Modifikationen vorgeschlagen worden. Zuerst hat Zuntz und auch v. Schrötter betont, dass die Ausscheidung des Stickstoffs durch Sauerstoffatmung vor und während der Dekompression wesentlich beschleunigt werden kann. In der Tat ist das Gefälle des Stickstoffs offenbar am grössten, wenn er gegen ein Gas diffundieren kann, das keinen oder nur wenig Stickstoff enthält. Gegen diese Idee, die übrigens v. Schrötter nie angewendet hat, ist namentlich von englischen Autoren der Einwand erhoben worden, dass der Sauerstoff unter hohem Druck sehr giftig ist, und daher die Methode zu gefährlich sei. In der Tat sehen wir beim Atmen von Sauerstoff unter Druck im Tierversuch einen merkwürdigen Symptomenkomplex entstehen. Ich hatte schon erwähnt, dass der respiratorische Stoffwechsel am Anfange einer O_2-Atmung unter Druck konstant bleibt, um später bis auf 50 pCt. der Norm zu sinken, wie schon Paul Bert fand. Gleichzeitig treten Krämpfe ein, und die Tiere sterben nach längerer oder kürzerer Zeit.

Bei der Sektion der Tiere findet man dann Veränderungen nur an den Lungen, die stark blutig angeschoppt erscheinen. Mikroskopisch findet sich ein Exsudat, das die Alveolen und kleinen Bronchen erfüllt, gelegentlich findet man neben der Hyperämie auch Stellen, in denen Blut in die Alveolen übergegangen ist. In schweren Fällen findet man kaum noch eine gesunde Stelle in den Lungen, und es erhebt sich die Frage, ob die Herabsetzung des respiratorischen Stoffwechsels und die Krämpfe nicht einfach als Erstickungserscheinungen infolge der massenhaften Ausschwitzung in die Alveolen anzusehen seien. Namentlich, wenn man bedenkt, dass die schwersten Lungenveränderungen in ganz kurzer Zeit (2—3 Stunden) entstehen können, ist diese Vermutung nicht von der Hand zu weisen. Doch trifft sie nicht zu. Setzt man Tiere unter sehr hohen Druck (8—9 Atmosphären reinen O_2), so entwickeln sich die Krämpfe sehr schnell, in etwa 10 Minuten. Tötet man dann die Tiere sofort, so findet man meist keine oder nur ganz unbedeutende Veränderungen an den Lungen. Beide Phänomene sind also unabhängig voneinander.

Dieser Vergiftungserscheinungen halber hat man also früher, namentlich in England, sich dem Sauerstoff gegenüber ablehnend verhalten. Ich habe dann zuerst einmal in zahlreichen Tierversuchen die toxischen Spannungen des Sauerstoffs festgestellt, dann an mir selbst und zuletzt auch an einer grösseren Anzahl Arbeiter Versuche mit O_2 unter Druck angestellt.

Ich möchte als praktisches Schema hinstellen, dass man einen Druck von 3 Atmosphären reinen O_2 30 Minuten aushalten kann. Ein solcher Druck und eine solche Zeit wird aber in praxi auch für die grössten Tiefen immer genügen, da man die O_2-Atmung immer mit der Haldane'schen Ausschleusungsart verbinden wird, von der gleich die Rede sein wird. Die praktischen Erfolge, die ich mit O_2 gehabt habe, waren, den theoretischen Grundlagen entsprechend, zufriedenstellend. Für den Grossbetrieb ist das Verfahren allerdings etwas kompliziert, so dass es bisher nur in besonderen Fällen und im Taucherbetriebe zur Anwendung gelangte.

Eine andere Ausschleusungsart ist die von Haldane angegebene „stage decompression", die staffelförmige Dekompression.

Haldane schlägt vor, die Dekompression nicht gleichmässig vorzunehmen, sondern zuerst sehr rasch eine gewisse Menge des Druckes abzulassen und dann sehr langsam weiter zu dekomprimieren. Auf diese Art wird eine erhebliche Tensionsdifferenz geschaffen und dadurch die N-Ausscheidung gefördert; es wird also auch die Gefährlichkeit der Zeit unmittelbar nach dem Ausschleusen erheblich herabgesetzt. Es kommt nun nur darauf an, den ersten schnellen Fall so gross zu machen, dass die Tensionsdifferenz möglichst gross ist, andererseits ihn nicht so gross zu machen, dass er selbst schon die Bildung von Gasblasen veranlasst.

Haldane meint nun folgendes: Bei den vielen, früher vorgenommenen, ganz plötzlichen Ausschleusungen sind Todesfälle erst von einem Ueberdruck von 1,4 Atmosphären, d. h. einem absoluten Druck von 2,4 Atmosphären vorgekommen, bei 2,3 Atmosphären nicht mehr. Man kann also von 2,3 auf 1,0 Atmosphären brüsk dekomprimieren, wobei vielleicht geringe Mengen Gasblasen entstehen werden, die aber nicht so gross sind, dass sie lebenswichtige Organe verstopfen können. Bei dem doppelten Druck nun, also von 4,6 Atmosphären, würde man, wie Haldane folgert, auf den doppelten Druck, also 2 Atmosphären, dekomprimieren können. Da nämlich nach dem Henri-Dalton'schen Gesetz die doppelte Menge N bei doppeltem Atmosphärendruck absorbiert wird, so wird sich bei einem proportionalen Fall des Luftdrucks genau die doppelte N-Menge entwickeln; da diese nach Boyle-Mariotte aber bei 2 Atmosphären nur den halben Raum einnimmt, wie bei 1 Atmosphäre, so würden bei Dekompression von 4,6 : 2 Atmosphären die Blasen genau den gleichen Raum einnehmen, wie bei Dekompression von 2,3 : 1 Atmosphäre. Da wir von den letzten Blasen aber wissen, dass sie unschädlich sind, so sind es auch die ersten. Die Dekompression kann also im Verhältnis von 2,3 : 1 Atmosphären brüsk vorgenommen werden, ohne dass sie gefährlich wird.

Ich habe versucht, einige Prämissen dieser Ueberlegungen experimentell zu prüfen. Zuerst ist vorausgesetzt, dass bei einer Senkung des absoluten Luftdrucks bei etwaiger Bildung kleinster Gasblasen die N-Ausscheidung durch die Lungen in der gleichen Weise vor sich geht, wie bei der Diffusion, wenn nur der Partialdruck des N herabgesetzt wird. Es liesse sich ja denken, dass dies nicht der Fall wäre. Ich habe mit der vorhin erwähnten Anordnung Versuche angestellt, die zeigten, dass diese Annahme richtig ist.

Die zweite Voraussetzung ist, die Gültigkeit des Henri-Dalton'schen Gesetzes für die Blasenbildung. Diese Annahme ist nun nie richtig, wie ich in vielen, darauf hingerichteten Versuchen gelernt habe. Es geht das auch schon aus den früheren Betrachtungen hervor, und ich konnte immer finden — mit N, mit CO_2 usw. —, dass die ausgeschiedene Gasmenge bei hohen Drucken grösser ist, als dem Henri-Dalton'schen Gesetz entspricht.

Aber diese geringe Rektifikation des Haldane'schen Gedankenganges schadet dem Prinzip nicht. Man wird eben nur etwas vorsichtiger sein müssen, als es nach der Haldane'schen Theorie sein müsste. Haldane selbst meinte, dass zwar 2,3 : 1 das äusserste Maass dessen sei, was gerade nicht gefährlich sei, doch hat er der Sicherheit wegen immer 2,0 : 1,0 dekomprimiert. Diese Maassregel erweist sich nach dem, was wir eben auseinandergesetzt, nicht als eine Sicherheit, sondern als eine absolut notwendige Forderung, *die namentlich bei sehr hohen Drucken* vielleicht manchmal nicht mehr zureichend sein wird. Ich habe diese Grenze in praxi auch bei niedrigen Drucken nie ganz erreicht.

Doch das ist Kleinkram, der der schönen und klaren Idee Haldane's keinen Abbruch tut. Die Statistik zeigte uns, dass Haldane in praxi recht hatte. Ich habe immer abwechselnd *einige Tage gleichförmig, dann wieder staffelförmig dekomprimiert*, mit dem Erfolge, dass die Haldane'sche Art in der Morbidität um 22 pCt. besser abschnitt. Wir werden also dieses ausserordentlich einfache Hilfsmittel auch in Zukunft weiter benutzen.

Während sowohl die Zuntz'sche als die Haldane'sche Methode danach streben, die Tensionsdifferenz zwischen dem N der Gewebe und der Aussenluft zu vergrössern, kann man eine *beschleunigte Ausscheidung des N auch dadurch erreichen, dass man* die Geschwindigkeit des Blutstromes erhöht. Je grösser das Minutenvolumen des Herzens, desto grösser wird auch die N-Ausscheidung sein. Dieser Gedanke liegt implicite in der Zuntz'schen Ueberlegung drin; er ist ferner kurz, aber klar von Haldane ausgeführt worden. Ich habe ihn dann zuerst experimentell, später auch praktisch zu prüfen gesucht.

Am nächsten *liegt es ja, den Kreislauf durch Medikamente zu* beschleunigen; ich habe zuerst die „belebende" Wirkung des Alkohols geprüft, doch wurde die N-Ausscheidung dadurch nicht beschleunigt. Dann stellte Herr Kauffmann auf meine Veranlassung Versuche mit intravenösen Digitalisinjektionen an; auch dadurch wurde das Schlagvolumen des Herzens kaum erhöht. Es zeigt sich da wieder, dass bei einem normalen Kreislauf alle solchen Medikamente wenig Einfluss haben. Es wurde dann die Vermehrung der Lungenventilation geprüft, deren *Einfluss schon erheblicher war. Immerhin* ist der Einfluss noch sehr gering, wenn nicht gerade ganz ausserordentliche Minutenvolumina der Lunge erreicht werden. So weit wie möglich, wird dieser Faktor schon unwillkürlich benutzt, denn die Luft in den Schleusen ist meist sehr schlecht und der CO_2-Gehalt steigt während der Dekompression bis auf 1 pCt. und mehr, wodurch sicherlich eine Vermehrung der Lungenventilation eintritt. Hier bietet sich also kein Angriffspunkt. Heisse Bäder erhöhen das Minutenvolumen etwas, sie bewirken namentlich eine *erhöhte Circulation in den Extremitäten; doch kommen sie* aus äusseren Gründen für die Prophylaxe nicht, wohl aber für die Therapie in Betracht, wobei sie sich, namentlich bei Bends, als gutes Adjuvans bewähren.

Den grössten Einfluss auf die Circulation sah ich durch Körperarbeit entstehen. Die Körperarbeit vermehrt in extremen Fällen das Minutenvolumen auf das 10fache, bei mittlerer Arbeit auf das 5 bis 7fache und bei ganz leichter Arbeit noch, die auch von ungeübten *Personen stundenlang ohne Unterbrechung* geleistet werden kann, auf das 3fache.

Diese Versuche schienen mir derart günstig für die Muskelarbeit, dass ich erfreut war, eine Gelegenheit zu haben, sie auch im Pressluftbetriebe zu verwenden. Im Bau des Elbtunnels befand sich eine etwa 25 m hohe Treppe, die so war, dass sie entweder in oder ausserhalb Pressluft sich befand. War sie ausserhalb Pressluft, so mussten die Arbeiter sie unmittelbar nach der Dekompression hinaufsteigen, also in dem Augenblicke, wo die Gefahr der N-Stauung am grössten war. Sie hatten dann etwa $1^1/_2$ Minuten relativ kräftige Arbeit zu leisten. Diese sehr kurzdauernde Arbeit genügte, um die Morbidität auf die Hälfte herabzusetzen. Es muss demnach angenommen werden, dass die Körperarbeit ein sehr wirksames Prophylakticum darstellt.

Es ist dabei allerdings zu bemerken, dass unsere Versuche nur bei 3 Atmosphären Druck angestellt sind und demnach nichts über die Verhältnisse bei höherem Druck aussagen. Es wäre sehr gut möglich, dass die Muskelarbeit bei diesem Drucke durch die Erschütterung eine vermehrte Gasblasenbildung zustande brächte, oder dass bei der Beschleunigung des Kreislaufs Gasblasen aus den Geweben in die Blutbahn verschleppt würden. Ich habe schon vorhin erwähnt, dass bei hohen Drucken gerade diese Möglichkeit schon normalerweise stärker in den Vordergrund tritt, so dass dann die Muskelarbeit gefährlich wirken könnte. Aber darüber fehlen uns, wie gesagt, noch alle Erfahrungen. Bei den Drucken jedoch, die für die Caissonarbeit in Betracht kommen, d. h. 1—3 Atmosphären Ueberdruck, ist die *Muskelarbeit das beste Hilfsmittel — bei langsamer* Dekompression natürlich —, das wir kennen.

Theoretisch sollte es möglich sein, die Pressluftkrankheit dadurch zu bekämpfen, dass man die Oberflächenspannung der Gewebsflüssigkeiten vergrössert und dadurch die Bildung von Gasblasen verhindert. Ich möchte diese Möglichkeit nur andeuten und darauf vorläufig nicht eingehen, bis ich sichere Beweise dafür habe, dass diese Möglichkeit auch wirklich realisierbar ist.

Ueber die Therapie ist wenig zu sagen. Das souveräne Mittel ist das Zurückbringen der Kranken in die Pressluft. Es ist ein Mittel, dass so spezifisch ist, dass keiner, der es je mit Verstand angewandt hat, es wird missen wollen. Die Vorgänge bei der Rekompression sind ziemlich verwickelter Natur. In erster Linie werden natürlich die Gasblasen, entsprechend dem Mariotte'schen Gesetz, auf ein kleineres Volumen zusammengepresst. Dadurch kann man die mechanischen Folgen der Gasblasenbildung beliebig verkleinern, wenn man nur einen Druck ausübt, der gross genug ist. Im allgemeinen wird man aber kaum jemals den Druck überschreiten, unter dem gearbeitet wurde. Die zweite günstige Folge des Wiedereinschleusens ist die Tatsache, dass jede weitere Blasenbildung dadurch verhindert wird. Es wird ferner allgemein gesagt, dass die Blasen bei dem hohen Druck leichter resorbiert werden als bei niederem. Das trifft nur in geringem Grade zu. So lässt sich leicht berechnen, dass bei Erhöhung des Luftdruckes auf das Doppelte die Diffusion nur um das $\frac{2}{\sqrt[3]{4}} = 1{,}26$ fache zunimmt. Gelegentlich wird auch O_2 zur Rekompression gegeben. Nach den Analysen Paul Bert's und Schrötter's beträgt *nämlich der N-Gehalt in* solchen Blasen im Durchschnitt 81 pCt. Da die N-Spannung der Gewebe gleich der der Alveolarluft, d. h. 79—80 pCt. ist, so beträgt das Gefälle für die Resorption des N der Blasen nur 1—2 pCt. der Atmosphäre. Hier müsste nun O_2-Atmung, wie Zuntz betont hat, ausserordentlich wirken, indem sie die Resorption der Blasen auf ca. das 50fache beschleunigt. In praxi wendet man neben *der O_2-Atmung* bei den Gliederschmerzen besonders Massage der Gliedmaassen an, ferner warme Bäder, die ebenfalls die N-Resorption verbessern.

M. H.! Ich bin am Ende meiner Ausführungen. Es findet sich in unserem Wissen noch manche Lücke, aber ich glaube Ihnen doch gezeigt zu haben, dass die grundlegenden Anschauungen Hoppe-Seylers und Paul Bert's durch die Arbeiten der neueren Autoren, von Schrötter, Zuntz, Haldane, Quincke — um nur einige Namen zu nennen — weiter ausgebaut worden sind, und dass wir die Physiologie und Pathologie des Lebens in verdichteter Luft mit seltener Klarheit zu übersehen vermögen.

Vorlaufige Mittheilung uber Caissonarbeiter

Von Dr. Richard Heller, Dr. Wilhelm Mager
und Dr. Hermann v. Schrotter

From: Wien. klin. Wochenschrift, vol. 8, 1895, pp. 475-476.

SUMMARY

Introductory Report on Caisson Workers

Page 475 deals only with construction and mechanisms of caisson.

Caisson was at Nussdorf; building engineer Mr. Karl Redlich. Professor received full cooperation from him to keep a clinical eye on all workers. Three MD's from Heller's Clinic were assigned to the project. One, usually v. Schroetter was always at the scene of the caisson work. v. Schroetter even went down with the men on occasion. The other two remained at the clinic. Project began on 1 February. All workers were in excellent health. As long as the pressure did not surpass 1.5 atmospheres, i.e., until May, there were, with the exception of insignificant difficulties on the part of the ears and very slight joint pains, no severe symptoms.

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Arrangements were made that every worker, who showed severe symptoms was immediately brought to the clinic. Thus we had the opportunity to observe the symptoms not only at the place of work, but to follow the entire course.

With very few exceptions it is characteristic that the symptoms appear first at 15 minutes to 1 hour after departure from the caisson and then very suddenly.

In the majority of cases the worker leaves his work perfectly well, and is seized either on his way home or after arrival at home, especially with sudden severe pains in the lower extremities, so that he collapses to the floor. Occasionally the ears are affected and there is some respiratory difficulty already when leaving the locked chamber.

In the character of a previous report we shall divide the observed disease picture into a few main groups.

Symptoms of the Auditory Organ

Aside from the slight humming in the ears and slight pain, sensed almost always when entering and leaving the chamber, which disappear immediately when the pressure has again become constant, there are sensations which last longer, as well as hemorrhages in the drum and middle ear and cases occur which show the Meniere symptoms.

Reduction in hearing ability in all these forms to a more or less degree are observed, sometimes only briefly, sometimes for a longer time.

Symptoms in the area of the extremities

The onset of very severe pain, without any traceable objective findings; the onset of severe pain, whereby the nerve trunks in their course are pressure sensitive to a high degree; pains with in part uniform swelling of the extremities, in part definitely combined with traceable exudation in the joints. Finally, the sudden onset of piercing pains in the large joints, especially the knee joints, which reach such an intensity, that the workers are unable to stand upright and, as though struck by lightning, collapse. Simultaneously with these pains there frequently is the sensation of "being dead" in the afflicted extremity.

In addition to the general symptoms from the side of the nervous system, we observed disturbances in sensitivity and pareses of the extremities.

Increase in volumes and edematous swellings of the extremities, frequently only one extremity, then both arms, or both legs, sometimes even combined as one upper and one lower extremity - of which on 14 June one case was presented to the Association of Physicians - which may be of such high degree, that the circumference between the normal and afflicted side may show a difference of several centimeters - in one case of 5 cm.

All symptoms of this group are characterized by the fact, that they usually disappear already after 3-5 days, so that the worker can return to his job.

Finally the severe forms, characterized by sudden unconsciousness, often of several hours duration, without apparent cyanosis and dyspnea, and such which begin with dyspnea and a high degree of cyanosis and may lead to collapse and death within a short time. The cyanosis here is peculiar in that the entire body shows in addition to the livid dark violet color a marbled appearance of the skin in even darker color.

Such a case, obducted by Hofrath v. Hofmann, which concerned a previously healthy 31 year old worker, showed blood overfill and edema of the lungs: (choking catarrh) as the cause of death.

To date this is the only case of death since this work began.

We do not, at present, feel justified, to report more, and wish to say only, that each of the named groups will undergo detailed study, and that Professor Gruber has offered his help with the affections of the ear.

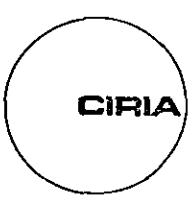
Investigation of air and temperature, blood gases and animal experiments will make the studies more understandable.

These experiences may have value from a profession-hygienic relation.

Translated by Mrs. Anne Woke, NMRI, 1972.

REPORT 44 FEBRUARY 1973

A Medical Code of Practice for work in compressed air



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Appendix 1 The new decompression tables

INTRODUCTION

by H. V. Hempleman (Superintendent, Royal Naval Physiological Laboratory)

Following observation of various civil engineering contracts over a period of several years it became obvious that the British decompression procedures described in 'Work in Compressed Air Special Regulations, 1958', were inadequate in that:

1. A decompression time of 2 min following exposures to all gauge pressures below 1.23 bar (or 18 lbf/in^2) was not safe as it was frequently followed by decompression sickness.
2. The bends rate increased markedly when the periods of exposure exceeded 4 h.
3. The bends rate amongst new starters was always high.
4. Both engineers and doctors had been in the habit of lengthening the decompression times given in the 1958 Regulations.
5. A high incidence of bone necrosis was occurring[1].

New decompression tables have been calculated on the basis of theoretical conclusions reached as a result of exposing animals and humans to pressures of air in the rigidly controlled conditions of the laboratory. The new tables represent a compromise between practicability and theoretical ideals.

METHOD OF CALCULATION

This is based on two principle assumptions:

Assumption 1

If a man is exposed to an absolute pressure of P_1 for some time t, the problems associated with decompression back to an absolute pressure of 1 bar are increased by a rise in P, and also by an increase in t. If after a long period at P_1 the man is to be decompressed rapidly to some lower pressure, P_2, then according to the Haldane concepts P_1/P_2 should be a constant and equal to 2. The new system modifies this and makes the value of P_1/P_2 ($=r$) dependent upon P_1 in the following manner:

$$P_1/P_2 = r = \frac{27.5714}{P_1^* + 12.407} \qquad *P_1 \text{ must be expressed in bar}$$

Thus as P_1 increases, the permissible pressure ratio (r) decreases. This expression fits the well-established observations described below. After very long exposures to compressed air at an absolute pressure of 1.9 bar, rapid decompression to an absolute pressure of 1 bar can be undertaken without any ill effects. Furthermore, the incidence of decompression sickness following 8-h shifts at a gauge pressure of 0.96 bar (or 14 lbf/in^2) is very low. Thus, it may be concluded that 1.9 is a safe decompression ratio for use at these low pressure values. For higher pressures, the New York State Regulations (1922)[2] which specify a rapid pressure drop to half gauge pressure, were very successful, as was Catton's[3] introduction of an intermediate stage. These observations imply the advisability of a diminution of the permitted ratio with pressure. For man the problem is open to some doubt (due to lack of appropriately controlled experimentation), but with animals the matter is beyond dispute and a cut-back in this ratio with increase of pressure is easily demonstrable. It is estimated, by analogy from these animal experiments, that for man the permitted ratio will be changed from 1.9 to 1.6 over the range from a gauge pressure of 0.96 bar (or 14 lbf/in^2) to 3.4 bar (or 50 lbf/in^2)

Assumption 2

This concerns the observation that for short exposure times it is possible to go safely to great pressures, whereas for long exposure times only relatively low pressures are safe. Thus the onset of decompression sickness would seem to be dependent upon the quantity of gas absorbed at pressure. The shape of the pressure-time curve for the onset of decompression sickness seems to be the same as that of the curve for the uptake of nitrogen by the whole body. This, in turn, is the same shape as a curve describing the quantity of gas diffusing into a slab of material when only one of the faces is exposed to the pressure of gas. Thus there is an exact and well known physical analogy to describe the uptake of gas curve, or the acquisition of danger curve.

The particular equation being used is:

$$\text{fractional saturation} = 1 - \frac{8}{\pi^2}\left\{e^{-kt} + \tfrac{1}{9}\,e^{-9kt} + \tfrac{1}{25}\,e^{-25kt} + \ldots\right\}$$

where $k = D\pi^2/4b^2$,

D = diffusion coefficient, and

b = thickness of the slab exposed on one side.

This is a solution to Fick's law

$$-\frac{dc}{dt} = D\frac{d^2c}{dx^2}$$

where c is the gas concentration (or partial pressure) at some distance x inside the slab, for the particular conditions of thickness b, the slab being initially free of nitrogen and then having one face suddenly exposed at time $t = 0$ to a fixed raised pressure of nitrogen or other gas.

This equation was fed into a computer for the particular value of $K = 0.007928$ which was chosen to give as near as possible 30% saturation after 22 min, and to represent the rate of removal of nitrogen from the body. This may not be conservative enough as it takes about 9 h to be 99% desaturated with gas using this equation. This may be compared with Haldane's 75-min tissue used in the present regulations which is 99% desaturated in almost the same time. Behnke[4] has referred to a 120-min tissue which would require 14 h to desaturate 99%. Nevertheless his measurements of the loss of nitrogen from body tissues when breathing oxygen do not support the consideration of any such prolonged values. In fact his data show that some men are rid of all measurable nitrogen in 6 h.

Calculation

These assumptions led to the following 'safety' scheme whereby it is assumed that the rate of uptake of gas is 1.5 times as great as the rate of elimination. There is some doubt whether the curve used for the elimination of gas represents a rate that is sufficiently slow, but it must be borne in mind that very conservative permitted pressure ratio changes should be used in conjunction with these gas elimination estimates and this will cancel any tendency to hurry the decompression.

As an example let it be supposed that a man is exposed to a gauge pressure of 3.4 bar (or 50 lbf/in^2) for 30 min, then in order to calculate the decompression one proceeds as follows:

After 30 min he is 42.9% saturated (from curve), thus the quantity of gas in the body (or slab analogy) is the same as if he had been at a gauge pressure of 1.46 (i.e. 3.4 x 42.9%) bar (or 21 lbf/in^2) for an indefinitely long period. The permitted ratio used from Assumption 1 given above, is:

$$r = \frac{27.5714}{P_1^* + 12.407}$$

* P_1 must be expressed in bar

but $P_1 = 1.46 + 1 = 2.46$ bar (absolute)

$\therefore \quad r = 27.5714/14.867 = 1.85$

Hence the first stage of the decompression is at an absolute pressure of 2.46/1.85 = 1.3 bar (or 19 lbf/in^2) or a gauge pressure of 0.3 bar (or 4.3 lbf/in^2). To be safe, therefore, the fast phase would end at a gauge pressure of 0.3 bar (or 4.3 lbf/in^2), but working in 0.2-bar (or 2.8-lbf/in^2) increments would mean stopping the fast phase at a gauge pressure of 0.4 bar (or 5.6 lbf/in^2).

The calculation next proceeds as follows:

The exposure to a gauge pressure of 3.4 bar (or 50 lbf/in^2) for 30 min, followed by a rapid drop in pressure to a gauge pressure of 0.4 bar (or 5.6 lbf/in^2), may be regarded as equivalent to adding together two exposures, one of which carried on indefinitely absorbing gas at a gauge pressure of 3.4 bar (or 50 lbf/in^2), followed after 30 min by a negative exposure of (3.4-0.4) (i.e. gauge pressure of 3.0 bar (or 43 lbf/in^2), which also carried on indefinitely). Ultimately, the two curves would become asymptotic, and the gas left in the body would be at a gauge pressure of 0.4 bar (or 5.6 lbf/in^2), but one does not wait any longer than is necessary to make the next pressure drop to a gauge pressure of 0.2 bar (or 2.8 lbf/in^2). At a gauge pressure of 0.2 bar (or 2.8 lbf/in^2), the permitted excess gas pressure is easily calculated from Assumption 1 as:

$$\frac{P_1}{P_2} \approx \frac{27.5714}{P_1{}^* + 12.407}$$

* P_1 must be expressed in bar

where P_2 = 0.2 + 1.0 = 1.2 bar (absolute) P_1 = 1.26 bar (absolute). The superimposing of the ingoing and outgoing curves is continued until it can be seen that an absolute gas pressure of 1.26 bar (or 18 lbf/in^2) is left. At this point a drop to a gauge pressure of 0.2 bar (or 2.8 lbf/in^2) is permitted. The duration of this stage is calculated by superimposing a gauge pressure 0.2 bar (or 2.8 lbf/in^2) negative curve on the existing two graphs. The calculation is continued in this simple manner until it is safe to reach atmospheric pressure with an excess gas gauge pressure of 0.92 bar (or 13.1 lbf/in^2) remaining. The only further fact to be borne in mind (see above 'safety' scheme) is that the fast graph is used for estimating gas uptake and there is a discontinuity at the moment of decompression when the slow elimination graph is employed.

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DECOMPRESSION ('BLACKPOOL') TABLES (IMPERIAL UNITS)

Exposure period 0 to ½ h

IMPERIAL UNITS

Maximum working pressure (lbf/in^2 g)	Stage pressure (lbf/in^2 g) (see Note 2)							Total time (min) (see Note 3)
	28	24	20	16	12	8	4	
14 to 16								–
16 to 18								–
18 to 20								–
20 to 22								–
22 to 24								–
24 to 26								–
26 to 28								–
28 to 30								–
30 to 32							5	5
32 to 34							5	5
34 to 36							5	5
36 to 38							5	5
38 to 40							5	5
40 to 42							10	10
42 to 44							10	10
44 to 46							15	15
46 to 48						5	10	15
48 to 50						5	15	20

NOTES:

1. Decompress at a rate not faster than 5 lbf/in^2 per min
2. Decompress between stages at a rate of 5 lbf/in^2 per min
3. Not including time between stages
4. Where alternative decompression procedures are given (e.g. 46 lbf/in^2) the longer decompression procedure should always be chosen

Exposure period over ½ h to 1 h

IMPERIAL UNITS

Maximum working pressure (lbf/in^2 g)	Stage pressure (lbf/in^2 g) (see Note 2)							Total time (min) (see Note 3)
	28	24	20	16	12	8	4	
14 to 16								–
16 to 18								–
18 to 20								–
20 to 22								–
22 to 24							5	5
24 to 26							5	5
26 to 28							10	10
28 to 30							15	15
30 to 32							20	20
32 to 34						5	20	25
34 to 36						5	30	35
36 to 38						5	35	40
38 to 40						10	40	50
40 to 42						10	45	55
42 to 44					5	10	50	65
44 to 46					5	15	50	70
46 to 48					5	20	50	75
48 to 50					5	25	55	85

NOTES:

1. Decompress at a rate not faster than 5 lbf/in^2 per min
2. Decompress between stages at a rate of 5 lbf/in^2 per min
3. Not including time between stages
4. Where alternative decompression procedures are given (e.g. 46 lbf/in^2) the longer decompression procedure should always be chosen

Exposure period over 1 h to 1½ h

IMPERIAL UNITS

Maximum working pressure (lbf/in^2 g)	Stage pressure (lbf/in^2 g) (see Note 2)							Total time (min) (see Note 3)
	28	24	20	16	12	8	4	
14 to 16							2	2
16 to 18							2	2
18 to 20							5	5
20 to 22							10	10
22 to 24							15	15
24 to 26							25	25
26 to 28						5	30	35
28 to 30						5	40	45
30 to 32						10	45	55
32 to 34						15	50	65
34 to 36						20	55	75
36 to 38					5	20	60	85
38 to 40					5	30	60	95
40 to 42					10	35	60	105
42 to 44					15	40	60	115
44 to 46				5	20	40	60	125
46 to 48				5	25	45	60	135
48 to 50				5	30	50	60	145

NOTES:

1. Decompress at a rate not faster than 5 lbf/in^2 per min
2. Decompress between stages at a rate of 5 lbf/in^2 per min
3. Not including time between stages
4. Where alternative decompression procedures are given (e.g. 46 lbf/in^2) the longer decompression procedure should always be chosen

Exposure period over 1½ h to 2 h

IMPERIAL UNITS

Maximum working pressure (lbf/in^2 g)	Stage pressure (lbf/in^2 g) (see Note 2)							Total time (min) (see Note 3)
	28	24	20	16	12	8	4	
14 to 16							2	2
16 to 18							5	5
18 to 20							10	10
20 to 22							20	20
22 to 24							30	30
24 to 26						5	40	45
26 to 28						5	50	55
28 to 30						15	50	65
30 to 32						25	50	75
32 to 34					5	25	60	90
34 to 36					5	35	60	100
36 to 38					10	40	60	110
38 to 40					15	45	60	120
40 to 42				5	20	45	60	130
42 to 44				5	25	50	60	140
44 to 46				10	30	50	60	150
46 to 48			5	10	35	50	60	160
48 to 50			5	15	40	50	60	170

NOTES:

1. Decompression at a rate not faster than 5 lbf/in^2 per min
2. Decompress between stages at a rate of 5 lbf/in^2 per min
3. Not including time between stages
4. Where alternative decompression procedures are given (e.g. 46 lbf/in^2) the longer decompression procedure should always be chosen

Exposure period over 2 h to 2½ h

IMPERIAL UNITS

Maximum working pressure (lbf/in^2 g)	Stage pressure (lbf/in^2 g) (see Note 2)							Total time (min) (see Note 3)
	28	24	20	16	12	8	4	
14 to 16							5	5
16 to 18							10	10
18 to 20							20	20
20 to 22							30	30
22 to 24						5	40	45
24 to 26						10	45	55
26 to 28						15	55	70
28 to 30						20	60	80
30 to 32					5	30	60	95
32 to 34					10	35	60	105
34 to 36					15	40	60	115
36 to 38				5	15	45	60	125
38 to 40				5	25	45	60	135
40 to 42				10	30	45	60	145
42 to 44				15	35	45	60	155
44 to 46			5	15	35	50	60	165
46 to 48			5	25	35	50	60	175
48 to 50			10	25	40	50	60	185

NOTES:

1. Decompress at a rate not faster than 5 lbf/in^2 per min
2. Decompress between stages at a rate of 5 lbf/in^2 per min
3. Not including time between stages
4. Where alternative decompression procedures are given (e.g. 46 lbf/in^2) the longer decompression procedure should always be chosen

Exposure period over 2½ h to 3 h

IMPERIAL UNITS

Maximum working pressure (lbf/in^2 g)	Stage pressure (lbf/in^2 g) (see Note 2)							Total time *(min)* (see Note 3)
	28	24	20	16	12	8	4	
14 to 16							5	5
16 to 18							15	15
18 to 20							25	25
20 to 22							40	40
22 to 24						5	50	55
24 to 26						15	50	65
26 to 28						20	60	80
28 to 30					5	30	60	95
30 to 32					10	35	60	105
32 to 34					15	40	60	115
34 to 36				5	20	40	60	125
36 to 38				5	25	45	60	135
38 to 40				10	30	45	60	145
40 to 42				15	35	45	60	155
42 to 44			5	20	35	50	60	170
44 to 46			10	20	40	50	60	180
46 to 48			15	25	40	50	60	190
48 to 50		5	15	30	40	50	60	200

NOTES:

1. Decompress at a rate not faster than 5 lbf/in^2 per min
2. Decompress between stages at a rate of 5 lbf/in^2 per min
3. Not including time between stages
4. Where alternative decompression procedures are given (e.g. 46 lbf/in^2) the longer decompression procedure should always be chosen

Exposure period over 3 h to 4 h

IMPERIAL UNITS

Maximum working pressure (lbf/in^2 g)	Stage pressure (lbf/in^2 g) (see Note 2)							Total time (min) (see Note 3)
	28	24	20	16	12	8	4	
14 to 16							10	10
16 to 18							20	20
18 to 20							35	35
20 to 22						5	45	50
22 to 24						10	55	65
24 to 26						20	55	75
26 to 28					5	30	55	90
28 to 30					5	40	60	105
30 to 32					15	40	60	115
32 to 34					20	45	60	125
34 to 36				5	30	45	60	140
36 to 38				10	35	45	60	150
38 to 40			5	15	35	45	60	160
40 to 42			5	20	40	45	60	170
42 to 44			10	25	40	45	60	180
44 to 46		5	10	30	40	45	60	190
46 to 48		5	20	30	40	45	60	200
48 to 50		10	20	35	40	50	60	215

NOTES:

1. Decompress at a rate not faster than 5 lbf/in^2 per min
2. Decompress between stages at a rate of 5 lbf/in^2 per min
3. Not including time between stages
4. Where alternative decompression procedures are given (e.g. 46 lbf/in^2) the longer decompression procedure should always be chosen

Exposure period over 4 h to 8 h

IMPERIAL UNITS

Maximum working pressure (lbf/in^2 g)	Stage pressure (lbf/in^2 g) (see Note 2)							Total time (min) (see Note 3)
	28	24	20	16	12	8	4	
14 to 16							15	15
16 to 18							30	30
18 to 20							45	45
20 to 22						5	55	60
22 to 24						15	60	75
24 to 26						30	60	90
26 to 28					5	35	60	100
28 to 30					10	45	60	115
30 to 32					20	45	60	125
32 to 34				5	30	45	65	145
34 to 36				10	35	45	70	160
36 to 38				20	35	45	80	180
38 to 40			5	25	40	50	85	205
40 to 42			10	30	40	50	90	220
42 to 44		5	15	30	40	55	100	245
44 to 46		5	20	35	40	60	110	270
46 to 48		10	25	35	45	65	120	300
48 to 50	5	10	30	40	45	70	130	330

NOTES:

1. Decompress at a rate not faster than 5 lbf/in^2 per min
2. Decompress between stages at a rate of 5 lbf/in^2 per min
3. Not including time between stages
4. Where alternative decompression procedures are given (e.g. 46 lbf/in^2) the longer decompression procedure should always be chosen

DECOMPRESSION ('BLACKPOOL') TABLES (SI UNITS)

Working period 0 to ½ h

SI UNITS

Maximum working pressure (bar)	Stage pressure (bar) (see Note 2)								Total time (min) (see Note 3)
	1.6	1.4	1.2	1.0	0.8	0.6	0.4	0.2	
0.0 to 0.2									–
0.2 to 0.4									–
0.4 to 0.6									–
0.6 to 0.8									–
0.8 to 1.0									–
1.0 to 1.2									–
1.2 to 1.4									–
1.4 to 1.6									–
1.6 to 1.8									–
1.8 to 2.0									–
2.0 to 2.2								5	5
2.2 to 2.4								5	5
2.4 to 2.6								5	5
2.6 to 2.8								5	5
2.8 to 3.0							5	5	10
3.0 to 3.2							5	5	10
3.2 to 3.4							5	10	15

NOTES:

1. Decompress at a rate not faster than 0.4 bar/min
2. Decompress between stages at a rate of 0.4 bar/min
3. Not including time between stages
4. Where alternative decompression procedures are given (e.g. 3.2 bar), the longer decompression procedure should always be chosen

Working period over ½ h to 1 h

SI UNITS

Maximum working pressure (bar)	Stage pressure (bar) (see Note 2)								Total time (min) (see Note 3)
	1.6	1.4	1.2	1.0	0.8	0.6	0.4	0.2	
0.0 to 0.2									–
0.2 to 0.4									–
0.4 to 0.6									–
0.6 to 0.8									–
0.8 to 1.0									–
1.0 to 1.2									–
1.2 to 1.4									–
1.4 to 1.6								5	5
1.6 to 1.8								5	5
1.8 to 2.0								10	10
2.0 to 2.2							5	15	20
2.2 to 2.4							5	20	25
2.4 to 2.6							10	25	35
2.6 to 2.8						5	10	35	50
2.8 to 3.0						5	15	40	60
3.0 to 3 2					5	5	20	40	70
3.2 to 3.4					5	10	25	40	80

NOTES:

1. Decompress at a rate not faster than 0.4 bar/min
2. Decompress between stages at a rate of 0.4 bar/min
3. Not including time between stages
4. Where alternative decompression procedures are given (*e.g. 3.2 bar*), *the longer* decompression procedure should always be chosen

Working period over 1 h to 1½ h

SI UNITS

Maximum working pressure (bar)	Stage pressure (bar) (see Note 2)								Total time (min) (see Note 3)
	1.6	1.4	1.2	1.0	0.8	0.6	0.4	0.2	
0.0 to 0.2									–
0.2 to 0.4									–
0.4 to 0.6									–
0.6 to 0.8									–
0.8 to 1.0									–
1.0 to 1.2								5	5
1.2 to 1.4								10	10
1.4 to 1.6							5	15	20
1.6 to 1.8							5	30	35
1.8 to 2.0						5	10	35	50
2.0 to 2.2						5	20	35	60
2.2 to 2.4						10	25	40	75
2.4 to 2.6					5	10	30	45	90
2.6 to 2.8					5	20	35	45	105
2.8 to 3.0				5	10	20	35	45	115
3.0 to 3.2				5	15	25	35	45	125
3.2 to 3.4									

NOTES:

1. Decompress at a rate not faster than 0.4 bar/min
2. Decompress between stages at a rate of 0.4 bar/min
3. Not including time between stages
4. Where alternative decompression procedures are given (e.g. 3.2 bar), the longer decompression procedure should always be chosen

Working period over 1½ h to 2 h

SI UNITS

Maximum working pressure (bar)	Stage pressure (bar) (see Note 2)								Total time (min) (see Note 3)
	1.6	1.4	1.2	1.0	0.8	0.6	0.4	0.2	
0.0 to 0.2									–
0.2 to 0.4									–
0.4 to 0.6									–
0.6 to 0.8									–
0.8 to 1.0									–
1.0 to 1.2								5	5
1.2 to 1.4								10	10
1.4 to 1.6							5	20	25
1.6 to 1.8							10	30	40
1.8 to 2.0						5	15	35	55
2.0 to 2.2						5	25	40	70
2.2 to 2.4					5	10	30	40	85
2.4 to 2.6					5	20	35	40	100
2.6 to 2.8				5	10	25	35	40	115
2.8 to 3.0				5	15	30	35	45	130
3.0 to 3.2			5	10	20	30	35	45	145
3.2 to 3.4			5	15	25	30	35	45	155

NOTES:

1. Decompress at a rate not faster than 0.4 bar/min
2. Decompress between stages at a rate of 0.4 bar/min
3. Not including time between stages
4. Where alternative decompression procedures at given (e.g. 3.2 bar), the longer decompression procedure should always be chosen

Working period over 2 h to 2½ h

SI UNITS

Maximum working pressure (bar)	Stage pressure (bar) (see Note 2)								Total time (min) (see Note 3)
	1.6	1.4	1.2	1.0	0.8	0.6	0.4	0.2	
0.0 to 0.2									–
0.2 to 0.4									–
0.4 to 0.6									–
0.6 to 0.8									–
0.8 to 1.0									–
1.0 to 1.2								5	5
1.2 to 1.4								20	20
1.4 to 1.6							5	30	35
1.6 to 1.8							15	40	55
1.8 to 2.0						5	25	40	70
2.0 to 2.2					5	10	30	45	90
2.2 to 2.4					5	20	35	45	105
2.4 to 2.6				5	10	25	35	45	120
2.6 to 2.8				5	20	30	35	45	135
2.8 to 3.0			5	10	20	30	35	45	145
3.0 to 3.2		5	5	15	25	30	35	45	160
3.2 to 3.4		5	10	20	25	30	40	45	175

NOTES:

1. Decompress at a rate not faster than 0.4 bar/min
2. Decompress between stages at a rate of 0.4 bar/min
3. Not including time between stages
4. Where alternative decompression procedures are given (e.g. 3.2 bar), the longer decompression should always be chosen

Working period over 2½ h to 3 h

SI UNITS

Maximum working pressure (bar)	Stage pressure (bar) (see Note 2)								Total time (min) (see Note 3)
	1.6	1.4	1.2	1.0	0.8	0.6	0.4	0.2	
0.0 to 0.2									–
0.2 to 0.4									–
0.4 to 0.6									–
0.6 to 0.8									–
0.8 to 1.0									–
1.0 to 1.2								10	10
1.2 to 1.4							5	20	25
1.4 to 1.6							10	35	45
1.6 to 1.8						5	20	40	65
1.8 to 2.0						10	30	40	80
2.0 to 2.2					5	15	35	40	95
2.2 to 2.4					10	25	35	45	115
2.4 to 2.6				5	15	30	35	45	130
2.6 to 2.8			5	10	20	30	35	45	145
2.8 to 3.0			5	20	25	30	35	45	160
3.0 to 3.2		5	10	20	25	30	40	45	175
3.2 to 3.4	5	5	15	25	25	30	40	45	190

NOTES:

1. Decompress at a rate not faster than 0.4 bar/min
2. Decompress between stages at a rate of 0.4 bar/min
3. Not including time between stages
4. Where alternative decompression procedures are given (e.g. 3.2 bar), the longer decompression procedure should always be chosen

Working period over 3 h to 4 h

SI UNITS

Maximum working pressure (bar)	Stage pressure (bar) (see Note 2)								Total time (min) (see Note 3)
	1.6	1.4	1.2	1.0	0.8	0.6	0.4	0.2	
0.0 to 0.2									–
0.2 to 0.4									–
0.4 to 0.6									–
0.6 to 0.8									–
0.8 to 1.0									–
1.0 to 1.2								15	15
1.2 to 1.4							5	30	35
1.4 to 1.6							15	40	55
1.6 to 1.8						5	25	45	75
1.8 to 2.0					5	15	30	45	95
2.0 to 2.2					10	20	35	45	110
2.2 to 2.4				5	15	25	40	45	130
2.4 to 2.6			5	5	25	30	40	45	150
2.6 to 2.8			5	15	25	30	40	45	160
2.8 to 3.0		5	10	20	25	30	40	45	175
3.0 to 3.2	5	5	15	25	25	30	40	45	190
3.2 to 3.4	5	15	20	25	30	30	40	45	210

NOTES:

1. Decompress at a rate not faster than 0.4 bar/min
2. Decompress between stages at a rate of 0.4 bar/min
3. Not including time between stages
4. Where alternative decompression procedures are given (e.g. 3.2 bar), the longer decompression procedure should always be chosen

Working period over 4 h to 8 h

SI UNITS

Maximum working pressure (bar)	Stage pressure (bar) (see Note 2)									Total time (min) (see Note 3)
	1.8	1.6	1.4	1.2	1.0	0.8	0.6	0.4	0.2	
0.0 to 0.2										–
0.2 to 0.4										–
0.4 to 0.6										–
0.6 to 0.8										–
0.8 to 1.0										–
1.0 to 1.2									20	20
1.2 to 1.4								5	35	40
1.4 to 1.6							5	20	40	65
1.6 to 1.8							10	30	45	85
1.8 to 2.0						5	20	35	45	105
2.0 to 2.2					5	10	25	40	50	130
2.2 to 2.4					10	20	30	40	55	155
2.4 to 2.6				5	15	25	30	45	60	180
2.6 to 2.8			5	10	20	25	30	45	70	205
2.8 to 3.0			10	15	20	30	40	50	80	245
3.0 to 3.2		5	15	15	25	30	45	55	100	290
3.2 to 3.4	5	10	15	20	25	35	45	60	120	335

NOTES:

1. Decompress at a rate not faster than 0.4 bar/min
2. Decompress between stages at a rate of 0.4 bar/min
3. Not including time between stages
4. Where alternative decompression procedures are given (e.g. 3.2 bar), the longer decompression procedure should always be chosen

Historical Milestones

Alphonse Jaminet on Caisson Disease (1871)*

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IN WAR and in peace, the physician tends to stand aside from other men and contemplate the human implications of the events that take place around him. It is for this reason that the medical histories of great wars have a special character. Indeed, it has been said that the medical historian knows war far better than the political, economic, or drum-and-trumpet writers of history.

The same holds true of the achievements of peace. It is probable that few of those who see the magnificent Eads Bridge at St. Louis reflect on the cost in terms of human morbidity.

James Buchanan Eads (1820–1887) first gained a small reputation salvaging sunken steamboats. During the Civil War he built ironclads for the federal government. From 1867 to 1874 he built the big steel bridge that traversed the Mississippi at St. Louis.

His physician, Alphone Jaminet (1825?–1890), is little known; the reader will find such details as are available in an essay by C. H. Kratovchil.[1] Jaminet's courageous and thrilling essay on caisson disease, quaintly printed and heavily italicized, is entitled Physical Effects of Compressed Air, and of the Causes of Pathological Symptoms Produced on Man, by Increased Atmospheric Pressure Employed for the Sinking of Piers, in the Construction of the Illinois and St. Louis Bridge over the Mississippi River at St. Louis, Missouri. The pamphlet contains 135 pages and was published in St. Louis in 1871.

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EXCERPTS FROM JAMINET

In the prosecution of a vast engineering undertaking, stupendous, even in its conception, as is the construction of a bridge over the Mississippi river, at St. Louis, Mo., to connect the Illinois shore with the State of Missouri, great difficulties had to be overcome, and among them the one of which we will speak hereafter.

To Mr. J. B. Eads, of this city, was reserved the honor to be the foremost who conceived and dared to undertake such an immense work—work replete with difficulties to overcome, to project and mature all the plans, devices and appliances necessary for the execution, accomplishment and success of such an unprecedented undertaking . . . . It was found necessary by the projector, to build four piers to support the three spans of five hundred and twelve feet each; one pier on the western shore, and three piers in the Mississippi river; said piers to be built on caissons made of very thick iron, with *an air-chamber underneath*, being nine feet high inside, and of the same area of the piers, which for the west pier in the river is 2,600 feet, for the east pier 3,600 feet, and for the east abutment pier 4,800 feet. Each caisson divided into three compartments by longitudinal timber partitions to support the deck or ceiling of the caissons, and at the same time the masonry work, which was to be built *over the air-chambers* during the progress of the sinking of the caissons. . . . Of the sinking of the two first piers, and filling up of the air-chambers with concrete, the result surpassed all expectations of its projector. It was only when, arrived at the bed of the river, and under the water, which had to be *excluded entirely from the air-chambers or caissons* by the compressed air forced by the air-pumps, that the air had to increase in density to equalise by its pressure the outside pressure caused by the water in the river. . . .

The sinking of the caissons and the building of the piers over them progressed, but, notwithstanding all the precautions taken, the pressure *increasing every day in the air-chambers*, and having reached twenty-four pounds to the square inch, the caisson being then fifteen feet in the sand at the east pier, and fifty feet under the surface of the river where the men were working, then, some of those at the east pier, *after coming out of the air-chambers*, and when in *the air-lock*,

* This study was based on research assisted by the National Institutes of Health (HE-10948).

or *after leaving the air-lock*, and returning into the normal atmosphere, commenced to suffer and complain of very severe pains in the arms and legs, and sometimes of shooting pains in the back. *None were affected when in the air chambers or caisson, but always after returning into the air-lock, or going out of the air-lock and returning to the normal atmosphere.*

The sinking of the piers becoming deeper, the pressure also increased, and when it had reached thirty-four pounds to the square inch, the men became more seriously affected; some of them with violent epigastric pains, and others with paresis, and some with slight paraplegia, of which they generally recovered in from twenty-four to forty-eight hours. Sometimes the paraplegia was more severe, and some were taken with still more serious symptoms, as paraplegia, involving the bladder and rectum. Notwithstanding the existing paralysis, some of those affected complained of violent pains about the middle of the spine, and radiating in every direction of the lower half of the body. . . .

After the recurrence of such facts and accidents, physicians were called at the bridge to see the men at work, and when taken sick, which was generally the case *when coming out of the air-lock, or after returning into the normal atmosphere. None, and we repeat it from official authority, were taken sick in the air-chambers*, and the sufferers were generally taken, in from a few minutes to one hour after they returned into the normal atmosphere, and in two cases only *did it occur in the air-lock as soon as the door opened into the normal atmosphere, and not in the air-chambers or caisson.* . . .

Having been for over six years Mr. J. B. Eads' physician, and meeting him frequently, we had the opportunity of becoming initiated in the furtherance of his great project to build *an arched bridge across the Mississippi river at St. Louis;* and with the means and devices of engineering which he intended to employ for prosecuting the work, and sinking of the piers, we became so interested in the matter, that from the time the project became a reality by the commencement of the work, we thought that questions of great importance to scientific men would be met with, and that the use of compressed air to exclude entirely the water from the air-chambers or caissons, *sunk at the depth of one hundred and fifteen feet, and perhaps more,* below the surface of the river, (*work never performed before at such a depth, the deepest ever before reached being sixty-five feet;*) that the air used at such a depth would have to be condensed to a pressure as high, may be, as fifty-five pounds to the square inch, and would certainly require close observations in its use as it might produce on the men therein engaged pathological phenomena, with more or less serious effects on health and life.

Hence, from the first day of the sinking of the caisson for the east pier, in November, 1869, we commenced observations and experiments. . . .

We were only three minutes and a half in the air-lock, to return into the shaft or normal atmosphere. I was the last to leave the air-lock, not feeling very well; and *after resting four times in ascending the stairs, I arrived at the surface of the pier, almost exhausted*, my pulse at 110 per minute. I sat down a few minutes, but did not feel any better. I was taken again with the same epigastric pain as in my former visit. I was dizzy, so that no sooner was I on board the boat which crossed us to shore than I had to sit down on the stairs of the cabin to prevent myself from falling; my pulse grew weaker, and after reaching the shore, I had to use great exertions to reach my buggy, only half a square distant. I succeeded in getting in. During that time the epigastric pain increased, having nothing to take to relieve me, an accident in the caisson having deprived me of my flask containing the cordial which I intended to use in case of necessity, of suffering as before from the same pain.

In the course of a few minutes I drove home, which I reached at half-past two o'clock P.M., *three-quarters of an hour after leaving the air-chambers or caisson.*. The last effort brought me to my office where in a few minutes I became paralysed. . . .

Being in my office paralysed and unable to speak for a few minutes, but conscious of what was passing around, I made signs to my wife and persons with her at the time not to move me at all, but to lower my head and to raise my feet as high as possible. In the course of a few minutes, I was able to articulate a few words, but with great effort, and to say what should be done to me. *I was to be left perfectly quiet on my back or my right side, my head on a level with my body, my legs stretched, and my feet elevated two feet above my head.*

Then I took a tea-spoonful of old Jamaica rum every five minutes three times in succession, and kept a small piece of ice in my mouth to quench my thirst. A few minutes after I commenced taking two large table-spoonsful of beef tea every five minutes. I was suffering from profuse cold perspiration, every effort to speak caused great suffering and fainting, my pulse was 106 per minute, both legs and my left arm were paralysed, still I was suffering in both with excruciating pains which I can only compare to pains felt after a fracture of the left leg, which I experienced some years ago. During the pains in my limbs, which increased at intervals, my pulse was 115 per minute.

I knew well that in my situation, as I said to my wife, that after doing all I directed to be done, if I was no better by half-past five o'clock that same evening that nothing more could be done.

About half an hour after reaching home, three o'clock P.M., my pulse was 100 per minute, but a little stronger; the pains were not so frequent, but as severe; it was impossible for me to move my legs and my left arm. Any attempt to remove my clothing occasioned fainting. . . .

At six o'clock P.M., the profuse perspiration ceased; my pulse remained 96 per minute, but full, with symptoms of fever, which gradually increased until half-past seven o'clock P.M., at which time *I considered*

myself out of immediate danger. The pains in the left arm and both legs were less frequent. I had intervals of comparative ease. At half-past nine o'clock P.M., I commenced to move my legs a little, as also my left arm.

I had no disposition to sleep. At half-past eleven P.M., the pain had left my left arm, and I was able to move it; but the pains had located in both knees, and was so intense as to cause me to groan. My pulse was still 96 per minute and full; my skin hot but moist.

At half-past two o'clock A.M. I slept, but was awakened from time to time by the suffering when trying to move; after half-past three o'clock A.M. I commenced to move my legs. Shortly after four o'clock A.M. I slept, and did not awake until after seven o'clock A.M., when I was able to sit up in my bed, but felt very weak, my pulse being 92 per minute, and my skin warm and moist. . . .

By advice of somebody, the men were ordered to wear a voltaic belt around the body, or a voltaic sole to be worn in each shoe or boot, between the sole and the foot, or two voltaic bracelets to be worn around each wrist—the voltaic element being composed of a series of zinc and silver plates overlapping each other about one eighth of one inch, said voltaic apparatus *intended as a preventive and cure for the pains the men who were working in the caissons complained of.*

During our visits to the bridge, we saw many of the men wearing *these voltaic apparatus, and by careful enquiry, we did not hear that much benefit had been derived from their use; for we saw men taken with very severe pains, who had been and were still wearing soles, belts, and bracelets, and were taken sick after coming out; and among them some became paralysed while wearing the apparatus, and some even died wearing them. . . .*

Warm baths and even hot baths were resorted to to relieve the sufferers, but with no marked benefit, except to stop for a while their pains; but as soon as they were removed from the bath, the pains returned; and some *were paralysed while in the bath, or immediately after.*

Notwithstanding all the attempts to prevent, cure, or relieve the sufferers, the number of cases increased daily. Cases of paraplegia occurred frequently, so that on February 15th, some of the men were actually sent to the city hospital.

* * *

Comment on Jaminet

Jaminet tells us that he had been the physician of Mr. J. B. Eads, the engineer, for more than six years. Apparently it was for this reason and no other that he was enabled to assume a medical role in connection with the great engineering project. Available biographical data provide no evidence that Jaminet had special skill or special training beyond that of the ordinary practitioner.

But if Jaminet lacked special training, he had no lack of courage. He repeatedly entered the air-locks and the caissons. Here he not only made the ordinary clinical observations that might be expected, but he also measured the boiling point of water at various pressures. Interestingly, he found it necessary to defend the relevance of such determinations: ". . . if we found that increased atmospheric pressure exerts such influence on its physical transformation from a liquid form to a gaseous one, is it not rational to infer the influence of increased atmospheric pressure to a much greater degree on an organized body as the human system?"

Jaminet's observations on himself are very triking, indeed classical. As he was leaving the air-lock he began to feel unwell. In climbing up t he pier he had to pause four times. He now had tachycardia, epigastric pain and dizziness. Three quarters of an hour after leaving the air-chambers he reached his home and office, where he became paralyzed and temporarily aphasic. However, he retained consciousness and was able to make observations. After a few minutes he regained speech, at least in part, and was able to supervise his own treatment. In addition to severe pains in the limbs he had profuse sweats, syncope and tachycardia and hence was probably in shock. The paralysis began to recede about 8 hours after onset and disappeared about 10 hours later. For a week afterward he was feeble.

The treatment that Jaminet ordered for himself during the height of his illness was simple. He was kept quiet on his back or right side, and his legs were elevated. He took rum, pieces of ice and quantities of beef tea. In contrast, laborers afflicted with bends used voltaic belts or bracelets and various liniments. Jaminet observed that some men became paralyzed while wearing the voltaic apparatus.

Other parts of the account quoted here, not included in these excerpts, deal with the general physiology and pathology of high pressure and with implications for the art of civil engineering.

The Eads Bridge stands as a memorial to a great engineer. Jaminet's little book stands as a memorial to a brave physicia .

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Prevention of Dysbaric Osteonecrosis in Compressed-Air Workers

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Dysbaric osteonecrosis can be prevented by instituting sophisticated engineering principles designed to avoid use of compressed air altogether, or to minimize exposure to pressure. Also important in the prevention of this disease are comprehensive medical supervision, including thorough preemployment examinations; the use of the Washington State decompression tables, as incorporated in the California code;[4, 5] and oxygen decompression in a closed system.[3]

Compressed air was first employed in tunnelling in 1879 at the Hudson River in New York.[13] In 1909 Keays[16] reported 3692 cases of dysbarism resulting from 557,000 decompressions in the construction of the East River Tunnels in New York. There were 20 deaths and an unknown incidence of osteonecrosis, since caisson disease was not described as an entity until 1911 by Bornstein and Plate[10] and independently by Bassoe.[2]

In 1942, Bell *et al.*[8] reported a radiologic survey of 32 compressed air workers in New York, none of whom had symptoms or gross signs indicative of bone lesions. The men had worked intermittently for 3–33 years in compressed air. The shortest continuous employment was 10 months, the longest, 36 months. Fourteen men gave a history of decompression sickness (DCS) but 18 stated that they had never had an attack of bends. Yet only 8 of the 32 workers were free of radiologic evidence of bone lesions.

Based on radiologic evidence of bone lesions, 63 claims for disability were made by tunnel workers in New York in October 1963. These claims related to the Lincoln Tunnel (Third Tube) operations of 1955–1957. Although Kooperstein and Schuman[19] reported only 44 cases of DCS out of 138,034 decompressions it is not possible to state with complete assurance that no bone lesions complicated this specific operation. It seems probable that some of the 63 processed claims for disability due to osteonecrosis in the Lincoln Tunnel workers may have occurred as a result of injury received prior to 1955, since preemployment radiological bone surveys were not performed.

The frequency of DCS was 0.56% (122,000 man-decompressions) during construction of the Dartford Tunnel (England) from 1957–59 where the maximum working pressure was 28 psig.[12]

The Decompression Sickness Panel of the British Medical Research Council studied

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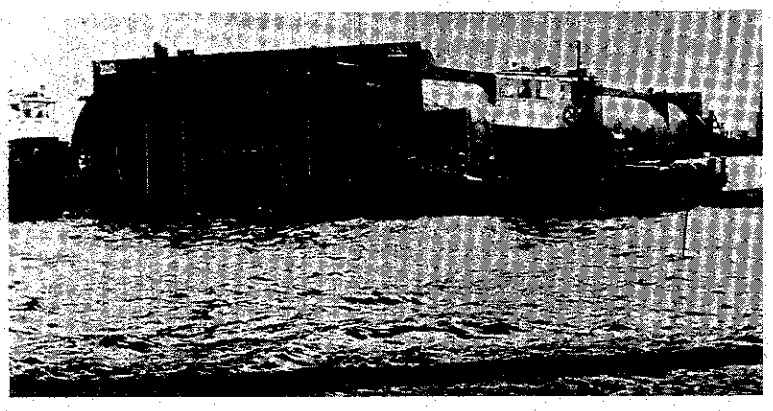

FIG. 1. Binocular tube sections were fabricated on shipways in San Francisco and launched with bulkheads in the ends. Tug boats maneuvered the tube section into position within the placing barge.

compressed-air workers on the Clyde Tunnels from 1958 to 1963 and found a bends rate of 0.29% and noted that 47 of 241 men (19%) had one or more lesions of osteonecrosis. The Panel in 1966 concluded: "At present strict adherence to the British Decompression Table does not prevent the onset of aseptic necrosis of bone, nor is there any clear indication of how it can be prevented."[21]

In the construction of the road tunnel under the River Tyne (England), 641 men worked in compressed air over a period of 31 months (1962–1965). The maximum pressure was 42 psig and the overall dysbarism rate for work at pressures of 18 psig and higher was 2%. Radiologic examinations were made of 171 men; avascular osteonecrosis was found in one or more bones of 44 men (26%).

Until 1963 virtually all U.S. caisson workers were decompressed according to modifications of the 1922 New York Code, which involved a "split shift" and short tables. But that sequence permitted considerable amounts of nitrogen to remain dissolved in the workers' tissues at the start of the second shift. Bone has a low tolerance for inert-gas supersaturation, hence the result was a high incidence of both DCS and osteonecrosis.

The Washington State Tables were introduced in 1963.[24] They are based on a continuous-shift concept with only one decompression per day, and are similar to current U.S. Navy decompression schedules.[27] They were first used in the Seattle tunnel construction of 1964–67, and in the construction of the Bay Area Rapid Transit System (BART) from 1967–69.[7]

BART was the first significant compressed air tunnelling operation in California and the largest civil engineering project ever performed on the West Coast of the United States. The 75-mile network includes duorail surface tracks, elevated lines, and subways linking San Francisco Bay and beneath the Oakland–San Francisco Bay Bridge. Of 64,576 feet of soft-ground tunnelling performed during this project, 22,600 feet were machine-shield-driven by men using compressed air under hazardous soil and obstacle conditions.

ENGINEERING PRACTICES IN THE BART PROJECT

The BART project was engineered to avoid completely the use of compressed air workers during construction of the Trans-Bay Tube. Prefabricated 320-ft-long sealed binocularlike tube sections, weighing 10,000 tons each, were floated into position (Fig. 1). After gravel ballast was added to overcome buoyancy, each tunnel section was lowered by 4 cable falls, suspended from a twin-hulled placing barge, into a previously dredged 3.6-mile-long trench extending across the bottom of San Francisco Bay (Fig. 2). Deep-sea divers, using conventional diving suits and hard helmets, worked at ap-

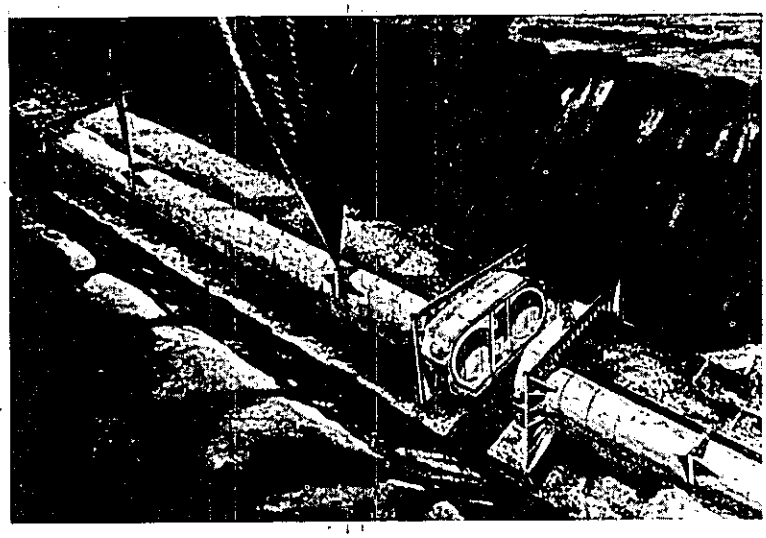

FIG. 2. Illustration of cable system used to slowly lower the tube sections from the barge, after gravel ballast is added to overcome bouyancy. The tube sections are lying within a trench and couplers are engaged to tighten the new section to the previous tube and hydrostatic pressure forces sections together even tighter. Later bulkheads are removed from inside the structure and permanent steel connections are welded in place without use of compressed air. (Reprinted with permission from Civil Engineering — ASCE, monthly publication of The American Society of Civil Engineers.)

proximately 100–120 ft depths, where they directed placement and mechanical linkage of the tube sections. No instance of decompression sickness was reported in these divers.

A large caisson (San Francisco Ventilation Structure) was likewise floated into position and installed at the western terminus of the Trans-Bay Tube, but it was also not necessary to use compressed air. Concrete was gradually added to the hollow walls of the prefabricated caisson, thereby progressively submerging it adjacent to the Ferry Terminal in approximately 90 feet of water. Divers were used, rather than compressed air workers, in directing linkage of the submersible Trans-Bay Tube to the caisson.

Of 64,576 feet of soft-ground tunnelling performed on the BART project, nearly half was hand-mined. Of the entire 12 miles of subway tunnelling, 9 miles were driven in free air and 3 miles (15,026 ft) under compressed air. However, only 135 ft were driven in compressed air in excess of 17 psig, over a period of 47 days.

Prior to the 1964 Seattle compressed air project hand-tunnelling methods were used. Tunnelling machines, a recent innovation, are now routinely used on engineering projects requiring compressed air. These machines have a large cutting wheel which scrapes ground off the face and drops it onto a conveyor belt, where it is carried to a muck train, through a muck lock, and is then vertically hoisted to the surface.

A typical tunnelling machine has a large cutting wheel (Fig. 3). Three radial doors on the face of the cutting wheel were opened by hydraulic rams. The cutting wheel was turned by planetary gears driven by hydraulic motors, which provided about 2 million ft-lbs of torque (Fig. 4). Shove jacks, with the capacity of 115 tons each, were used to hold the cutter against the face during excavation. The forward progress, or shove, sufficient to install a liner ring in the tail of the shield, was 2.5 ft. Although manpower requirements were about equal for both machine-tunnelling and hand-tunnelling methods, those contractors using tunnelling machines averaged advances of 40 ft per day as compared with 25 ft in the hand-mining projects.

About 5100 ft of twin subway tunnels north of the 16th Street Mission Station and an additional 3500 ft of twin tunnels south of the station were driven under compressed air. In both instances the original water level was above the crown of the tunnels.

To reduce the pressure of compressed air, dewatering procedures were introduced by drilling wells, 40–140 ft deep, into which submersible pumps were installed. Pumping began prior to tunnel excavation and the water table was lowered approximately 50 feet. It was often impossible to draw water down below the level of the tunnel invert, and air pressure was needed to counterbalance water pressure at the heading. These tunnels were constructed about 50 ft below the surface of the ground and air pressure varied from 9 psig to a maximum of 17 psig.

That portion of the system requiring compressed air at sufficient pressure to cause dysbaric osteonecrosis, *i.e.* over 17 psig, involved construction of the binocular tunnels from the Spear Street Ventilation Shaft, in the center of Market Street in San Francisco, to the center of the caisson (San Francisco Ventilation Structure). These tunnels are located in a completely filled area. In 1888 the shoreline of the San Francisco Bay was located where First Street is presently situated. It was unknown as to whether or not there would be sunken ships along the tunnel alignment. The access and ventilation shaft for this section of tunnel is located between Main and Spear Streets, 3½ blocks seaward from the shoreline in 1888. The tunnel is completely founded within New Bay Mud which is a very unstable material. It was also suspected that an old timber pier might be buried under the street surface since it had been built as an extension of Market Street from First Street to the present location of the Ferry Terminal. In addition, the tunnel passes within a few feet of an old rubble seawall and through a forest of piles supporting the foundations of the Ferry Terminal. The final obstacle confronting this portion of the project, and that which required progressively increasing levels of compressed air, was the unstable back fill and clay blanket surrounding the caisson. Unfortunately, the lower end of Market Street was also the site of major destruction to buildings, which were constructed on unstable ground, during the 1906 San Francisco earthquake.

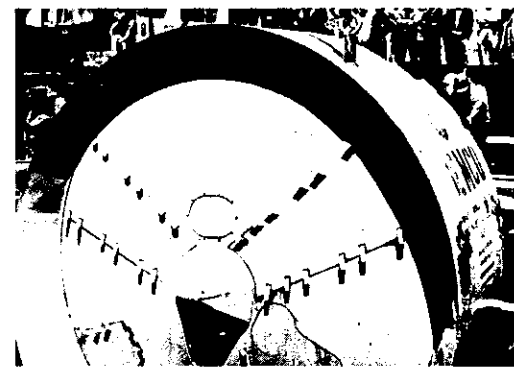

FIG. 3. Photograph of the cutting wheel of the soft-ground tunnelling machine, which scrapes dirt away from the face and drops it through doors onto a conveyor belt.

Timber-pile obstructions were handled by compressed air workers with extreme caution since each pile was a potential "blow hole" whereby compressed air pressure could suddenly be lost, with serious potential consequences for the workers. A total of 896 piles had to be disposed of, including one concrete and one steel pile. Locating the piling before each shield advance involved considerable delay. Of the 93 man-hours expended per foot of tunnel construction, 68 were required for excavation, ring erection, and grouting, and 5.2 for pile removal.

When horizontal tunnel excavation had progressed about 200 ft, a muck-lock (Fig. 5) and man-lock were installed adjacent to the working area. Compressed air supplied to the heading was cooled and filtered to

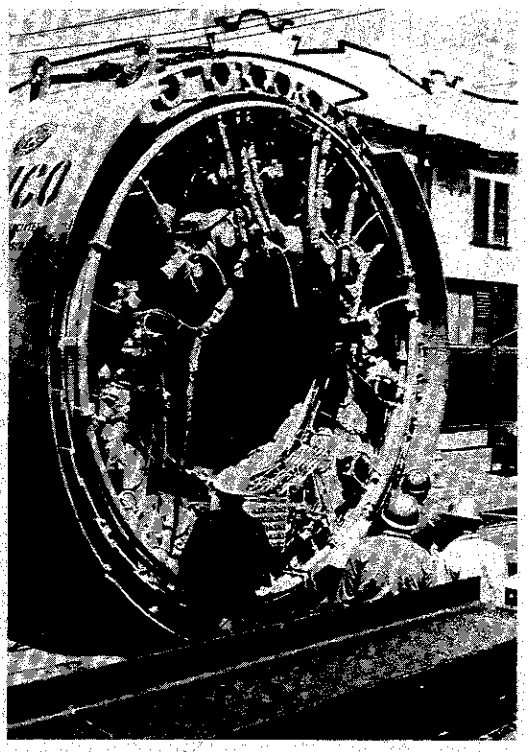

FIG. 4. Rear view of the cutting-wheel of the tunnelling machine, showing shove jacks on the outer ring and planetary gear housings on the inner ring.

prevent excessive fogging; burning and smoking inside the tunnels were prohibited.

The working day in compressed air was divided into 4 6-hr shifts for each tunnel. An average heading crew consisted of 23 men with a support crew of 15. Those activities performed during a typical soft-ground tunnel-driving cycle included shield advance, ring erection, grouting, and installation of hog rods. Pneumatic impact wrenches were ordinarily used to tighten the bolts between ring segments, pneumatic reciprocating pumps to inject grouting cement, and pneumatic chipping hammers to introduce lead strips into caulking grooves. Unfortunately, much of this work had to be performed overhead, resulting in significant stress to the workers' shoulder joints. Behind the shield was a platform where the soft-ground miners used a pneumatic hoist to lift the ring segments into position. The compressed air workers were responsible for erecting the steel tunnel liners and for bolting the rings together (Fig. 6). Through use of tunnelling machines and other hydraulic equipment, however, the heavy overhead lifting usually required of these workers was minimized.

It was during the final phase of tunnelling, when the pressure had to be increased, that the majority of severe cases of decompression sickness (Type II) developed. Maximum pressure in the left tunnel was 36 psig for 5 days and, in the right tunnel, 35 psig for 24 hours.

MEDICAL PRACTICES IN THE BART PROJECT

A Transit Compressed Air Medical Center in San Francisco serviced all BART operations conducted under compressed air. The Center performed all medical services required by the "Compressed Air Safety Orders" issued by the Division of Industrial Safety of the State of California.[11] Every prospective workman in the compressed air projects was required to be qualified by medical examination. After continuous hyperbaric work for one year, he was re-examined to reconfirm his qualification.

Each applicant completed a preemployment health-history form and underwent a comprehensive physical examination, including 11 roentgenograms. He was then subjected to a pressure test in the medical lock before being approved.[4] From June 1967 to November 1969, 1633 initial examinations and 256 annual examinations were performed. Of those examined, 81.1% were qualified for compressed air work and 18.9% were disqualified, principally because of excessive weight and pulmonary abnormalities.

Over 17,000 skeletal roentgenograms were made on more than 2000 workers. Thirty-

three osteonecrosis lesions of varying maturity were discovered in 12 pre-employment examinations; 8 additional applicants had suspicious lesions and were rejected. Of the 12 subjects, 11 had potentially disabling juxta-articular lesions affecting one or both humeral heads (Fig. 7); only 2 had involvement of the femoral heads.

It is significant that all these applicants, with one exception, were allegedly asymptomatic of joint involvement. It would therefore not have been possible to establish a diagnosis of chronic dysbaric osteonecrosis in these men without routine roentgenograms. Two of these rejected workers had previously been exposed to maximum pressures of 16 and 18 psig, respectively, without decompression sickness, but both had a history of alcoholism.[14] All other rejected examinees had previously worked in compressed air for at least one year, and had been exposed to pressures in excess of 30 psig. Only 3 of these applicants admitted having experienced an attack of dysbarism; 7 had previously been exposed to maximum pressures in excess of 45 psig. Eight other applicants (2.6%) were disqualified because of sickle-cell hemoglobinopathy.[15]

DECOMPRESSION PRACTICES IN THE BART PROJECT

The Medical Center had 3 compression chambers for testing workmen and for treating decompression sickness (DCS). Each had 2 compartments. The inner one, used for treatment, was equipped with oxygen; the small outer one allowed an attendant to enter without altering the inner compartment's pressure (Fig. 8). Because using compressed oxygen for treatment created a substantial fire hazard, each chamber was equipped with a sprinkler system capable of spraying the interior.

A pressure chamber was carried in an ambulance so that a severely injured workman might be extricated from the tunnels without undergoing decompression. Still under compression in the portable chamber, the workman was transported to the Center's medical chamber where his injuries could be treated during decompression.

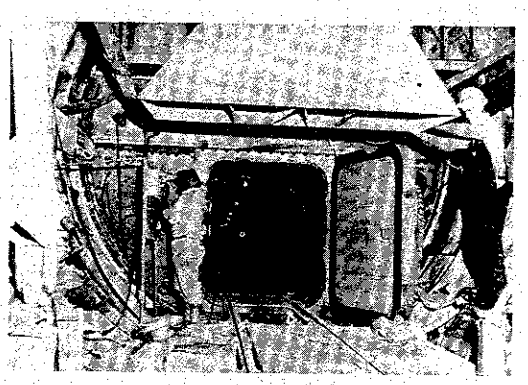

FIG. 5. Photograph of muck lock through which a muck train carries tunnelling supplies, dirt, and debris.

From November 1967 to May 1969, 80,360 man-decompressions were performed at pressures between 9 and 36 psig. There were 135 instances of DCS involving 85 men among approximately 400 compressed air workers — 128 of Type I (minor) and 7 of Type II (serious). The frequency of DCS was 0.16%. In constructing the tunnels from the ventilation shaft to the ventilation caisson 473,000 man-hours were worked, followed by 22,359 decompressions. There were 116 episodes of DCS (110 Type I and 6 Type II); 46 men suffered repeat attacks.

In 2 instances a relatively low pressure was associated with postdecompression symptoms following 6-hr work shifts — 13 psig in one case and 11.5 psig in the other. At relatively high pressures a rather high incidence of DCS was experienced, despite curtailed hours of work. As mentioned, work at higher pressures lasted only one week; hence the time was too short to evaluate the role of acclimatization. However, there appeared to be selective susceptibility in that of the

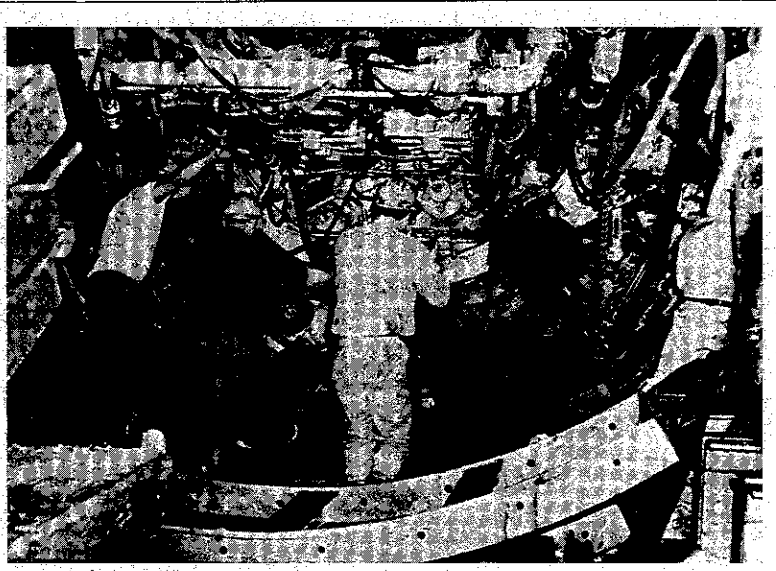

FIG. 6. Photograph of compressed air (shield) workers standing on a working platform on top of the conveyor, located immediately behind the heading and tunnelling machine. They are preparing to erect the next tunnel ring.

85 workers involved, 52 had one attack and 33 suffered repeated ones. One man was treated 6 times for DCS, and 10 of the 33 susceptible individuals had a second attack within 48 hours of the earlier one. No criteria were delineated from these examinations to separate the susceptible workers from those who were apparently resistant, or at least did not report for treatment (approximately 75%). The interval between decompression and the onset of symptoms was prolonged, 5 or 6 hours, which may possibly reflect the individual's reluctance to undergo recompression therapy or, possibly, to driving the 10- to 50-mile distance to the Medical Center.

Only 133 of the 832 miners originally employed for compressed air work remained on the job and were available for their first annual examination. Results of a radiological bone survey were negative in all these men. Subsequent roentgenographic evaluations have likewise been negative. But since tunnelers are often an itinerant, migratory labor group, follow-up clinical and roentgenographic examinations are virtually impossible.

Eight years have passed since the last compressed-air exposure of the BART project. No worker with clinical or roentgenographic evidence of dysbaric osteonecrosis has been reported, and no workmen's compensation claims have been filed in California as a result of the project.

DISCUSSION

Dysbaric osteonecrosis is the major health hazard to which compressed air workers are exposed. The magnitude of the problem is continuously studied by the Central Registry for DCS formed by the British Medical Research Council in 1964. Records are currently available for 2200 compressed air workers in Great Britain of whom 383 (17%) show 977 definite lesions of osteonecrosis, 348 of which are juxta-articular. Dysbaric osteonecrosis was found to be twice as common in the humeral heads (230) as the femoral heads (118).[26]

As a result of this increased incidence of osteonecrosis, the 1958 British Regulations were replaced by the British "Blackpool" tables, which have been used on all caisson projects in the United Kingdom since 1966.[9] These tables resulted in an incidence of DCS (bends rate) of 0.67% on the Dungeness B Power Station Contract. However, 5 of 59

(9%) workers studied on the project had developed definite lesions of osteonecrosis.[26]

Several civil and engineering projects have been completed in the Western Hemisphere since the BART project ended in 1969.

Pre-employment examinations were not performed in the early phase of the Milwaukee, Wisconsin Sewerage Tunnel project, and until 1970 the workers were decompressed according to a modification of the 1922 New York Code. Nellen and Kindwall[22] studied these workers and in 1972 reported 59 men with osteonecrosis, 33 of whom had shoulder lesions.

These 1922 New York Tables (1959 Brazilian modification) were also used in construction of the Costa e Silva Bridge that spans Guanabara Bay to connect the cities of Rio de Janeiro and Niterói, and which required 452 compressed air caisson foundations for the horizontal approaches to the shipping channel (Fig. 9).[23] From 1971 to 1972 there were 1226 cases of DCS in 45,000 man-decompressions (2.80%); the maximum working pressure was 51 psig. The incidence of osteonecrosis is unknown.

In order to reduce this intolerable risk of DCS (and to prevent osteonecrosis), the Washington State/California tables were used during construction of Phase I (17 kolometer long) of the Sao Paulo, Brazil Metro System. Pre-employment examinations and X-rays were performed on 2680 workers, and 73% were accepted. From 1973 to 1974, 2195 meters were excavated under compressed air using tunnelling machines. Engineering techniques permitted the working pressure to be maintained below 14 psig. Ten cases of DCS occurred in 59,284 man-decompressions (0.016%), which were attributed to the fact that the tables were not adjusted for the altitude of Sao Paulo. No osteonecrosis has been found through 1975.

More than 38,000 man-decompressions from pressures to 34 psig were required on the Seattle Tunnel Project through 1967, and

FIG. 7. Anteroposterior roentgenogram of the right shoulder of a 47-year-old compressed air worker with a diffusely sclerotic lesion within the juxta-articular region of the right humeral head and an irregular metaphyseal lesion. This applicant had been employed in compressed air for 6 years to a maximum pressure of 35 psig and had experienced DCS.

in 1977 Sealey[25] completed a 10-year follow-up study and found no evidence of osteonecrosis. The Washington State/California Tables became the U.S. federal standard in 1971. However, 3 compressed air workers have since developed osteonecrosis, all of whom were exposed to working pressures between 36–44 psig during the later phase of the Milwaukee Project (1971–1972).[17] Koch and Nishi (1972)[18] made a comparison of the various decompressure procedures currently used for compressed-air work.

Compressed air decompression tables were first modified for high altitude (2250 meters, 11 psig) during construction of tunnels in Mexico City[1] to reduce the frequency of DCS (and osteonecrosis). Similarly, the 22 km long Caracas, Venezuela Metro complex is now under construction at 900 meters altitude (13.17 psig), and the U.S. tables have

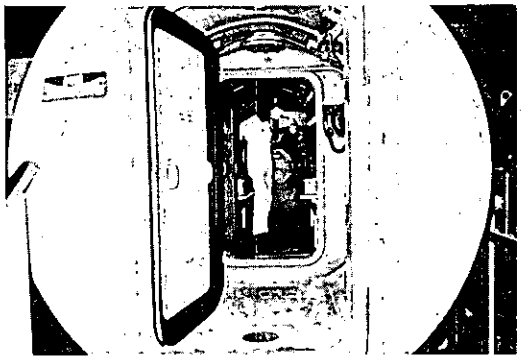

FIG. 8 Photograph showing the front and rear compartments of a medical lock at the Transit Medical Center. The technician is standing within the inner treatment lock.

been modified for altitude. It is anticipated that engineers will be able to keep the maximum pressure under 22 psig to compensate for the overburden and hydrostatic pressures encountered during excavation in the deep valley of Caracas. Also, new equipment has been developed to automatically monitor and control pressure and gas concentrations in the tunnels. Computerized tables for continuous isobaric decompression from tunnel saturation habitats have also been developed.

PERIODIC RESIDENCE IN COMPRESSED-AIR

Saturation diving has been perfected for the off shore oil industry and this technique can now be applied to compressed air workers to reduce the incidence of pressure-related disease. Recently, Behnke, Bell and Jones[6] developed a program using a transportable saturation habitat system at the tunnel complex from which compressed air workers make excursions. This saturation system should significantly reduce the operating expenses for the contractors and minimize or eliminate decompression sickness and osteonecrosis altogether. The risk of osteonecrosis has resulted in extremely high insurance premiums to compensate those workers with permanent partial disabilities resulting from juxta-articular lesions.

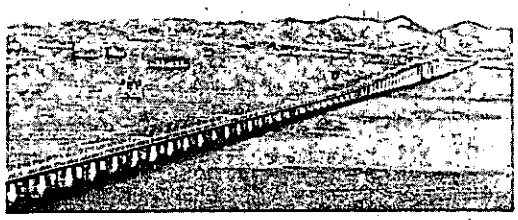

FIG. 9. Aerial photograph of the Silva Bridge from Rio de Janeiro to Niterói, showing the supports in the foreground which require compressed-air caisson foundations. (Courtesy of Camargo Correa S.A. Brazil.)

It has been shown repeatedly that habitation in dry chambers and undersea habitats is feasible for at least 2 weeks in air atmospheres at depths equivalent to 50 feet of sea water or FSW (22.2 psig). Larsen and Mazzone (1967)[20] conducted tests showing that a 4-hr no-decompression excursion can be made to a simulated depth of 100 FSW (44.5 psig) from a saturation pressure of 15.6 psig (35 FSW). The following tabulation indicates the scope of no-decompression excursions that are considered theoretically safe (Table 1). The feasibility of 2 work shifts daily per man remains to be tested with and without 0_2 inhalation following saturation exposures at 15 psig.

If the pressure in an undersea habitat can be safely raised to an upper level of 22.2 psig (50 FSW), it should be possible to conduct work at tunnel pressures up to 32 psig for indefinite periods followed by isobaric higher working pressures 0_2 could be inhaled for short periods at habitat pressure (Table 2).

SUMMARY

Osteonecrosis is a major hazard when compressed air is used in civil engineering projects (tunnel or caisson work), but could be prevented by applying specific engineering and medical principles. The risk of decom-

TABLE 1. Prototype Oxygen Decompression Table for Tunnel Workers*

Tunnel Pressure psig	*Work Shift hrs*	*Calculated dc Time (minutes)*	
		Total	*Per hr of Work***
20	6	64	10
30	6	105	18
36	6	117	20
40	4	120	30

* Preliminary but not finalized tests have been satisfactory. Oxygen is inhaled in *closed* individual systems with stringent precautions to prevent fire.
** For a continuous or intermittent work shift.

pression sickness is minimal if working pressure can be maintained below 11 psig. Pressure levels below 17 psig minimize the risk of dysbaric osteonecrosis. Engineering consideration should therefore be given to avoiding the use of compressed air altogether, or minimizing the pressure necessary in tunnel, caisson, or diving work. Engineering principles should also include: (A) use of prefabricated tunnels deployed with minimum direct supervision by divers breathing compressed air; (B) dewatering, probing, and elimination of obstacles in the heading; (C) use of machine-tunnelling apparatus and mechanically operated erector arms, which reduce the requirement for pneumatic hand-operated equipment and heavy overhead lifting; (D) maintaining a man-lock and emergency lock adjacent to the working area. Persons with antecedent dysbaric osteonecrosis or coexistent illnesses associated with avascular osteonecrosis should be screened by comprehensive pre-employment examinations (including special laboratory studies and roentgenograms) and disqualified for work in compressed air environments.

In both the U.S. and U.K. experience, it has not been possible to limit the hazard of decompression sickness. However, during the past 55 years steps have been taken in New York State to reduce the incidence of dysbarism and the complication of bone necrosis by shortening hours of work. Tables have been computed by the State of Washington that greatly extend decompression time following prolonged pressure exposure. But use of these tables does not appear to reduce the incidence of dysbarism. Nevertheless, only 3 cases of bone necrosis have been found using them. To circumvent future dysbarism-related injury in compressed air work, the following procedures are suggested: (A) 0_2 decompression under conditions favoring isobaric N_2 elimination from tissues; (B) residence in compressed air habitats with pressure adjusted to that of the tunnel. The

TABLE 2.

Habitat Pressure		*Work Shifts*					
		4 Hours		*6 Hours*		*8 Hours*	
psig	*ft*	*psig*	*ft*	*psig*	*ft*	*psig*	*ft*
0	0	13.4	30	11.6	26	10.7	24
4.5	10	20.9	47	17.8	40	16.5	37
8.9	20	28.1	63	24.1	54	22.3	50
13.4	30	35.6	80	30.7	69	28.1	63
17.8	40	43.2	97	37.0	83	34.3	77
22.2	50	49.4	113	43.2	97	40.0	90

feasibility of these procedures has been demonstrated in diving practice, but they remain to be implemented in compressed air tunnel operations.

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COMPRESSED-AIR ILLNESS

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This paper is based largely upon a report, made by the writer in 1909[1], of 3692 cases of compressed-air illness which resulted at the Pennsylvania East River Tunnels during the time that he was medical director. It will present a brief general description of the subject of compressed-air illness, special attention being paid to its cause and to its prevention.

Triger,[2] a French engineer, who designed the first practical caisson in 1839, mentioned the occurrence of pains in the extremities of workmen employed. In 1868, Le Roy de Méricourt[3] published the first medical report of illness among sponge-divers. Since Triger's report many contributions have been made to the subject of compressed-air illness. A full review of the literature of the subject may be found in *Caisson Sickness* by Leonard Hill, a book published this year.

ETIOLOGY—CAUSES

Various theories have been advanced to explain the symptoms occurring among compressed-air workers. The earliest theory to receive general recognition was that advocated by Pol and Wattelle[4] in 1854, the so-called mechanical-congestion theory. In 1878 Paul Bert[5] proposed the theory, supporting it by logical reasoning and by experiments, which is now universally accepted. It is

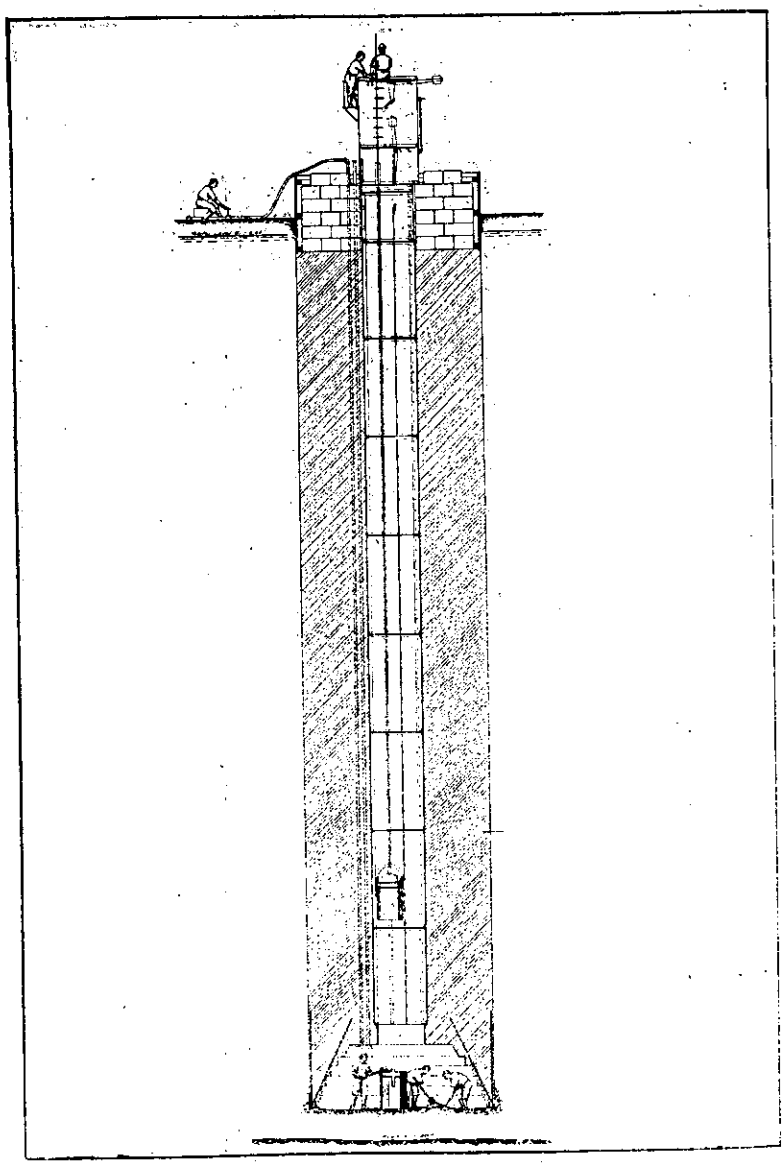
[1] Keays, "Compressed-Air Illness, With a Report of 3692 Cases," *Researches from the Department of Medicine, Publications of Cornell University Medical College*, Vol. II, pp. 1-55.

[2] Triger, "Compte rendus." *Acad. des Sciences*, 1841, tome XIII, p. 884

[3] De Méricourt, *Bull. de l'Académie de Méd.*, 1868, XXXIII. *Ann. d'Hygiene Publ. et de Méd. Légale*, 1869, second series, XXXI.

[4] Pol and Wattelle, "Memoire sur les Effets de la Compression de l'Air." *Annal. d'Hyg. Publique et de Méd. Légale*. Paris, 1854.

[5] Bert, *La Pression Barométrique*. Paris, 1878.



CROSS SECTION OF CAISSON IN FULL OPERATION

Workers ("Sand Hogs") At Bottom of Caisson Work Under Atmospheric Pressure Sufficient to Prevent Water From Flowing In As Sand is Shoveled Up

Too Rapid Decompression, As in Going Suddenly Out into the Normal Atmosphere, Causes Compressed-Air Illness

a surprising fact that Bert's explanation was practically disregarded for several years, while the mechanical-congestion theory continued to be accepted, especially by the early American writers.

Briefly stated, Bert's theory is as follows: The blood of a man or of an animal, when in compressed air, takes into solution an increased quantity of oxygen and nitrogen from the air, the quantity of the gases absorbed being in direct proportion to the increase of pressure. The gases taken up by the blood are gradually distributed to the fluids of the various tissues. With rapid decompression the nitrogen gas bubbles off in the blood. These bubbles act as emboli, block up the capillaries in one or another part of the body and, by cutting off the blood supply or by direct mechanical violence, cause the symptoms of compressed-air illness. Symptoms of illness may be prevented by making decompression slow enough to allow the absorbed nitrogen to escape from the lungs. Further experimentation by Von Schrötter,[6] Hill and his associates,[7] and others, have confirmed his theory. Post-mortem findings, moreover, in many fatal cases of compressed-air illness, both in men and in animals, give conclusive proof that this theory is correct.

From this theory, as well as from practical experience, the chief etiological factors have been deduced as follows: (1) In general, the higher the pressure, the greater the chances of illness; (2) the longer the time of pressure, the greater the chances of illness; and (3) the more rapid the decompression, the greater the chances of illness.

Let us now consider these three factors in brief detail.

1. *The degree of pressure.*—Practical experience has shown that cases of compressed-air illness seldom happen at pressures up to fifteen pounds per square inch above normal.[8] Fatal cases seldom result from pressures below thirty pounds. The lowest pressure from which death has been reported is twenty-one pounds, and there seems to be some doubt as to the authenticity of this report. Among

[6] Heller, Mager and von Schrötter, *Die Luftdruckerkrankungen*, Vienna, 1900.

[7] Hill and Macleod, "Caisson Disease and Diver's Palsy," *Journal of Hygiene*, 1903, p. 401; Hill and Greenwood, *Proceedings Royal Society*, B. Vol. 77, p. 442, 1906; Vol. 79, p. 21 and p. 284, 1907.

[8] The figures in regard to pressure given in this paper all refer to the number of pounds per square inch above normal atmospheric pressure, which is a little less than 15 pounds.

twenty fatal cases of compressed-air illness resulting at the Pennsylvania East River Tunnels, only two were caused by pressures below thirty pounds, one at twenty-eight pounds, the other at twenty-nine pounds. The following table, taken at random from the records of the Pennsylvania East River Tunnels, illustrates the influence of only slight additions of pressure upon the percentage of cases of illness, when pressures in the neighborhood of thirty pounds were being used.

TUNNEL A. MANHATTAN SITE.

Month	Number of Man-shifts	Length of Shifts	Average Pressure Above Normal	No. Cases of Comp.-Air Illness	Per Cent
Jan. '07	3751	8 hours	28.5 lbs.	7	.18+
Feb. '07	4141	6 hours (2-3 hr. periods)	31 lbs.	25	.60+
Mar. '07	4902	"	31.5 lbs.	33	.67+
Apr. '07	4018	"	32 lbs.	39	.97+

It may be stated that, with other conditions the same, the number of cases of illness will depend directly upon the degree of pressure.

2. *The time under pressure.*—When pressures of one atmosphere or more are being used, the time spent under pressure is an important etiological factor. It is obvious that if less time is spent in compressed air than is necessary for complete saturation of the body fluids, the chances of symptoms developing upon decompression will be less than if that time is equalled or exceeded. The exact time in which complete body saturation takes place has never been determined. No doubt it varies in different individuals. It is certainly hastened by work and exercise. Some parts of the body saturate quickly and others slowly. Fat especially saturates slowly, both on account of its poor blood supply and because it has the property of absorbing about six times as much nitrogen as the other body fluids. Haldane and Boycott[9] estimated that half saturation of the body occurs in about twenty-five minutes, and almost full saturation in about ninety minutes.

[9] Boycott, Damant and Haldane, "The Prevention of Compressed-Air Illness," *Journal of Hygiene*, Vol. VIII, No. 3, June, 1908.

In the Pennsylvania East River Tunnels, when pressures of 30 lbs. and more were being used, all new men, before being allowed to work, were given a preliminary test at the prevailing tunnel pressure which lasted 90 minutes, decompression being at the rate of two pounds per minute. In 2719 preliminary tests only three cases of compressed-air illness were encountered. Two of these were mild cases of pain, and the third was a case of paralysis of the lower extremities. After the preliminary test, those who took it satisfactorily were allowed to work 90 minutes when six-hour shifts were in progress. In 2000 men who worked for 90 minutes in pressures averaging 32 lbs., seven cases of compressed-air illness resulted, all being mild cases. The small number of cases in the former group would indicate that complete saturation had not taken place in 90 minutes. The influence of work in hastening absorption would account for the increased number of cases in the latter group.

The following table, made up from the records of the Pennsylvania East River Tunnels, throws some practical light upon the question of the time of nearly complete body saturation and of the effect of work, and also indicates the effect of fatigue, as shown by a comparison of the number of cases following the first and the second three-hour periods of six-hour daily shifts:

Average Pressure (estimated)	Time under Pressure	Number of Men	Cases of Comp.-Air Illness		Remarks
			No.	Per cent.	
31 lbs.	1½ hours	2719 Preliminary test, not working	3	0.18+	2 cases ordinary pain. 1 case paralysis legs.
32 lbs.	1½ hours	2000 (estimated) Working	7	0.35+	All ordinary cases (pain, vertigo, etc.)
29 lbs.	2 hours	6000 (estimated) Working	13	0.21+	1 case pain and prostration, not severe. Rest, ordinary cases.
33 lbs.	3 hours 1st half 6-hr. shift	43,680 (est.) Working B. & D. Tunnels, Manhattan	152	0.35+	4 fatal. 2 pain and prostration. 3 partial paralysis. Rest, ordinary cases.
33 lbs.	3 hours 2nd half 6-hr. shift	"	317	0.72+	2 fatal. 1 pain and prostration. 1 partial paralysis. Rest, ordinary cases.

The decreased percentage of cases of illness from two hours work, as compared with that from one and one-half hours work, is accounted for by the lower pressures in the former case. At the same pressure, other factors being equal, two hours work would probably be followed by more cases than one and one-half hours work. In comparing results from three-hour shifts with those from one and one-half and two-hour shifts, it should be noted that in the former case the percentages were based chiefly upon old workmen; but in the latter the percentages were based entirely upon new men.

3. *The time of decompression.*—All authorities agree that the rate of decompression is a most important factor in determining the number of cases of compressed-air illness, as well as in determining their severity. During decompression the absorbed gases are liberated from the body fluids and blood in the form of bubbles, and are excreted through the lungs. The rapidity with which these gases are set free, and the size of the gas bubbles, depend directly upon the rate at which the pressure is removed. Consequently rapid decompression increases the chances of illness and slow decompression diminishes them. It is not known how long it takes for complete desaturation; like saturation it probably differs in individuals. The practical problem is to find, if possible, a safe rate of decompression. From practical experience it has been learned that with pressures up to 15 or 20 lbs. rapid decompression seldom gives rise to any symptoms, and probably never, even after long exposures of six to eight hours, to those due to large quantities of free gas in the circulatory system. An explanation of this, which appears logical, is that at these pressures not enough gases can be absorbed to embarrass the circulation even when suddenly liberated. That rapid decompression from pressures of four or more atmospheres is more dangerous than slow decompression has been repeatedly demonstrated in animal experimentation.

Bert concluded, from experiments with animals, that all trouble could be avoided by allowing thirty minutes for decompression from pressures between two and three atmospheres and sixty minutes for decompression from pressures between three and four atmospheres. Von Schrötter considers an allowance of twenty minutes per atmosphere safe; and Hill and his associates found twenty minutes per atmosphere safe for a large number of animals exposed to satur-

ation. Haldane,[10] on the other hand, advocates the interrupted or stage method of decompression. Starting from the fact that rapid decompression from 19 lbs. to normal atmospheric pressure is comparatively safe, he argued that it would be correspondingly safe to decompress rapidly from four to two atmospheres, or from six to three atmospheres, and he found this true in a series of experiments with animals. He proposes the following rate of decompression for caisson and tunnel work:

Working Pressure in Pounds per Square Inch	Number of Minutes for each Pound of Decompression after the First Rapid Stage.		
	After first 3 hours' exposure	After second or third 3 hours' exposure following an interval for a meal.	After 6 hours or more of continuous exposure
18–20	2	3	5
21–24	3	5	7
25–29	5	7	8
30–34	6	7	9
35–39	7	8	9
40–45	7	8	9

His first rapid stage of decompression reduces the pressure in about three minutes to a point equal to one-half the actual pressure. To illustrate, if the working pressure is 40 lbs., the actual pressure equals 55 lbs. One-half of 55 or 27.5 equals the actual pressure, or 12.5 lbs. equals the gage pressure. Applying this table to decompression from 40 lbs., one would reduce the pressure in about three minutes to 12.5 lbs. and then allow 87.5 minutes for decompression after the first three hours' exposure.

Haldane presents strong theoretical reasons in proof of the advantages of the stage method of decompression. In his own experiments with goats, however, the beneficial results of stage decompression, as compared with the uniform decompression of equal time, are less apparent than the theory would lead one to expect. Hill and Greenwood[11] tested the effects of uniform and stage decompression on pigs without showing any decided advantage for the latter method. Hill says: "The conclusion to be drawn, then, from experiments on animals is that there is evidence in favor of stage decompression after

[10] Haldane, "The Hygiene of Work in Compressed Air," *Journal of the Society of Arts*, Vol. XVI, p. 214. Jan. 1908.
[11] Hill, *Caisson Sickness*, Longmans, N. Y., 1912.

short exposures, but no decisive evidence of its superiority after long exposures. The theory is a captivating one, but experiment has not brought that conclusive support which was to be expected." In this statement by short exposures is meant periods of one hundred and twenty minutes or less.

Bornstein compared the effects of stage and uniform methods at the Elbe Tunnel Works, Hamburg, (two atmospheres), with the following results:

Days	Workers	Cases of Illness
20 stage	526	15
16 uniform	528	17
18 stage	529	12
16 uniform	529	14
14 stage	536	12

The percentage on the basis of man-shifts for the stage method is 0.15; and for the uniform method 0.19. These results show only a slight advantage for stage decompression, but they are not conclusive.

It would seem, then, that in the case of men working long periods in compressed air in pressures above 20 lbs., the question of the time taken for decompression is of more importance than the question of the method of decompression. Hill claims that exercise and the breathing of oxygen, both of which aid in the elimination of nitrogen gas, during decompression will safely permit of the reduction by at least one-half of the times of decompression advocated by Haldane.

In the Pennsylvania East River Tunnels, during a period of five hundred and fifty-seven days, with about one thousand men a day working in compressed air at pressures varying from 15 lbs. to 36 lbs., and a decompression period at the rate of one minute for each two pounds of pressure, there were reported to the medical department 3692 cases of compressed-air illness with twenty deaths. About ten thousand different men in all worked during this time. On the basis of the number of men working, the percentage of illness was 36.92 and the percentage of fatal cases 0.2. On the basis of man-shifts, estimating one thousand men a day for five hundred and fifty-seven days, or 557,000 man-shifts, the percentage of illness was 0.66 and the percentage of death 0.0035. The substitution of the

rate of decompression now required by the New York State law for tunnel work, of three pounds every two minutes up to 36 lbs. and of one pound per minute for pressure above 36 lbs., would no doubt have reduced the number of cases of illness, as well as the number of serious and fatal cases, but it seems highly improbable that it would have prevented all illness and death.

In considering the etiology of compressed-air illness it must be remembered that, beside the questions of pressure, time of compression, and rate of decompression, there are many other factors to be reckoned with, which might be called predisposing causes. Briefly stated these are as follows:

Age.—Boys, on account of underdevelopment, and men past forty are generally acknowledged to be bad subjects for compressed-air work.

Build.—Fat individuals are bad risks in compressed-air work and should be avoided.

Organic disease.—Persons with organic disease should not be subjected to work in compressed air because, even if they are not more susceptible to compressed-air illness, they are certainly less able than those with normal organs to stand the effects of such illness.

Alcoholism.—Alcoholics are bad risks for the same reason that those with organic disease are bad risks.

Newness to work.—"Green" men are more likely to have symptoms of compressed-air illness than old workmen.

Fatigue.—This appears to play a decided part in the causation of compressed-air illness.

Ventilation.—C O_2 within reasonable limits probably has no effect. Poisonous gases, such as C O and H_2S, may play a part in etiology.

The personal element.—This is a factor which I believe plays a large part in the causation of compressed-air illness. I have used this term for want of something more definite. Just what conditions may exist to make certain individuals susceptible to compressed-air illness or to cause those who have apparently been immune suddenly to develop symptoms, sometimes serious, I cannot say. It has seemed to me probable that certain individuals may lack the ability to excrete the gases from the blood at the physiological rate during decompression and that such a condition may arise at any time in men who have been free from it. In my experience I have found that certain men, who from careful examination appeared especially fit subjects,

fell easy victims to the effects of compressed air. In the work on the Pennsylvania East River Tunnels several old workmen had fatal illnesses while working under apparently the same conditions under which they had worked safely for months.

Symptoms

The time is too short to allow of a detailed report in this paper of the symptoms of compressed-air illness. They are various in form and depend first upon the amount of gas set free in the blood, and second upon what organs are affected by the gas emboli. In many cases, as when soft tissues or unimportant organs are involved, gas emboli will give no symptoms. A small gas bubble causes pain when present in some unyielding tissue, such as nerve sheath or periosteum; it causes vertigo when in the semicircular canal; paralysis when in a motor area of the spinal cord; and sudden death when in a vital center of the medulla, or possibly in the coronary artery. Large accumulations of gas in the blood stream cause general pains and prostration, and in extreme cases collapse, coma, and sudden death.

In my study of 3692 cases I made the following classification, giving the number and percentage of cases falling under each group, as follows:

	No.	Per cent
A.—*Cases showing pain in various parts of the body, "bends"*	3278	88.78+
Cases with pain also having local manifestations	9	.26+
B.—*Cases showing pain and prostration*	47	1.26+
C.—*Cases showing symptoms referable to the central nervous system:*		
1. Brain (hemiplegia)	4	.11+
2. Spinal cord:		
(a) Sensory disturbance	36	
(b) Motor disturbances	34	
(c) Sensory and motor disturbance	10	
Total (Spinal cord)	80	2.16+
D.—*Cases showing vertigo, "staggers"*	197	5.33+
E.—*Cases showing dyspnoea and sense of constriction of the chest, "chokes"*	60	1.62

F.—*Cases showing partial or complete unconsciousness with collapse*	17	.46+
Grand total	3692	99.98+

Fatal Cases
- Group B..... 6
- Group C..... 5
- Group F..... 9

20 or .54+ per cent.

Pathology

The results of autopsy in fatal cases have fallen largely under two classes: first, those which died after long illnesses and showed lesions of the spinal cord, such as disseminated and transverse myelitis and hemorrhage, with consequent complications, such as pneumonia, cystitis, pyonephritis, bed sores, etc.; and second, those which died soon after decompression, many of which showed the presence in greater or less degree of free gas in the circulatory system. Von Schrötter, in an analysis of one hundred and thirty-seven fatal cases reported between the years 1854 and 1897, found twenty reported autopsies showing lesions of the spinal cord and their complications, and eighteen reported autopsies in rapidly fatal cases of which eleven showed the presence of free gas in the circulatory system. In the twenty fatal cases reported by me, five fell within the first group, and of these two came to autopsy and showed lesions of the cord and complications; fourteen fell within the second group and of these, in twelve autopsies reported, eight showed the presence of free gas in greater or less degree in the circulatory system. In cases of sudden death, when no discoverable lesions have been found, it seems fair to suppose that death has been due to the involvement of vital centers by emboli too small to be detected. In several of our fatal cases no sign of organic disease could be found.

Treatment

Recompression is the most efficient means of treatment. This was recommended by Pol and Wattelle in 1854; Bert demonstrated its value in animal experimentation about 1871; and Mr. E. W. Moir made the first practical use of the medical lock at the old Hudson

River Tunnel. He there proved its efficiency, thus making it a necessary equipment in caisson and tunnel work.

The medical air-lock, as used on the Pennsylvania East River Tunnels, consisted of an air-tight steel cylinder about six feet in diameter and twelve feet in length, closed at one end. At the other end was an entrance by means of an air-tight door which opened inwards. The cylinder was divided into two compartments by means of a transverse partition, which had a door opening toward the inner compartment. Compressed-air pipes and outlet valves supplied both chambers, so that the pressure could be raised or lowered from either chamber. This arrangement enabled the physician or attendant to enter or leave the chamber in which the patient was being treated without disturbing the pressure of that chamber. Valves were also placed outside the lock so that the pressure could be regulated from without. The inner chamber was fitted with two bunks, one on either side, upon which patients could lie, and with electric lights, telephone, clock, pressure gage, thermometer, and electric heater. A means of ventilating the inner chamber was also supplied. Heavy glass windows were placed on a line in both doors so that one could watch from outside the patient, pressure gage, and thermometer.

Recompression should be instituted as soon as possible after the appearance of symptoms, the pressure being raised quickly to the working pressure. Relief of symptoms, when afforded, usually occurs before this point is reached. Soon after reaching full tunnel pressure decompression should be begun at a rate not less than one pound per minute, and in severe cases much more slowly. At the Pennsylvania East River Tunnels we thought our results were best when decompression was made rather quickly down to 10 or 15 lbs., and then continued very slowly. During decompression the patient, if able to do so, should move about and exercise the affected part. In severe cases massage and passive movements should be administered by an attendant, and in unconscious cases artificial respiration should also be performed. If symptoms return after one recompression, a second recompression should be made. We sometimes had to recompress three or four times before permanent relief was obtained. In cases of simple pain, where there is a return of symptoms after recompression, relief, frequently permanent, may be obtained by the use of counter-irritation with liniments, the vibrator, or the Faradic current, or by hot applications. A hot bath for the

return of pain after recompression is beneficial, but would hardly be indicated in cases where there is prostration.

The results of treatment in 3692 cases in the Pennsylvania East River Tunnels were as follows:

In 3278 cases of pain in various parts of the body about 90 per cent got relief from one or more recompressions. Recompression failed to give any relief in only about .5 per cent of the cases of this class, and in some of these the failure was undoubtedly due to improper recompression or to failure of the patient to exercise while decompressing.

In forty-seven cases of pain and prostration, thirty-eight were relieved or cured by recompression, all ultimately recovering, but six had only temporary improvement and died. The other three refused the medical lock, and recovered after illnesses of about a week.

In eighty cases with symptoms referable to the central nervous system the results were as follows:—

Four cases of hemiplegia were all cleared up permanently by recompression; of thirty-six cases of sensory disturbance, thirty-four were relieved by recompression, two refused the medical lock and were improved by medical treatment; of thirty-four cases of motor disturbance, partial or complete paralysis of the legs, twenty-three were benefited by recompression and either cleared up at once or recovered later, in eleven recompression caused no improvement and of these five ultimately died, three had permanent spastic paraplegia, and three were lost sight of; of ten cases of sensory and motor disturbance, nine were permanently relieved, and one was improved, but the final result was not learned.

In one hundred and ninety-seven cases showing vertigo, with or without vomiting, pain, prostration and dyspnoea, one hundred and eight had complete relief from recompression, eighty-two had partial relief from recompression, and seven refused the medical lock.

In sixty cases of dyspnoea and sense of constriction of the chest, all cleared up with one recompression except two which required a second recompression.

In seventeen cases of partial or complete unconsciousness and collapse eight were cured or relieved by one or more recompressions, but nine had little or no relief and died. Oxygen given to several of these severe cases during decompression afforded no appreciable benefit.

Prevention of Compressed-Air Illness

How to prevent compressed-air illness is a most important question. Modern demands in engineering require the use of compressed air. Recompression, while an efficient means of treatment in mild cases, often fails to prevent disability and death in severe ones. If high pressures are to be used, all means should be employed to prevent illness. These should consist of thorough medical examinations of workmen and especially of new candidates. In cases where "green" men must work in high pressures, 25 lbs. or over, preliminary tests should be given and, if satisfactorily passed, a short working shift should first be tried. Careful supervision of the workmen should be exercised, and occasional reexaminations made, especially after any absence from work. The men should be instructed as to the dangers of rapid decompression, should be made to move about during and after decompression, and should be warned that neglect to seek medical advice at once upon the appearance of any symptoms may result disastrously. They should also be informed of the bad effects of excesses of all kinds, of improper hygiene, and of intercurrent illness.

The following table indicates briefly what can be done by medical examination and proper supervision to eliminate the predisposing causes mentioned under the subject of etiology:

Predisposing factors	*Can be prevented*
Age (improper)	Yes
Build (fat)	Yes
Organic disease	To a large extent
Alcoholism	To a large extent
Newness to work	Partly
Fatigue	No
Ventilation (bad)	To a large extent
Personal element	No, not with our present knowledge.

The chief means of preventing illness must be found in the arrangement of shifts and decompression periods to suit the pressures. In this connection we find the old conflict between labor and capital. The workman is willing to reduce the shift but rebels at what seems to him an unnecessary time for decompression. The contractor, on the other hand, desires to offset long shifts by long decompressions.

Laws have already been passed in different countries regulating

the length of shifts and decompression periods. Such a law has been passed, however, in but one state (New York) in this country. As time goes on further legislation will no doubt be needed and this could be made much more efficient if full information in regard to all cases of compressed-air illness could be reported to the state and reviewed by some competent person or board, who should recommend the necessary changes in the laws. What is now most needed is an exhaustive study of the practical application of theories which have been well worked out. In studying the causes of compressed-air illness, one should not forget that many factors play a part, and that, since the human organism is concerned, it is not a purely physical question. The results of comparatively few experiments with animals should not be looked upon as final. In the same way, the results, under certain conditions, with a comparatively few men should not be considered conclusive. While much may be done by proper regulations to diminish cases of illness and death in compressed-air work, I believe that, when pressures of two or more atmospheres are being used, it should be classed as a dangerous occupation on account of individual conditions, not now understood, which I have called the personal element.

Acute Decompression Illness

A REPORT OF FORTY-FOUR CASES

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DECOMPRESSION illness, more commonly spoken of as the "bends," has been a known clinical entity from the earliest days of the professional sponge fishermen of the Mediterranean and the pearl fishermen of Ceylon. Other terms for this condition are "divers' paralysis," "caissons disease," and "compressed air illness," while those who work in compressed air are familiar with it under such symptomatic terms as the "chokes," "staggers," "itch," and "fits."

Death or permanent paralysis was an all too common and accepted hazard for those who exposed themselves to inadequate decompressions. It was known then and it is known today that the symptoms of this condition appear only after decompression and never during compression.

In 1890, Bert placed a rabbit under high pressure using ordinary air, and, on autopsy, after rapid decompression, found nitrogen bubbles throughout the entire body. Using pure oxygen, however, no bubbles at all were noted after similar rapid decompression. He was the first to postulate the theory of too rapid decompression releasing nitrogen bubbles as emboli in the blood stream instead of allowing gradual loss of nitrogen through the lungs.

Decompression illness, properly speaking, is less a true disease and more a physical phenomenon. It can be explained most simply by the illustration of the capped bottle of charged soda water in which all of the gas is in solution owing to the increased pressure inside the bottle. When this pressure is released suddenly, e.g., when the cap is removed, the gas emerges from the solution as bubbles and will continue to do so until the partial pressures of the gas in the liquid and in the surrounding atmosphere are equalized. Exactly the same phenomenon occurs, too, in the human blood stream. Compressed air is dissolved in the blood, but, when released too rapidly, nitrogen bubbles appear and act as emboli which emigrate to all points of the body.

The symptomatology follows directly the area of circulatory blockage by the nitrogen bubbles as well as the total amount of free gas liberated. For example, small amounts of gas in a bursa or beneath a tight fascia may cause severe pain in a joint — a relatively minor albeit painful condition. A similar blockage in a cerebral area can cause diverse sensory or motor disturbances, including paralyses or even death.

In general, the behavior of compressed air follows the standard principles set down in these few physical laws:

1. Charles' Law — At constant pressure, change of volume of a gas is proportional to the change of temperature.

2. Boyle's Law — At constant temperature, volume of a given mass of gas varies inversely as the pressure.

3. Henry's Law — With a constant temperature, the quantity of gas which goes into solution is proportional to the partial pressures of the gases concerned.

4. Dalton's Law of Partial Pressures — In a mixture of several gases or vapors that do not react on each other chemically, the pressure exerted is approximately the same as if each constituent exerted the full pressure it would exert if each alone filled the entire volume.

THE CASES described in this paper occurred during the compressed air phase of the driving of the Third Tube of the Lincoln Tunnel by The Port of New York Authority during the period January 15, 1955, to June 23, 1956. This was a shield-driven tunnel extending eastward from Weehawken, New Jersey, to New York City.

The shield had a diameter of 32 feet and was driven forward by massive hydraulic jacks, each push measuring 32 inches. This process was repeated 2131 times, the total distance involved being 5486 feet. This was accomplished by gangs of sandhogs working around the clock, 24 hours a day, six and sometimes seven days a week, and under pressures that went as high as 34 pounds per square inch gauge (P.S.I.G.)* The men worked in close quarters at hard manual labor either behind or in front of the shield, with irregular and often poor footing, in damp, water-

Material gathered in collaboration with our colleagues at the Lincoln Tunnel Third Tube Project, MICHAEL WULWICK, M.D., FRANCIS X. REYNOLDS, M.D., STEPHEN SUGAAR, M.D., SAMUEL J. MEDNOW, M.D.

*Absolute pressure = gauge pressure + atmospheric pressure (e.g., +14.7 lbs.).

dripping areas and under conditions that are considered properly to be hazardous. Also exposed regularly to the compressed air were the corps of engineers, carpenters, electricians, safety engineers, and others who functioned on this construction job.

Past experience in compressed air construction was such that insurance costs rose to a prohibitive figure. In this case, The Port Authority was self-insured and the medical management of this project became the exclusive responsibility of The Port Authority Medical Department.

Almost two years of preparation preceded the actual onset of operations. The prime objective was to minimize, and if possible eliminate, every medical hazard normally associated with previous compressed air work. Owing to the high risks and resultant high costs of compressed air illness, with its concomitantly high insurance rates, it became necessary to entertain an entirely new concept. The employer, therefore, became his own insurer and was then able to devote himself fully and unselfishly to the improvement of the health and safety of the workers.

To handle the medical aspects of this job, an extremely well-equipped and well-manned medical building was set up by and under the complete supervision of The Port of New York Authority. This was unique in the history of compressed air tunnels. It consisted of a spacious separate building, 3000 sq. ft. in size, located at the entrance to the work shaft. To man this extensive physical setup, there were four doctors on duty six hours a day around the clock, a nurse on duty 24 hours a day, a laboratory technician, x-ray technician, and a secretary. Accurate and detailed daily medical records were kept and statistics compiled periodically as the job progressed. Medical coverage was maintained for compressed air illness even on nonworking days. In addition, a medical lock for the treatment of compressed air illness was maintained in the building and all medical personnel were trained in its use. This consisted of a large metal tubular chamber divided into two sections, each of which could be controlled separately for use as a decompression chamber and for treatment of compressed air illness. Each was fully equipped with the latest and most modern methods of therapy, including gauges inside and outside, tanks of oxygen and of helium and oxygen, explosion-proof electrical heaters, and explosion-proof bully eyes for vision.

Prior to being permitted to work in compressed air, every man had to pass a stringent medical examination, with emphasis on the special aspects of compressed air work, careful attention being given to the ear, nose, throat, heart, lungs, joints, and urine.

Having passed this physical, the applicant was then tested in the medical air lock by the physician. He was subjected to pressure equal to that being used in the tunnel at the time (15 - 35 P.S.I.G.) to see if he could adjust satisfactorily. The ear drums were carefully inspected, the patient having been instructed previously in the Valsalva maneuver for clearing his ears when they blocked. Then and only then was the applicant allowed to go into compressed air. Furthermore, every man who had never been in compressed air previously was given another checkup at the expiration of his first work shift to observe any untoward effects.

The entire working population of the Lincoln Tunnel (Third Tube) exposed to compressed air was given a thorough examination every two months to determine continued suitability for compressed air work. Every man who was out of work for three days for any reason was rechecked by the Medical Department before being allowed back to work; and a re-examination was necessary for any and all workers who had not been in compressed air for 10 days or more regardless of the cause.

COMPRESSED air was first turned on January 17, 1955. All told, 138,034 decompressions were performed. This involved a constantly changing worker population that equaled approximately 300 men at any one time. A total of 44 cases of acute decompression illness were encountered and treated at our medical installation. This represents a percentage of .0318%, or 3.18 cases per 10,000 decompressions (Table I).

TABLE I.

Decompressions	Bends	Percent
138,034	44	.0318

The first case occurred on December 23, 1955, some 11 months and some 76,000 decompressions after the compressed air was begun. The gauge pressure did not exceed 15 P.S.I.G. for this period, which confirms the clinical experience of other investigators — that cases of decompression illness are uncommon below a gauge pressure of 15 P.S.I.G.

It was a matter of considerable interest to us to analyze the factors involved in the occurrence of these 44 cases of compressed air illness. There were a total of 832 individual preplacement examinations. Of these 704, or 84.61%, were accepted and 110, or 13.22%, rejected; while another 18, or 2.17%, for miscellaneous reasons did not finish the examination. We feel that this is a high percentage of workers accepted, particularly considering the stringency of the examination. However, our purpose was to provide a worker population suitable for this particular type of occupation, and our doctors were trained and experienced in recognizing which disabilities were and which disabilities were not reconcilable with compressed air work (Table II).

TABLE II.
ANALYSIS OF WORKER POPULATION

Total Number of Men Examined	832
Total Number of Men Accepted	704, or 84.61%
Total Number of Men Rejected	110, or 13.22%
Did Not Finish Examination	18, or 2.17%

TABLE III.

Presenting Site of Symptoms	Number of Cases	Percent of Cases
Upper Extremity	12	27.27
Lower Extremity	25	56.82
Both Extremities	5*	11.37
Abdomen	1	2.27
Nausea	1	2.27
Total	44	100%

*One case also had generalized itch.

The majority of the 44 cases presented symptoms relating to one or more extremities (Table III). The upper extremities were indicted in 12 cases, or 27.27%; while the lower extremities were involved in 25 cases, or 56.82%. Five patients, or 11.37%, had pain in both lower and upper extremities as a presenting symptom. One of these five cases also had a generalized itch. Only one patient, or 2.27%, evinced clinical abdominal distress, and one other patient, or 2.27%, had nausea as his primary symptom. It was encouraging for us to note as the job progressed that the majority of cases were limited to the extremities since these presented fewer problems in therapy. It was our opinion that the careful selection of workers and the comprehensive medical control of the working conditions in routine decompression schedules used on the job were strong contributory factors in both the low incidence and lack of severity of the compressed air cases.

An attempt was made to analyze the gauge pressures at which the cases occurred. As noted in Table I, there was a total of 138,034 separate decompressions, with an incidence of .0318. This figure is far and away the best ever reported, and considerably less than had been feared or anticipated.

The men worked two three-hour shifts per day with a rest period of three hours when the pressure was maintained up to 22 P.S.I.G. At this pressure range, five cases, or 11.37%, occurred (Tables IV, V, and VI). Four of these took place at 20 P.S.I.G., and one at 18 P.S.I.G. No cases occurred below 18 P.S.I.G., which is in accord with the best previous opinions on the subject, namely, that the occurrence of "bends" is rare under 15 P.S.I.G.

Between 22 and 30 P.S.I.G., the men worked two shifts per day of two hours duration each, with a rest period of three and a half to four hours. At this level, there were 35 cases, or 79.54%, of compressed air illness, every one of which occurred between 28 P.S.I.G. and 30 P.S.I.G. No brief is made for the concentration of "bends" in the narrow range, except to note that the pressure was at the upper limits of its 22-30 P.S.I.G. range.

When the pressure was raised above 30 P.S.I.G., the men were placed on a two-shifts-a-day schedule, one and a half hours per work shift, with a rest period of five hours. Four cases occurred, or 9.09%, all of them mild and therefore easily treated.

Another evaluation of considerable interest was the question of lapse of time between leaving the decompression chamber after a work shift and the onset of the presenting symptom (Table VII). It was found that three cases, or 6.81%, had pain immediately on leaving the work lock, or decompression chamber. Two of the cases involved both knees and one case involved the right knee. Eight other cases, or 18.18%, had an onset of symptoms within 30 minutes after leaving the work lock. Five cases, or 11.37%, occurred within 60 minutes; while four cases, or 9.09%, had pain within a 90-minute period. Before two hours had elapsed, six other cases, or 13.64%, had presenting symptoms; whereas seven cases, or 15.91%, took place within three hours after leaving the work lock. Within four hours, there were five cases, or 11.37%; and four cases, or 9.01%, occurred within four to eight hours after leaving the decompression chamber. There was one delayed case, or 2.27%, whose presenting symptom appeared between 12 and 24 hours after leaving the compressed air chamber. There was one patient who was extremely uncooperative and no adequate history was available.

It can be seen then from Table VII that 25% of all the cases had symptoms which appeared before 30 minutes had elapsed after leaving the decompression chamber; while more than half, or 59.09%, of the cases had symptoms which

TABLE IV.

P.S.I.G.	Number of Cases of Decompression Illness	Percent of Cases
0 - 16	0	00.00
16 - 22	5	11.35
22 - 30	35	79.54
30 - 35	4	9.10
Total	44	100%

TABLE V.

P.S.I.G.	Number of Shifts Worked Per Day	Duration of Work Shift	Rest Time Between Work Shifts
0 - 16	2	3 hours	3 hours
16 - 22	2	3 hours	3 hours
22 - 30	2	2 hours	3½ - 4 hours
30 - 35	2	1½ hours	5 hours

TABLE VI.

P.S.I.G.	Number of Cases of Decompression Illness	Percent of Cases
0 - 16	0	00.00
16 - 19½	1	2.27
20 - 27½	4	9.09
28 - 30	35	79.54
30 - 35	4	9.09
Total	44	100%

TABLE VII.
DURATION OF TIME BETWEEN LEAVING WORK LOCK AND ONSET OF SYMPTOMS

Time	Number	Percent
Immediate	3	6.81
30 min.	8	18.18
60 min.	5	11.37
90 min.	4	9.09
120 min.	6	13.64
180 min.	7	15.91
240 min.	5	11.37
4-8 hrs.	4	9.09
8-12 hrs.	0	—
12-24 hrs.	1	2.27
Miscellaneous*	1	2.27
Total	44	100%

*Uncooperative.

evinced themselves before two hours had elapsed. All but six of the cases, to include the uncooperative patient in this figure, had presenting symptoms before four hours time. Each of the five remaining in the last category came in with mild symptomatology limited to the extremities. All were easily treated — only three requiring recompression. The other two cases subsided rapidly with conservative therapy. From our experience, therefore, almost 90% of the cases which occurred had symptoms which presented themselves within four hours after leaving the decompression chamber, and none of the cases occurring after that time required more than the simplest therapy.

A constant check was maintained on the routine decompression schedules which were in operation at the work site. These schedules were made up with the cooperation of the United States Navy and covered all pressures to which the workers were subjected. Separate schedules were figured out for each level of pressure and for each work shift, taking cognizance of the difference in nitrogen absorption between the first and second work shifts. A three-stage decompression was used routinely, and, for example, after the first work shift at 20 P.S.I.G., the total decompression time was 9½ minutes; whereas, after the second shift at the same pressure, the total decompression time was 14½ minutes. Similarly at 34 P.S.I.G., the total decompression time after the first work shift was 25 minutes; whereas, after the second work shift at the same pressure, total decompression time was 42 minutes. These tables will show that they follow Halden's 2-1 Rule, namely, that you can always halve the pressure without causing symptoms. This method of decompression was used 138,034 times, and only 44 instances of symptomatology were reported to us.

The treatment schedules were also drawn up with the valuable assistance of the United States Navy (Table VIII). This treatment schedule is detailed and specific in its analysis of indications and therapy. However, as in any other problem in

TABLE VIII.
TABLE OF RECOMPRESSION TREATMENTS FOR DECOMPRESSION SICKNESS

	"BENDS" — PAIN ONLY				SERIOUS SYMPTOMS	
Compress 10 min. Decompress 1 min. between stops	Pain relieved at Pressures Less than 30 lbs. Use Column 1A if O_2 is not available.		Pain relieved at Pressures Greater than 30 lbs. Use Column 2A if O_2 is not available. If pain does not improve within 30 min. at 75 lbs., the case is probably not bends. Decompress according Column 2 or 2A.		Serious symptoms include any one of the following: 1. Unconsciousness 2. Convulsions 3. Weakness or inability to use arms or legs 4. Any visual disturbances 5. Dizziness 6. Loss of speech or hearing 7. Severe shortness of breath or "chokes"	
					Symptoms Relieved within 30 minutes at 75 lbs. Use Column 3	Symptoms Not Relieved within 30 minutes at 75 lbs. Use Column 4
STOPS	TIME IN MINUTES UNLESS OTHERWISE INDICATED.					
P.S.I.G.	1	1A	2	2A	3	4
75			30 (Air)	30 (Air)	30 (Air)	30 to 120 (Air)
65			12 (Air)	12 (Air)	12 (Air)	30 (Air)
55			12 (Air)	12 (Air)	12 (Air)	30 (Air)
45	30 (Air)	30 (Air)	12 (Air)	12 (Air)	12 (Air)	30 (Air)
35	12 (Air)	12 (Air)	12 (Air)	12 (Air)	12 (Air)	30 (Air)
25	30 (O_2)	30 (Air)	30 (O_2)	30 (Air)	30 (O_2 or Air)	6 Hrs. (Air)
22	30 (O_2)	30 (Air)	30 (O_2)	30 (Air)	30 (O_2 or Air)	6 Hrs. (Air)
18	30 (O_2)	30 (Air)	30 (O_2)	30 (Air)	30 (O_2 or Air)	6 Hrs. (Air)
14	5 (O_2)	60 (Air)	60 (O_2)	2 Hrs. (Air)	12 Hrs. (Air)	First 11 Hrs. AIR Then 1 Hr. O_2 or AIR
8	5 (O_2)	60 (Air)	5 (O_2)	2 Hrs. (Air)	8 Hrs. (Air)	First 1 Hr. AIR Then 1 Hr. O_2 or AIR
4	5 (O_2)	2 Hrs. (Air)	5 (O_2)	4 Hrs. (Air)	2 Hrs. (Air)	First 1 Hr. AIR Then 1 Hr. O_2 or AIR
0	5 (O_2)	1 Min. (Air)	5 (O_2)	1 Min. (Air)	1 Min. (Air)	1 Min. (O_2)

TABLE IX.
NUMBER OF CASES TREATED WITH RECOMPRESSION

Conservative Treatment	12,	or 27.28%
Recompression Therapy	31,	or 70.45%
Miscellaneous*	1,	or 2.27%
Total	44	100.00%

*Uncooperative, refused therapy.

medical therapeutics, much is left to the clinical judgment of the medical observer. In this type of case, as in any other, there is no substitute for experience and a sound clinical judgment is essential and invaluable in properly evaluating the symptomatology and diagnoses involved, and then following logically with the proper therapy. As can be noted, recompression to 45 P.S.I.G. is required in Schedule 1 and 1A; whereas, Schedules 2, 2A, 3 and 4 require recompression to 75 P.S.I.G. before beginning stage decompression therapy.

The use of oxygen or a mixture of oxygen and helium substantially reduces the treatment time, and this was done wherever it was practicable. In our experience it was never found necessary to use other than Schedules 1 or 1A, which speaks well for the relative mildness of the cases encountered and for the excellence of the decompressions schedules used on the job.

Twelve of the cases, or 27.28%, were treated conservatively without the use of any recompression (Table IX). The remainder of the cases were treated with recompression according to the 45-lb schedule or variations thereof. Only two patients required hospitalization for further observation. There were no deaths attributable to compressed air in this entire operation, nor is there evidence thus far of any permanent disability resulting from exposure to compressed air at the time.

Comment

FROM AN over-all point of view it appears that much benefit was derived from the establishment of a thoroughly equipped and well staffed medical station directly on the job site, under the complete supervision and control of the Medical Department of The Port of New York Authority. This made possible a close follow-up of the working conditions and adherence to the decompression schedules at the work lock and was of immense value in the uplift of worker morale. A careful screening of the applicants for compressed air work was a major factor in the unprecedentedly low incidence of "bends," .0318%. In other words, for every 10,000 decompressions there were 3.18 cases of "bends." The largest number of cases in any range of pressure was found to be in the upper levels, e.g., at 20 P.S.I.G. and 28 P.S.I.G. The 44 cases, in general, were considered to be relatively mild in nature and this is attributable to the excellence of the working decompression schedules. The treatment was handled under the established United States Navy schedules and only two patients required hospitalization. There were no deaths or crippling disabilities.

Summary

FORTY-FOUR cases of acute compressed air illness occurred in 128,034 decompressions presented, which were incurred in the process of building a shield-driven compressed air tunnel under the Hudson River. Emphasis is placed on the careful selection and preplacement examination of the workers as well as the unique character of the medical control by the Medical Department of The Port of New York Authority. The work schedules and treatment schedules are presented. The aim of the Medical Department's program was the prevention of compressed air illness. The most modern methods of therapy were made available on the job site.

It is our belief that, given a careful preemployment screening and physical examination, adequate proper schedules of work time and decompression time, and full cooperation between labor, management and the Medical Department, acute decompression illness can virtually be eliminated as a hazard in future compressed air work

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EXPERIMENTAL STUDIES ON OXYGEN DECOMPRESSION

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INTRODUCTION

It has been recognized that the use of oxygen during decompression is in principle quite effective in preventing decompression sickness (Bert, 1878; Ham and Hill, '05). The practical use of this procedure called O_2 decompression in caisson work, however, is seldom found (Jones, Crossin, Griffith, Sayers, Schrenk and Levy, '40; Nashimoto, '65), as hyperbaric oxygen (OHP) may have toxic effects and also increase fire hazards. The purpose of our study was to make a new O_2 decompression table for compressed air work and to investigate its effectiveness upon the prevention of decompression sickness and the saving of decompression time.

METHODS

During the experiment the working pressure of the pneumatic caisson was from 1.75 kg/cm^2 to 2.8 kg/cm^2 and the working time was from 2 to 10.5 hr. Decompression was performed according to the schedule made for this experiment. Table 1 and 2 show the examples of our table and Figure 1 represents the relationship between working time and total decompression time at various working pressures. The half saturation times of tissues projected in calculating the table were 5, 10, 20, 40, 75 and 120 min, and the value of 1.36 was taken as allowable ratio of tissue nitrogen to ambient pressure.

To prevent O_2 poisoning, O_2 began to be breathed at the first stop of decompression. Futhermore for the avoidance of fire hazards, a specially designed O_2 breathing apparatus was used. The air lock of the pneumatic caisson was equipped with sets of the O_2 breathing apparatus, which

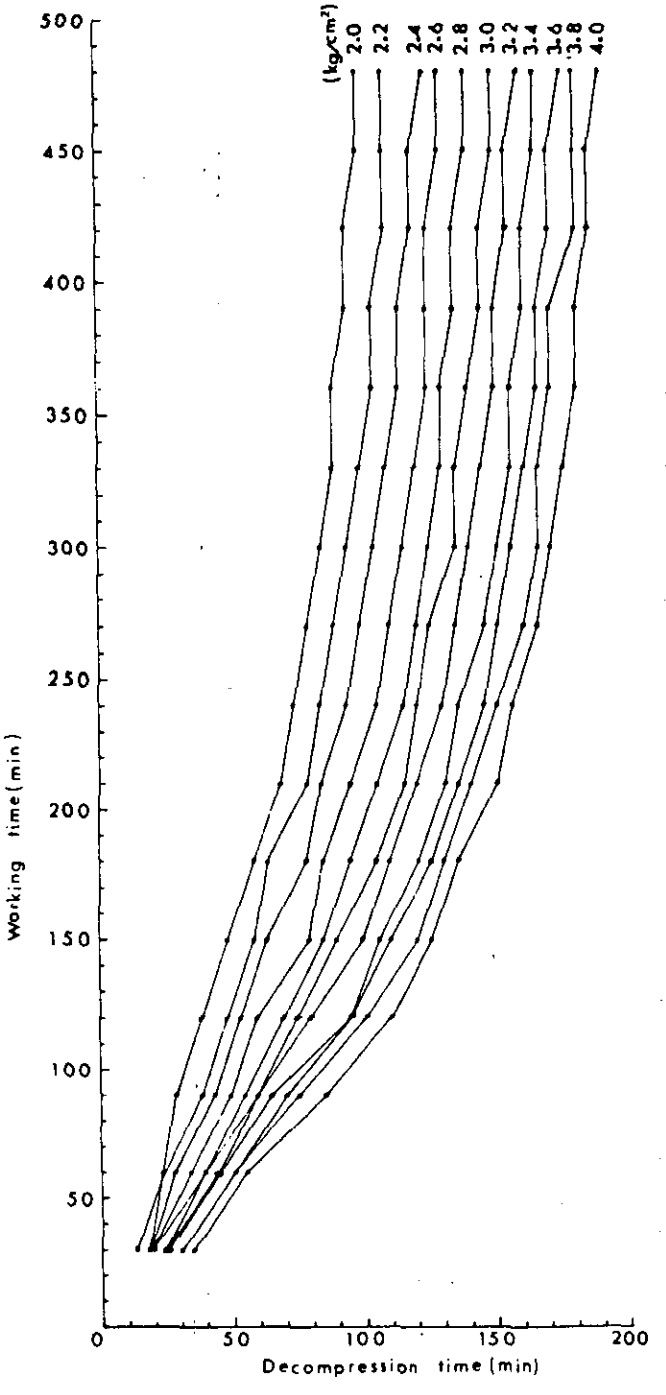
TABLE 1: Oxygen decompression table at 2.0 kg/cm²

Working time (min)	Decompression stops min at kg/cm² 0.9	0.6	0.3	Total decompression time (min)
30	5		5	13
60	5	5	10	23
90	5	5	15	28
120	5	10	20	38
150	5	10	30	48
180	5	15	35	58
210	5	20	40	68
240	5	25	40	73
270	5	25	45	78
300	10	25	45	83
330	10	25	50	88
360	10	30	45	88
390	10	35	45	93
420	10	35	45	93
450	10	35	50	98
480	10	40	45	98

TABLE 2: Oxygen decompression table at 4.0 kg/cm²

Working time (min)	Decompression stops min at kg/cm² 2.1	1.8	1.5	1.2	0.9	0.6	0.3	Total decompression time (min)
30	5			5		5	15	35
60	5			10	5	10	20	55
90	5			10	10	20	35	85
120	5		10	10	15	20	45	110
150	5	5	5	10	20	30	45	125
180	5	5	10	10	20	35	45	135
210	5	5	10	15	25	40	45	150
240	5	5	15	15	30	35	50	155
270	5	5	15	20	30	40	45	165
300	5	10	15	25	30	35	45	170
330	5	10	15	25	30	40	45	175
360	5	10	20	25	30	40	45	180
390	5	15	20	25	30	35	45	180
420	5	15	20	25	30	40	45	185
450	5	15	25	25	30	35	45	185
480	5	15	25	25	30	35	50	190

FIG 1: Working time plotted in relation to decompression time for compressed air works at various pressures, based upon values from our table.



released the expired O_2 automatically out of the air lock.

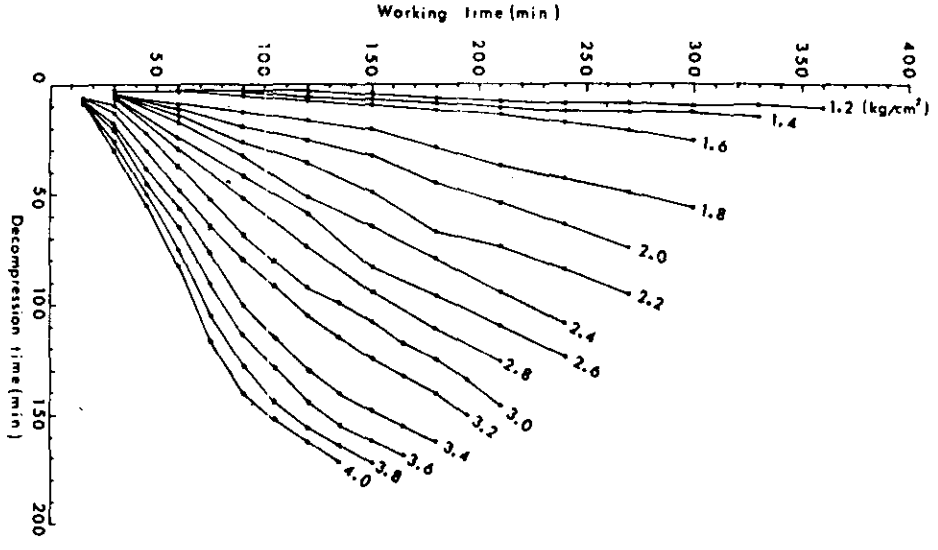
In a total of 1,417 trials, 1,361 subjects breathed O_2. In an air decompression group 5 cases of bends occurred and its incidence was 8.93% while in the O_2 decompression group 18 cases of bends occurred and its incidence was 1.32% (Table 3).

TABLE 3: Incidence of decompression sickness in oxygen decompression group and air decompression group

Type of decompression	Number of decompressions	Case of decompression sickness	Incidence (%)
Air	56	5	8.93
O_2	1361	18	1.32

$$X_0^2 = 1501 > X^2(1;\ 0.005)$$

FIG 2: Working time plotted in relation to decompression time for compressed air works at various pressures, based upon values from ordnance on prevention of compressed air hazards in Japan.



As indicated in Table 3, the incidence of decompression sickness following the O_2 decompression was markedly low compared with that of air decompression. Furthermore it can be seen from Figure 1 and 2 that in the case of prolonged work at higher pressures the decompression time of our table is, far, shorter than the decompression time on the tables currently used in our country. These results apparently indicate that our table is effective in preventing decompression sickness and saving decompression time in compressed air work carried out at comparatively high pressures.

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Safe Exit from the Hyperbaric Environment

Medical Experience with Pressurized Tunnel Operations

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Increasing numbers of civil engineering projects requiring work in compressed air, the exploration and development of the continental shelf, and the operation of hospital hyperbaric chambers, has increased the need for study of the problems of safe exit from a hyperbaric environment.

By the beginning of the Twentieth century the problems of decompression sickness in diving, caisson and tunnel work had become so troublesome that in 1906, the British Admiralty appointed a committee which included J. S. Haldane, who in 1907,[1] described the now classic principles of stage decompression. Haldane's original thesis considered the human body as consisting of a number of diffusors or tissue compartments with characteristic half times to which were applied basic gas transport equations.

Aseptic bone necrosis was first described in 1911–1912, by Bornstein and Plate,[2] as a pathologic entity among some 500 "bends" cases associated with the construction of the Elbe Tunnel at Hamburg.

The Ciba Foundation, in October 1965, sponsored a small international working party, organized by the British Medical Research Council Panel on Decompression Sickness, for consideration of decompression problems in civil engineering. Much of the material in this paper was presented at the working party and published in its proceedings,[3] and brought up-to-date at meetings of the BMRC panel in October 1967, and November 1968.

In the United States each state has its own safety regulations for construction work. Prior to 1963, most U. S. regulations for tunnel, shaft and caisson construction requiring compressed air followed the New York state "split shift" standards. Under these standards, which required an interval during the shift in free air, as working pressure exceeded 35 psig, effective work periods at the heading became impractical.

Development of Recent Washington State Standards

In February 1963, anticipating major tunneling in the Seattle area, the current Washington State Standards for compressed air work were adopted.[4] This adoption was preceded by an intensive two-year study by an *ad hoc* committee which included representation from labor, general contractors, and the engineering profession. We had advice from many experts in decompression problems, including: Capt. Albert R. Behnke, M.D., U.S.N. (Ret.); Capt. Gerald J. Duffner, M.D., U.S.N.;[5] Dr. William Fredrick, Detroit, (Wayne County Health Dept.); and Edward S. Robinson, M.D. and L.A. Patterson,

M.D., medical consultants to the Highbury Tunnel Project in Vancouver, B. C., Canada.

California and Michigan have adopted similar standards. A U.S.A. Standards Institute subcommittee is now working on model compressed air safety standards similar to Washington State's. These standards allow continuous work shifts in compressed air and are based on a hypothetical three-tissue compartment concept of 30, 60, and 120 minute half-saturation times. If routine decompression requires more than 75 minutes, the contractor must provide a comfortable "low pressure" decompression chamber with sanitary facilities. Pre-placement and periodic physical examinations of all compressed air workmen must include x-rays of shoulders, hips, knees and chest, and a lock test to determine a man's ability to equalize pressure.

When the working chamber pressure exceeds 13 psig, (pounds per square inch gauge) a medical lock facility must be continuously staffed by a certified medical lock attendant, for a minimum of five hours following the last man's exit from the working chamber. A physician and attendant must be on call 24 hours, seven days a week.

The design of Seattle's Metropolitan sewer system includes a major 17,000 foot (12-foot bore) trunk line from the north city limits, the Lake City district, thence 250 to 350 feet beneath the University district to a trunk line along the Lake Washington Ship Canal. The raw sewage is conducted to the West Point treatment plant and the treated effluent is discharged at a depth of 240 feet, three-fourths mile off-shore into Puget Sound.

Decompression Sickness: More than 38,000 decompressions from pressures of 13 to 34 psig were required during the 32 months of construction of the 17,000 foot Lake City tunnel. During this time there were 210 occasions to treat 85 men for relief of decompression sickness symptoms (Table I).

About one-third of the treatments followed a modified U.S. Navy air recompression procedure. Two-thirds of the treatments utilized the "minimal-recompression oxygen-breathing" approach develped by Workman[6] and Goodman at the U.S. Navy Experimental Diving Unit.

Two men were treated twelve times. About one-third of the men accounted for three-fourths of the treatments. Thirty-eight men, each decompressed more than 100 times from pressures above 17 psig, denied having experienced decompression sickness symptoms. None of the men lost time directly due to decompression symptoms.

Aseptic bone necrosis is a chronic condition which may follow even a single compressed air exposure. It does not become evident until months or even years following the hyperbaric exposure. Pathologically it consists of one or more areas of dead bone. When aseptic necrosis occurs in the head, neck, or shaft of a long bone it probably does not cause symptoms; however, when it occurs near the articular cortex (juxta-articular) of the hip or shoulder joint, it is frequently followed by structural joint failure, collapse of the articular cortex and permanent partial disability. The British Medical Research Council Decompression Sickness Panel has established guidelines for the interpretation of bone x-rays. These lesions are classified as: (A) Juxta-articular (clinically or potentially disabling; (B) Head, neck or shaft (rarely disabling). Impressions are recorded as definite, doubtful, or negative. The BMRC Central Registry has recently prepared an Atlas of radiographs demonstrating the appearance of these classes of bone lesions and relating their occurrence to the nature of compressed air exposure.[7]

Most of the Seattle men had no history of previous compressed air exposure, but pre-placement x-rays show that approximately one-third had benign changes in the trabecular patterns, many of which could be confused with inert gas induced changes.

It has now been longer than four years since more than 100 men were first exposed to air pressures above 14-34 psig, for four hours or more. All were decompressed according to the Washington State Standards. To date there has been no definite reported case of aseptic bone necrosis. More than 25 of these men have had follow-up x-rays of the ex-

TABLE I

BENDS TREATMENT — LAKE CITY TUNNEL — SEATTLE, WASHINGTON
OCTOBER 1964 — MAY 1967

Working pressure		No.	Bends	
psig	Kg/cm²	man shifts	Treatments	(%)
13–17	1.0–1.2	10,000	12	0.12
18–20	1.25–1.4	11,000	33	0.30
21–25	1.5–1.7	13,000	90	0.70
26–29	1.8–2.0	1,600	24	1.5
30–34	2.1–2.4	3,000	51	1.7
13–34	1.0–2.4	38,600	210	0.54

tremities for three and one-half years following their initial hyperbaric exposure.

A serious deficiency of present Standards is that none have provisions for continuing x-ray follow-up. Fortunately we have been able to follow 25 of the men from the Lake City tunnel project who went to other tunnel projects in Seattle and San Francisco.

A 1967 review with a member of the BMRC panel of 26 sets of x-rays from men, each of whom had been decompressed more than 500 times at the Lake City tunnel, revealed two who had doubtful changes in the trabecular patterns of the shaft; none had definite changes; none had juxta-articular changes.

In the past, most studies of aseptic bone necrosis among compressed air workers revealed an incidence of definite benign lesions of 40 to 50% and disabling lesions of the femoral and humeral heads of 12 to 25%.

At the BMRC panel meeting in October 1967, a report was made on workmen at the Dungeness nuclear power station on the south coast of England. Total decompressions and work pressures there were comparable to those in Seattle. Using BMRC trial decompression tables (approximately midway between current [1958] British regulations and Washington State regulations) there was a reduction from current British experience of 75% in central nervous system symptoms; 33% in recompression for extremity pain; 65% in juxta-articular bone lesions; and 33% in head, neck and shaft lesions.

Conclusions

The application of the Washington State Standards for compressed air work, "generally at pressures between 13 and 34 psig appears to allow safe continuous work in compressed air at least up to 34 psig. Approximately four years following their initial exposure to pressures above 14 psig, no men have filed claims for decompression disability, and no men have shown definite evidence of decompression bone injury (three have doubtful changes); none have had evident decompression injuries to the central nervous system.

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CAISSON DISEASE

A STUDY BASED ON THREE HUNDRED CASES OBSERVED AT THE QUEENS-MIDTOWN TUNNEL PROJECT, 1938

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Caisson disease is an industrial hazard encountered in the building of bridges, tunnels and skyscrapers where compressed air is employed. In the past this malady has caused permanent disability and death in many instances. Certain principles of prophylaxis and new concepts of treatment are here presented aiming to reduce this industrial hazard.

THE CAUSATION OF CAISSON DISEASE

Caisson disease is caused by nitrogen gas, a physical agent. Emboli are produced by the formation of nitrogen gas bubbles in the tissues and blood stream which interfere with normal life processes.

A homogeneous mixture of gases in the atmosphere covers the earth to a height of approximately 4½ miles. The atmospheric pressure is the weight of these gases on the earth's surface and is expressed in pounds per square inch. Although atmospheric pressure varies slightly, it is approximately 15 pounds per square inch.

The interchange of gases in the lungs and blood of a person who is in a compressed air atmosphere obeys the law of physics governing the solution of a gas in a liquid.[1] The quantity of nitrogen and oxygen dissolved by the blood varies directly as the pressure. The increased amount of oxygen absorbed is readily metabolized because it is an active gas chemically. This is not true of nitrogen, which is inert and is not utilized by the body.[2]

The increased amount of nitrogen dissolved in the blood is absorbed by the various tissues of the body according to their ability to hold nitrogen in solution. Fat and fatty tissues will dissolve much more nitrogen because nitrogen is five times more soluble in fat than in other tissues and body fluids.[3] The amount of tissue saturation with nitrogen depends on the amount of air pressure and the length of time the body is exposed to this pressure.

When a person who has worked in compressed air is exposed immediately to normal atmospheric pressure, a phenomenon occurs similar to the sudden opening of a bottle of charged water. For example, bubbles of carbon dioxide will evolve from the charged water and will continue until equilibrium of partial pressures of carbon dioxide in the atmosphere and in the liquid is obtained. A similar phenomenon occurs in the blood and the body tissues under sudden release of pressure. The dissolved nitrogen gas evolves in the form of bubbles, producing blocking of the circulation and tearing of tissues with resultant symptoms of caisson disease. Bert's experiments add further evidence for the support of the nitrogen gas emboli theory as the cause of this disease.[4]

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PATHOLOGY

Accumulation of evidence from postmortem examinations further supported the gas emboli theory as the cause of caisson disease.[5] Fatal cases grouped themselves into a rapidly fatal group and a delayed fatal group. In the rapidly fatal group, death is caused by nitrogen emboli to the vital centers of the brain, the coronary vessels and the pulmonary arteries.

In the delayed death groups, death is caused by secondary complications following neurologic manifestations of the disease. After long standing paralysis of the lower extremities, bedsores, sepsis, anemia, pneumonia and exhaustion usually develop. The significant pathologic changes in the delayed death group are found in the spinal cord. The lumbar and thoracic regions of the cord show areas of necrosis and softening with degeneration and destruction of ascending and descending fibers.

SIGNS AND SYMPTOMS

Onset of Symptoms.—The onset of symptoms of the disease is relatively rapid. Of the 300 cases observed 60 per cent occurred during the first hour, 35 per cent during the second hour and 3 per cent during the third hour. Six cases occurred after twelve hours, amounting to 2 per cent of the total.

Presenting Symptoms.—Pain (the "bends"): The presenting symptom of the disease was pain. The cases observed formed groups clinically as follows: pain generalized, pain localized and pain with prostration and collapse. The pain of compressed air disease may vary in intensity, depending on the site of bubble formation and the amount of gas evolved in the tissues. The pain may thus be mild and transient or severe and excruciating. The occurrence of pain in various parts of the body according to incidence is as follows: legs 50 cases, unilateral or bilateral, occurring generally about the knees and ankles; arms 60 cases, unilateral and bilateral, involving several joints. It may radiate or follow the course of a peripheral nerve. Abdominal bends may be of such severity that shock, collapse and prostration occur, forming the next clinical group. Here pain in the abdomen is outstanding. It is often accompanied by signs of circulatory collapse because of the great amount of gas in the abdominal vessels mechanically impeding the circulation. The appearance of mottling and blotching with subcutaneous hemorrhages is further evidence denoting large amounts of free gas in the circulation. These are prodromal signs of coma and collapse, which should be carefully watched for. To the compressed air worker these symptoms are known as the "bends." The reason for this vernacular expression is obvious. The pain is of such severity as to make the afflicted one bend over to obtain relief. The pain is caused by the presence of bubbles of nitrogen gas in the tissues and the plugging of small arteries by nitrogen gas emboli. The lodging of nitrogen gas emboli in the gastrointestinal and mesenteric vessels is undoubtedly the cause of abdominal bends. Likewise, when bubbles of gas form in unyielding structures and tissues of the body such as ligaments, fascia, connective tissue, periosteum, synovial membranes, muscle spindles, joint capsules, skin and sweat glands, pain is the result. The greater the amount of gas, the greater will be the stretching of the unyielding tissues with the resultant increase in pain. Most compressed air workers suffer on decompression

5. Bert, Paul: La pression barométrique; recherches de physiologie expérimentale, Paris, G. Masson, 1878.

with mild fleeting pains in the various parts of the body which should be differentiated from true caisson disease.

Vertigo (the "staggers"): Next in the order of incidence are the cases in which symptoms resembling Ménière's syndrome are outstanding. The symptoms are dizziness or vertigo, staggering or loss of equilibrium, nausea or vomiting, abnormal ocular movements (nystagmus) and tinnitus, or ringing in the ears. Of the 30 cases observed at the Queens-Midtown Tunnel in 1938, there was vertigo in 6, vomiting and vertigo in 6, vertigo, vomiting, staggering and nystagmus in 10 and vertigo, nausea and tinnitus in 8. These symptoms are evidently caused by the evolution of nitrogen bubbles in the internal ear, labyrinth, cochlea and semicircular canals. To the compressed air worker this syndrome is known as the "staggers." A worker suffering from the "staggers" resembles a man who has indulged in alcoholic excess. Unless the worker's identifying badge is seen, the man is believed to be an alcoholic addict and is treated as such. This is one important reason why compressed air workers should wear their identifying badge where it can be readily seen and detected.

Air Hunger (the "chokes"): Dyspnea is characteristic of this group. These patients appear acutely ill and present a condition which is alarming. However, they yield readily to treatment, provided it is given immediately. Compressed air workers suffering from this symptom complex resemble an asthmatic patient. Physical examination of the chest reveals bilateral medium and fine moist and musical rales. These patients also resemble persons with heart disease suffering with sudden left ventricular failure and transitory pulmonary edema. This clinical picture is familiar to the compressed air worker and is known as the "chokes." Fifteen cases of the "chokes" were observed at the Queens-Midtown Tunnel. The symptoms are caused by varying amounts of nitrogen emboli in the pulmonary arteries.

Cutaneous Manifestations (the "itch"): The various cutaneous manifestations noted in the cases studied were pruritus (the "itch"), erythema and mottling and blotching. There were 20 cases presenting cutaneous manifestation of the disease: 6 presented only pruritus, 5 a combination of pruritus, erythema and blotching of the skin. Erythema and mottling of the skin were present in 6 cases. The intense itching is caused by nitrogen bubbles in the sweat glands of the skin. The erythema and purplish mottling of the skin denote stasis of blood in the cutaneous vessels as a result of nitrogen emboli in the skin capillaries. Cutaneous signs are usually early signs of compressed air illness. They signify possible ensuing symptoms of much greater severity. Therefore persons presenting cutaneous manifestations should be carefully observed for severer symptoms. Of 6 cases in which mottling and blotching of the skin were present, the "staggers" developed in 2 and the "chokes" in 4.

Neurologic Manifestations: This group of cases is important from the point of view of its disabling character and the possibility of permanent damage to the central nervous system. Patients with central nervous system symptoms who are not treated promptly are apt to develop permanent disability.

The nerve cells and tissues of the central nervous system are vulnerable to ischemia and pressure from nitrogen bubbles with consequent pressure necrosis. Thus the reasons for permanent damage can readily be seen. Nitrogen bubble formation can occur in any part of the brain or spinal cord. Nitrogen emboli can form locally in the blood vessels or be carried to the central nervous system by the blood stream from other parts of the body. The central nervous system symptoms produced by compressed air disease can simulate those caused by any other disease or injury of the central nervous system. Complete unconsciousness and collapse to numbness and tingling of an extremity can be expected.[6]

Paralysis of the bladder and bowels is common in spinal cord cases. The majority of afflicted persons recover with treatment, while some remain with permanent weakness of the lower limbs. In some instances the patient dies after a lingering illness, death being caused by secondary complications such as cystitis pyelonephritis, bedsores, pneumonia, exhaustion and anemia. Twenty-five cases of central nervous system symptoms occurred at the Queens-Midtown Tunnel with brain involvement, hemiplegia 3 cases, monoplegia 2 cases, internal strabismus 2 cases, nystagmus 2 cases, diplopia 2 cases; with spinal cord involvement, sensory, numbness and tingling of both legs 5 cases, motor, paresis of both legs 4 cases, paralysis of both legs 2 cases, sensory and motor disturbance, numbness and tingling and paresis 3 cases. Urinary and bowel incontinence are present in all spinal cord cases in addition to the symptoms mentioned. Recovery was complete with treatment except in 1 case of paralysis of both legs. Urinary and bowel control were regained but weakness of both limbs remained.

DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

The diagnosis of caisson disease is not difficult. Although the symptoms are varied and depend on the parts of the body involved, there should be no doubt as to the diagnosis provided the patient is conscious and can give a history of exposure to compressed air during the preceding twelve hours. The identification badge that the compressed air worker wears conclusively confirms the diagnosis. It is conceivable that the identifying badge might not be worn and the worker might be in coma and unable to give a history. Furthermore, compressed air workers are susceptible to other injury or illness in addition to caisson disease. In such instances the diagnosis becomes more difficult and a careful differential is always necessary. A severe case of abdominal bends can simulate an acute surgical condition of the abdomen and conversely an acute surgical condition of the abdomen can simulate abdominal bends. True caisson disease must be differentiated from mild cases of myalgia, arthralgia and neuralgia. Aside from caisson disease, 135 cases of mild pain in the extremities were observed. Most of these cases responded to physical therapy and medication. The pains were located chiefly in the joints and extremities. They were described as vague aches and pains in the thighs, legs, arms, knees, ankles, elbows, wrists, shoulders and along the course of the peripheral nerves. The pains

6. Clark, E. A.: Effects of Increased Atmospheric Pressure upon the Human Body, M. Arch., St. Louis 5: 1-30 and 295-300, 1870-1871. Cazamian: Hématomyélie par décompression brusque chez un scaphandrier; paraplégie spasmodique, Arch. de méd. nav. 98: 212-224, 1912. Genet, L.: Atrophie optique partielle et maladie des caissons, Bull. Soc. d'opht. de Paris, 1933, pp. 318-321. Callan, L. W.: Double Choked Disks Associated with Compressed Air Disease (Caisson Disease), Arch. Ophth. 36: 509-512, 1907. Hoinet: La maladie des scaphandriers, Bull. Acad. de méd., Paris 55: 756-764, 1906. Bassoe, Peter: Compressed Air Disease, J. Nerv. & Ment. Dis. 38: 368-369, 1911; The Late Manifestations of Compressed Air Disease, Tr. XV Internat. Cong. Hyg. & Demog. (1912) 3: 626-638, 1913.

were transitory and not severe enough to incapacitate the patient but were aggravated with change in temperature.

Physical examination revealed three clinical groups as follows: pains limited to muscles, myalgias; pains limited to joints, arthralgias; pains limited to the course of a peripheral nerve, neuralgias. Combinations of the three groups were also seen. It is believed that these cases are the result of the decided change in temperature on compression and decompression, the unusually damp atmosphere of the tunnel environment and the poor local tissue circulation resulting from fatigue following strenuous physical effort.

COMPLICATIONS

The complications of caisson disease are limited to the bones and joints. The symptoms of onset are insidious and are delayed from six months to a year or more following repeated attacks of the disease. A case of bone necrosis was reported in 1888 by Twynam.[7] Cases of chronic arthritis were reported by Bornstein and Plate[8] in 1911 and 1912 following repeated attacks of the disease. Bassoe[9] in 1913 reported several cases of arthritis deformans. Christ[10] in 1934 reported joint lesions. It is possible that nitrogen emboli in end arteries of nutrient vessels to bones might cause necrosis and degenerative changes in bone. Four cases of aseptic bone necrosis attributed to caisson disease were reported by Kahlstrom, Burton and Phemister[11] in 1939.

PROGNOSIS

The mortality of caisson disease has dropped to an exceedingly low figure at the present time because of the efficiency of the recompression treatment. Prior to the use of the medical lock the mortality rate was high. Blick[12] in 1909 reported 30 per cent mortality among pearl divers, 60 out of 200 patients dying before medical aid could be given. Janinet[13] in the St. Louis bridge construction reported 119 cases with permanent paralysis in 52 and death in 14, representing a 14 per cent mortality. Dominguez[14] reported 106 cases of serious paralysis with 14.9 per cent mortality. During the building of the Brooklyn bridges the mortality was 3 per cent. During the work on the Hudson River tunnels the advantages of recompression were amply shown on the installation of a medical lock. After the medical lock was employed the mortality rate dropped from 25 per cent to 1 per cent. The mortality rate in building the Pennsylvania Railroad East River tunnels was 2 per cent. In 300 cases observed during the building of the Queens-Midtown Tunnel there was no mortality from this disease. In cases of sudden collapse and unconsciousness the prognosis is graver than in cases presenting only pain in the extremities. Those in which paralysis is present are difficult to cure, and advice as to the outcome should be guarded.

7. Twynam, G. E.: A Case of Caisson Disease, Brit. M. J. 1:190, 1888.

8. Bornstein and Plate: Ueber chronische Gelenkveränderungen entstanden durch Presslufterkrankung, Fortschr. a. d. Geb. d. Röntgenstrahlen 18: 197-206, 1911-1912.

9. Bassoe, Peter: Compressed Air Illness, Illinois M. J. 17: 462-469, 1910.

10. Christ, A.: Ueber Caissonkrankheit mit besonderer Berücksichtigung einer typischer Erkrankung des Hüftgelenkes, München. med. Wchnschr. 81: 843, 1934.

11. Kahlstrom, S. C.; Burton, C. C., and Phemister, D. B.: Aseptic Necrosis of Bone, Surg., Gynec. & Obst. 68: 129-146 (Feb.) 1939.

12. Blick, G.: Notes on Diver's Paralysis, Brit. M. J. 2: 1796-1798, 1909.

13. Janinet, A.: Physical Effects of Compressed Air, St. Louis, R. & T. A. Ennis, 1878.

14. Dominguez, A. G.: Caisson Disease o parálisis de los buzos, Rev. de med. y cir. de la Habana. 17: 359-363, 1912.

PROPHYLAXIS AND PREVENTION

In addition to nitrogen embolus formation, certain secondary conditions predispose an individual toward caisson disease. They are age, systemic disease, obesity, alcoholism and fatigue.

It is the consensus that the ideal age for compressed air workers is between 20 and 40 years, since during these years the cardiovascular system is at its peak of greatest efficiency and best able to withstand the hardship of increased air pressure. Diseases of the heart, lungs and kidneys and peripheral vascular diseases are grounds for rejection. These conditions should be carefully ruled out during the first examination. Obese men are bad risks because of the great solubility of nitrogen in fat. Men who are known to be habitual drinkers are poor risks because of the effect of alcohol on the circulation and should be rejected.

A man who is acutely ill should not be admitted to compressed air until he has recuperated. Acute infection of the upper respiratory passages should temporarily disqualify a man for employment, because the infection usually involves the eustachian tubes and ostiums of the sinuses, causing adhesions of the walls and consequent closure. When one is entering the compression chamber the ear drum is stretched, causing severe pain. This is known as "ear block." Infection of the mucous membrane of the ostiums of the sinuses causes acute edema. Valvelike action occurs, allowing air to enter the sinus; but its escape is prevented. Air under pressure becomes trapped in the sinus, causing severe pain. This is known as "sinus block." Acute infection of the sinus may follow from organisms driven into the sinus by the compressed air, requiring surgical intervention. Failure of the eustachian tubes to open to equalize the pressure on either side of the tympanic membrane will result in rupture of the tympanum with consequent infection of the middle ear.[15] Fatigue predisposes to emboli and the "bends" because of its effect on the circulation, causing slowing of the elimination of nitrogen gas.

There is no immunity to caisson disease. Consequently the most important step in the prophylaxis is the physical examination with special emphasis on the heart, lungs, circulatory system, circulatory efficiency and cardiac reserve. The importance of age, weight and habits should not be overlooked.

Approximately 20 per cent of the men examined at the East River tunnels were rejected. Men who show symptoms of caisson disease after one or two trial test shifts would be rejected. Many of the men suffer from repeated mild attacks of pain and itching of the skin, but there is no need for rejection on such mild symptoms.

The ultimate prevention of the disease depends on the proper elimination of nitrogen from the tissues during decompression. There is only one route by which the nitrogen in the body tissues and blood can be eliminated, and that is through the lungs by the circulation. Any condition affecting the efficiency of the circulation is likely to affect the efficiency of the elimination of the nitrogen gas from the tissues. During the decompression stage the value of exercise in stimulating the circulation cannot be overemphasized. The extreme importance of slow decompression should always be borne in mind. The working time under

15. Crosson, J. W.; Jones, R. R., and Sayers, R. R.: Helium-Oxygen Mixtures for Alleviation of Tubal and Sinus Block in Compressed Air Workers, Pub. Health Rep. 55: 1487-1496, 1940. Lovelace, W. R., II; Mayo, C. W., and Boothy, W. M.: Aero-Otitis Media, Proc. Staff Meet. Mayo Clin. 14: 9-96, 1939.

pressure should always be held within safe limits with adequate rest periods between shifts. This is important, because the amount of nitrogen absorbed depends to a large extent on this time factor. The inhalation of oxygen and oxygen-helium mixtures during the decompression period to hasten the nitrogen release from the body is a valuable prophylactic measure. Sudden changes in temperature should be avoided. Therefore the temperature of all air locks should be controlled by suitable heating apparatus to keep the temperature as constant as possible.

TREATMENT

The essential treatment of caisson disease is the return of the patient to the compressed air. In previous years, men who were seized with an attack voluntarily returned to the compression chamber for the relief of their symptoms. Today this treatment is given in a compression chamber known as a "medical air lock." [16]

Only those who have witnessed the treatment of a case of compressed air illness can realize the efficacy of recompression. Recompression should be started as soon after the onset of symptoms as possible, because the sooner the bubbles of nitrogen are redissolved the sooner will the circulation be established and pain relieved. The possibility of permanent damage to vital structures such as the brain and spinal cord will be materially reduced by immediate recompression. It has been noted that if treatment is delayed following the onset of symptoms a higher pressure is necessary to give relief. Long delay in recompression may result in permanent injury to the cord because of anemia as a result of the circulation being blocked by nitrogen emboli. It is true that recovery will occur in certain mild cases without recompression, but there are no criteria by which we can determine which cases suddenly become serious. It is most advisable therefore to treat all definitely diagnosed cases of the disease by recompression immediately.

Of 300 patients treated at the Queens-Midtown Tunnel airlock, 85 per cent were completely relieved, 12 per cent were partially relieved and 3 per cent had no relief. Experience has established that symptoms in most cases are relieved by recompression to a pressure equal to that to which the worker was exposed. Occasionally it is necessary to go 5, 10 or 15 pounds higher before complete relief is obtained.[17]

The consensus favors waiting twenty to thirty minutes before starting the decompression process. Observations have proved that this waiting period has given the best result. In many instances symptoms recurred if decompression was started immediately with no waiting period, requiring another recompression. To avoid repeated recompressions, it was found advisable to introduce this waiting period before starting the decompression process. Despite the waiting period, however, symptoms are apt to recur requiring one or more additional recompressions.

It was noted that if the men were made to exercise the affected limb during the decompression process it aided materially in obtaining a permanent relief. The inhalation of pure oxygen and oxygen-helium mixtures during decompression has given encouraging results in many instances. These gases hasten the elimination of dissolved nitrogen from the blood and hence decrease the tendency toward the disease.[18] The importance of stimulating drugs as adjuncts in treatment should not be minimized. Strychnine, epinephrine and caffein are valuable circulatory stimulants and one should not hesitate to use these drugs in cases of circulatory collapse. In cases of respiratory failure, artificial methods should be instituted. Physical therapy and general nursing care should be given whenever necessary.

SUMMARY

1. Three hundred cases of caisson disease occurred without mortality during the building of the New York-Queens Midtown Tunnel in 1938.

2. Serious disability in these cases was also practically nil. This remarkable result may be attributed to:

The selection of workers between the ages of 20 and 40 years, free from acute or chronic disease and with freedom from pulmonary, cardiovascular, renal, peripheral vascular or gastrointestinal diseases and obesity.

Prompt recompression of all subjects exhibiting the slightest symptoms of caisson disease, thereby minimizing neurologic phases of the disease, which ordinarily when neglected prove most disabling or fatal.

The prophylactic inhalation of oxygen and oxygen-helium mixtures in the decompression stage, thus hastening nitrogen release.

The rigid regulation of the duration of the working shifts and rest period between shifts according to prescribed pressure-time codes.

20 West Seventy-Second Street.

16. The first recompression chamber in the United States was installed during the building of the New York Hudson tunnels under the North River in 1894. This was known as a "medical lock" and because of its efficiency it was made essential to the equipment of all compressed air work.

17. Keays, F. L.: Compressed Air Illness with a Report of 3,690 Cases, Pub. Cornell Univ. M. Coll., Dept. Med. 2: 1-55, 1909. Shilling, C. W.: Compressed Air Illness, U. S. Nav. M. Bull. 36: 9 and 235, 1938.

SOME PROBLEMS OF WORKING IN AN HYPERBARIC ENVIRONMENT

by

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" Prae monitus prae munitus "

Hunterian Lecture delivered at the Royal College of Surgeons of England on 10th March 1965

by

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THE PIONEER WORK of Boerema in Amsterdam and Illingworth in Glasgow has recently focussed the attention of surgeons on the possible advantages to be gained from the use of hyperbaric oxygen therapy. Whether such therapy is to be given at the time of operation or at some other time, as for instance in the treatment of a head injury, acute coronary occlusion or anaerobic infection, surgeons, physicians and nursing staff may have to expose themselves to the high-pressure environment when attending to the patient. Unlike the patient, the doctors and nurses will breathe air at high pressure, not oxygen.

Such exposures to a compressed air environment carry with them certain dangers. These dangers are well known to civil engineers, since some types of constructional work are only possible when compressed air is used to keep the workings dry as, for instance, when building a tunnel under a river. Naval divers and frogmen also face the same dangers.

THE NATURE OF THE DANGER

Most, but not all, of the untoward effects of working in compressed air are associated with decompression, i.e. coming out of the hyperbaric environment. Exposure to a compressed air environment in itself even up to pressures of 4 Atmospheres Absolute has generally been thought to be innocuous provided that proper temperature, humidity and ventilation rates are maintained, and except for a change in voice pitch there is little subjective effect to be noticed. The disturbances which can occur during decompression probably result from the appearance of nitrogen or air bubbles in the tissues or in the blood. It is interesting to note that Hunter was well aware of the danger of gas bubbles in the circulation. When carrying out some experiments in which he injected various drugs as well as air into the veins of dogs, he reported that of all the things he tried the most lethal and the one which had the most rapid effect was the injection of air (Palmer, 1835).

Why do bubbles occur in the tissues and blood during decompression from a high-pressure environment? Normally the gases of the atmosphere —oxygen, nitrogen and carbon dioxide—are in solution in the body tissues to a degree which is related to the pressure at which these gases are present

in the atmosphere and the tissues are said to be saturated with the gases for that pressure. Exposure to pressures greater than atmospheric leads to more of these gases going into solution until a state of saturation for the higher pressure is reached. This saturation process takes time and the time is different for each tissue of the body, depending on the richness of its blood supply. Some tissues become saturated in minutes, some take several hours. Eventually a new state of equilibrium is reached when all the tissues have become saturated at the new pressure. If a man saturated with the gases of the atmosphere in a high-pressure environment suddenly comes out of that environment to one at normal atmospheric pressure, then he will have a relative excess of gas in his body and his tissues can be said to be supersaturated. He is in fact like the bottle of soda water which is liable to fizz when the cap is suddenly taken off. In man and animals spontaneous bubble formation during decompression is said to be due to the supersaturation by nitrogen because the body can use up excess oxygen fairly quickly and it can normally deal with carbon dioxide satisfactorily. Once a nitrogen bubble has formed, however, its contents will quickly come into equilibrium with the gases of the blood and consist of a mixture of nitrogen, oxygen and carbon dioxide. The syndromes which result from the appearance of bubbles in the tissues and blood constitute what is called decompression sickness, and this can take several forms. Broadly speaking, decompression sickness can be divided into two types, Type I and Type II (Golding *et al.*, 1960). Both types can occur during decompression or within the first few minutes after decompression, or there may be a delay of several hours before symptoms are manifest.

Type I decompression sickness (" the bends ")

This consists of pain in the region of a major joint. The knee is the most frequently affected joint, followed by the hip, which in compressed air workers, as opposed to divers, is more commonly affected than the shoulder. In order to get some relief from the pain, the patient tends to adopt a characteristic attitude of flexion. It is said that this attitude led to the origin of the term " the bends " because, in New York, at the turn of the century fashionable ladies of the town were affecting a stance which they called the " Grecian Bend " (Fig. 1) and men working on the caissons for the Brooklyn Bridge who suffered from Type I decompression sickness were ribbed by their mates that they were adopting the latest fashion and so had " the bends ".

Although the pain of " the bends " may be severe, there is no constitutional upset and the patient feels perfectly well.

Type II decompression sickness

This is a more serious condition than " the bends " and it may present in one of several ways. If bubbles arise or lodge in the central nervous system, neurological symptoms may result with paraplegia and par-

aesthesia. Visual scotomata and upsets of balance called "the staggers" can also result as a secondary result of bubble formation. Bubbles may lodge in the coronary vessels to give rise to the signs and symptoms of a coronary thrombosis, or they may be trapped in the vessels of the lungs to give discomfort in the chest, difficulty in breathing and cyanosis, a syndrome which is known as " the chokes ".

Fig. 1.The " Grecian Bend ".

In many Type II cases of decompression sickness where the cardiovascular system or the respiratory system is affected, the men are ill—they are sweating, pale, hypotensive, peripherally vasoconstricted, they have apprehensions of death and will die unless treated quickly.

The symptoms of both Type I decompression sickness (" the bends ") and Type II decompression sickness can almost invariably be relieved by returning the patient to the pressure at which he was working. Back at pressure, the causative bubbles are compressed and the situation is brought under control.

Once the situation is controlled, time can be taken to consider the next move. The aim must be, of course, to get the man out of pressure without causing the symptoms to re-appear. This is done by lowering the pres-

sure very slowly and stopping or even increasing the pressure again if symptoms re-appear. Usually about three hours are required to treat a Type I case, but it can occasionally take an extraordinarily long time to get a man who has been treated for the neurological symptoms of Type II decompression sickness out of pressure safely. I know of one compressed air worker who had to be treated for nine days before he could be brought to atmospheric pressure, but when he did get out he was symptom-free and had no further complications. If a man has an acute paraplegia following decompression and he is not treated promptly by recompression, then the paraplegia will be permanent. All cases must be returned as soon as possible to a centre where there are facilities for recompression.

Caisson disease of bone

Type I and Type II decompression sickness are the acute conditions which may result from being decompressed following a period of exposure to compressed air. There is also a chronic condition which can follow this sort of work (even one exposure to compressed air may be sufficient) and this is known as caisson disease of bone. It does not become evident until some months or even years after the exposure to the hyperbaric conditions which caused it. Caisson disease of bone is also known as avascular necrosis or aseptic necrosis of bone. Pathologically the lesion consists of an area of dead bone.

A patch of dead bone in the centre of the shaft of the humerus or femur is generally thought to be of little consequence since it probably will not cause symptoms, but an area of dead bone underlying an articular surface is a serious matter. In the course of time, the cortex of the bone may collapse under the stress of weight-bearing to give rise to pain aggravated by movement. Furthermore, the consequent irregularity of the joint surface will lead to the development of a secondary osteo-arthritis in the joint.

THE SOURCE OF PRESENT INFORMATION

My interest in decompression sickness started 20 years ago during the war and has been sustained by the problems presented by the increasing activity in the development of our road systems in Great Britain, which has necessitated the digging of many under-river tunnels where compressed air has been necessary.

You may be wondering how there can be a similarity between a tough workman who digs a tunnel under a river with a pick and shovel and a surgeon who works at the operating table in a hyperbaric theatre. I hope to convince you that there is a similarity and to show you where it lies.

First it is necessary to appreciate how an under-river tunnel is constructed. Figure 2 illustrates the 32-feet diameter tunnel which is now being built under the Tyne at Newcastle. It can be seen that the tunnel passes through boulder clay, which is water impermeable except where

there are " faults " or cracks, and through river deposits and coal measures which are water permeable. Where the ground is water permeable, and where there are " faults " in the boulder clay, it is necessary to use compressed air to keep the water out.

Tunnelling was started on both sides of the river in free air and proceeded until the tunnel faces became too wet to proceed further with safety. Bulkheads were then built and on the Northumberland side a vertical shaft was sunk, from the bottom of which a small 12-feet diameter tunnel was first driven under the river. The working face was reached through a lock, beyond which everything was in compressed air kept at sufficient pressure to hold the water out. It is very important to use just sufficient pressure to keep the tunnel workings dry as the use of too much pressure will blow a hole in the river-bed and not only result in loss of pressure but also in flooding of the tunnel. This hazard must always be borne in mind and it is usual to construct an escape gangway near the top of the tunnel for

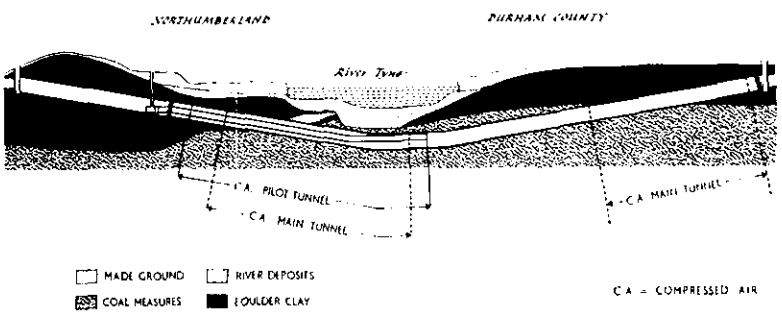


Fig. 2. Cross section of the Tyne Road Tunnel (under construction 1965) showing the extent of the pilot tunnel and the areas where compressed air had to be used.

the use of miners in an emergency. Flooding did occur once during the construction of the Tyne Tunnel, but, fortunately, all the men working in the tunnel at the time escaped unharmed. However, not only was the tunnel flooded, but so much ground was washed into it that many weeks were required to clear up the debris. Before this could be done, however, the hole in the river bed had to be closed by dumping barge loads of clay into it—an expensive and time-consuming procedure.

The small diameter tunnel which is built first is called the pilot tunnel. The need to build it arises from the fact that, since the lower edge of the working face will be at a greater distance below the surface of the river than the upper edge, there will be a greater hydrostatic pressure at that point (Fig. 3). With a 12-feet pilot tunnel 50 feet below the surface of the river, the hydrostatic pressure at the upper edge of the working face will be 22 p.s.i.g. and at the lower 27 p.s.i.g. The pressure of compressed air necessary to keep the bottom of the face dry will be 27 p.s.i.g. so that there will be an excess pressure of 5 p.s.i.g. at the top edge. This will lead

to some leakage of air but not sufficient to cause disruption of the river bed. If the 32-feet diameter tunnel were built straight away, it would require a compressed air pressure of 35 p.s.i.g. to keep the lower part of the face dry and there would be an excess pressure of 13 p.s.i.g. at the top edge. This would lead to such a rapid loss of air that the river bed would certainly be breached with consequent flooding of the tunnel.

Once the pilot tunnel is built, the ground around it can be treated by injecting out through its walls a material which will render the surrounding soil less water pervious. Later, the full-sized tunnel of 32 feet is built round the pilot tunnel through the treated ground using a low pressure of compressed air. At the same time the pilot tunnel is dismantled.

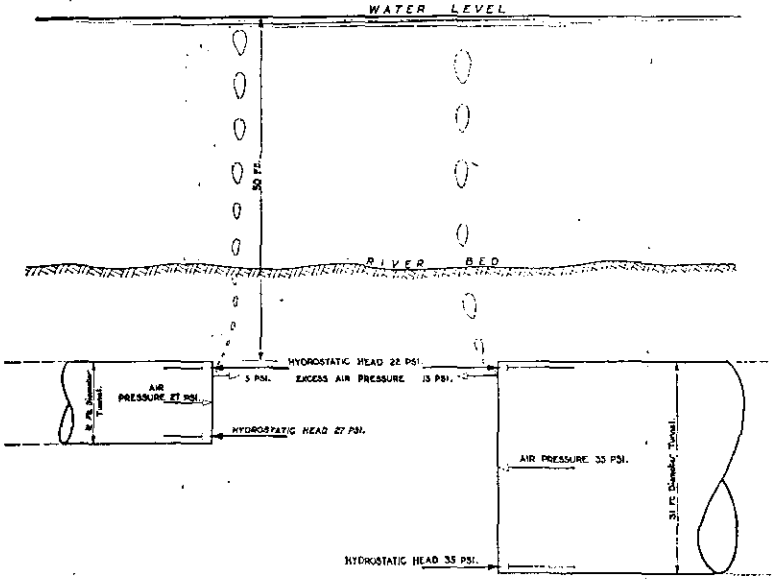


Fig. 3. Effect of tunnel diameter on pressure differential at top of working face.

The principle on which these tunnels are constructed is to build a series of iron rings, each consisting of a number of segments (Fig. 4*a*). In the centre of each segment is a grouting hole, through which, in the case of the pilot tunnel, the ground treatment material mentioned above can be forced and, in the case of the final full-diameter tunnel, cement can be forced into the surrounding ground to form a protective layer outside the ironwork of the tunnel. The grouting holes are eventually closed by a screw plug. When converting the small-diameter tunnel to the final large-size tunnel, a large-diameter face has to be worked and use is often made of a shield (Fig. 5). This consists of a large circular diaphragm, round the periphery of which is located a series of hydraulic rams which bear against the last ring to have been constructed. The face of this shield is divided

up into little compartments, into each of which a man can go to shovel out the earth in front of his compartment. Once all the earth has been removed for a distance of 30 inches in front of the shield, the hydraulic rams are operated and the whole shield is advanced; the rams are then retracted and a new ring is built into the space created. The whole operation is then repeated over and over again. It is very difficult to steer

(*a*)

(*b*)

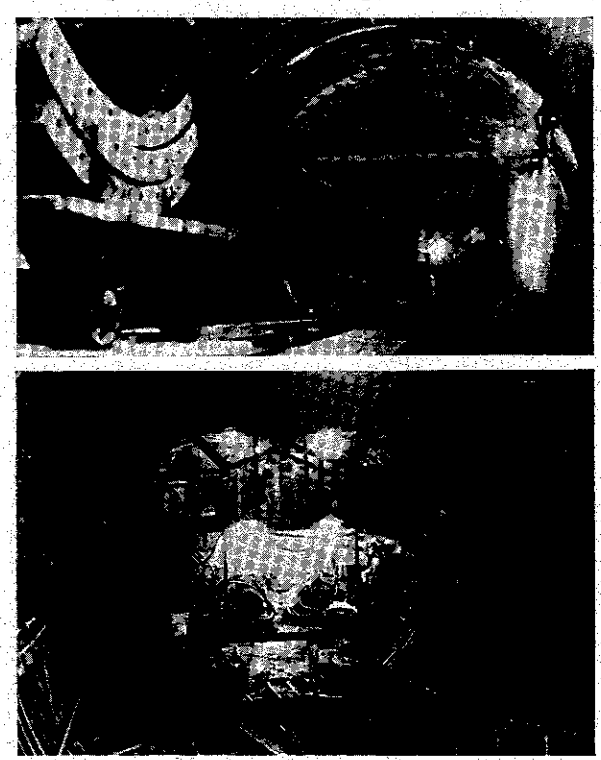


Fig. 4. (*a*) To show the way in which iron segments (seen on left) are bolted together to form the " rings " of the tunnel. (*b*) Ancillary equipment which follows the shield as it is moved forward.

the shield, and as the engineers usually start tunnelling on both banks of the river simultaneously, in order to save time, a great deal of skill is required if the tunnels are to meet accurately under the river.

As the shield moves forward, it has to be followed by a great deal of ancillary equipment (Fig. 4*b*).

Once the tunnel gets under way, there is an increasingly large volume of air to be kept at high pressure so that it is necessary to provide several large-capacity compressors. Not only are maintenance compressors required, but emergency systems must be provided. At least one compressor system must be independent of the national electricity supply.

A master control room must be set up from whence the pressures in the different sections of the tunnel can be controlled. The tidal variation of the river Tyne at the point where the tunnel is being built is about 15 feet a day, so that the air pressure in the tunnel must be adjusted as the tide changes to avoid flooding as the tide rises or excessive loss of air as the tide ebbs.

Normally tunnellers work eight-hour shifts under hyperbaric conditions and, of course, the aim is to bring these men at the end of that time back

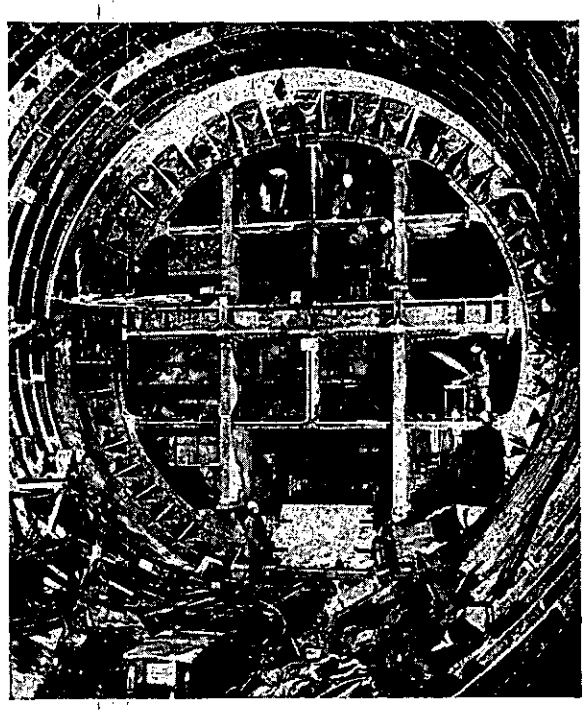


Fig. 5. A shield in the course of erection. The hydraulic rams round its periphery can be clearly seen.

to atmospheric pressure without causing the development of bubbles in their blood or tissues. In civil engineering practice in Great Britain, decompression procedures are used which are set out in the Ministry of Labour and National Service Special Regulations (1958). The procedure adopted is based on the original work of Boycott, Damant and Haldane (1908), in which they stated that so long as the pressure differential between the tissues and the ambient environment did not exceed 2 : 1, no spontaneous bubbling would occur. The tables used were devised on the assumption that after four hours' exposure a man would be fully saturated with the ambient gases so that the decompression times for exposures of

four hours and over are the same. The nature of the decompression is a two-stage procedure in which a rapid drop in pressure to half absolute pressure is allowed in not less than two minutes followed by a second-stage slow fall in pressure for which the rate of change is given in lb./min. For example, after an eight-hour shift at 32 p.s.i.g., the men go into a decompression lock where the pressures can be changed without affecting the tunnel pressure. The pressure in the lock is then dropped rapidly (in just over two minutes) to 9 p.s.i.g. and then slowly at the rate of nine minutes for each pound until atmospheric pressure is reached in 81 minutes. Thus a total time of 83 minutes is required for the decompression. As can be imagined this is an irksome procedure for a workman who has just done an eight-hour shift. The men are discouraged from going to sleep during decompression as it is so difficult to know when something untoward happens to a sleeping man, and should he become paraplegic or unconscious this would not be realized until the end of the decompression period.

By law a full-time lock-keeper must be employed and he is in charge of the decompressions. He is responsible for adjusting the valves to make sure that the pressure is reduced according to the decompression tables, as well as for keeping a register of the exposure times of all those going in and out of the compressed air workings. A certain degree of intelligence and ability to control men is desirable in a lock-keeper but not always obtained. In order to minimize the human factor as far as possible use is often made of an electro-mechanical device, known as a Fisher valve, which can be set up to provide automatically the correct decompression for a given exposure.

In spite of adhering to the procedures laid down in the Decompression Table, it is recognized that decompression sickness will still occur. For this reason, and in order to be able to treat the rare individual who flagrantly disobeys the regulations and consequently suffers from decompression sickness, the law requires that a treatment centre shall be provided where recompression locks are always available. The only treatment for decompression sickness is recompression, that is, placing the affected individual back into a compressed air environment at a pressure slightly above that at which he was working. This procedure usually rapidly relieves the condition and must then be followed by a decompression, the exact rate of which is primarily determined by the necessity to avoid a recurrence of the symptoms.

Because of the long decompression times required after shifts at the higher pressures, there are occasionally men who through ignorance believe that they are " tough " enough to be able to come out of compressed air without the need for properly regulated decompression. A possible method of escape from the compressed air which avoids the manlock and its lock-keeper exists in most tunnels since it is common practice to operate, in addition to the manlock, a muck lock, through which the

trucks containing the excavated earth are brought out of the workings. Naturally the pressures in the muck lock are changed as rapidly as possible since only earth-filled trucks are normally in them. A man who is prepared to flout the regulations can travel out with the " muck ".

I personally know of two men who have taken this quick way out, and both are now permanent paraplegics. Of course, to prevent this sort of thing is really a matter of discipline, but rules, for some, are made to be broken.

One way of avoiding this particular type of flagrant disobedience is to provide no " muck lock ". The excavated earth from the tunnel must then be pulverized in an enormous mincing machine and mixed with water to make a sludge which can be pumped out of the tunnel through pipes. This system defies a man to go out with the muck! Such a scheme was tried at Dartford, but the engineering problems involved were such that mechanical failures of the apparatus were numerous and led to considerable loss of working time. As can be imagined this system was extremely unpopular with the contractors, however desirable it might have been from the safety and medical points of view.

POSSIBLE FACTORS AFFECTING THE INCIDENCE OF DECOMPRESSION SICKNESS

As has been indicated earlier, it is an unfortunate fact that, even when men adhere strictly to the decompression arrangements provided for them, many will still suffer from decompression sickness at some time or another. In an effort to determine whether there is a specific cause for these cases of decompression sickness, various factors have been investigated.

Inaccuracy of decompression

One matter which must be examined is the extent to which slight inaccuracies in carrying out the decompression procedure will influence the decompression sickness rate. Where the decompression is controlled manually by a lock-keeper, much may depend on his skill. Paton and Walder (1954) found that whereas when the rate of fall of pressure during decompression was greater than that prescribed by the British regulation there was an increase in the incidence of bends. However, when the rate of fall was less than that prescribed, there was no such increase in the incidence of bends although on theoretical grounds this should have led to an inadequate decompression.

Individual susceptibility

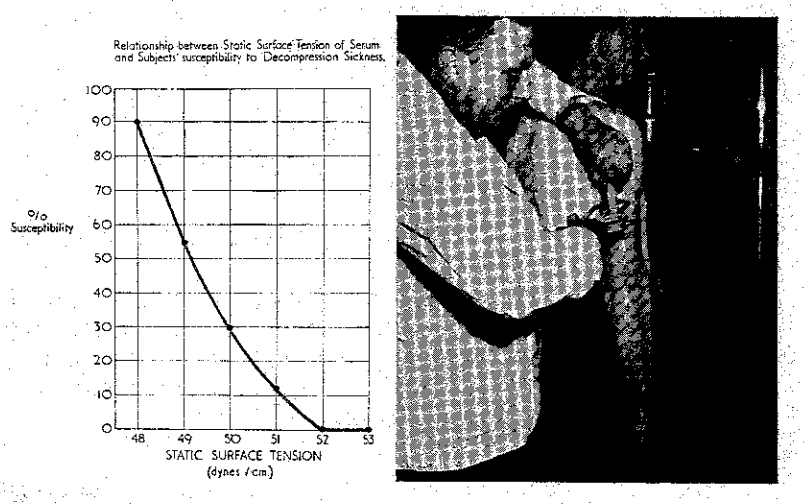
There is always the question of a man's individual susceptibility to decompression sickness.

Age. There is no doubt that age is a factor—men over 40 are at greater risk than men under 40 (Paton and Walder, 1954).

Blood surface tension. Another interesting observation made by me (Walder, 1948) in connection with the susceptibility of pilots undergoing

decompression is that the surface tension of the subject's blood serum seems to be related to his susceptibility to decompression sickness (Fig. 6*a*). This association was predicted on the theoretical grounds that the initiation of gas bubbles in a supersaturated fluid, the rate of growth, ultimate size and force required to move a bubble along a vessel will all be related to the surface tension of the fluid in which the bubble exists.

Fatness. There are many suggestions in the literature that the fatness of a man is important in determining his susceptibility to decompression sickness. This hypothesis is based on the fact that nitrogen is five times more soluble in fat than water and that the fatty tissues of the body are often poorly supplied with blood vessels, so it is assumed that nitrogen



(*a*) (*b*)

Fig. 6. (*a*) The relationship between the static surface tension of the blood serum and the susceptibility to decompression sickness (51 men, $t = 18.54$, $P<0.001$). (*b*) Measuring the skinfold thickness over the triceps with special calipers.

will take a long time to be cleared from fatty regions and zones supersaturated with nitrogen will be left during decompression to give rise to the danger of bubble formation. In practice it is extremely difficult to gauge a man's fat content. Many methods have been suggested but few are satisfactory or suitable for application to compressed air workers. Ponderal indexes determined from weight and height measurements do not provide an accurate answer.

One way in which fat content can be determined is to measure the specific gravity of a man, but this requires that he shall be weighed under water—not a very acceptable procedure outside the laboratory. Quite recently, it has been shown that skinfold thickness is closely related to the amount of fat that a man carries (Fletcher, 1962). Special calipers are used to measure pinched-up folds of skin (Fig. 6*b*). The sites at which

the skin fold is said to give the most reliable indication of total body fat are: (i) over the triceps, and (ii) below the angle of the scapula. Some preliminary experiments in which skinfold measurements of men working on the Tyne Tunnel have been related to their susceptibility to decompression sickness show that although there is a statistical relationship between these two factors it does not appear to be a very close one.

Acclimatization

It is interesting to note that men who expose themselves regularly to compressed air day after day seem to become less susceptible to attacks of decompression sickness as time goes on; in other words, it appears that men can become acclimatized to this type of work (Paton and Walder, 1954). Table I shows the incidence of bends in a group of 90 men exposed daily to the same pressure over a period of time. When they started their decompression sickness rate was high but, as the days went by, it fell until it reached quite a low level. Acclimatization appears to take about 14

TABLE I

THE EFFECT OF REPEATED DAILY EXPOSURES TO WORK IN COMPRESSED AIR (NUMBER OF COMPRESSIONS) ON THE MEAN DAILY BENDS RATE (% BENDS) IN A GROUP OF 90 MEN

Number of compressions ..	1–5	6–10	11–15	16–20	21–25	26–30	31–35	36–40	41–45	46–60
Bends %	7.3	3.6	1.3	0.44	0.89	1.3	1.8	1.8	0.44	0.67

days before the maximum effect is obtained. Ceasing to work in compressed air leads to de-acclimatization. This is a gradual process and takes about 10 days before it is complete. It therefore appears that for maximum protection against decompression sickness it is best, once daily periods of work in compressed air are started, to continue regularly each day rather than to work in compressed air sporadically.

TYPE II DECOMPRESSION SICKNESS FOLLOWING SHORT EXPOSURES

If, as has been suggested, it takes at least four hours before all the tissues of the body have become saturated with the ambient gases at a given pressure, then it would be expected that the risk of suffering from decompression sickness should be small following very short exposures to pressure. Experience has demonstrated, however, that this is not necessarily so and that some men, even after short exposures followed by a correct decompression, can suffer from the severe Type II decompression sickness.

There was, for example, the case of a managing director of a firm of consultant engineers who were building a tunnel. He was a man of about 50 years who has been in and out of compressed air all his working life. One day he went into the compressed air at a pressure of 25 p.s.i.g. for three-quarters of an hour in order to make sure that all was going well with the tunnel. At the end of his decompression, he collapsed with

Type II decompression sickness. He was recompressed at once and his life saved. On subsequent examination, he was found to have a cyst in the lower zone of his right lung.

Another similar case involved a plumber who went into the compressed air at a tunnel to do a job and, whilst being decompressed, he fell asleep, but at the end of his decompression he was found to have a paraplegia. Fortunately for him, he was immediately recompressed and his paraplegia cured, but it took nine days of very careful decompression before it was possible to get him out of the recompression lock symptom-free. Subsequent careful clinical investigation showed that the only physical abnormality to be found was a cyst in the lower zone of his right lung.

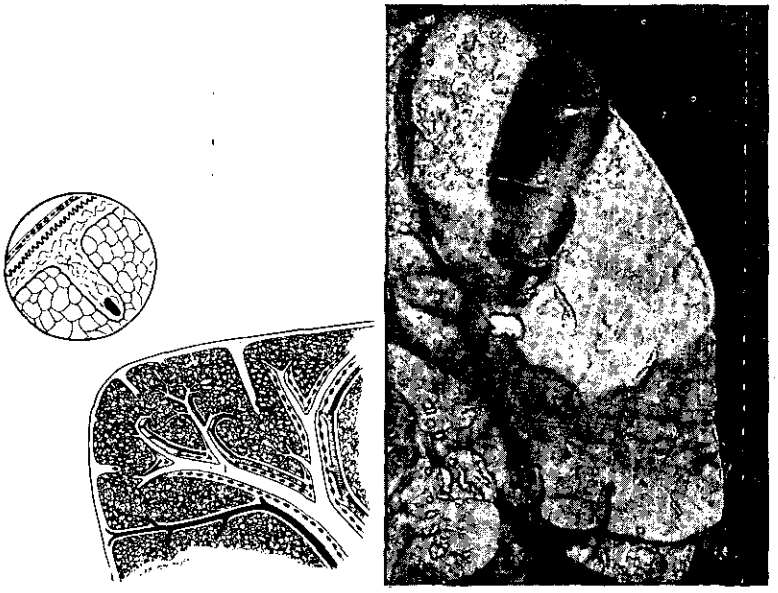
At about the same time a man who had been working on the construction of the Clyde Tunnel was found dead shortly after being decompressed at the end of a shift in compressed air. A radiograph of his chest taken just before starting the post-mortem examination revealed a cyst on the mediastinal aspect of the right lung.

These experiences led me to postulate that perhaps if for some reason air trapping occurred in the chest whilst the subject was at pressure, and I had in mind the blocking of a bronchus by a mucosal plug or oedema, then any subsequent decompression of the individual might result in the trapped high-pressure air expanding to cause cyst formation with lung damage and the possible introduction of air into the circulation. The volume of air introduced into the circulation would not necessarily have to be very large to cause major bubbling because, if the blood in some parts of the circulation was supersaturated with gas, then seeding it with quite small bubbles could release this dissolved gas and lead to their very rapid expansion.

In order to see if such a mechanism could account for the clinical conditions which had been observed, some animal experiments using guinea pigs were devised (Walder, 1963). Anaesthetized guinea pigs were exposed to compressed air and lead shot dropped down their tracheae in an effort to bring about bronchial blockage. The guinea pigs were then decompressed to see if cyst formation would occur behind the blocked bronchus. In fact no cysts developed and the guinea pigs did not suffer from Type II decompression sickness or bubbles in the circulation.

A second series of experiments was then carried out in which a bronchospasm was induced with histamine in guinea pigs exposed to compressed air. In these experiments subsequent decompression did result in the appearance of bubbles in the circulation and many of the animals so treated died. Air had been trapped behind the bronchioles in spasm and somehow this air had found its way into the circulation to result in the death of many of the animals. Even short exposures to 15 p.s.i.g. for 5 mins. could result in air passing from the lungs to the pulmonary veins when bronchospasm had been induced.

This was interesting but it was not creating exactly the conditions which had been seen in man, since no cyst-like structures developed in the guinea pig lung. It was therefore decided to compare the structure of guinea pig lung with that of man in order to see if this could account in some way for the different behaviour of human lung in the presence of trapped air compared with guinea pig lung. It soon became obvious that certain anatomical differences exist between the lungs of man and guinea pigs. An important difference in the present context seems to be that in man the visceral pleura is applied loosely to the outer alveoli and every few centimetres inter-alveolar septa dip down from the visceral pleura between the



(*a*) (*b*)

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Fig. 7. (*a*) Inter-alveolar septa in human lung. Note pulmonary vein radicle at base of septa. (*b*) Formation of an air-containing bleb due to splitting along the inter-alveolar septa when the pressure in the bronchus rises to 1.5 p.s.i.g. (75 mm. Hg) (pig).

alveoli; the outer alveoli are covered by a thin, elastic lamina. The septa are filled with a loose connective tissue and at the bottom of each lies a radical of the pulmonary venous system (Fig. 7*a*).

Study of this structural pattern makes it appear possible that if a group of alveoli on one side of a septum should become distended there could well occur a differential movement along the axis of the septum to create a shearing force through the loose connective tissue so that tearing would occur and almost certainly involve alveoli walls at the point where they are least well supported.

It was found that pig lung has a similar structure to that of man. Experiments with post-mortem human lungs and with pig lungs have enabled this hypothesis for the mechanism by which trapped air could enter the circulation to be confirmed.

Figure 7*b* shows a pig lung in which one bronchus has been intubated so that one area of lung alveoli can be distended preferentially. When the intra-alveolar pressure is 1.5 p.s.i.g. (77 mm. Hg) greater than that of the adjacent area, shearing occurs down the line of the limiting inter-alveolar septum and the surface of the distended alveoli split to admit air into the loose connective tissue layers of the septum. This air then tracks under the visceral pleura, which is raised up in the form of a bleb. Increasing the pressure in the distended alveoli to 2 p.s.i.g. (100 mm. Hg) leads to the development of a hemispherical bleb. When the roof of this bleb is removed, the underlying alveoli are found to have been compressed to form a saucer-shaped depression so that the whole bleb in cross section is circular, and radiographically looks identical to the cysts seen in the patients described above. Of great significance is the fact that examination of the floor of the bleb reveals that the initiating tear in the inter-alveolar septa involves the pulmonary vein radicle, so that a pathway is created for the high-pressure air in the bleb to pass into the pulmonary venous circulation. It therefore appears possible that high-pressure air trapped in one region of the lung could in fact on decompression be forced into the circulation, thus inoculating the circulation with a gas phase to initiate bubbling wherever a state of gas supersaturation exists. This would be Type II decompression sickness. If the volume of air introduced was itself sufficiently great to interfere with the circulation without the release of any gas in solution, then the condition would correctly speaking be one of air embolism.

CAISSON DISEASE OF BONE

As has already been mentioned, caisson disease of bone is a late manifestation which may follow work in compressed air. This condition consists of an aseptic necrosis of the bone most commonly occurring in the proximal end of the humerus, the proximal or distal ends of the femur, or in the proximal end of the tibia some three months to ten years after exposure to compressed air. Symptoms are present only if the patch of necrotic bone is so situated that it results in the collapse of an articular surface with consequent distortion of the overlying articular cartilage. Once collapse has occurred, secondary osteo-arthritic changes almost invariably supervene in the joint. Characteristically in caisson disease of bone, the articular cartilage remains healthy and of normal thickness so that the joint space as seen on radiographic examination is often unnarrowed, even in the late stages when osteo-arthritic changes have supervened. Unfortunately, caisson disease of bone is frequently bilateral and, when it affects the hip joints, can cause severe disability in an otherwise fit and strong, heavy manual labourer (Fig. 8).

Shaft lesions (Fig. 9*a*) are also seen, but as these are unlikely ever to give rise to symptoms they are not of great significance to the compressed air workers. Until recently, no true assessment of the prevalence of this condition has been made, partly due to the difficulty in studying compressed air workers caused by their itinerant habits and partly due to the fact that not all cases of aseptic necrosis of bone due to work in compressed air are recognized as such, particularly when the radiographic picture is dominated by the secondary osteo-arthritis.

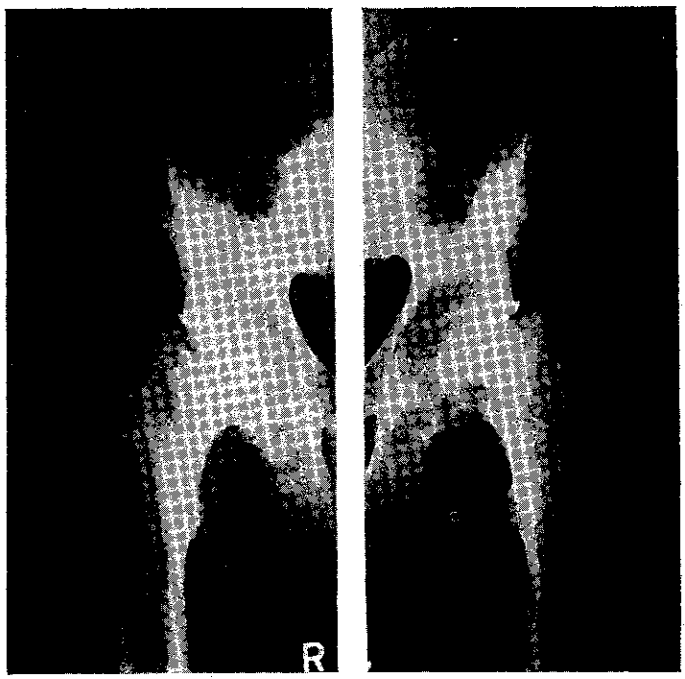
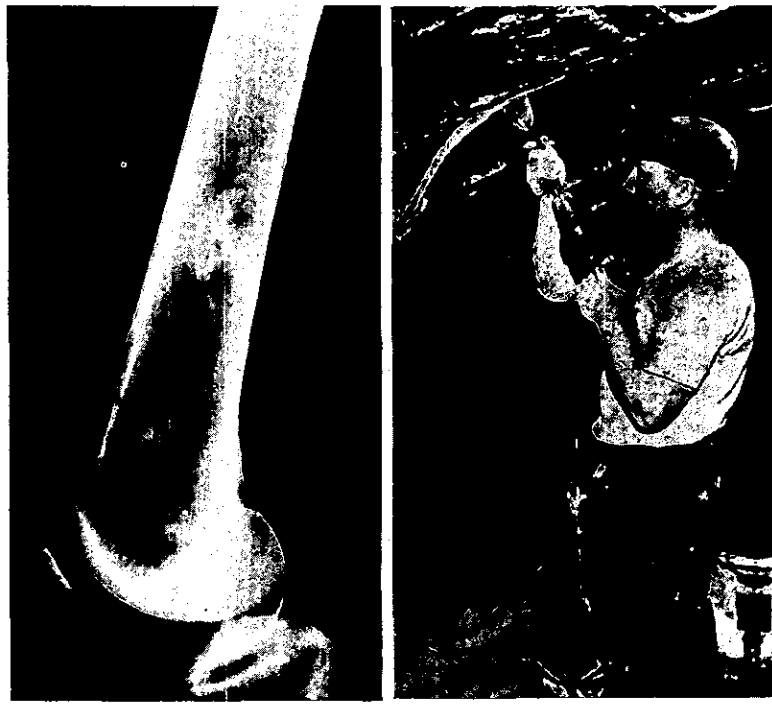


Fig. 8. Bilateral caisson disease of the hips with secondary osteo-arthritic changes.

A study of the compressed-air workers remaining at the end of the Clyde Tunnel contract in 1963 has revealed a much higher incidence than was hitherto suspected. As many as 10 per cent of compressed-air workers probably suffer from a disabling bone lesion despite taking all the precautions at present prescribed for this form of work. The mechanism by which these lesions are caused is not fully understood, so that what additional precautions should be taken to avoid this hazard are not known. The present position with regard to bone lesions in compressed-air workers is discussed in detail by McCallum and Walder with others (in the press).

THE RISKS OF WORKING IN AN HYPERBARIC CHAMBER

Can the risks to which compressed-air workers are exposed really be compared with those to which a doctor or surgeon is exposed in an hyperbaric oxygen chamber? At first sight, there are some obvious differences in the circumstances under which the two groups work. For instance, under-river tunnels are often very wet and sometimes men may have to work standing in several inches of water. The relative humidity is often



(*a*) (*b*)

Fig. 9. (*a*) Caisson disease of bone—shaft lesion. (*b*) Caulking.

as high as 98 per cent, conditions which will not occur in hyperbaric chambers. In fact, however, it can be shown that dampness does not significantly influence the bends rate. It seems to matter little whether the environment is wet or dry.

Another possible factor which might be expected to influence the incidence of bends is the nature of the job which the man performs. For instance, working in a cramped position, as when digging in the compartment of a shield (Fig. 10), might be expected to give rise to more bends than working in an upright position. Tightening up nuts and bolts of the tunnel segments with enormous spanners or caulking (Fig. 9*b*) might

be expected to make the shoulders of such men more vulnerable to attacks of bends than their knees or hips, but it transpires that the job a man performs has little influence on the likelihood of his getting the bends.

NITROGEN NARCOSIS

Finally, mention must be made of yet another hazard which has nothing to do with decompression but which might be of considerable importance to surgeons operating in high-pressure air environments. I refer to nitrogen narcosis, a condition which is well known to divers and familiarly

Fig. 10. Working in a compartment of the shield.

called the " narks ". It is thought to be due to the effect of high partial pressure of nitrogen on the brain and results in a progressive narcosis. It has not in the past been considered as a risk at the pressures normally experienced by compressed-air workers. Recently, however, because of the suggestion that some tunnelling engineers were making silly mistakes when carrying out mathematical calculations in compressed air instead of waiting until they were in free air, the possibility that nitrogen narcotic effects might operate even at air pressures of 3 Atmospheres Absolute and below has been investigated by Poulton *et al.* (1964) under the auspices of the Medical Research Council's Panel on Decompression Sickness. Groups of men were tested for their efficiency at card sorting using the Himalayan Card Sorter.

In this technique, each man is given two shuffled packs of cards. These he places one at a time according to suit into the appropriate slot of a box having four slots in its lid. The time interval between correctly placing one card and the next is electronically recorded and the time intervals between each selection is subsequently analysed using a computer.

Each man was tested twice, once at atmospheric pressure and once at $3\frac{1}{2}$, $2\frac{1}{2}$ or 2 Atmospheres Absolute pressure. An additional group of men sorted cards twice at atmospheric pressure. When the task was carried out for the first time, all the groups of men performing at raised pressure were found to yield a reliably greater proportion of very slow responses than the group of men performing at normal pressure. However, when the task was carried out for a second time at $3\frac{1}{2}$ Atmospheres Absolute pressure, no reliable effect was shown. Thus exposure to compressed air affected performance only while the task was being learned. Age, length of experience in compressed air and the duration of the exposure to compressed air, which was never less than 10 minutes, did not influence the effect.

The practical implications of these findings are clear. Whenever a skill involving complex mental operations is undertaken after some time of exposure to compressed air at 2 Atmospheres Absolute or greater, it cannot necessarily be assumed that it will be carried out as adequately as at normal pressure. This applies particularly if a new, unrehearsed situation arises.

ELIMINATION OF THE HAZARDS

Unfortunately, we do not know at present any way in which the dangers of working in compressed air can be completely eliminated. The extent of the hazard to hyperbaric oxygen chamber personnel will no doubt become clear as experience in this field increases.

It does, however, seem reasonable to assume, in view of the experience relating to the serious Type II decompression sickness and the related experimental findings, that personnel with lung abnormalities should be excluded from this type of work and that any tendency to suffer from bronchospasm should be considered as an absolute bar to working in compressed air.

As far as Type I decompression sickness is concerned, an attack of bends may be related to the subsequent development of a bone lesion, but the relationship is not clear, nor is it possible to make any suggestions at the moment as to how bone lesions might be avoided. There is no doubt that the tendency to suffer from bends is greater over the age of 40 years and is greater in obese individuals than in thin ones.

Breathing oxygen before and during decompression, by speeding the elimination of nitrogen from the tissues, should diminish the risk of suffering from bends. As far as civil engineering work is concerned, oxygen

breathing does not commend itself as a solution to the decompression sickness problem because of the concomitant risk of fire and explosion, but perhaps in medical therapeutic chambers safety discipline could be maintained at a sufficiently high level to offset the added risk.

A Medical Research Council Central Compressed Air Registry has recently been established in the University of Newcastle-upon-Tyne with the specific object of obtaining more information about the dangers of working in compressed air so that the steps which should be taken to eliminate the hazards can be defined.

CONCLUSION

Those who are about to enter or who have already entered the hyperbaric oxygen therapy field may find this lecture discouraging. This is not my object. I merely wish to emphasize that there are several possible dangers associated with working in compressed air and these must not be ignored. Forewarned is forearmed.

ACKNOWLEDGEMENTS

I would like to acknowledge the support which I have received over the years from the Medical Research Council and the members of its Decompression Sickness Panel in carrying out some of the studies which are reported here.

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AN OBJECTIVE APPRAISAL OF THE BLACKPOOL (U.K.) AND WASHINGTON STATE (U.S.A.) DECOMPRESSION TABLES

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The difficulty of assessing the relative merits of decompression tables stems from the fact that the incidence of decompression sickness at any contract depends not only on the decompression tables in use but also on several other factors, some of which indirectly affect the way in which the tables are used. Such factors as the reliability of the data and the selection, acclimatisation, length of shift and working pressure of the men have been previously discussed (Walder, '67). So complex is the problem that perhaps the bone lesion rate might be a more reliable and in most circumstances a more important parameter than the reported bends rate.

Since it is unlikely that any two contracts using different decompression tables will ever be sufficiently similar for these other factors to be discounted, one way of overcoming some of the difficulties is to match one contract with another for pressures and durations of exposures worked, the two most important factors in influencing the decompression sickness rate.

Both in Great Britain and the United States new decompression tables for compressed air workers have been introduced over the last few years. On one side of the Atlantic, Duffner's Washington State Tables were first officially introduced in 1963. They have now been used in contracts at the Lake City Tunnel Seattle, the BART Project, San Francisco and are currently being used on a contract at Milwaukee (in all, 48,665 man decompressions). On the other side of the Atlantic, Hempleman's Blackpool tables were introduced in 1966 and were first used on a number of small contracts and then on a major contract from 1966–1968. This contract was concerned with the construction of water cooling ducts

under the sea in connection with a nuclear power station known as Dungeness B (in all 36,121 man decompressions). The data for the whole Dungeness B Contract is now available so that it is possible to compare a large contract where the Blackpool Tables were used with the three major American contracts carried out with the *Washington State Tables*.

There is one important difference between the ways in which the Washington State Tables and the Blackpool Tables are used. With the former the work period is reduced as the working pressure increases so that the total time for work plus time taken to decompress approximates to a total of 8 hours (Seattle Conference, '62). On the other hand the Blackpool Tables are used at all pressures for an 8 hr shift (i.e. 8 hr of work) which is then followed by the necessary period for decompression. In Table 1 the maximum limits of exposure time for work with the Washington State Tables at Seattle, San Francisco and Milwaukee are indicated.

TABLE 1: Limitations of Exposure Time when using the Washington State Tables

Pressure (p.s.i.g.)	Work Period (hr)
< 18	8
18 – 23	7
23 – 29	6
29 – 37	5
37 – 48	4
48 <	3

Decompression Sickness

Figures 1, 2 and 3 show for each pressure range

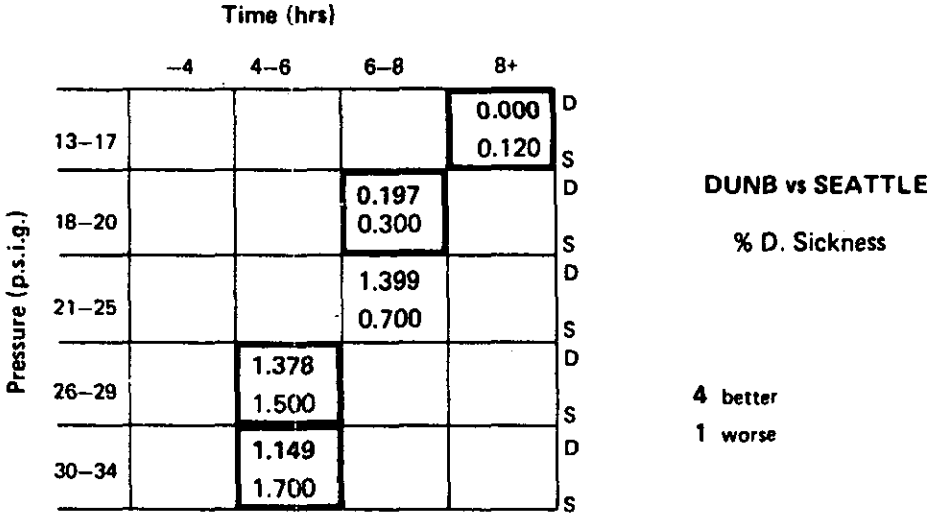
1) in the case of the Dungeness B Contract the percentage of man decompressions following the exposure time range shown at the head of the column which resulted in decompression sickness.

2) In the cases of Seattle, San Francisco and Milwaukee the percentage of man decompressions following all exposure time ranges up to and including the range shown at the head of the column.

Thus for the Dungeness B contract the worst case has been presented since there is no possibility that the percentage of decompression sickness has been diminished by the inclusion of man decompressions from exposures of lesser durations than those indicated.

From Figure 1 it can be seen that the decompression sickness incidence at Dungeness B was better than at Seattle except in the pressure range 21–25 p.s.i.g.

FIG 1: Percentage prevalence of decompression sickness for various ranges of pressure and time of exposure. In each square the upper figure (D) refers to Dungeness B (only includes results for the exposure range indicated) and the lower figure(S) to Seattle (includes results for exposure up to and including the range indicated).



When similar comparisons are made between Dungeness B and San Francisco it can be seen that the use of the Blackpool Tables gave a lower incidence of decompression sickness in all five ranges of pressure (fig. 2).

The proportion of exposures followed by decompression sickness at Dungeness B was less than that at Milwaukee in two ranges of pressure 26–30 p.s.i.g. and 31–35 p.s.i.g. (fig. 3).

It seems then that the Blackpool Tables are at least better in some time and pressure ranges than the Washington State Tables in preventing decompression sickness.

Another method of comparison has been to plot separately for the Dungeness B Contract (Blackpool Tables) and for the three U.S.A. Contracts together (Washington State Tables) the percentage of total man decompressions (that is decompressions from all durations of exposure) resulting in decompression sickness at each pressure. (fig. 4).

From these points a least squares regression line was drawn for the data for each Decompression Table. To make the correlation as fair as possible the points were assumed to occur with the same frequency as the actual number of exposures that they represent, so that the weight of even

FIG 2: Percentage prevalence of decompression sickness for various ranges of pressure and time of exposure. In each square the upper figure (D) refers to Dungeness B (only includes results for the exposure range indicated) and the lower figure (SF) to San Francisco (includes results for exposure up to and including the range indicated).

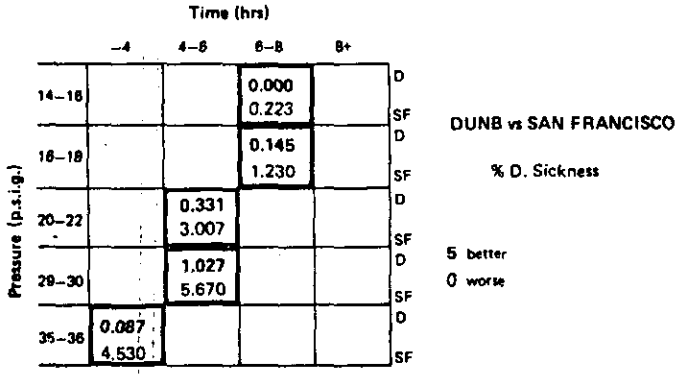


FIG 3: Percentage prevalence of decompression sickness for various ranges of pressure and time of exposure. In each square the upper figure (D) refers to Dungeness B (only includes results for the exposure range indicated) and the lower figure (M) to Milwaukee (includes results for exposure up to and including the range indicated).

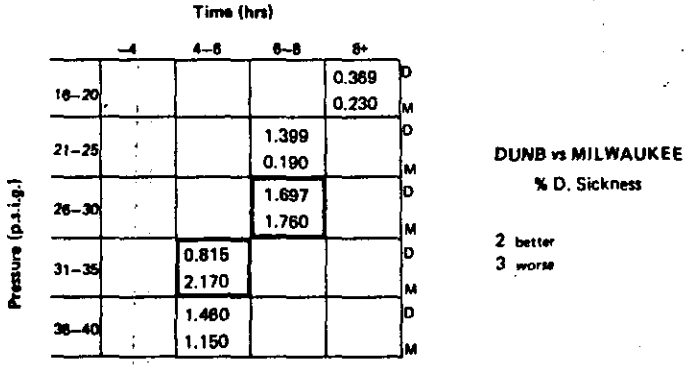
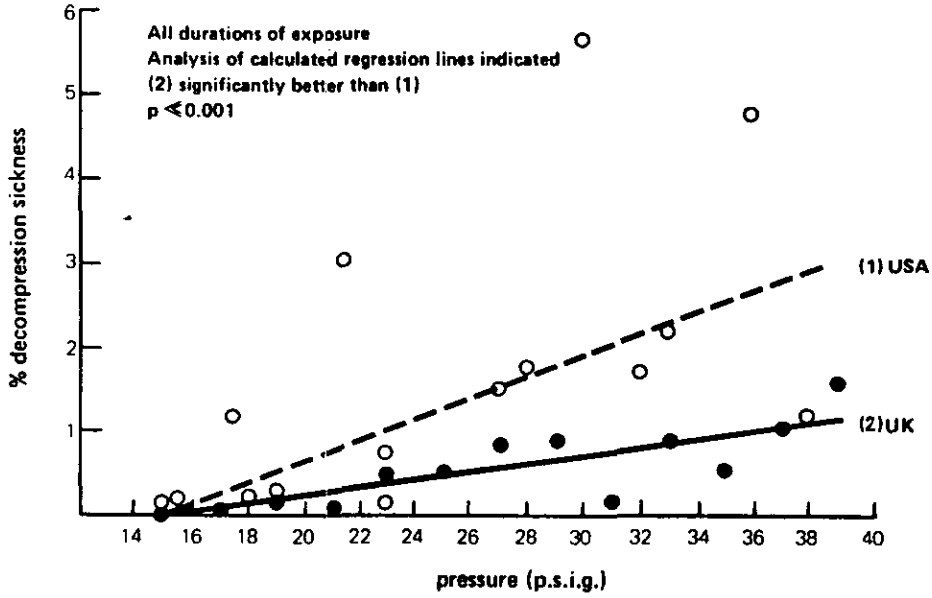


FIG 4:

COMPARISON OF THE BLACKPOOL (UK) AND WASHINGTON STATE (USA) DECOMPRESSION TABLES



the lightest point is still quite considerable as it represents 326 exposures (the heaviest point represents 13,000 exposures). Throughout pressure was assumed to be the independent variable.

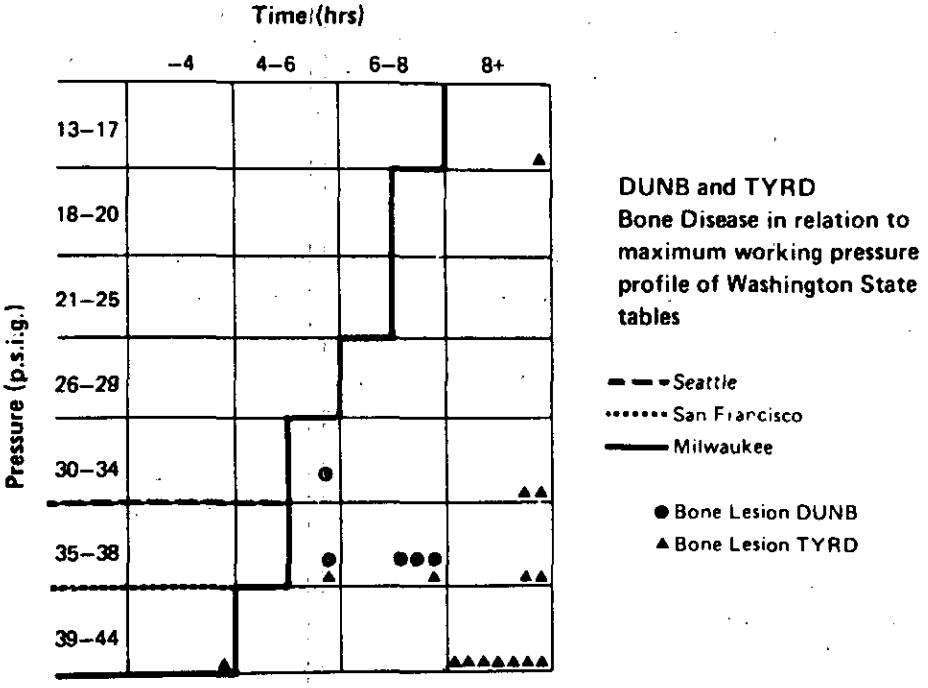
In addition to the lines themselves the correlation coefficients and the standard deviation of the slopes were calculated. From these, it was possible to determine the statistical significance, if any, of the difference between the slopes of the lines representing the results for the two decompression tables. To try to improve the accuracy further the information throughout was grouped for increments of pressures of 2 lbs and all the calculations were repeated. In all cases improved correlations were obtained.

It is seen from the graph that the results from the Blackpool Tables, as used at the Dungeness B Contract, are again better than those from the Washington State Tables. The regression lines differ to a high degree of statistical significance ($t = 173$ $p \ll 0.001$).

Bone Lesions

In Figure 5 the men who have worked only with the Blackpool Tables (Dungeness B) and who have developed definite bone lesions are shown in relation to their compressed air experience (in terms of pressures and durations of exposures worked). It can be seen that the experience of all these men has extended beyond the allowable ranges of the Washington

FIG 5: Men with bone lesions attributable to working at Dungeness B and those with bone lesions attributable to working on the Tyne Road Tunnel shown on a matrix which indicates the limiting profile for the use of the Washington State Tables.



State Tables. In addition the men who have worked only with the British 1958 *Table (Tyne Road Tunnel) and who have developed definite bone* lesions are similarly shown. It can be seen that with one exception their experience also extended outside the range of the Washington State Tables.

Therefore it may be concluded that if the Blackpool Tables had been used instead of the Washington State Tables at Seattle, San Francisco and Milwaukee only one definite bone lesion would have occurred. It is claimed that so far no definite bone lesions have been detected as a result of using the Washington State Tables (Koch and Nishi, '72). Since one bone lesion is not statistically different from no bone lesions when considering the total number of exposures involved, it would appear that in so far as preventing bone necrosis is concerned over the domain tested, it is not possible to say whether the Washington State Tables are better or worse than the British Blackpool Tables.

The point must be made that because some sections of a decompression table are satisfactory in avoiding decompression sickness or bone necrosis it does not mean that the whole table is sound. Only proper testing with detailed documentation will give a true assessment.

The comparisons made between the U.K. Blackpool Tables and the

U.S.A. Washington State Tables in this paper are unnecessarily complex because of the non-uniform way in which the data for the Washington State Tables has become available.

One of the advantages of centralizing and unifying the system of data collection as has been done by the M.R.C. Decompression Sickness Panel with the assistance of the Construction Industry Research and Information Association in the United Kingdom is that it enables these detailed and very important comparisons to be made between all aspects of different contracts.

ACKNOWLEDGEMENTS

Thanks for financial help are due to the Medical Research Council and to the Construction Industry Research and Information Association. Messrs. V.B. Thickett and P. Trowbridge have given invaluable assistance in the preparation of this paper.

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CHRONIC CO_2 TOXICITY

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2

CHRONIC CO_2 TOXICITY

K. E. SCHAEFER

Prolonged exposure to elevated levels of CO_2 in ambient air has been a cardinal problem in submarine medicine and is of concern to longer operations in other closed environments, e.g., shelters, aircraft, and spacecraft. It also plays a role in certain industries, such as meat packing and breweries, where people are exposed to elevated CO_2 concentrations during the 8-h working day.

The first significant contribution to chronic CO_2 toxicity in man was a study from a U.S. Navy laboratory. Under the direction of one of the pioneers in underwater medicine, A. R. Behnke, Consolazio et al. (1947), working at the Naval Medical Research Institute in Bethesda, Maryland, reported that human subjects could tolerate up to 5% CO_2 and 12 to 13% O_2 for 72 h. Twenty percent of the men complained about headaches and occasional nausea. Some impairment in specific motor performance was noted. The conclusion drawn from this experiment was that despite crew discomfort, the saftey of a submarine need not be jeopardized as a result of exposure to 5% CO_2 and 12 to 13% O_2. The purpose of these investigations was to determine the emergency limits for increased CO_2 and lowered oxygen simulating submarine conditions.

A summary of chronic CO_2 toxicity studies carried out during World War II on German submarines, published by Schaefer (1951), demonstrated a variety of impairing effects of prolonged exposure to approximately 3% CO_2 on respiration, metabolism, circulation, heat exchange, and performance. Schulte (1964) evaluated the experiences on U.S. Navy submarines and stated that exposure to 2% CO_2 resulted in dyspnea and headaches on mild exertion after several hours. A large-scale, systematic study on 21 subjects exposed to 1.5% CO_2 for 42 d was carried out at the Naval Medical Research Laboratory in New London. Significant adaptive changes in acid-base balance (Schaefer et al., 1964) and calcium-phosphorus metabolism (Schaefer et al., 1963) were found.

Exposure to relatively low CO_2 concentrations (submarine studies) causes renal responses quite different from those of exposure to higher CO_2 concentrations, such as are used in the clinically-oriented studies of Schwartz and his coworkers. The periods required to reach maximal compensation of pH were 24 d in the former and about 5 d in the latter (Schwartz et al., 1964; van Ypersele et al., 1966). Schaefer (1979) presented a summary of available data in the literature on the times to reach maximal compensation of pH, including data of Clark, Sinclair, and Welch (1971) on 3% CO_2 and Guillerm and Radziszewski (1979) on 2% CO_2. The graph shows a systematic difference in the response to levels of CO_2 of 3% and above, compared with that of lower CO_2 concentrations. In the former conditions, the renal regulation (bicarbonate reabsorption) is fully active, while in the latter it becomes less effective. Bone buffering, which has a slow time constant, seems to become the dominant factor.

Recent animal studies on phasic changes in bone CO_2 fractions and calcium and phosphorus metabolism (Schaefer et al., 1980) provide confirmatory evidence for this suggestion. Moreover, exposure to 1% CO_2 caused kidney calcification (Schaefer et al., 1979).

A classical study of the effects of exposure to 15 mm Hg PCO_2 (2% CO_2) on the maximal work capacity in man was carried out by Luft, Finkelstein, and Elliott (1974). Two percent CO_2 (15 mm Hg $P_{I_{CO_2}}$) is the highest acceptable level of ambient CO_2 for emergencies in spacecraft. Respiratory gas exchange acid-base balance and electrolytes were measured during and after maximal exercise. The authors demonstrated significant impairment of the individual's maximal exercise capacity because inhalation of CO_2 impeded respiratory discharge of CO_2. Metabolic acidosis generated by anaerobic processes in muscles during exercise can no longer be attenuated by respiration, and the endpoint is precipitated by a critical rise in hydrogen ion concentration. Sinclair, Clark, and Welch (1971) also found a reduced CO_2 output in exercise during acute and chronic exposure to 3% CO_2 (21 mm Hg).

A significant part of the studies listed in this collection of important papers on chronic hypercapnia provided the basis for U.S. Navy standards for nuclear submarines, consisting of three exposure-level limits: (1) 1 h emergency level—19 mm Hg (2.5% CO_2); (2) 24 h continuous exposure level—7.6 mm Hg (1%); (3) 90 d continuous exposure—3.8 mm Hg (0.5%). The 1971 *Documentation of the Threshold Limit Values* of the American Conference of Governmental Industrial Hygienists lists 0.5% CO_2 for an 8 h work day, referring to some of the papers cited in this report.

CHRONIC CO_2 TOXICITY

K. E. SCHAEFER

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Clark J. M., Sinclair R. D.; Welch B. E.: Rate of acclimatization to chronic hypercapnia in man, in Lambertsen CJ (ed): *Underwater Physiology. Proceedings of the Fourth Symposium on Underwater Physiology*. New York, Academic Press, 1971, pp 399–408. Copyright 1971, Academic Press.

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RATE OF ACCLIMATIZATION TO CHRONIC HYPERCAPNIA IN MAN

J. M. Clark, R. D. Sinclair, and B. E. Welch

The logistics of manned undersea and space exploration require that life-support systems be contained in sealed environments from which the CO_2 produced by cellular metabolism must be continually removed. Partial or total failure of the CO_2-removal system will expose the inhabitants of the environment to increased P_{CO_2}. Because such a failure may occur at any time, the tolerance limits in normal man to acute and chronic hypercapnia must be determined.

It is well known that prolonged exposures to elevated Pa_{CO_2} generate a process of acclimatization that greatly increases tolerance to hypercapnia (1, 3, 9, 24, 26). This acclimatization includes reduction of the ventilatory response to hypercapnia (1, 6, 10, 20, 22) and partial or complete reversal of the initial increase in $[H^+]$ in body fluids (3, 5, 9, 23–26). Determining the rate of acclimatization is of particular importance, because CO_2 accumulation in a sealed environment will probably be gradual and may therefore allow sufficient time for compensatory mechanisms to increase CO_2 tolerance effectively.

Previous Studies

Previous studies providing data on the rate of acclimatization to chronic hypercapnia are summarized in Table I (6, 10, 20, 22–24). Although there are many indices of acclimatization to hypercapnia, ventilatory response to CO_2 and maximal compensation of arterial pH were selected as the bases of comparison in the table. There is general agreement that the duration of exposure to chronic hypercapnia required to produce maximal compensation of arterial pH is about 3–5 days. The single reported exception of 23 days was based upon venous pH measurements that probably did not reflect corresponding changes in the arterial blood. However, the duration of chronic hypercapnia observed to produce a significant reduction in the ventilatory response to inspired CO_2 ranged from 13 hr to 40 days. In the latter case, the ventilatory response to CO_2 was not specifically tested until after 40 days of exposure, and the

TABLE I

RATE OF ACCLIMATIZATION TO CHRONIC HYPERCAPNIA

Ambient P_{CO_2} (mmHg)	Species	Index of Acclimatization		Source
		Significant reduction in ventilatory response to CO_2	Maximal compensation of arterial pH	
11	Man	40 days	23 days (venous pH)	Schaefer, Hastings, Carey, & Nichols (22)
18–21	Man	3 days	—	Habisch (10)
21	Man	3 days	3 days	Schaefer (20)
21	Man	13 hr	—	Chapin, Otis, & Rahn (6)
107	Guinea pig	—	3 days	Schaefer, McCabe, & Withers (23)
50–121	Dog	—	3–5 days	Schwartz, Brackett, & Cohen (24)

change may therefore have occurred before that time. With the exception of the study by Chapin *et al.* (6), little attention has been given to the possibility that significant respiratory acclimatization may occur within the first 24 hr of exposure to hypercapnia.

Recent Experimentation

We conducted a series of experiments to study extensively the rate of respiratory acclimatization to chronic hypercapnia in normal man. Some of the data from three of these sets of experiments will be presented here. In the first experiment, four subjects were exposed to an ambient P_{CO_2} of 30 mmHg for 11 days; in the second experiment, four different subjects were exposed to the same ambient P_{CO_2} for 5 days; and the third experiment consisted of a 30-day exposure of four additional subjects to an ambient P_{CO_2} of 21 mmHg. Each experiment was designed to obtain repeated measurements of ventilation and to obtain acid–base indices of arterial blood and lumbar cerebrospinal fluid (CSF) during hypercapnia.

EXPOSURE TO AN AMBIENT P_{CO_2} OF 30 MMHG FOR 11 DAYS

Effects of the 11-day exposure to an ambient P_{CO_2} of 30 mmHg on ventilation, $P_{a_{CO_2}}$, and CSF P_{CO_2} are shown in Fig. 1. The exposure was preceded by a 5-day control period and followed by a 5-day recovery period. Average ventilation tripled at the start of CO_2 breathing and then decreased slightly after the first day, remaining essentially constant for the rest of the exposure. After an initial elevation of about 2 mmHg, the mean $P_{a_{CO_2}}$ increased by an additional 3 mmHg during the first day of hypercapnia and was not changed after 5 and 9 days of exposure. Average valves of CSF P_{CO_2} measured after 1 and 10 days of exposure were elevated in both instances by about 6 mmHg. During the recovery period, ventilation rapidly returned to normal, and $P_{a_{CO_2}}$ was normal when it was first measured after 3–4 days of recovery.

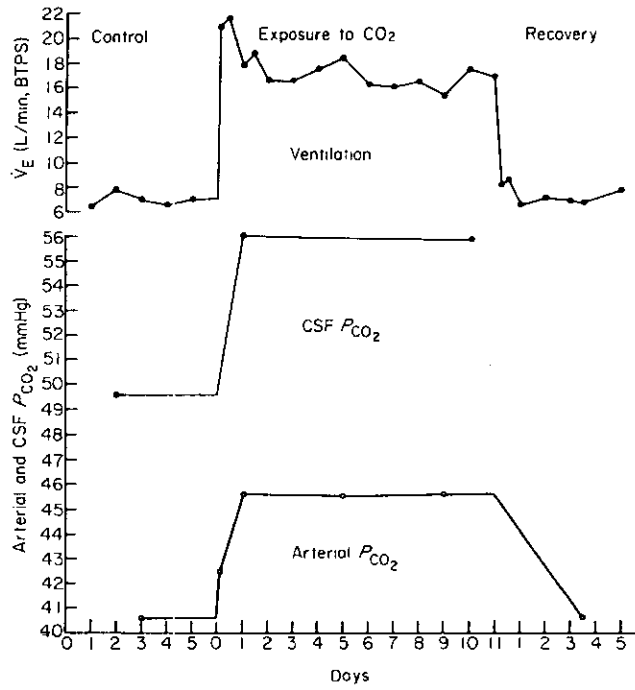

FIG. 1. Effect of an 11-day exposure to an ambient P_{CO_2} of 30 mmHg upon ventilation, Pa_{CO_2}, and CSF P_{CO_2} in man. The exposure period was preceded by a 5-day control period and was followed by a 5-day recovery period. Ambient O_2 concentration was maintained at about 19–21% throughout the experiment. Ambient P_{CO_2} was less than 2 mmHg during control and recovery periods. The data, which represent the average results of four subjects, were obtained from unpublished observations of S. J. Menn, R. D. Sinclair, J. M. Clark, and B. E. Welch.

EXPOSURE TO AN AMBIENT P_{CO_2} OF 30 MMHG FOR 5 DAYS

Because the results of the 11-day study indicated that respiratory acclimatization to hypercapnia was essentially complete after 1 day of exposure, a second experiment was designed to study more carefully the first 24 hr of hypercapnia and the first 24 hr of recovery (Fig. 2). This experiment involved a 5-day exposure to an ambient P_{CO_2} of 30 mmHg, which was preceded by a 3-day control period and followed by 2 days of recovery.

Complete data were obtained for three of the four subjects, and only these three were included in the average results. Ventilation and Pa_{CO_2} were measured simultaneously at 4-hour intervals during the first day of exposure and the first day of recovery. Average ventilation doubled at the start of CO_2 exposure and then continued to increase slightly during the first day of exposure. It decreased during the second day, and remained essentially constant for the remainder of the exposure.

Arterial P_{CO_2} increased immediately by almost 4 mmHg, reaching its maximum elevation after 20 hr of exposure. It then decreased during the next 4 hr to a level about 5 mmHg above the control value, and was unchanged after 2 and 5 days of exposure. The sustained Pa_{CO_2}

elevation of 5 mmHg agreed closely with the results of the previous 11-day exposure. Changes in average CSF P_{CO_2} appeared to parallel those in arterial blood; and CSF P_{CO_2} was only 0.5 mmHg less after 24 hr of hypercapnia than it was after 5 days of exposure. During the recovery period, ventilation returned promptly to normal. Arterial P_{CO_2} decreased initially to 2.5 mmHg above the control value, continued to decrease during the first 8 hr of recovery, increased after 16–20 hr of recovery, and finally returned to normal. After 2 days of recovery, CSF P_{CO_2} was about 1 mmHg above the control value.

Average pH and bicarbonate ($[HCO_3^-]$) data from the same experiment are summarized in Fig. 3. Arterial pH decreased immediately by 0.025 units, reached its lowest level after 20 hr of exposure, and then increased progressively until it returned to normal by the fifth day of exposure. Average CSF pH was lowest after 8 hr of exposure, and then increased by the end of exposure to a level about 0.01 units below the control value. Both arterial and CSF $[HCO_3^-]$ increased progressively in parallel fashion to reach their maximum elevations by the fifth day of exposure. During the recovery period, all parameters returned to normal with the exception of CSF pH, which was lower than the control value after 2 days of recovery; concomitantly, CSF P_{CO_2} was slightly elevated (Fig. 2).

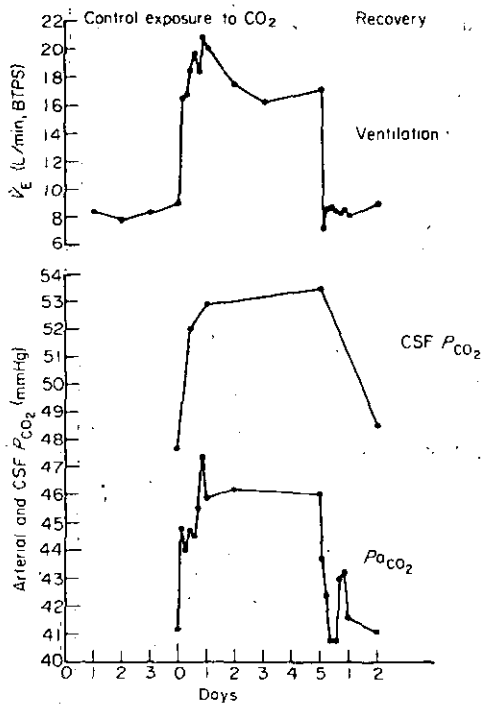

FIG. 2. Effect of a 5-day exposure to an ambient P_{CO_2} of 30 mmHg upon ventilation, Pa_{CO_2}, and CSF P_{CO_2} in man. Control data were obtained just before the start of the exposure period and on 3 previous days. The exposure period was followed by a 2-day recovery period. Ambient O_2 concentration was maintained at about 20–22% throughout the experiment. Ambient P_{CO_2} was less than 2 mmHg during control and recovery periods. The data represent the average results of three subjects.

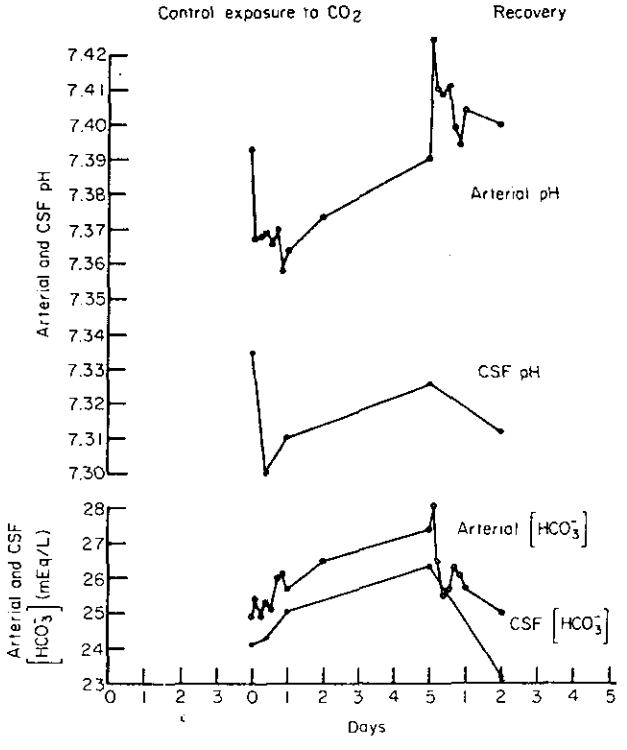

FIG. 3. Effect of a 5-day exposure to an ambient P_{CO_2} of 30 mmHg upon pH and $[HCO_3^-]$ of arterial blood and CSF in man. Data were obtained from the same experiment described in the legend for Fig. 2.

Data from the 5-day exposure showing the relationship of ventilation to arterial P_{CO_2} and pH are shown in Fig. 4. After 24 hr of exposure, the Pa_{CO_2}–ventilation response curve shifted to the right of the control curve. The curves obtained after 2 and 5 days of exposure indicate that there may have been a slight additional shift to the right along with the continued elevation of arterial and CSF $[HCO_3^-]$ (Fig. 3). After 24 hr of air breathing, the P_{CO_2}–ventilation response curve shifted back to the left to overlap the control curve and appeared to shift still further to the left after 2 days of recovery. Although the shifts in the Pa_{CO_2}–ventilation response curves appear to be small in magnitude, comparison of the ventilatory responses obtained at a constant Pa_{CO_2} shows that ventilation after 5 days of hypercapnia was about 10–12 L/min less than it was at the same Pa_{CO_2} during the exposure and recovery periods.

Schaefer (20) has reported a similar shift to the right of the PA_{CO_2}–ventilation response curve in normal men exposed to chronic hypercapnia, and Katsaros *et al.* (11) produced the same result by acute administration of $[HCO_3^-]$. The data of Katsaros *et al.* show that the shift to the right of the Pa_{CO_2}–ventilation response curve caused by acute elevation of arterial $[HCO_3^-]$ was accompanied by a shift of the arterial pH–ventilation response curve to the left toward higher pH levels. During prolonged hypercapnia, however, the initial shift of the Pa_{CO_2}–ventilation response curve to the right was accompanied by a similar shift of the pH–ventila-

tion response curve toward lower pH values. As arterial [HCO_3^-] increased, the pH–ventilation response curve moved in the direction of higher pH values to the left of the control curve. During the recovery period the pH–ventilation response curve moved to the right again, in conjunction with a decreasing arterial [HCO_3^-].

Exposure to an Ambient P_{CO_2} of 21 mmHg for 30 Days

Respiratory control data from the third experiment essentially confirm the findings in the two earlier experiments. Figure 5 shows the effects in four subjects of a 30-day exposure to an ambient P_{CO_2} of 21 mmHg on the relationship of ventilation to arterial P_{CO_2} and pH. After 24 hr of hypercapnia, the P_{aCO_2}–ventilation respones curve shifted slightly to the right of two control curves obtained at the start of CO_2 exposure and 2 days previously. The corresponding arterial pH–ventilation response curve again shifted initially to the right toward lower pH levels. After four days of hypercapnia, arterial [HCO_3^-] reached maximum elevation, and the initial decrease in arterial pH was completely compensated. At this time, the P_{aCO_2}–ventilation response curve was less than 1 mmHg to the right of the 24-hr exposure curve, whereas

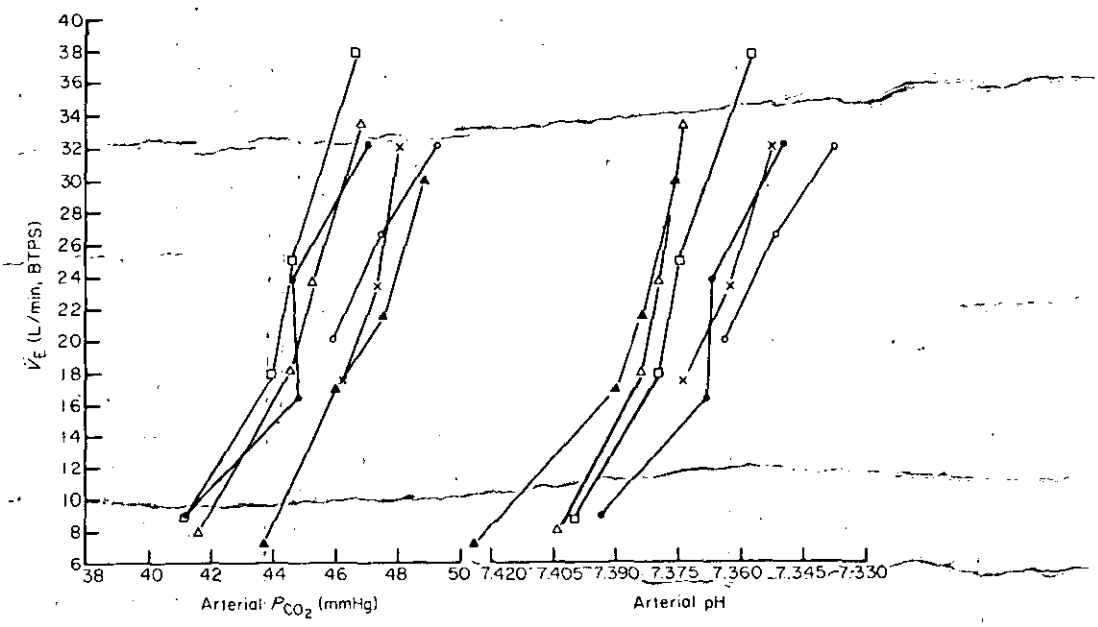

Fig. 4. Effect of a 5-day exposure to an ambient P_{CO_2} of 30 mmHg upon the relationship of ventilation to arterial P_{CO_2} and pH in man. Data were obtained from the same experiment described in the legend for Fig. 2. Measurements of ventilation, P_{aCO_2}, and arterial pH were obtained at the times indicated in the figure. In the arterial blood of normal subjects during acute administration of CO_2, the relationship of change in P_{CO_2} to change in pH has a slope of −0.0075 pH units/1.0 mmHg P_{CO_2} (14). The abscissa was drawn to the same scale in order that a change on the P_{CO_2} axis would produce an identical change on the pH axis if arterial [HCO_3^-] remained constant. (●) Start exposure; (○) 1 day exposure; (×) 2 days exposure; (▲) 5 days exposure; (△) 1 day recovery; (□) 2 days recovery.

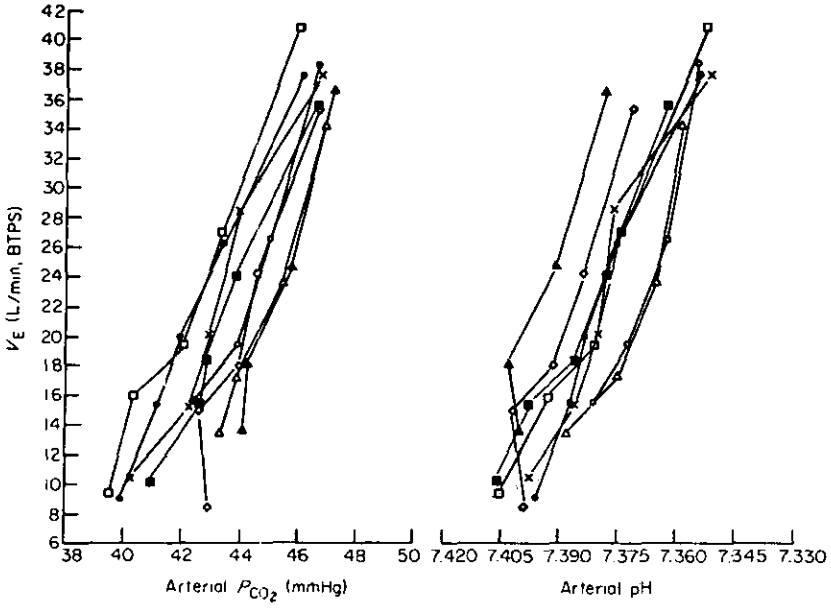

FIG. 5. Effect of a 30-day exposure to an ambient P_{CO_2} of 21 mmHg upon the relationship of ventilation to Pa_{CO_2} and pH in man. The 30-day exposure to CO_2 was preceded and followed by a 14-day period of air breathing. Measurements of ventilation, Pa_{CO_2}, and arterial pH were obtained at the times indicated in the figure. The data represent the average results of four subjects. A change in P_{CO_2} of 1 mmHg on the abscissa is equivalent to a pH change of 0.0075 units. (●) Control day 13; (×) start exposure; (○) 1 day exposure; (▲) 4 days exposure; (△) 14 days exposure; (◇) 30 days exposure; (■) 1 day recovery; (□) 4 days recovery.

the pH–ventilation response curve was shifted to the left by about 0.025 pH units. After 14 days of hypercapnia, the Pa_{CO_2}–ventilation response curve was still in the position of the 4-day curve, but the pH–ventilation response curve had shifted back to the right to become superimposed upon the 24-hr curve.

Following 30 days of hypercapnia, the Pa_{CO_2}–ventilation response curve was superimposed upon the 24-hr curve, whereas the pH–ventilation response curve was shifted to the left toward the 4-day curve. After 1 and 4 days of air breathing, the Pa_{CO_2} and pH–ventilation response curves shifted toward the control curves and became superimposed upon them. Comparing the ventilatory responses obtained at a constant Pa_{CO_2} shows that ventilation was reduced by about 8–10 L/min following acclimatization to hypercapnia.

Discussion

The data summarized in Figs. 4 and 5 indicate that the reduction of ventilatory response to CO_2 occurring during the first 24 hr of chronic hypercapnia cannot be attributed to a reduced stimulus level in respiratory chemoreceptors which are directly exposed to the $[H^+]$ of arterial blood. On the contrary, arterial pH measurements obtained after 24 hr of hypercapnia show that these chemoreceptors are exposed to $[H^+]$ at least equal to and probably

greater than the control level of acidity. Reduced ventilatory response to hypercapnia without a compensatory decrease in arterial [H^+] could be accounted for by a decreased stimulus level in the central chemoreceptors whose acid–base environment may be quickly influenced by changes in Pa_{CO_2}, but which are only slowly modified by alterations in arterial pH. The existence of such central chemoreceptor response has been demonstrated by Lambertsen *et al.* (16–18).

Comparison of the close agreement of the Pa_{CO_2}–ventilation response curves during CO_2 exposure with the much wider range of the arterial pH–ventilation response curves provides additional evidence that respiration during acclimatization to prolonged hypercapnia is predominantly controlled by central chemoreceptors which are not directly influenced by changes in arterial pH. The apparent lack of a change in the ventilatory response slope to increased Pa_{CO_2} or [H^+] does not support the concept that reactivity of the respiratory control centers is diminished during prolonged hypercapnia.

Elevations in Pa_{CO_2} were observed 16–20 hr after exposure to both an ambient P_{CO_2} of 30 mmHg and an ambient P_{CO_2} of 21 mmHg, and again after 16–20 hr of recovery in each instance. In all four cases, increased Pa_{CO_2} occurred when the subjects normally would have been sleeping. These data indicate that the decreased ventilatory response to CO_2 that occurs during sleep (4, 15) may also occur to some degree at the same time of day even when the subject is awake. Eger *et al.* (8) and Koepchen *et al.* (13) have also reported a diurnal variation in the ventilatory response to hypercapnia. Hormones—such as norepinephrine, epinephrine, ACTH, and cortisone—can all increase respiratory response to CO_2 administration (2, 7, 12, 13, 28). It is possible that diurnal variation in hormone blood levels (19, 27) may be partially responsible for the apparent diurnal variation in the ventilatory response to hypercapnia. The data summarized in Figs. 4 and 5 were obtained within a few hours after the subjects were awakened and should not therefore have been influenced by diurnal variation.

Conclusions

The results of the present studies of the rate of man's acclimatization to chronic hypercapnia agree with the findings of most previous investigators that maximal compensation for the initial decrease in arterial pH during exposure to hypercapnia requires as long as 3–5 days. However, the results of these experiments indicate that most of the reduction in ventilatory response to CO_2 occurs within the first 24 hr of exposure and, therefore, agree generally with the earlier observations of Chapin *et al.* (6). The rapid rate of respiratory acclimatization to chronic hypercapnia appears to be related to acclimatization of some central component of respiratory control that is not directly influenced by changes in arterial pH. Compensation for the initial decrease in arterial pH may cause a further reduction of ventilatory response to CO_2 that is smaller than the earlier reduction.

It should be emphasized that these preliminary conclusions are based upon data obtained from small numbers of subjects. There are obvious individual variations in both objective and subjective responses to CO_2 (14, 21), and the rate of acclimatization to hypercapnia may also vary among individuals. Furthermore, many of the changes observed in the present investigation are small in magnitude and difficult to measure by present-day techniques. More definitive information can be obtained by exposing larger numbers of subjects to higher levels of inspired P_{CO_2}, if such exposures are made safe by using suitable indices of CO_2 toxicity and if they can be subjectively tolerated.

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EFFECTS ON MAN OF HIGH CONCENTRATIONS OF CARBON DIOXIDE IN RELATION TO VARIOUS OXYGEN PRESSURES DURING EXPOSURES AS LONG AS 72 HOURS[1]

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The limits of 3% carbon dioxide and 17% oxygen in ambient air have been accepted in the American Submarine Service as compatible with efficient performance of personnel for extended periods of time. Although considerable experimental data have accumulated on the influence of carbon dioxide on respiration (1–4), the investigations, with the exception of those of Miller (5), have been limited to short-term exposures. Furthermore, other than the studies of Case and Haldane (6), little attempt has been made to correlate the changes in respiration caused by combined oxygen deficiency and carbon dioxide excess with psycho-physiological functions.

With respect to the oxygen saturation of blood, the prime consideration is not the partial pressure of oxygen in ambient air, but the much lower alveolar oxygen pressure. If the lungs could be more effectively ventilated, it should be possible to raise the alveolar oxygen pressure to levels approaching that in the ambient air. The problem is to determine the carbon dioxide concentration in the ambient air that will bring about maximal pulmonary ventilation without undue physical impairment. This will permit the alveolar oxygen pressure to approximate the partial pressure of oxygen in ambient air.

TEST PROCEDURES

General

In six experiments of 35 to 72 hours' duration, groups of 4 to 77 male subjects (age range 18 to 45 years) occupied sealed steel chambers which allowed a free air space of approximately 500 cu. ft. per man. The first experiment was an indoctrination run. In the second experiment of 52 hours' duration (4 subjects), the exhaled carbon dioxide was not absorbed and oxygen was not replenished. In the third experiment (4 subjects), carbon dioxide likewise was not absorbed but the ambient oxygen was not permitted to fall below 19%. In the fourth experiment of 72 hours' duration (4 subjects), carbon dioxide in excess of 5% was absorbed; oxygen was not replenished. In experiments 5 and 6, the carbon dioxide in excess of 5% was again absorbed; oxygen was not replenished. In experiment 5, 37 men breathed recirculated air for 60 hours and in experiment 6, 77 men were subjected to similar conditions for 50 hours.

[1] The material in this article should be construed only as the personal opinions of the writers and not as representing the opinion of the Navy Department officially.

In the first four experiments an Effective Temperature of approximately 85° was maintained to simulate hot tropical conditions with a dry bulb of 90° F. and a relative humidity of 75%. In experiment 5, the Effective Temperature averaged 75° with a dry bulb of 80° F. and a relative humidity of 65%; in experiment 6, the Effective Temperature averaged 59°, with a dry bulb of 60° F. and a relative humidity of 90%.

Biochemical, physiological and psychological measurements and observations were made. The following daily schedule was followed in the first four experiments and slight modifications were made in experiments 5 and 6.

0800–1030	psychological tests	1400–1800	test program repeated
1030–1130	physiological tests	1800–2000	dinner—rest period
1130–1200	biochemical tests	2000–2400	test program repeated
1200–1400	lunch—rest period	2400–0800	sleep period—breakfast

Biochemical

In the early experiments, blood was drawn from the brachial artery. Due to the frequency of needle insertion as well as technical difficulties, samples of 'arterialized' venous blood were drawn in the later experiments. These were obtained by immersing the hand in hot water (45°C.) for 20 minutes and with the hand still immersed, drawing blood from one of the dorsal veins of the hand (7). Blood obtained in this manner was used for gas analysis in lieu of arterial blood.

Alveolar air samples were taken according to the technic described by Dill (8). All subjects were trained for several days before the start of the experiments to insure proper sampling technic.

The plasma pH was calculated by means of the Henderson-Hasselbalch equation from data obtained from analysis of alveolar air and arterial blood or 'arterialized' venous blood (9, 10).

Physiological

The following measurements were made in the course of the experiments: pulse rate, blood pressure, body temperature, pulse rate response to exercise and respiratory rate and minute volume. The observers followed a strict routine in making all measurements in order to reduce to a minimum the variability in data usually obtained with inexperienced subjects. During a typical test procedure, the subject reclined quietly for 15 minutes, after which the pulse rate, blood pressure and body temperature were obtained. He was next allowed to assume a sitting position while the respiratory measurements were made. Finally, he engaged in light activity for the purpose of recording response to exercise.

Pulse beats were counted for 30 seconds. Blood pressure was measured by auscultation, the diastolic pressure being taken at the point of sound disappearance. Pulse pressure was computed as the difference between systolic and diastolic pressures. Body temperature was obtained with standard clinical thermometers, rectal temperatures being employed in the first four experiments,

and oral temperatures in the last two. To obtain the respiratory data in the first four experiments, expired air was collected by means of a face mask connected to a Tissot spirometer; dry gas meters were employed in experiments 5 and 6 in place of spirometers. The respiratory rate was counted for a full minute and minute volume was measured for a period of 5 minutes. Exercise response was evaluated on the basis of performance in the step-up test (11). For this test the subject stepped up and down, using the same leg, on an 18-inch box, 20 times in 30 seconds, pulse counts being made immediately after and two minutes after cessation of exercise. A 'cardiovascular score' was computed by the formula (11):

C.V.S. = (5″ to 20″ pulse count) plus (1′45″ to 2′15″ pulse count).

Psychological

Fourteen different tests were used in the psychological battery. Principles which guided the selection of tests were: that test procedures cover a wide range of functions; that tests have high enough reliability to make possible an evaluation of individual performance; and that tests be used that were known to be satisfactory as criteria of anoxia. The functions tested were:

Vision. Foveal flicker frequency was measured as one significant aspect of central photopic vision (12). The dark-adapted form-acuity threshold was measured with a T-shaped test object similar to that of the Navy radium plaque adaptometer (13).

Audition. Measures were made of the ability to discriminate differences in pitch and loudness (14), and of the absolute auditory threshold over a wide range of pitch.

Equilibrium. Ability to stand still and erect was measured by recording anterior-posterior body sway with eyes open and closed (15). Ability to maintain balance during movement was measured by requiring the subject to walk a one-inch rail without shoes (15).

Hand-arm steadiness. This was measured by the ability to keep the end of a rod in a fixed position.

Eye-hand coordination. Two tests of this function were used: the Koerth pursuit rotor, which requires a smooth continuous pattern of movement for one hand; and a complex tapping test, which requires irregular and non-symmetrical movement of both hands simultaneously (16).

Strength. A Smedley hand dynamometer was used, following a procedure that requires steadily increasing outputs of energy to the point where the subject is no longer able to improve (17).

Symbolic functions. Three paper-and-pencil tests were used: the Johnson Code Test, which requires continuous application and attention in a series of letter-for-letter translations (18); the computation test, which is a series of mixed addition and subtraction problems (18); and the number-checking test, which requires the comparison of pairs of numbers to determine whether they are alike or different (19).

Except in experiment 6 and on one test in experiment 5, all subjects had ex-

tended practice on the tests before the experiments began, in order to minimize the effect of rapid learning and irregular adaptation to test conditions. Control of motivation was not possible, but there was reason to believe that motivation was relatively high and constant. The subjects knew the purpose and nature of the research and knew approximately, if not exactly, how well they were doing on each test. There were no special rewards or inducements to good performance but a general social facilitation and normal competitive spirit developed among the subjects; i.e., morale was judged to be good.

EXPERIMENTAL DATA AND DISCUSSION

General

The cost of maintaining adequate oxygenation of hemoglobin when the ambient oxygen is as low as 12% and carbon dioxide as high as 5% is an approximate 2½-fold increase in minute breathing volume, a rise in pulse rate of approximately 10 beats per minute, some impairment in specific sensorimotor performance,

TABLE 1. *Summary of conditions to which the subjects were exposed*

EXPERIMENT NUMBER	NUMBER OF MEN	DURATION	HIGHEST CO_2	LOWEST O_2	HOUR WHEN AMBIENT CO_2 APPROACHED 5%
		hrs.	*per cent*	*per cent*	
1	4	34	5.95	14.18	29
2	4	52	6.54	13.45	34
3	4	51	6.75	19.22	37
4	4	72	5.42	10.45	32
5	37	60	5.27	12.21	34
6	77	50	5.18	13.21	34

headache affecting 20% of the personnel, and occasionally nausea. Throughout all experiments involving 130 man exposures, only three men were removed from the closed spaces. One of these men showed apprehension; another, exhaustion; and a third, a steadily increasing blood pressure. At no time were these men in a critical condition.

The period immediately following inhalation of outside air may be attended by transient dizziness and headache. Observers exposed periodically for one to two hours to the recirculated compartment air repeatedly developed headaches and experienced a transient taste and smell of ammonia upon leaving the compartment. However, the apparently complete recovery of both subjects and observers was rapid.

The data (table 1) show that the highest carbon dioxide concentration was 6.75%, the lowest oxygen concentration 10.45%. Although these concentrations were tolerated, the symptoms of headache and respiratory difficulty, especially during physical effort, sharply increased whenever the carbon dioxide rose appreciably above 5%.

Special significance is attached to experiment 3 in which the oxygen was main-

tained at a level approaching normal although the carbon dioxide was permitted to approach 7%. In this experiment it was found that measurable improvement over the performance in other experiments did not result from the added oxygen.

The remarkably consistent values of carbon dioxide output per man, of 0.326 l/min. STP (0.69 cu. ft/hour) and oxygen consumption 0.387 l/min. STP (0.82 cu. ft/hour), agree with those obtained by previous investigators in tests performed during and subsequent to the first World War.

It is noteworthy that the alveolar carbon dioxide pressure, respiratory minute volume, and pulse rate show very little change until the atmospheric carbon dioxide approaches the 3% level. Above the 3% level, these functions begin to increase rather sharply.

Biochemical Data

Ambient carbon dioxide and oxygen concentrations. In experiment 3, the carbon dioxide rose to a value of 6.75 at the end of 51 hours but the oxygen was maintained at a level of 20% ± 0.8 during this period (fig. 1). In experiment 4, carbon dioxide absorption was begun at the end of 45 hours to maintain the carbon dioxide level at 5% until the termination of the test at the end of 72 hours. Oxygen was not added and the concentration fell to 12.8% during the 56th hour where it remained for several suceeding hours (fig. 2). At this time, nitrogen was added at a constant rate to compensate for outboard leakage. In experiments 5 and 6, carbon dioxide absorption was begun during the 35th hour when the concentration reached 5% and continued for 25 and 15 additional hours, respectively (fig. 3, 4).

Comparison of values of ambient with alveolar carbon dioxide and oxygen concentrations. As a result of the increased ventilation, the oxygen percentage in the lungs during the rebreathing of air falls at a slower rate than it does in the ambient air. The difference between ambient and alveolar oxygen pressures (ΔpO_2) varies from 40 to 52 mm. Hg at the beginning of the tests and declines steadily to values ranging from 11 to 19 mm. Hg at the conclusion of the experiment (table 2, fig. 5). The difference between alveolar and ambient carbon dioxide (ΔpCO_2) diminishes similarly from about 42 mm. Hg (chamber open to outside air) to about 10 mm. Hg when the ambient carbon dioxide reaches 46 mm. Hg (exp. 2, table 2).

Effects of high carbon dioxide concentrations on plasma pH and carbon dioxide content. The plasma pH values (table 3) indicate a slight increase in acidity, 7.44 to 7.38 in one experiment and 7.40 to 7.38 in another, when the carbon dioxide of the ambient air increased from 0.03% to 5%. Plasma carbon dioxide increased from 58.6 to 59.5 vols. % in one experiment, and from 58.2 to 64.6 vols. % in another. These changes may be classified as slight and are at variance with the results obtained by Miller (5). They further illustrate the remarkable rôle played by hyperventilation in protecting the body against the accumulation of carbon dioxide in the presence of high ambient concentrations of this gas.

Oxygen concentrations in ambient and alveolar air and the corresponding equivalent altitudes. An ambient oxygen pressure of 100 mm. Hg without increased

carbon dioxide in the air is associated with an alveolar oxygen pressure of 58 mm. Hg. Corresponding values are found at simulated altitudes of 10,000 feet (20). The same ambient oxygen pressure (100 mm. Hg), however, in combination with 5% carbon dioxide in air is associated with an alveolar pressure of 86 mm. Hg. This value corresponds to a simulated altitude of but 4000 feet (fig. 6).

Effects of carbon dioxide on oxygen saturation of blood. The percentages of oxyhemoglobin in two experiments (4 and 5) when carbon dioxide in ambient

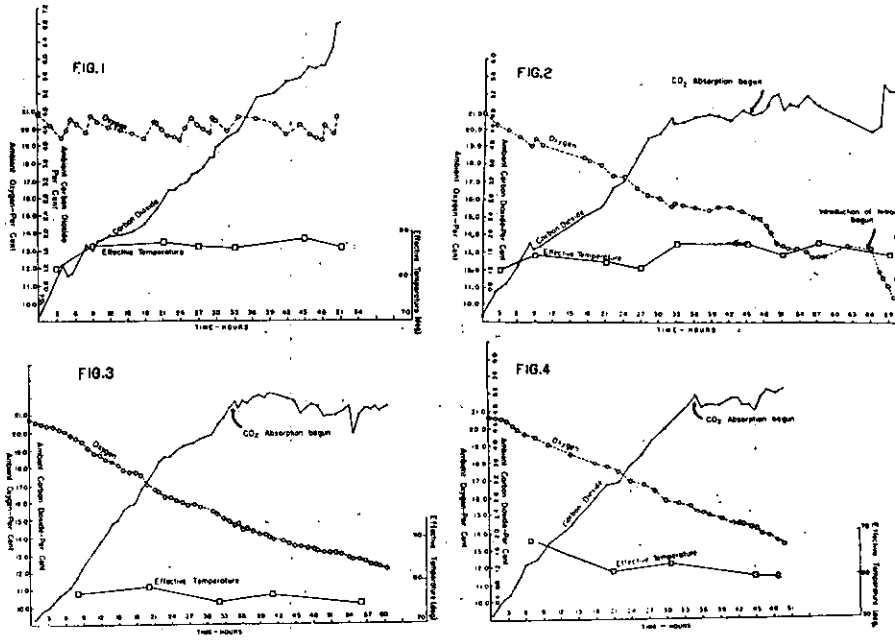


FIG. 1. Experiment 3, the rise in CO_2 maintaining constant O_2 during 52 hours recirculation of compartment air.

FIG. 2. Experiment 4, the rise in CO_2 and fall in O_2 during 72 hours recirculation of compartment air. During the 65th hour nitrogen and some carbon dioxide was introduced into the compartment.

FIG. 3. Experiment 5, the rise in CO_2 and fall in O_2 during 60 hours recirculation of compartment air.

FIG. 4. Experiment 6, the rise in CO_2 and fall in O_2 during 50 hours recirculation of compartment air.

air is 5% show considerable elevation over percentages expected in the absence of CO_2 when the oxygen pressure in inhaled air is reduced (table 3, fig. 7). These relatively high saturation values are due to the maintenance of a high alveolar oxygen pressure (table 2) resulting from hyperventilation. In association with an ambient carbon dioxide pressure of 36 mm. Hg an oxygen pressure of 72.5 mm. Hg (corresponding to that at a simulated altitude of 17,000 feet) saturates hemoglobin 87% (fig. 7). In the absence of carbon dioxide in the inhaled air, the saturation of hemoglobin would have been of the order of 76%. However,

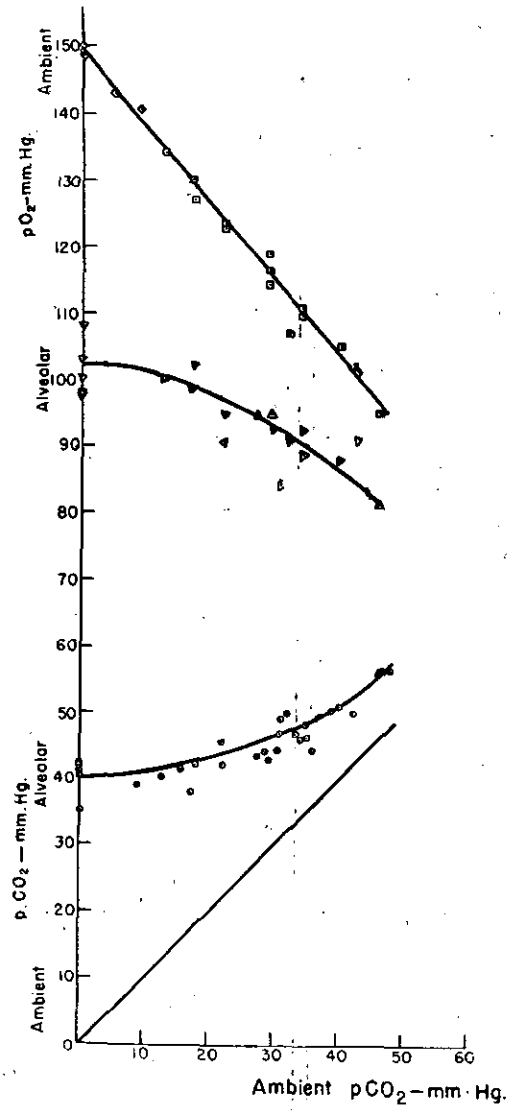
on the basis of the data submitted no further gain in alveolar oxygen or hemoglobin saturation is to be expected by increasing the ambient carbon dioxide

TABLE 2. *Effects of increased ambient carbon dioxide on alveolar air*

NUMBER EXPERIMENT	NUMBER OF SUBJECTS	DATE	HOURS OF EXPOSURE	AMBIENT AIR				ALVEOLAR AIR				ΔpCO_2[1]	ΔpO_2[1]
				CO_2	O_2	pCO_2	pO_2	CO_2	O_2	pCO_2	pO_2		
		1944		*Per cent*		*mm. Hg*		*Per cent*		*mm. Hg*		*mm. Hg*	*mm. Hg*
1	4	11 May	Rest	0.03	20.94	0.2	150.1	5.76	14.18	40.8	100.4	40.6	49.7
	4		4	1.28	19.62	9.2	140.5	5.49	14.60	39.3	103.7	30.1	36.8
	4		10	2.41	18.32	17.3	131.2	5.94	13.75	42.3	98.5	25.0	32.7
	4	12 May	23	3.84	16.63	27.5	119.1	5.81	13.28	43.5	95.0	16.0	22.1
	4		28	4.79	15.50	34.3	111.0	6.50	13.01	46.4	92.5	12.1	18.5
	4		34	5.95	14.18	42.6	101.5	7.08	12.55	50.4	89.3	7.8	12.2
2	4	17 May	Rest	0.03	20.94	0.2	150.1	5.92	14.55	41.9	103.0	41.7	47.0
	4		4	0.75	20.23	5.3	143.4	4.90	16.05	33.7	112.8	26.6	30.6
	4		10	1.79	18.97	12.6	134.4	5.74	14.20	40.4	100.0	27.8	34.4
	4	18 May	22	3.15	17.48	22.3	123.7	5.95	13.49	42.2	95.2	19.9	28.5
	4		28	4.07	16.42	28.8	116.3	6.22	13.09	44.1	92.9	15.3	23.4
	4		34	4.83	15.50	34.1	109.6	6.61	12.95	46.3	89.0	12.2	20.0
	4	19 May	46	5.66	14.52	40.0	102.8	6.93	12.39	49.3	88.2	12.3	18.4
	4		51	6.54	13.45	46.2	95.2	7.87	11.45	55.8	81.4	9.6	13.8
3	4	25 May	Rest	0.03	20.94	0.2	150.1	5.81	13.85	41.1	98.1	39.9	52.0
	4		18	2.21	19.34	15.9	138.5	5.85	14.84	41.4	105.6	25.5	32.9
	4		34	4.32	20.57	31.0	147.5	6.57	17.79	46.8	127.0	15.8	20.5
	4	26 May	42	5.41	19.54	38.8	140.0	7.10	16.86	50.7	123.7	11.9	16.3
	4		51	6.72	20.52	48.2	147.2	7.92	18.98	56.7	135.8	8.5	11.4
4	4	31 May	Rest	0.03	20.94	0.2	148.5	4.95	15.08	35.5	108.2	35.3	40.3
	4	1 June	17.5	2.47	18.13	17.4	127.5	5.39	14.50	38.0	102.2	20.6	25.3
	4		28	4.19	16.25	29.4	114.4	6.14	13.53	42.9	95.0	13.4	19.4
	4	2 June	42	4.60	15.22	32.3	106.8	6.54	13.01	46.0	91.2	13.5	15.6
	4		52	4.98	13.27	35.0	93.2	6.64	10.85	46.5	76.1	11.5	17.1
	4		58	4.78	12.45	33.6	87.3	6.54	10.73	45.9	73.5	12.3	13.8
	4	3 June	66	4.36	13.21	30.6	92.6	6.33	10.04	44.4	70.5	13.8	22.1
	4		72	5.13	10.45	36.2	73.5	6.35	8.72	44.5	60.7	8.3	12.8
5	10	13 July	Rest	0.03	20.94	0.2	148.8	5.96	13.77	42.3	97.6	42.0	51.2
	8	14 July	19	3.07	17.53	22.2	122.7	6.38	12.73	45.5	90.6	22.3	32.1
	10	15 July	31	4.32	15.50	30.7	110.0	6.98	11.91	49.6	84.4	18.9	25.6
	7	16 July	54	4.98	12.83	35.2	90.8	6.88	10.23	48.5	72.1	13.3	18.7

[1] ΔpCO_2 and ΔpO_2 are defined as the difference between ambient and alveolar pO_2 or pCO_2.

above 36 mm. Hg. An increase of carbon dioxide beyond 36 mm. Hg failed to decrease ΔpO_2 and a level is reached where the law of diminishing returns applies (fig. 6).



mm. Hg.			
Ambient Air		Alveolar Air	
pCO_2	pO_2	pCO_2	pO_2
0.2	150.1	40.8	100.4
9.2	140.5	39.3	103.7
17.3	131.20	42.3	98.5
27.5	119.1	43.5	95.0
34.3	111.0	46.4	92.5
42.6	101.5	50.4	89.3
0.2	150.1	41.9	103.0
5.3	143.4	—	—
12.6	134.3	40.4	100.0
22.3	123.7	42.2	95.2
28.8	116.3	44.1	92.9
34.1	109.6	46.3	89.0
40.0	102.8	49.3	88.3
46.2	95.2	55.8	81.4
0.2	150.1	41.1	98.1
15.9	—	41.4	—
31.0	—	46.8	—
38.8	—	50.7	—
48.2	—	56.7	—
0.2	148.5	35.5	108.2
17.4	127.5	38.0	102.2
29.4	114.4	42.9	95.0
32.3	106.8	46.0	91.2
35.0	—	46.5	—
33.6	—	45.9	—
30.6	—	44.4	—
36.2	—	44.5	—
0.2	148.8	42.3	97.6
22.2	122.7	45.5	90.6
30.7	—	49.6	—
35.2	—	48.5	—

Note: All alveolar points are averages of from 4 – 10 subjects

FIG. 5. Effects of carbon dioxide on alveolar air at various oxygen concentrations.

TABLE 3. *Effects of increased ambient carbon dioxide on gas equilibria in blood*

EXPERIMENT NO.	DATE	TIME	AMBIENT AIR		ALVEOLAR AIR		BLOOD				PLASMA	
			pCO_2	pO_2	pCO_2	pO_2	O_2 cont.	O_2 cap'y	HbO_2	CO_2 cont.	CO_2 cont.	pH
			mm. Hg		*mm. Hg*		*vol. %*	*vol. %*	*% sat.*	*vol. %*	*vol. %*	
4[1]	6/6	0830	0.2	149.0	39.2	101.3	18.68	19.63	95.3	47.8	58.6	7.44
	6/1	0800	17.4	127.5	38.0	102.2	19.79	20.85	95.0	48.4	58.9	7.45
	6/2	0800	32.3	106.8	46.0	91.2	18.71	20.22	92.6	51.2	59.9	7.38
	6/3	0800	32.4	92.6	44.3	70.5	19.24	21.27	90.5	50.2	60.4	7.40
	6/3	1400	36.0	73.5	44.6	61.2	18.16	20.33	89.3	48.9	59.5	7.38
5[2]	7/13	0830	0.2	149.0	42.4	97.3	19.94	20.34	95.5	47.9	58.2	7.40
	7/16	0700	35.2	90.8	48.5	72.1	18.44	19.93	92.5	53.3	64.6	7.38

[1] Average of 4 subjects.
[2] Average of 5 subjects.

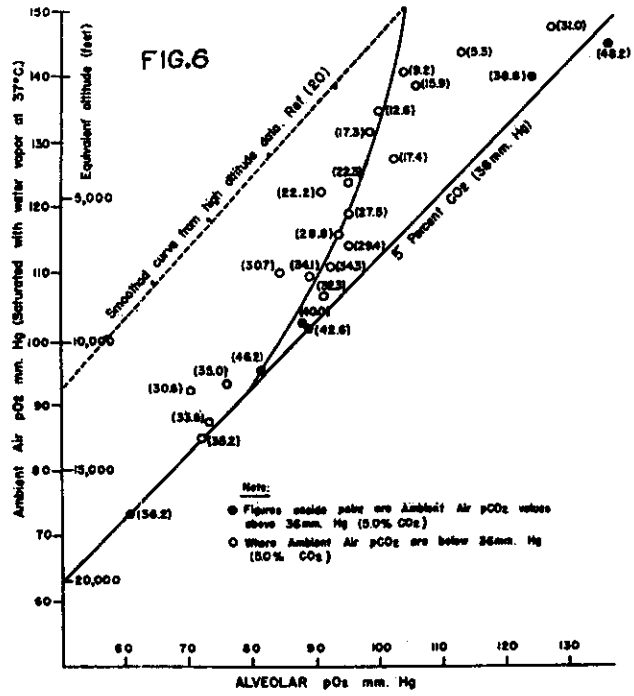


FIG. 6. Effects of carbon dioxide on oxygen pressure in alveoli at various ambient oxygen concentrations.

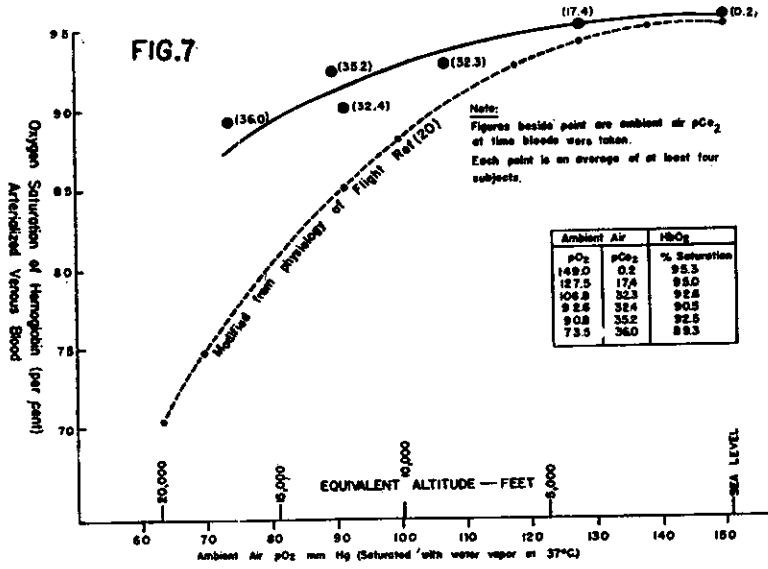


FIG. 7. Effects of carbon dioxide on oxygen saturation of hemoglobin at various ambient oxygen concentrations.

Physiological Data

High concentrations of carbon dioxide in the ambient air impose a physiological stress by raising the alveolar carbon dioxide pressure and thereby reducing the pressure gradient which is so favorable to the unloading of this gas from the

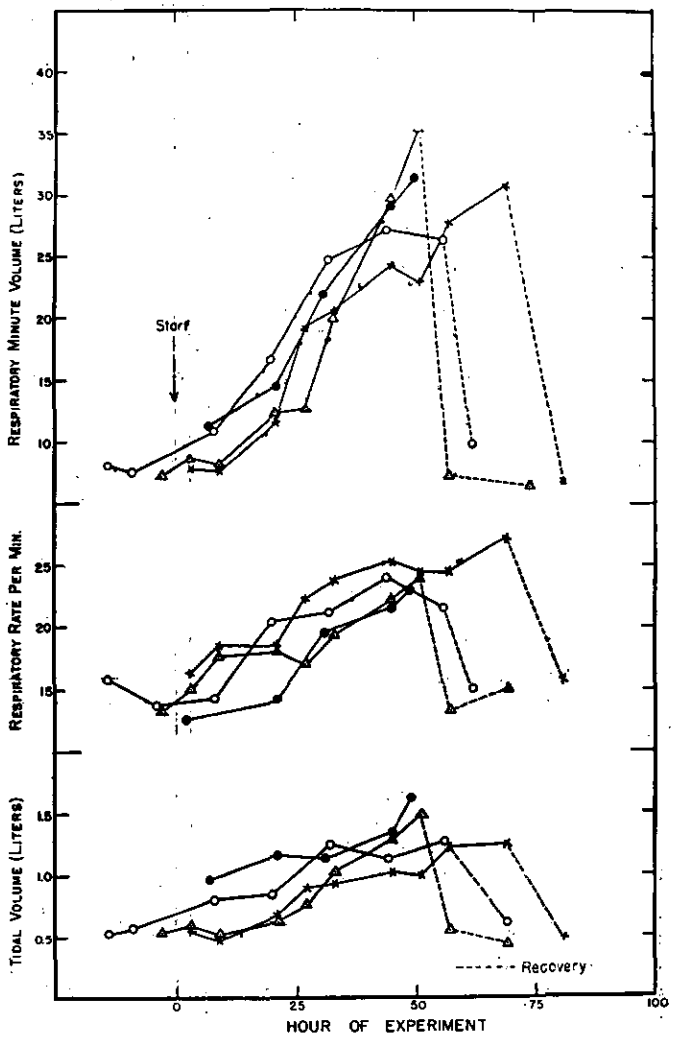


FIG. 8. Effects of carbon dioxide on mean respiration rate, tidal and minute volume. Experiment 3 = △, 4 = x, 5 = ○, and 6 = ●.

pulmonary blood. Hence with heightened alveolar carbon dioxide pressure, it can be assumed that the amount of carbon dioxide unloaded from each unit of blood passing through the alveolar capillaries is reduced. To overcome the barrier imposed by the high ambient carbon dioxide the organism responds by increasing pulse rate, respiratory rate and tidal volume. The pulse rate response

is probably indicative of an increased cardiac output which augments the rate of carbon dioxide transport from the tissues to the lungs, while the respiratory response ensures a more effective removal of carbon dioxide from the alveoli.

Respiration. The most prominent physiologic response to the altered oxygen and carbon dioxide concentrations was the change in respiration. In the course of each experiment, the respiratory rate and the tidal volume approximately doubled and the minute volume was two to three times its normal value (figure 8). It was found that an increase in normal ventilation minute volume of over 300% can be maintained for many hours without serious or persistent effects. Some subjects complained of soreness of the respiratory musculature at the end of the experiments but this symptom disappeared within one or two days.

The increase in respiratory minute volume produced by 3% carbon dioxide was of the order of one and a half times normal, compared with a two- to three-fold increase brought about by 5% carbon dioxide.

Pulse rate. A characteristic mean increase of approximately 10 beats per minute over the normal resting rate occurred when the carbon dioxide concentration reached 5% (fig. 9). That this increase was in response to the increased carbon dioxide pressure rather than to the lowered ambient oxygen pressure was proved by experiment 3, in which the rising carbon dioxide concentration was accompanied by a similar rise in pulse rate, although the oxygen concentration was maintained between 19 and 21%. Figure 9 also shows an approximate difference of 10 beats per minute at equivalent carbon dioxide concentrations between experiments 3 and 4, and 5 and 6. This difference is attributed to effect of temperature on pulse rate. Experiments 3 and 4 were carried out at Effective Temperatures of 85 and 88°, and experiments 5 and 6 at 75 and 60°, respectively (fig. 1–4). Regardless of the effect of temperature on pulse rate, a rise always accompanied an increase in carbon dioxide concentration.

Pulse rate response to exercise paralleled the increase in carbon dioxide (fig. 9). This finding, as in the case of the resting pulse rate, cannot be attributed to the decreased ambient oxygen pressure. It will be noted that in experiment 5 there was a sharp rise of about 8 points in the C. V. S. obtained two hours after the chamber was opened and ventilation with outside air started (recovery point)[2]. In other experiments the C. V. S. was not ascertained until 6 to 9 hours after exposure to outside air. It appears therefore that the exposure to outside air results in a rise in the C. V. S. (two-hour measurement) followed by a fall to pre-experimental level at the end of 6 to 9 hours. Explanation of this rise is difficult, but it can be said that the return to outside air was the most drastic change to which the subjects were exposed, and which in part is reflected by the increased pulse rate response to exercise.

Blood pressure. There were no characteristic changes in blood pressure (fig. 10). In two of the experiments, both the systolic and diastolic pressures showed a tendency to increase but pulse pressure did not change.

Body temperature. Rectal and oral temperatures require separate considera-

[2] The period of re-exposure to outside air.

tion (fig. 11). In experiments 3 and 4, involving few subjects, rectal temperatures were taken, while in experiments 5 and 6 convenience dictated the use of oral thermometers. In the control observations oral temperatures were, as has been commonly observed, roughly one-half degree lower than rectal temperatures. In experiments 3 and 4, the rectal temperatures rose within 5 to 10 hours after the

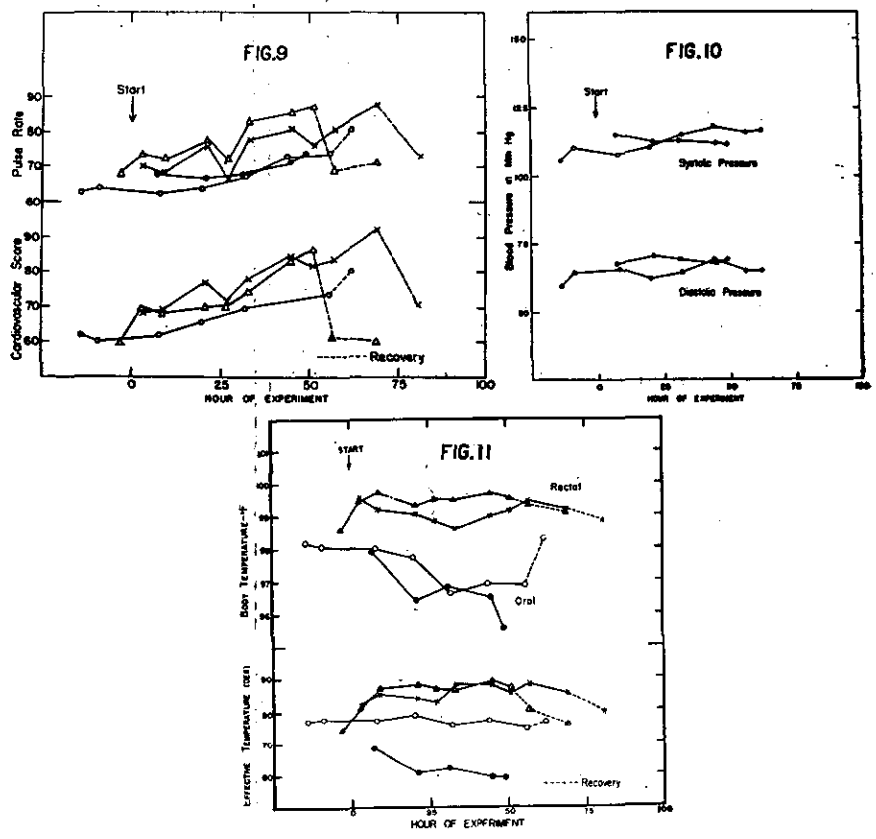


FIG. 9. Effects of carbon dioxide on mean pulse rate and cardiovascular score. Experiment 3 = △, 4 = x, 5 = ○ and 6 = ●.

FIG. 10. Effects of carbon dioxide on mean systolic and diastolic pressure. Experiment 5 = ○ and 6 = ●.

FIG. 11. Mean oral and rectal temperatures and compartment Effective Temperatures. Experiment 3 = △, 4 = x, 5 = ○ and 6 = ●.

start of an experiment to higher levels and dropped almost as rapidly at the close of an experiment. This rise is attributed to the high Effective Temperatures of the experimental chamber (88 and 85°). On the other hand, experiment 5 (Effective Temperature, 75°) and experiment 6 (Effective Temperature, 60°) imposed a heat conservation problem as indicated by the considerable decrease in oral temperature. The subjects were inadequately clothed, particularly in experiment 6, and felt cold. The fall in oral temperature may in part be due to

mouth breathing which many subjects found necessary at high ambient carbon dioxide concentrations as well as to the increased heat loss due to hyperventilation.

TABLE 4. *Subjective symptoms with respect to the subjects, recorded as a fraction (personnel affected/personnel interviewed)*

	HOUR OF TEST	AMBIENT AIR		CEREBRAL FULLNESS	HEADACHE[1]	NASAL CONGESTION	NAUSEA	SORE THROAT	DRY THROAT	DRY OR SORE THROAT	FELT GOOD	FELT FAIR
		CO_2	O_2									
		per cent										
Exp. 5												
Chamber	46.5	4.8	13.5		15/35	14/34	5/35			16/34		
closed	58.5	5.0	12.5		16/34		2/34					
Chamber open	1.5 hr. after test	0.03	20.9		7/34		1/34					
Exp. 6												
Chamber	3	0.5	20.5	—	2/20	3/20		1/20	0/20		19/20	1/20
closed	7	1.3	19.5	1/18	0/18	0/18		0/18	0/18		17/18	1/18
	11	1.9	18.6	1/15	0/13	0/15		0/15	0/15		15/15	0/15
	15	2.4	18.3	1/16	0/16	3/16		1/16	0/16		16/16	0/16
	19	2.8	17.7	1/35	0/35	0/35		3/35	0/35		31/35	4/35
	23	3.3	17.3	1/17	0/17	1/17		0/17	0/17		17/17	0/17
	27	3.9	16.5	0/17	3/17	4/17		1/17	0/17		15/17	2/17
	29	4.2	15.9	1/10	2/10	2/10		0/10	1/10		6/10	4/10
	31	4.4	15.6	1/18	1/18	1/18		0/18	2/18		15/18	3/18
	35	5.0	15.1	0/16	0/16	1/16		0/16	0/16		16/16	0/16
	39	4.8	14.6	0/14	4/14	4/14		2/14	1/14		11/14	3/14
	43	4.8	14.1	4/16	3/16	0/16		0/16	0/16		8/16	8/16
	47	5.1	13.7	1/10	3/10	0/10		0/10	3/10		8/10	2/10
	50	5.2	13.2	6/76	18/76	8/76		6/76	18/76		50/76	23/76[2]
Chamber open	1.5 hr. after test	0.03	20.9	4/76	3/76	—		—	—		—	—

[1] Headaches were for the most part transient and not severe. One man was removed from the chamber because of headache, nausea, vomiting, and a blood pressure rise to 146 mm.

[2] *All personnel were in good condition the following morning.* Only 3 of 76 individuals complained of malaise at the 50th hour.

Mouth breathing and increased heat loss. The increased rates of ventilation encountered in these experiments caused an increase in rate of heat loss via the lungs. In experiment 6, the subjects were exposed to uncomfortably low temperatures and high humidities. If we assume the temperature to be 61°F., the relative humidity to be 90% and the minute volume of a seated man to be 30 liters, then each man loses about 41.9 cal. per hour through the lungs (21). The

metabolic rate of a seated man weighing 70 kgm. is roughly 100 calories per hour. Hence, under these conditions a man loses about 42% of the heat which he is producing via the lungs. When he is breathing at a more normal rate of 10 liters per minute, he loses only 14% of his heat via this channel. Consequently, thermal insulation adequate for normal breathing becomes inadequate when the rate of ventilation is increased without concurrent increase in rate of metabolism.

In experiments 3 and 4 the subjects breathed humid air at a temperature of over 90°F. Under these conditions the heat loss via the lungs was negligible. Thus, it can be seen that with respect to temperature regulation an increased rate of ventilation without coincident increase in the rate of heat production is a definite liability at low temperatures and is not an appreciable asset at high temperatures unless the relative humidity is low.

Subjective symptoms. Subjective reactions were recorded in experiments 5 and 6 (table 4). The usual symptoms, sore throat, nasal congestion and headache, were experienced about 40 hours after the start of the experiments. In experiment 5, about 40% of the subjects complained of all these symptoms; in experiment 6, dry throats and headaches occurred in 18%, and nasal congestion in about 10%. However, all personnel felt well the morning after the conclusion of each experiment. In the first four experiments, transient headaches occurred frequently after leaving the sealed spaces. A phenomenon of interest was the fleeting smell and taste of ammonia when outside air was breathed following exposure in high carbon dioxide atmospheres.

Psychological

Although there were some unquestionable decrements in test performance in these experiments, the results lead to an interpretation that the losses, when they occur, were not of such magnitude or character as to interfere appreciably with efficiency of personnel performing naval tasks. Five per cent carbon dioxide is not a comfortable concentration for prolonged inhalation, but the data show that its depressing effect is not great. Compensatory mechanisms appear to come into play to mitigate the adverse effects of long exposures. Other conditions, e.g., the extreme Effective Temperature in the early experiments may also have operated to reduce efficiency. Since these conditions would be expected to affect test scores in the same direction as increased carbon dioxide or reduced oxygen, the changes found are maximal if attributed to the major variables of carbon dioxide excess and oxygen deficiency.

The psychological test data have been analyzed to answer five questions.

What changes in performance occurred during the experiments (table 5)? There was no consistent significant effect upon any of the auditory or visual functions measured, nor upon any of the paper-and-pencil test scores, after the subjects practiced. The eye-hand coordination tests showed a slight decline in most cases. Hand dynamometer scores declined 3 to 10% in well-practiced subjects. Even though statistically significant, these changes are believed to be of small practical importance. The amount of body sway consistently increased, and, for the most part, the increases approach statistical significance. Some part, at

TABLE 5. *The difference in performance between the first and last test in the closed chamber*

Each column presents the data for an experiment. Description of the time and conditions of each test period is given at the head of the columns. Items and group means relating to the first test are in the lines labeled (1); those concerning the last test, in (2).

		EXPERIMENT					
		1	2	3	4	5	6
Time to middle of test period from closing chamber	(1)	1½ hr.	1½ hr.	1½ hr.	1½ hr.	7½ hr.	6 hr.
	(2)	31½ hr.	49½ hr.	49½ hr.	69 hr.	57½ hr.	49 hr.
Per cent CO_2 (av.) during test	(1)	0.5	0.6	0.5	0.5	1.1	1.1
	(2)	5.4	6.1	6.0	5.3	4.8	5.1
Per cent O_2 (av.) during test	(1)	20.2	20.4	20.4	20.5	19.6	19.7
	(2)	14.8	14.0	19.8	11.2	12.5	13.4
Number of subjects		4	3	3	4	[2]	12
Critical flicker frequency (flashes per sec.)	(1)	41.0	43.8		44.5		
	(2)	40.7	40.4		42.9		
	t	<1.0	1.86		1.72		
Dark adaptation threshold (log $\mu\mu$ lamberts)	(1)					3.7	
	(2)					3.7	
	t					0.0	
Pitch discrimination (decile rank)[3]	(1)	2.0	3.0	4.0			
	(2)	4.5	6.3	4.7			
	t	1.35	4.94[1]	<1.0			
Loudness discrimination (decile rank)[3]	(1)	5.2	6.3	4.0			
	(2)	8.2	6.3	4.3			
	t	2.22	0.0	<1.0			
Audiometer, 128 dv. (decibels)[3]	(1)				18.1		
	(2)				13.8		
	t				<1.0		
Audiometer, 1024 dv. (decibles)[3]	(1)				18.8		
	(2)				18.1		
	t				<1.0		
Audiometer, 8192 dv. (decibels)[3]	(1)				−2.5		
	(2)				3.1		
	t				5.02[1]		
Body sway, eyes open (mm. in 2 min.)[3]	(1)	223	500	200	251	174	
	(2)	390	865	244	394	204	
	t	2.75	3.95	1.24	3.07	1.55	

TABLE 5—*Continued*

		EXPERIMENT					
		1	2	3	4	5	6
Body sway, eyes closed (mm. in 2 min.)[3]	(1)	364	714	421	304	216	
	(2)	566	1214	737	550	308	
	t	2.36	1.76	3.12	2.19	2.38	
Railwalking (feet walked in 10 trials)	(1)	47	49	56		46	
	(2)	36	51	49		40	
	t	1.28	<1.0	2.18		1.57	
Hand-arm steadiness (contacts per min.)[3]	(1)	48.4	16.0	54.9	31.8	50.0	
	(2)	133.8	87.8	123.5	98.7	100.2	
	t	15.59[1]	3.72	10.04[1]	2.50	11.76[1]	
Complex tapping (contacts per min.)	(1)	164	170	188	195	159	
	(2)	148	143	179	163	164	
	t	1.40	3.24	<1.0	1.17	<1.0	
Pursuit rotor (contact during 30 sec.)	(1)	24.65	25.90	27.37	26.35	12.85[4]	
	(2)	22.08	25.34	26.31	24.79	16.77	
	t	2.09	<1.0	2.59	1.90	5.31[1]	
Hand dynamometer (kgm.)	(1)	54.5	55.7	56.3	52.6	56.1	56.6[4]
	(2)	49.2	52.0	54.7	49.0	51.8	57.6
	t	2.50	1.58	2.52	2.51	4.26[1]	<1.0
Computation (problems in 6 min.)	(1)	87.8	73.3	116			
	(2)	69.2	78.7	118			
	t	3.48[1]	<1.0	<1.0			
Computation (problems in 10 min.)	(1)				165	167	
	(2)				154	155	
	t				1.0	2.46[1]	
Code test—15 min. (letters per 90 sec.)	(1)	26.7	25.9	32.2			
	(2)	25.1	27.7	32.8			
	t	<1.0	<1.0	<1.0			
Code test—30 min. (letters per 90 sec.)	(1)				28.5	29.3	26.5[4]
	(2)				27.7	29.7	30.2
	t				<1.0	1.05	4.45[1]
Number checking (number correct in 3 min.)	(1)	51.8	55.3	67.0			
	(2)	47.2	55.3	64.3			
	t	<1.0	0.0	<1.0			

[1] Values for t and N show that the difference between these means is significant at the .05 level of confidence, or lower.

[2] Number of subjects in experiment 5 was 17, except as follows: dark adaptation, 4; body sway, 5; hand-arm steadiness, 15.

[3] A lower score indicates better performance.

[4] The subjects had little or no practice before the experiment.

least, of this increase is a result of heavy breathing. Control of gross body movement is not so severely affected by heavy breathing as is static equilibrium, for railwalking scores showed only an inconsistent trend downward. Of the functions measured, hand-arm steadiness showed the greatest change, but again

TABLE 6. *Comparison of performance at the beginning and the end of the time during which the CO_2 concentration was approximately 5%*

Each column presents the data for an experiment. Description of the time and conditions compared is given at the head of each column. Items and group means of performance relating to the beginning of the time at 5% CO_2 are in the lines labeled (1); those concerning the end of the time at 5% CO_2 are labeled (2).

		EXPERIMENTS		
		4	5	6
Time to middle of test period since closing chamber	(1)	37½ hr.	34 hr.	31 hr.
	(2)	61½ hr.	58½ hr.	48 hr.
Per cent CO_2 (av.) during test	(1)	4.7	4.8	4.1
	(2)	5.2	4.8	5.0
Per cent O_2 (av.) during test	(1)	15.6	15.1	15.8
	(2)	12.0	12.5	13.5
Number of subjects		4	[2]	12
Critical flicker frequency (flashes per sec.)	(1)	41.8		
	(2)	43.0		
	t	2.43		
Audiometer, 128 dv. (decibels)[3]	(1)	26.0		
	(2)	10.6		
	t	3.37[1]		
Audiometer, 1024 dv. (decibels)[3]	(1)	16.8		
	(2)	18.4		
	t	<1.0		
Audiometer, 8192 dv. (decibels)[3]	(1)	1.2		
	(2)	6.0		
	t	<1.0		
Body sway, eyes open (mm. in 2 min.)[3]	(1)	260	248	
	(2)	368	204	
	t	2.82	1.73	
Body sway, eyes closed (mm. in 2 min.)[3]	(1)	353	415	
	(2)	490	308	
	t	2.25	2.22	
Hand-arm steadiness (contacts per min.)[3]	(1)	99.1	90.7	
	(2)	104.9	100.2	
	t	<1.0	1.58	

TABLE 6—*Continued*

		EXPERIMENTS		
		4	5	6
Complex tapping (contacts per min.)	(1)	202	153	
	(2)	182	164	
	t	1.38	2.54[1]	
Pursuit rotor (contact during 30 sec.)	(1)	26.39		
	(2)	24.16		
	t	1.44		
Hand dynamometer (kgm.)	(1)	47.6	53.8	58.3[4]
	(2)	48.0	51.8	57.6
	t	<1.0	1.56	<1.0
Computation (problems in 10 min.)	(1)	161	156	
	(2)	162	155	
	t	<1.0	<1.0	
Code test—30 min. (letters per 90 sec.)	(1)	27.9	28.8	29.4[4]
	(2)	28.6	29.7	30.2
	t	<1.0	3.16[1]	1.22

[1] Values for *t* and *N* show that the difference between these means is significant at the .05 level of confidence, or lower.

[2] Number of subjects in experiment 5 was 17, except as follows: body sway, 5; hand-arm steadiness, 15.

[3] A lower score indicates better performance.

[4] The subjects had no practice before the experiment.

body movements, resulting from heavy breathing, were obviously an important determining factor.

To what extent does performance change when oxygen percentage gradually decreases and carbon dioxide is maintained at 5% (table 6)? The data of experiments 4, 5, and 6 are relevant to this question. The statistical analysis consisted in comparing performance when the carbon dioxide first reached 5% with performance just prior to return to normal air. In using the data of experiment 4, the small number of cases made advisable the averaging of the scores of the first two and the last two test periods during the 40 hours that the carbon dioxide was at a 5% level.

The results (table 6) show very few changes of significance. Only three of the comparisons show differences significant below the .05 level of confidence, and that for the audiometer (128 double vibrations[3]) is questionable because of mechanical difficulties during the testing. The other two show improvement. The conclusion to be drawn from this analysis is that the subjects were able to maintain their performance levels in all tests during prolonged exposure to 5% carbon dioxide even when the ambient oxygen percentage was decreasing to 12. Further-

[3] Hereinafter, 'dv.'

more, there is evidence in some tests of adaptation to the conditions of the experiments, with consequent improvement in performance during the last 20 hours.

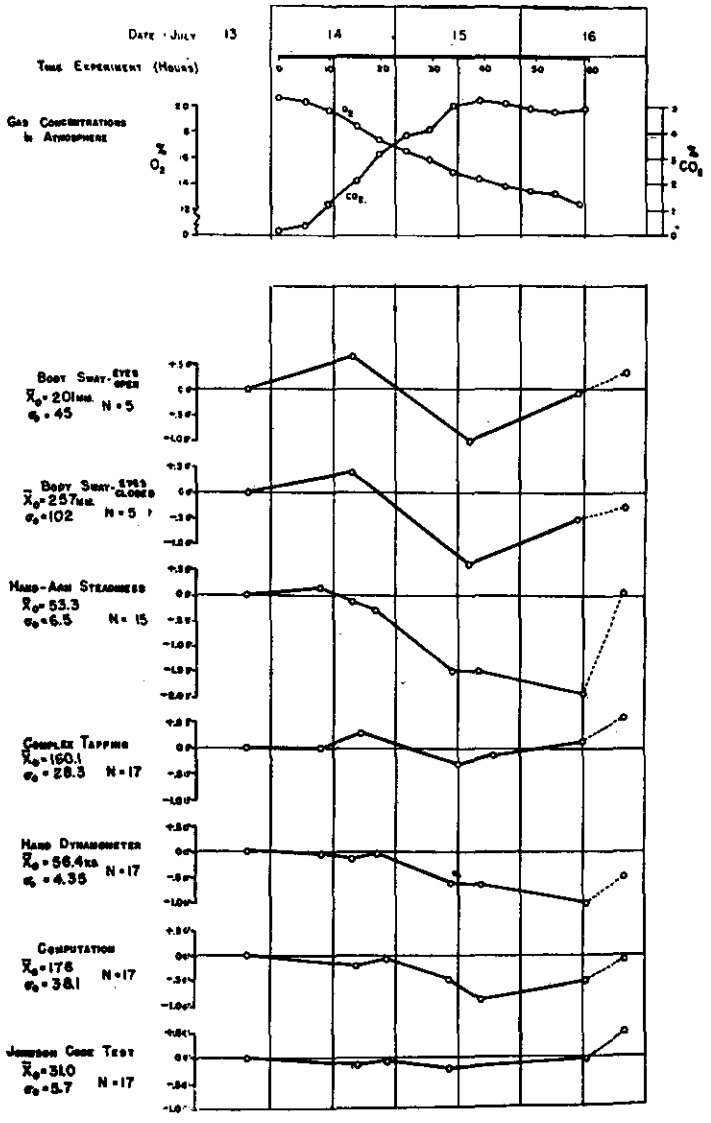


FIG. 12. Effects of increasing ambient carbon dioxide and decreasing ambient oxygen concentrations on psychomotor performance (experiment 5). All ordinates are given in standard deviation units of the score distribution in the last practice period. All scores are plotted so that positive deviation indicates improvement in performance, regardless of the raw score magnitude.

Graphs based on the data obtained from seven of the tests used in experiment 5 are shown in figure 12. All scores are plotted in comparable units, based on the standard deviation of the score distribution of the last practice session, taking

TABLE 7. *Extent and significance of the differences in performance between the last test during rebreathing and the 'recovery test'*

Each column presents the data for one experiment. Description of the conditions compared is at the head of each column. Group means of performance during the last test in the closed chamber are in the lines labeled (1); those for the 'recovery test' are labeled (2).

		EXPERIMENTS				
		1	2	3	4	5
Time of starting test in recovery period		9 hr.	2 hr.	9 hr.	2 hr.	4½ hr.
Highest per cent CO_2 reached		5.95	6.54	6.75	5±	5±
Lowest per cent O_2 reached		14.18	13.45	19.22	10.45	12.21
Number of subjects		4	3	4	4	[2]
Critical flicker frequency (flashes per sec.)	(1)	40.7	40.4		39.0	
	(2)	41.5	46.3		42.9	
	t	1.90	3.53		2.26	
Pitch discrimination (decile rank)[3]	(1)	4.5	6.3	5.5		
	(2)	3.8	8.3	2.2		
	t	<1.0	3.52	2.18		
Loudness discrimination (decile rank)[3]	(1)	8.2	6.3	4.2		
	(2)	5.2	7.3	1.5		
	t	1.73	<1.0	1.62		
Audiometer, 128 dv. (decibles)[3]	(1)				13.8	
	(2)				9.4	
	t				2.34	
Audiometer, 1024 dv. (decibels)[3]	(1)				18.1	
	(2)				13.8	
	t				2.74	
Audiometer, 8192 dv. (decibels)[3]	(1)				3.1	
	(2)				−1.8	
	t				1.63	
Body sway, eyes open (mm. in 2 min.)[3]	(1)	390	865	294	394	204
	(2)	293	218	115	214	190
	t	1.75	1.78	2.89	4.92[1]	<1.0
Body sway, eyes closed (mm. in 2 min.)[3]	(1)	566	1214	754	550	308
	(2)	505	502	282	244	288
	t	<1.0	1.36	5.55[1]	2.49	<1.0
Railwalking (feet walked in 10 trials)	(1)	36	51	50		
	(2)	35	58	62		
	t	<1.0	<1.0	1.66		

TABLE 7—*Continued*

		EXPERIMENTS				
		1	2	3	4	5
Hand-arm steadiness (contacts per min.)[3]	(1)	133.8	87.8	105.8	98.7	100.2
	(2)	23.8	14.8	38.2	41.5	49.4
	t	13.56[1]	4.16	12.26[1]	2.54	6.37[1]
Complex tapping (contacts per min.)	(1)	148	143	187	163	164
	(2)	182	167	209	213	178
	t	2.43	1.73	1.38	2.38	2.96[1]
Pursuit rotor (contact during 30 sec.)	(1)	22.08	25.34	25.85	24.79	
	(2)	25.12	25.49	27.83	26.44	
	t	1.85	<1.0	3.10	2.12	
Hand dynamometer (kgm.)	(1)	49.2	52.0	53.9	49.0	51.8
	(2)	52.6	55.0	55.0	50.4	54.0
	t	2.64	1.71	1.10	<1.0	2.24[1]
Computation (problems in 6 min.)	(1)	69.2	78.7	111		
	(2)	82.2	74.3	129		
	t	5.73[1]	<1.0	1.74		
Computation (problems in 10 min.)	(1)				154	155
	(2)				184	173
	t				1.73	3.41[1]
Code test—15 min. (letters per 90 sec.)	(1)	25.1	27.7	33.2		
	(2)	28.7	30.2	38.6		
	t	4.92[1]	2.19	2.17		
Code test—30 min. (letters per 90 sec.)	(1)				27.7	29.7
	(2)				31.8	33.7
	t				2.36	6.35[1]
Number checking (number correct in 3 min.)	(1)	47.2	55.3	65.8		
	(2)	53.5	51.7	80.8		
	t	1.58	1.00	6.12[1]		

[1] Values for t and N show that the difference between these means is significant at the .05 level of confidence, or lower.

[2] Number of subjects in experiment 5 was 17, except as follows: body sway, 5; hand-arm steadiness, 15.

[3] A lower score indicates better performance.

the average of this distribution as zero. It will be noted that only hand dynamometer and steadiness scores continued the downward trend during the last 20 hours of rebreathing. For the other tests, the lowest scores occurred between the 30th and 40th hours and subsequently improved.

Is there any advantage in the maintenance of ambient oxygen at approximately 20% if carbon dioxide is allowed to increase to 5%? This question was answered by

comparing the data of the third experiment with those of experiments 1, 2, and 4. Changes in performance between the time the chamber was closed and the time, about 35 hours later, when the carbon dioxide concentration had reached about 5%, were compared under the two conditions of oxygen concentration. The conclusion of this analysis is that 19 to 21% ambient oxygen offers no advantages over oxygen reduced to 15% if the carbon dioxide concentration is concomitantly increased to 5%. In 14 comparisons of changes in test performance, 6 favored conditions of decreased oxygen; no difference was significant at the .05 level of confidence.

TABLE 8. *Improvement with practice on the hand dynamometer test during 50 hours' rebreathing, carbon dioxide concentration being 5% during the last 15 hours*

	EXP. 6	CONTROL GROUP A	CONTROL GROUP B
Number of subjects	12	18	10
First practice score (kgm.)	56.6	52.6	46.5
Sixth practice score (kgm.)	56.8	54.2	49.2
Difference	.2	1.6	2.7
Difference from Experiment 6 group in improvement		+1.4	+2.5
t		<1.0	1.52

TABLE 9. *Improvement with practice on the Johnson Code Test during 50 hours' rebreathing, carbon dioxide concentration being 5% during the last 15 hours*

	EXP. 6	CONTROL GROUP
Number of subjects	15	18
First test score (letters per 90 sec.)	26.6	26.7
Fourth test score (letters per 90 sec.)	29.8	30.9
Improvement	3.2	4.2
Difference from Experiment 6 group in improvement		+1.0
t		1.18

To what extent does performance improve on return to normal air? This is an important question since there is a decrement in some tests, (table 5) and it is important to know whether the unfavorable reactions persist. Table 7 compares performance in the last test period during rebreathing with that in the recovery period (fourth to fifth hour). Of 57 differences, 52 show some average improvement in performance during the recovery period and 12 are significant at the .05 level of confidence or lower.

What is the effect of the experimental conditions on expected improvements from practice (tables 8, 9, and fig. 13)? In experiment 5 the subjects had only two practice sessions with the pursuit rotor before closing the experimental chamber. They had four more practice periods while the chamber was closed, and one in

the recovery test period. The learning curve for the group, compared with three other groups tested with the same apparatus and procedure (fig. 13), suggests that the effect on pursuit rotor learning when living in an atmosphere where concentration of carbon dioxide builds up to 5%, is roughly equivalent to that of living in an atmosphere where the Effective Temperature is above the comfort zone (22). The subjects in experiment 6 had no previous practice on the hand dynamometer or the code test. Their improvement (tables 8, 9) is slightly but not significantly less than that of groups learning under normal conditions. Although there is some indication in these data of interference or inhibition imposed by the experimental conditions during the learning period, the effect is not

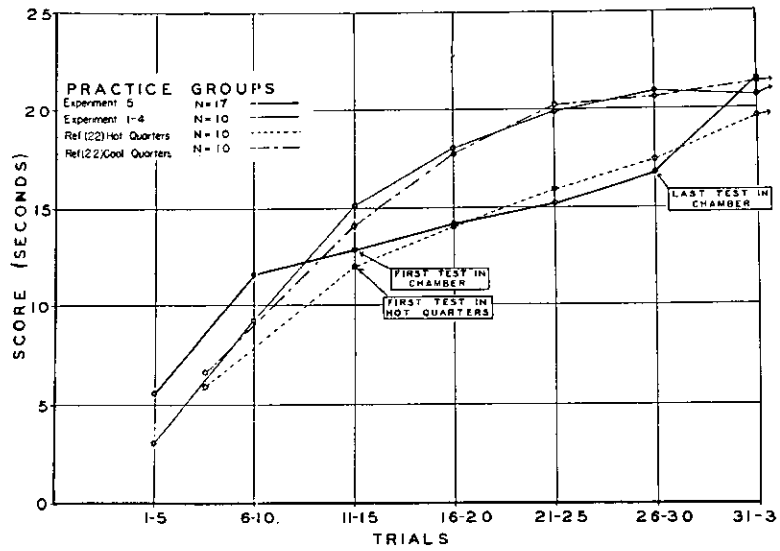


FIG. 13. Pursuit rotor learning under several experimental conditions. Each curve covers a period of four days, with two, five-trial practice periods each day in most cases. The subjects of experiments 1—4 and the 'cool quarters' group were learning under essentially normal conditions. The 'hot quarters' group lived in an environment where the Effective Temperature remained above 85°.

greater than that found in well-practiced performance, when judged by the critical ratio of the changes.

SUMMARY

1. In six experiments men breathed recirculated air for periods of 35 to 72 hours in sealed spaces of such size as to provide 500 cu. ft. of air volume per man.

2. Exposure in atmospheres of carbon dioxide concentrations up to 5% and reduced oxygen concentrations as low as 12% did not seriously impair the physical condition and efficiency of the subjects as evaluated by biochemical, physiological, and psychological tests. Minor symptoms of headache, nasal congestion, and dryness of the throat quickly disappeared when outside air was breathed.

3. In an atmosphere of 5% carbon dioxide and 12% oxygen, healthy men are able to maintain an adequate oxygen pressure in the lungs, blood and tissues because an increase in respiratory minute volume (hyperventilation) and an increase in pulse rate (circulation) prevent a corresponding reduction in oxygen concentration in lungs and blood despite the decrease in ambient oxygen from 21 to 12%. Consequently, in long exposures to atmospheres of high carbon dioxide content (5%) it is not necessary to maintain the oxygen concentration of the recirculated air at the normal value.

4. Concentrations of carbon dioxide much above 5% are not well tolerated. This value appears to be a limiting level for healthy young men if exposures are prolonged.

5. Under these conditions the carbon dioxide output was found to be 0.326 l/min. STP (0.69 cu. ft. per man hour) and the oxygen consumption was 0.387 l/min. STP (0.82 cu. ft. per man hour).

The completion of this project was made possible only by the skilled assistance and perseverance of the following men: V. Broom, H. Collison, L. Hayward, H. Hinshaw, S. Hollander, A. Leggett, W. Platt, J. Shaner, C. Spear, C. Stevens, T. Watson and L. Williamson.

We wish to acknowledge the assistance of investigators from the Naval Research Laboratory, Anacostia, D. C., and the Medical Research Department, New London, Connecticut.

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SECTION 2. Laboratory Studies

Effects on man of 30-day exposure to a P_{ICO_2} of 14 torr (2 %): application to exposure limits

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Guillerm, R., and E. Radziszewski. 1979. Effects on man of 30-day exposure to a P_{ICO_2} of 14 torr (2 %): application to exposure limits. Undersea Biomed. Res. Sub. Suppl.: S91–S114.—Pulmonary function, acid-base balance, renal electrolyte excretion, hematology, biorhythms and psychomotor test results were studied in six men during 30 days of exposure to a P_{ICO_2} of 14 torr (F_{ICO_2} = 0.02) with pre- and postexposure periods on air. Alveolar and arterial P_{CO_2} increased and remained constant throughout the CO_2 exposure ($\Delta P_{ACO_2} = \Delta P_{aCO_2} = 2.5$ torr); the rise in expiratory minute volume ($\Delta \dot{V}_E$ = 60%) was related to the increased tidal volume. Oxygen uptake and carbon dioxide output increased about 10% because of the ventilatory work overload. Physiological dead space increased 8% without an alveolar-arterial P_{CO_2} difference. Respiratory acidosis was mild ($\Delta pH \simeq 0.01$) and the renal response was slight. There was no variation in plasma electrolytes, except a slight decrease in potassium. Red blood cell count decreased, showing a confinement effect. Adaptation to exercise was slightly impaired. Results of electrobiological and psychomotor tests and biorhythm evaluations showed no variation; application of these findings to CO_2 exposure limits is discussed.

chronic hypercapnia
ventilation
alveolar CO_2 tension
arterial CO_2 tension
physiological dead space
acid-base balance
plasma electrolytes
urine electrolytes
hematology
psychomotor tests
biorhythms
CO_2 exposure limits

The advent of nuclear submarines and space vehicles raises the problem of man's ability to adapt to the new conditions he has to face, in particular those of a prolonged stay in a confined atmosphere. Several elements connected with long-duration confinement (accumulation of various contaminants, the relative decrease in physical activity, and the lack of sunlight and the usual synchronizers) are in fact likely to bring about changes in some of the crew's

biological and psychophysiological constants. These modifications may have an effect on the health of subjects and on their safety as well; it is therefore essential, from the health and operational points of view, to know the far-reaching effects of the different environmental factors upon the organism.

Among the numerous contaminants on a submarine, carbon dioxide is the most important because it is a metabolic gas with a tendency to accumulate if not properly eliminated.

Most of the experiments of the effects on humans of prolonged exposure to an atmosphere enriched with carbon dioxide have been carried out on submarines (Schaefer 1961; Schaefer, Nichols, and Carey 1963; Peck 1971; Gortner, Messier, Heyder, and Schaefer 1971; Messier, Heyder, and Schaefer 1971; Gray, Morris, and Brooks 1973).

Analysis of the results of these different works leads to the following observations:

1) Interpretation of results is difficult, because, as Davies (1973) noticed, any variation observed may be due to the combined effects of factors other than carbon dioxide, such as carbon monoxide and the great number of other contaminants generally present on submarines. Thus, in studies of calcium metabolism (Schaefer et al. 1963; Davies 1973; Gray et al. 1973) the relative lack of physical exercise and sunlight and the daily ingestion of demineralized water would obviously affect this variable, so that in these conditions the variations observed can hardly be attributed solely to hypercapnia.

2) In addition, the low $F_{I_{CO_2}}$ picked up on board generally induces only small variations in the different variables, similar to normal physiological variations and well within the accuracy limits of the analytic techniques.

This accounts for certain contradictions, such as the absence of variation in $P_{A_{CO_2}}$ (Peck 1971) and the decrease in hypercapnia (Gortner et al. 1971; Messier et al. 1971); in these conditions, it is difficult to assign the electrolytic variations occasionally observed to a hypercapnia that is not demonstrated by changes in Pa_{CO_2}.

Experimental laboratory studies of chronic hypercapnia have been carried out in man by Clark, Sinclair, and Welch (1971). They only studied ventilatory adaptation and the acid-base balance of arterial blood in men exposed for 5 to 8 days at a $P_{I_{CO_2}}$ of 21 or 30 torr. Similarly, we carried out a research program (1968–1973) involving long-duration experiments conducted in a large air-tight environmental chamber with voluntary subjects (see Table 1).

During these different experiments, we studied the effects of hypercapnia on ventilatory function, acid-base balance of arterial blood, electrolyte shifts, renal response, circulatory function, hematological parameters, adrenocortical activity, electrobiological parameters (ECG, EEG), and psychomotor performance in resting and, for some variables, in exercising subjects.

The results have led to a summary report (Radziszewski 1974) and to several publications (Guillerm, Radziszewski, Abran, Hee, and Badre 1972; Guillerm, Radziszewski, Abran, and Badre 1973; Radziszewski, Guillerm, Badre, and Abran 1976); they provide complementary

TABLE 1

MATRIX OF CONDITIONS OF HUMAN HYPERCAPNIC STUDIES AT CERTSM (1968–1973)

$F_{I_{CO_2}}$ %	2	3	4	4.5
$P_{I_{CO_2}}$, torr	14	21	28	32
Duration (days)	30	8	8	2
Number of Subjects	6	15	15	10

qualitative and quantitative data on man that allow the tolerance limits on experimental bases, according to the $P_{I_{CO_2}}$ and the periods of exposure, to be specified.

The present work deals with experience at a $P_{I_{CO_2}}$ of 14 torr; total experimental duration was 46 days, and the hypercapnia exposure lasted for 30 days. In the discussion, the results are compared with the data from the literature as well as to those we obtained during earlier experimental series (mentioned in Table 1).

MATERIALS AND METHODS

The experiment took place in a large environmental chamber (100 cm). Light was supplied by fluorescent tubes and a side window which let sunlight in; temperature was maintained at 24°C ± 1°C, relative humidity at 70% ± 5%, oxygen partial pressure ($P_{I_{O_2}}$) at 150 ± 5 torr, and the carbon dioxide partial pressure ($P_{I_{CO_2}}$) at the level fixed by the protocol ($P_{I_{CO_2}}$ ± 1 torr). All the ambient parameters were regulated automatically.

An analysis of the atmosphere of the chamber was made periodically by gas chromatography, to ensure no contamination by contaminants that would require specific absorbers.

Six healthy, young, non-smoking volunteers selected after physical and psychological examination were subjected for 46 consecutive days to the following conditions: 8 days at a $P_{I_{CO_2}} \simeq 0$ torr (control period); 30 days at $P_{I_{CO_2}}$ of 14 torr (hypercapnic period); and 8 days at a $P_{I_{CO_2}} \simeq 0$ torr (recovery period). Carbon dioxide was added to and eliminated from the chamber at 0700 in the morning, without the knowledge of the subjects, and lasted about 30 min.

During the experiment, the subjects were not completely isolated from the outside world, for they kept their watches, had radios and TV sets and could communicate by telephone. In addition to the investigations, the subjects had to carry out, every other day between 2300 and 0700, and each in turn, a 3-h night shift involving reading meters, recording figures, supervising, and taking various measurements.

Diet was normal, cooked outside the chamber, and handed in at mealtimes (0800, 1200, and 1900) through a small lock; each subject was given a liter and a half of tap water and 250 ml of wine every 24 h.

Nature and chronology of the investigations

A large number of biological investigations (respiratory function, circulatory function, acid-base balance), biochemical determinations (on blood and urine specimens), and electrobiological studies (electrocardiogram and electroencephalogram) on both resting and exercising subjects as well as psychomotor tests and circadian rhythm studies were carried out at regular intervals throughout the 46 days of the experiment.

Electrocardiogram and arterial blood pressure measurements were recorded on waking between 0700 and 0730 in the morning in bed-resting subjects. Then the subjects were asked to get up and weigh in.

Blood studies

Between 8 and 9 a.m., venous blood (15 ml) was drawn on fasting subjects and immediately divided into 3 tubes:

The first tube was heparinized; the tube content was centrifuged at 3000 r/min and the plasma obtained was used to determine sodium and potassium (using an Il-Meter 348 flame

photometer with automatic dilution), as well as chloride (Schales and Schales 1941) and cortisol (Murphy 1967). The second tube contained EDTA disodium salt for hematologic studies; red blood cell count, mean blood cell volume and hematocrit were calculated automatically (Coulter-Counter, S). The third tube contained non-anticoagulant; the serum was used to determine inorganic phosphorus (Technicon Autoanalyzer), magnesium (volumetric microanalysis using titanium-yellow (Masson 1957)) and calcium (complexometric determination using the Patton and Reeder indicator (Tronchet 1958)).

At 10 a.m., arterialized capillary blood (50 μl) was collected from the ear lobes into two tubes, vasodilatation being achieved by rubbing the lobe with β-butoxy-ethyl nicotinate (Finalgon) 10 min before sampling. To make sure that the subjects were under steady-state respiratory conditions, the blood samples were taken at the time ventilatory measurements (see respiratory studies) were made; pH was measured immediately after the collecting of blood samples (Radiometer pH 27; electrode E 5021) and the pH values were taken into account only when the difference between both tubes did not exceed 0.01 U. The pH values measured at 38°C were corrected to body temperature (37°C) by adding 0.0148 pH unit (according to the method of Rosenthal 1948).

Pa_{CO_2} was calculated by measuring pH after equilibration of venous blood at two known CO_2 tensions (Astrup microtonometer, Radiometer, Copenhagen) and using the Siggard-Andersen nomogram.

Bicarbonate (HCO_3^-) concentration in plasma was calculated from the Henderson-Hasselbalch equation:

$$pH = 6.10 + \log \text{bicarbonate} / 0.0301\ Pa_{CO_2}$$

Urine studies

Twenty-four hour urine specimens were stored in a refrigerator in a bottle containing 10 ml of a mercurothiolate solution and a film of paraffin. They were collected daily in the morning after collection of the night urine and were used for pH and volume measurements as well as for determination of chloride (Cl^-) (according to the method of Mohr), ammonium ions (NH_4^+) (formol-titration (Ronchese 1907)) bicarbonate (gas chromatograph connected to Van-Slyke's apparatus), and titratable acidity (TA). Daily net acidity (NA) was calculated for each subject.

All determinations were carried out within 48 h of sample collection.

Resting respiratory studies

Respiratory and pulmonary gas exchange measurements were made between 1000 and 1200 h. The subjects were comfortably seated in an armchair and they inhaled air through a mouthpiece fitted with valves. Their noses were occluded with adhesive tape to eliminate the trauma caused by nose clips, which favor reflex hyperventilation. These measurements were carried out during the steady-state period, over a period of 2 min and after a relaxation period of about 8 min.

The expiratory minute volume, $\dot{V}_E$, was read on a precision dry-gas spirometer with a small pressure drop (1 cmH_2O/liter/s). Expired gases were analyzed continuously by means of an infrared analyzer (Beckman LB1) connected to a potentiometric recorder with a high amplitude and a short response time (100 msec for an amplitude of 15 cm); the alveolar carbon dioxide tension ($P_{A_{CO_2}}$) was measured in the middle of the alveolar plateau (Lacoste 1964) over several consecutive respiratory cycles.

All expired gases were collected in a Douglas bag and were used to measure both the oxygen concentration ($F_{E_{O_2}}$) and the carbon dioxide concentration ($F_{E_{CO_2}}$) in the expired gas mixture, and to calculate oxygen consumption ($\dot{V}_{O_2}$), carbon dioxide output ($\dot{V}_{CO_2}$), respiratory quotient (equation of Rahn and Fenn 1955) and physiological dead space, V_D (Bohr equation 1890).

Electrobiological studies and psychomotor testing

These studies were carried out between 0300 and 0500 h.

The electroencephalogram recording (EEG) consisted of a control period (opening and closing of the eyes, wave stopping reaction) together with a sequence of exposure to intermittent light stimuli (light stimulation at 7 Hz, 5 Hz, and 3 Hz during 1 min for each frequency) followed by a 1-min recovery period. A spectral analysis of the EEG performed in real-time with a digital computer (Atreeg computer, CSF) made it possible to observe the distribution of the prevailing frequencies and to determine the modulation of both the α (8 to 12 Hz) and θ (4 to 8 Hz) rhythms, thanks to a frequency resolution of 0.25 Hz.

Psychomotor tests were numerous and of several types; they included collective tests (coding test, Zazzo's double task) as well as individual tests (choice reaction time, Couve-Lezine's classification test). Each test was the occasion for a detailed analysis during which both the speed and accuracy of execution of the task were determined.

Circadian rhythm studies

Once a week for 48 h (on Saturdays and Sundays), the following physiological variables were recorded every 4 h: oral temperature, peak expiratory flow, grip strength, arterial blood pressure, urinary volume and pH, and potassium excretion.

Exercise studies

Twice a week at about 5 p.m., the subjects were put through a 10-min exercise test with a 150-watt load (Elema-Schölander bicycle ergometer). During the last minute of exercise, they were provided with a mouthpiece connected to a Tissot spirometer in which expired gases were collected to determine $\dot{V}_E$, $\dot{V}_{CO_2}$, $\dot{V}_{O_2}$, and R; $P_{A_{CO_2}}$ (Beckman LB_1) and electrocardiogram (with 2 electrodes positioned on the chest and one grounding lead on the forehead) were recorded at the same time.

RESULTS

Daily means have been compared with the mean of all values obtained during the control period, according to the Student *t*-test applied to matched series of reduced strength. For most of the measured parameters, significant interindividual variations were noted; consequently, to understand this report more easily, only the daily means have been plotted on the figures and tables enclosed in this paper.

It should be remembered that CO_2 was added between 0700 and 0730 h; the ventilatory values as well as the blood analysis and acid-base balance values that are plotted on the figures for the first day of hypercapnia therefore correspond to the acute phase of the experiment, that is, after 2 to 3 h of exposure to CO_2.

Resting respiratory studies

Data on alveolar CO_2 tension, expiratory minute volume, and tidal volume are presented in Fig. 1. The data from which the graphs were constructed are summarized and statistically evaluated in Table 2.

After 2 h of exposure at a $P_{I_{CO_2}}$ of 14 torr, the expiratory minute volume increased 60% from 7.8 liters BTPS/min to 12.5 liters BTPS/min; such an increase was statistically significant ($P < 0.001$) and was essentially due to a rise in tidal volume (+ 48%; $P < 0.001$), since the respiratory rate did not change significantly (NS). An average increase in $P_{A_{CO_2}}$ of 1.5 torr was achieved ($P < 0.05$).

After 24 h of exposure, initial hyperventilation had decreased 4% (NS) and continued to fall by 6% (P 0.05) after 9 days. $P_{A_{CO_2}}$ was increased by one additional torr after 24 h of hypercapnia; the total 2.5 torr overload remained remarkably stable over the 30 days of exposure (Fig. 1).

Finally, the recovery period was marked, on the one hand, by an immediate return of the expiratory minute volume to a steady level not very different from the value measured during the control period and, on the other hand, by a gradual decrease in $P_{A_{CO_2}}$, which stabilized as early as the 24th h (Day 2).

Figure 2 and Table 3 display data on oxygen uptake, carbon dioxide output, and respiratory quotient; these data show that hypercapnia induced an increase in $\dot{V}_{O_2}$ and $\dot{V}_{CO_2}$ of approximately 10% (P 0.05) with no significant change in respiratory quotient. The post-hypercapnia period was characterized by a mild increase in the respiratory quotient (from 0.91 to 0.98) during the first 24 h.

Finally, physiological dead space, V_D, calculated from the Bohr equation, increased 8% (P 0.05) during the whole exposure to hypercapnia (see Table 3); during the recovery period, the V_D values did not deviate from the control period values.

Blood studies

The mean Pa_{CO_2} values were equal to those of $P_{A_{CO_2}}$ both during the pre-and post-exposure periods and during the exposure period (see Table 4); the mean arterial P_{CO_2} overload observed was also 2.5 torr.

Acid-base balance

During the control period (Fig. 1), the mean pH of arterialized capillary blood was 7.38 and the bicarbonate concentration in plasma varied between 21.5 and 22 mEq/liter.

After 2 h of exposure, 4 subjects out of 6 showed no detectable change in pH; in the other 2 subjects, hypercapnia caused a very mild respiratory acidosis. The mean pH value in the 6 subjects (7.377 ± 0.008) did not deviate significantly from the values measured during the control period. An increase in bicarbonate concentration of 0.6 mEq/liter (P 0.001) in plasma was also observed.

From the 2nd to the 24th h of exposure, the mean pH value decreased gradually as a result of the late development of an acidosis in a third subject. By the 3rd day of exposure, the mean pH in the 6 subjects (7.37 ± 0.005) showed a significant deviation from the control of pH level (P 0.01).

Between the 3rd and the 8th day of hypercapnia, acid compensation seemed to be beginning already; pH deviation was no longer significant. Compensation of the respiratory acidosis seemed complete after 15 days in all the subjects. Daily values of bicarbonate concentration in

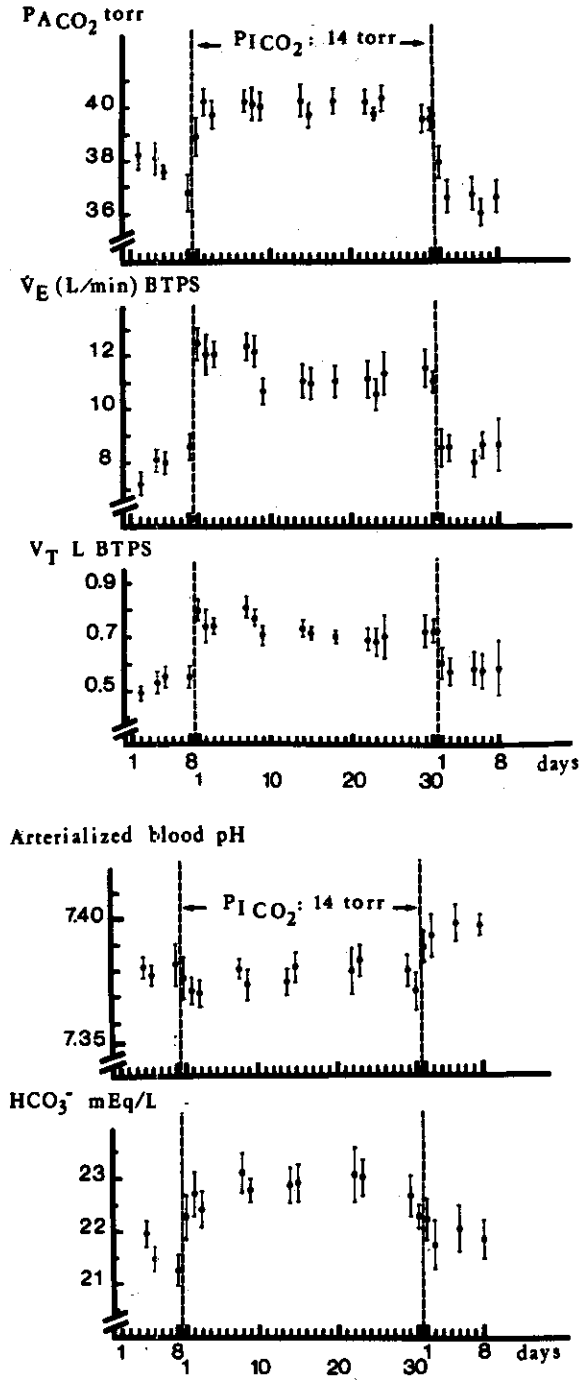

Fig. 1. Effect of 30 days of exposure to a $P_{I_{CO_2}}$ of 14 torr on alveolar CO_2 tension ($P_{A_{CO_2}}$), expiratory minute volume ($\dot{V}_E$), tidal volume (V_T), arterialized blood pH, and plasma bicarbonate (HCO_3^-); values are means ± SD for 6 subjects.

TABLE 2

EFFECTS OF 30-DAY EXPOSURE TO P_{CO_2} OF 14 TORR ON $P_{A_{CO_2}}$, VE, VT, RR, CAPILLARY pH AND PLASMA HCO_3^-

Parameter		Control, Air	Hypercapnia						Recovery on Air		
			2–3 h	Day 2	Day 3	Day 8	Day 15	Day 29	3 h	Day 2	Day 8
Alveolar CO_2 tension, torr	Mean	37.5	38.9*	40.2*	39.7*	40.1*	40.2*	39.5*	37.9	36.6	36.6
	SD	0.3	0.7	0.5	0.5	0.6	0.5	0.5	0.6	0.6	0.6
	n	30	6	6	6	6	6	6	6	6	6
Expiratory minute volume, liter/min, BTPS	Mean	7.83	12.50*	11.95*	12.10*	12.24*	11.02*	11.60*	8.62	8.61	8.54
	SD	0.18	0.58	0.82	0.57	0.55	0.59	0.72	0.74	0.54	0.46
	n	30	6	6	6	6	6	6	6	6	6
Tidal volume, *liter*, BTPS	Mean	0.540	0.800*	0.740*	0.740*	0.770*	0.715*	0.720*	0.600	0.570	0.580
	SD	0.088	0.041	0.064	0.028	0.029	0.020	0.061	0.056	0.050	0.095
	n	30	6	6	6	6	6	6	6	6	6
Respiratory rate	Mean	15.0	15.8	16.4	16.5	15.0	15.4	16.3	14.6	15.5	15.2
	SD	0.5	1.0	1.0	1.0	1.0	0.8	0.5	1.0	1.0	1.0
	n	30	6	6	6	6	6	6	6	6	6
Arterialized capillary blood pH	Mean	7.380	7.377	7.372	7.371*	7.380	7.381	7.380	7.388	7.392*	7.396*
	SD	0.002	0.008	0.005	0.005	0.006	0.005	0.006	0.006	0.008	0.004
	n	24	6	6	6	6	6	6	6	6	6
Plasma bicarbonate	Mean	21.65	22.23*	22.70*	22.41*	23.08*	22.91*	22.65*	22.21*	21.68	21.81
	SD	0.15	0.56	0.33	0.54	0.50	0.26	0.47	0.60	0.83	0.30
	n	24	6	6	6	6	6	6	6	6	6

*Differences significant at the 5% level or better.

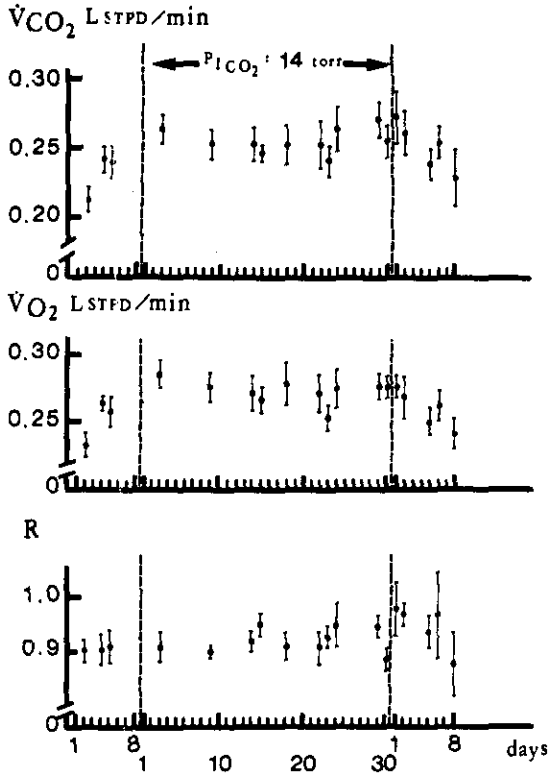

Fig. 2. Effect of 30 days of exposure to a $P_{I_{CO_2}}$ of 14 torr on carbon dioxide output ($\dot{V}CO_2$), oxygen uptake ($\dot{V}O_2$) and respiratory quotient (R). Values are means ± SD for 6 subjects.

TABLE 3

EFFECT OF EXPOSURE TO P_{CO_2} OF 14 TORR ON $\dot{V}O_2$, CO_2 EXCRETION, R, AND VD

		Control Period, Air	Hypercapnia	Recovery Period, Air
Oxygen uptake, liter/min, STPD	Mean	0.248	0.272*	0.258**
	SD	0.004	0.004	0.005
	n	30	60	30
Carbon dioxide output, liter/min, STPD	Mean	0.232	0.255*	0.250**
	SD	0.005	0.004	0.007
	n	30	60	30
Respiratory quotient	Mean	0.92	0.92	0.95**
	SD	0.02	0.01	0.02
	n	30	60	30
Physiological dead space, liters, BTPS	Mean	0.140	0.152*	0.143
	SD	0.004	0.003	0.006
	n	30	72	30

*Differences significant at the 5% level or better; **because of daily variations, the pooled data were not evaluated statistically.

TABLE 4

MEAN Pa_{CO_2} AND Pa_{CO_2} VALUES BEFORE, DURING, AND AFTER EXPOSURE TO A PI_{CO_2} OF 14 TORR

		Control Period	PI_{CO_2} Exposure, 14 torr	Recovery Period
Alveolar P_{CO_2}	Mean	37.67	39.79	36.95
	SD	0.27	0.15	0.30
	n	24	66	24
Arterial PCO_2	Mean	37.35	39.81	37.15
	SD	0.63	0.36	0.61
	n	24	66	24

plasma increased slightly during the first 20 days of exposure; the total increase was 1 mEq/liter (P 0.001).

The recovery period was marked by a gradual decrease in plasma bicarbonates during the first 24 h. Acid-base values were significantly above the values measured during the control period (+ 0.001 pH unit during the first 24 h; +0.02 pH unit after 5 and 8 days).

Venous plasma electrolytes

Changes in venous plasma electrolytes (Fig. 3) were relatively mild, on the whole. Natremia increased from the 24th h to the 15th day of exposure (+2 mEq/liter; P 0.02); it then decreased during the second half of the exposure period. Kaliemia gradually decreased from the 48th h to the last day of exposure ($\Delta K^+ = -0.4$ mEq/liter; P 0.05). The plasma calcium level remained stable and was comparable to that observed during the control period except for a transitory increase after 2 h of exposure ($\Delta Ca^{++} = 0.04$ g/liter). The plasma phosphorus level decreased during the first two days of hypercapnia ($\Delta P_i = -0.07$ g/liter), and returned to control values between the 15th and 20th days.

Changes in plasma magnesium level were in the opposite direction to that of inorganic phosphorus concentration; the initial increase observed during the first two days ($\Delta Mg^{++} = 0.01$ g/liter) was followed by a gradual decrease in the magnesium concentration in plasma between the 8th and 20th days.

The recovery period was essentially characterized by a transitory reduction in Ca^{++} after 2 h of exposure and by a more or less rapid return of the Na^+, K^+, Mg^{++} and P_i values to control levels.

Urine studies

Urine studies revealed the following changes (Fig. 4): changes in urine pH, volume, and chloride concentration were not regular and did not appear to be very much affected by hypercapnia. Excretion of NH^+_4, HCO^-_3, titratable acidity and net acidity remained relatively stable during the first 8 days of exposure, and daily means were comparable with the control period values. During the second week under hypercapnic conditions, a rise in NH^+_4 excretion (P 0.02) and to a lesser degree, in titratable acidity (NS), was observed, which resulted in a marked increase (NS) in net acidity. From the third week of exposure on, NH^+_4 ion excretion continued to rise, while both titratable and net acidities were subnormal.

Finally, the recovery period was marked by a considerable reduction in net acidity, which reduction was maximum and significant over the first 48 h. This can be explained by the

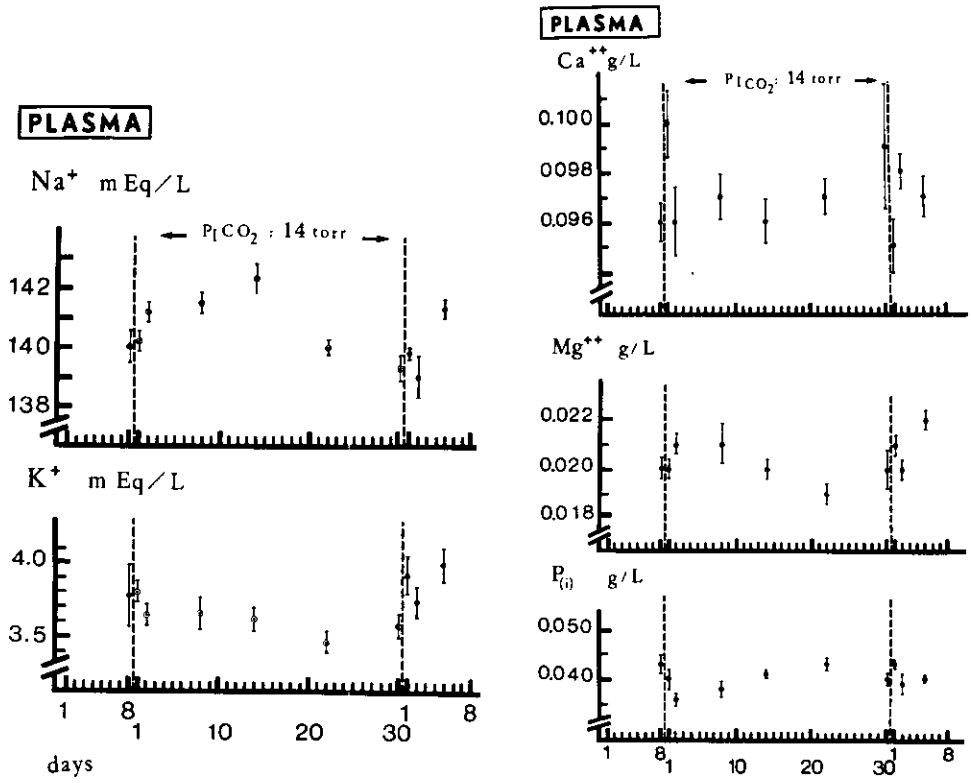

Fig. 3. Effect of 30 days of exposure to a $P_{I_{CO_2}}$ of 14 torr on venous plasma electrolytes; values are means ± SD for 6 subjects.

increased HCO_3^- excretion, which was accompanied by a reduction in NH_4^+ and titratable acidity. During the same period, urinary pH rose above the control level (P 0.01).

Hematology

A gradual reduction in hematocrit (Fig. 5) was observed during the 30 days of exposure; this 10% reduction (P 0.02) was caused primarily by a decrease in red blood cell count (9%; P 0.001) and, to a lesser extent, by a reduction in mean red blood cell volume (4%; NS). During the recovery period, both hematocrit and red blood cell count remained at a low level.

Adrenocortical response

No significant changes in plasma cortisol concentration were noted during the 46 days of the experiment (Table 5).

Basal heart rate, systolic and diastolic blood pressure

Heart rate ($\overline{X}$ = 60 bpm), systolic blood pressure ($\overline{X}$ = 10.9 mmHg) and diastolic blood pressure ($\overline{X}$ = 6 mmHg) remained stable and did not appear to be affected by hypercapnia.

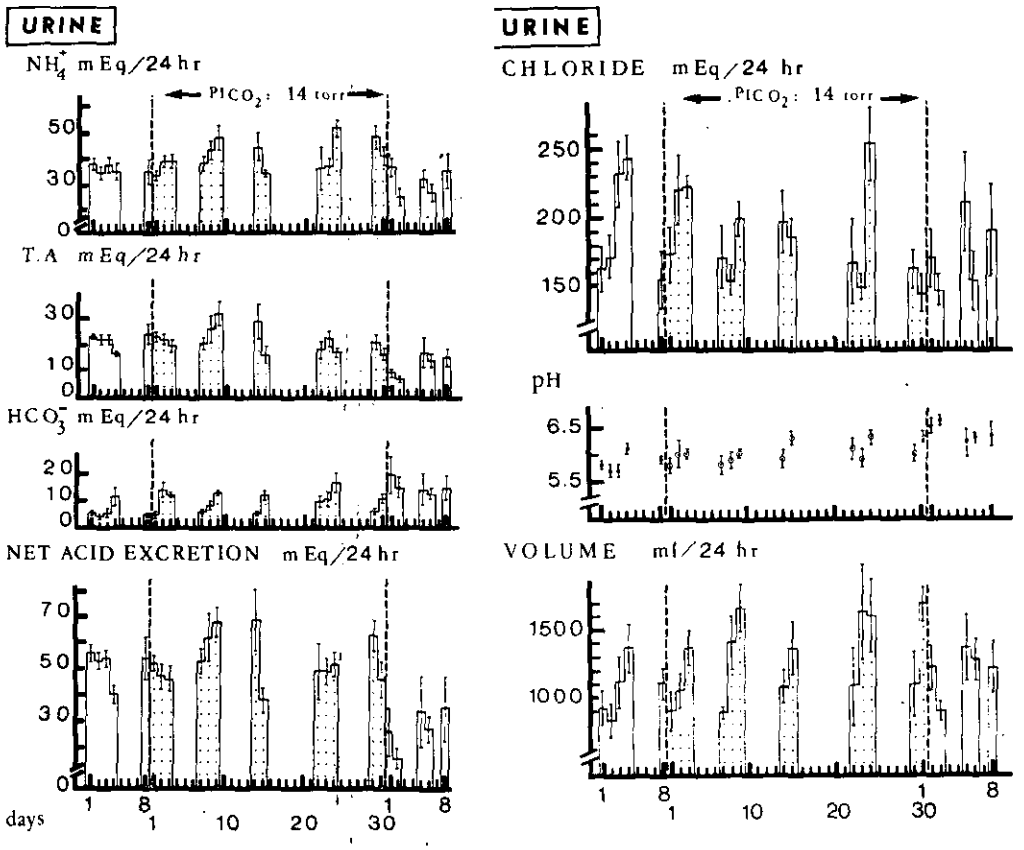

Fig. 4. Effect of 30 days of exposure to a $P_{I_{CO_2}}$ of 14 torr on urinary excretion of electrolytes and on urinary pH and volume; values are means ± SD for 6 subjects.

Body weight

The average body weight of the 6 subjects showed an increase of 1.5 kg during the first three days of the experiment and 0.5 kg on subsequent days.

Electrobiology

Hypercapnia at a $P_{I_{CO_2}}$ of 14 torr caused no significant changes in the electrocardiogram, electroencephalogram, and critical fusion frequency.

Psychomotor testing

As a general rule, in all the tasks assigned to the subjects, a progressive increase in the speed of execution was noted during the first 20 days of the experiment, followed by a subsequent stabilization. Such a development occurred without any significant increase in the number of errors. The results obtained during the coding and classification tests are presented in Fig. 6, as an illustration.

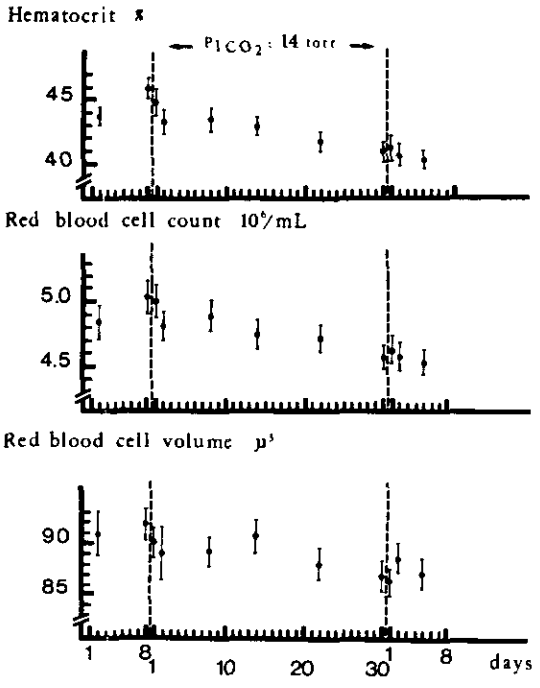

Fig. 5. Effect of 30 days of exposure to a $P_{I_{CO_2}}$ of 14 torr on hematocrit, red blood cell count and red blood cell volume; values are means ± SD for 6 subjects.

TABLE 5

EFFECT OF 30-DAY EXPOSURE TO P_{CO_2} OF 14 TORR ON BLOOD VARIABLES, PLASMA ELECTROLYTES, AND CORTISOL

			Hypercapnia		
		Control Period	Days 1–15	Days 16–30	Recovery Period
Hematocrit, %	Mean	44.77	43.58	41.32*	40.76*
	SD	0.62	0.42	0.54	0.49
	n	12	24	12	18
Red blood cell count, 10^6/ml	Mean	4.93	4.86	4.64*	4.58
	SD	0.09	0.06	0.07	0.06
	n	12	24	12	18
Plasma cortisol, μg/100 ml	Mean	17.08	19.25	16.13	18.47
	SD	0.99	0.74	1.46	0.76
	n	12	24	12	18
Plasma sodium, mEq/liter	Mean	139.6	141.3*	139.6	140.0
	SD	0.3	0.2	0.3	0.3
	n	12	24	12	18
Plasma potassium, mEq/liter	Mean	3.95	3.68	3.52*	3.88
	SD	0.13	0.04	0.05	0.07
	n	11	24	12	18

*Differences significant at the 5% level or better.

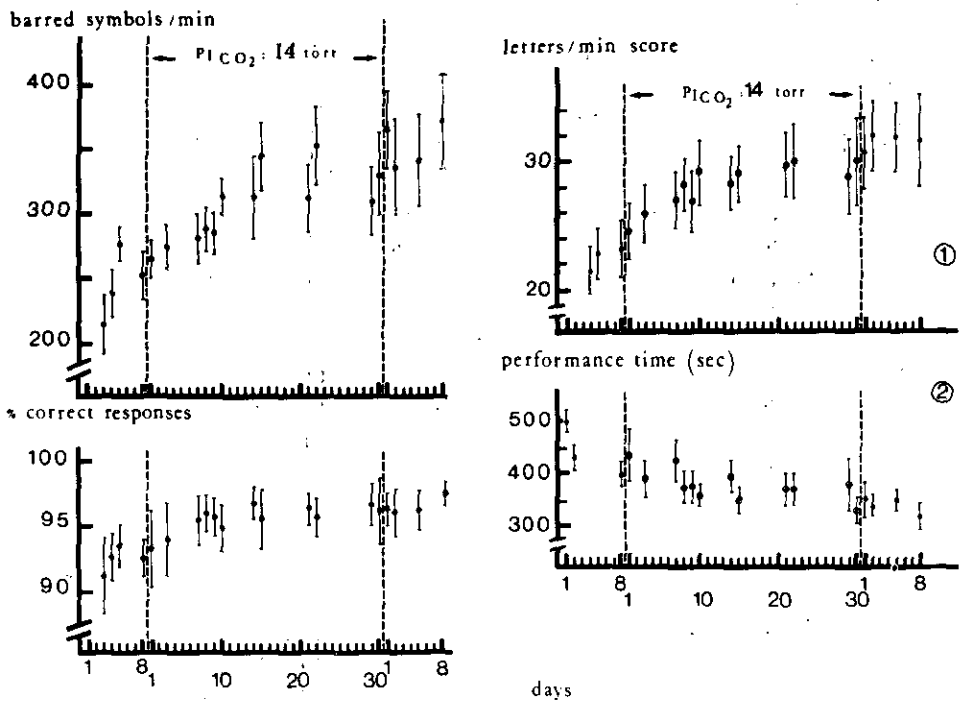

Fig. 6. Effect of prolonged exposure to a P_{ICO_2} of 14 torr on psychomotor performance. *Left*, Zazzo double task results: velocity (barred symbols/min) and % of correct responses. *Right*, (1) Coding test velocity, and (2) Couve - Lezine performance time; values are means ± SD of 6 subjects.

Self-appreciation of psychic state

All subjects tolerated the 45 days of confinement quite well. They reported that time dragged toward the middle of the experiment and this subjective evaluation was supported by responses to the questionnaires they filled out. During this period the subjects' mood and enthusiasm showed a drop. These psychological manifestations diminished later on. After the 45-day confinement, all 6 subjects felt tired for about 10 days and experienced a sensation of "heavy legs."

Circadian rhythm studies

Characteristics of the detected rhythms were defined by the following parameters: acrophase (peak of the cosine function used to approximate the observed time series data), amplitude, and mesor (rhythm-adjusted 24-h mean).

Detailed results and a description of the method of analysis were published earlier (Guillerm, Radziszewski, and Reinberg 1975). The most important finding was that neither a 3-h period of night work every other day nor an unusual amount of CO_2 in the breathing air altered the parameters characterizing the circadian rhythms considered.

Exercise studies

During the last minute of 10-min exercise with a 150-watt work load, the daily mean values of the various parameters measured during the control period were: $\dot{V}_E \simeq 82$ liters BTPS/min; respiratory rate $\simeq 30$ c/min; heart rate $\simeq 176$ beats/min; $\dot{V}_{O_2} \simeq 2.8$ liter STPD/min, $\dot{V}_{CO_2} \simeq 2.9$ liter STPD/min; $R \simeq 1$.

During hypercapnia, the $\dot{V}_{O_2}$, $\dot{V}_{CO_2}$, and R values, and the respiratory and heart rate values did not change and could be compared with the values obtained under normocapnic conditions, but the expiratory minute volume, $\dot{V}_E$, increased about 17%. This increase remained constant throughout the exposure period and was caused primarily by an increase in tidal volume.

As far as $P_{A_{CO_2}}$ was concerned, and taking into account the discussions dealing with the validity of $P_{A_{CO_2}}$ measurements during exercise, only the relative variations between normocapnic and hypercapnic conditions during exercise will be taken into consideration, all things being equal. Thus, the $P_{A_{CO_2}}$ values measured during the exercise period under hypercapnic conditions were 4 to 5 torr above the values observed under normocapnic conditions (it should be remembered that the overload at rest is only 2.5 torr).

DISCUSSION

As already mentioned, chronic hypercapnia studies carried out on submarines have encountered great difficulties. On the one hand, it remains to be proved that the effects observed are actually specific to hypercapnia. On the other hand, low carbon dioxide concentrations ($F_{I_{CO_2}} \leq 1\%$) cause only low-amplitude changes, which are hardly within the precision limits of current techniques for measuring physiobiological parameters. This may explain the discrepancies and uncertainties in the literature, which is why it was decided to conduct laboratory investigations in an environmental chamber. After exposures of shorter duration at a $P_{I_{CO_2}}$ of 21, 28, or 32 torr, it was also decided to apply a partial pressure ($P_{I_{CO_2}}$) of 14 torr for a 1-month period, which pressure is sufficient to produce detectable amplitude changes and yet low enough to be tolerated well.

During such a long experiment, carried out even under the best laboratory conditions, we were confronted with the effects of a change in life styles, which probably caused changes in some constants. To distinguish these effects from those of carbon dioxide proper, an 8-day control period at normal atmosphere was introduced in the experimental protocol, to enable the subjects to adapt to new conditions. Such a control period also made it possible for the subjects to get used to the various examinations in the experimental protocol.

The duration of confinement normally has some effects during 30 days of exposure to hypercapnia, and from a strictly methodological point of view, the results obtained in hypercapnia ought to have been compared with those recorded under normocapnic conditions imposed on the same subjects for the same time. However, although this method is appealing from a theoretical point of view, it could not be carried out, but the 8-day recovery period made it possible, to a certain degree, to distinguish the hypercapnic effects from those of confinement.

Finally, to limit to a certain extent the effects of relative body inactivity, the subjects performed 10 min of exercise on a bicycle ergometer, with a 150-watt work load. In the following discussion, the effects of hypercapnia on the various functions will be analyzed successively.

Resting respiratory studies

During the first 24 h of exposure to a $P_{I_{CO_2}}$ of 14 torr, the initial hyperventilation diminished slightly, and $P_{A_{CO_2}}$ increased an additional torr, which raised the total alveolar and arterial overload to 2.5 torr. This evolution can be compared with that observed during exposures to a $P_{I_{CO_2}}$ of 21, 28, or 32 torr.

All the observations made during the first 24 h of various hypercapnic experiments are summarized in Fig. 7; the $\dot{V}_E$ and $P_{A_{CO_2}}$ values measured after 2 and 24 h of exposure are plotted with the changes in arterial pH corresponding to each situation. According to this figure, the relative decrease in hyperventilation at a $P_{I_{CO_2}}$ of 14 and 21 torr (G_1, G_2) does not appear to be secondary to reduction of the $P_{A_{CO_2}}$ and arterial pH stimuli. This reduction mechanism is not likely to be related to the changes in the acid-base balance of the cerebrospinal fluid because of the short time lag between these changes and arterial blood changes (Clark et al. 1971; Saunier, Schibi, and Colas 1967).

It also looks as if the part played by peripheral chemoreceptors whose time constant is very short (Bouverot, Flandrois, Puccinelli, and Dejours 1965) may be disregarded. Hyperventilation attenuation may be explained by a decrease in respiratory center sensitivity to the P_{CO_2} stimulus.

It is noteworthy that the 2.5 torr alveolar overload alone was able to keep hyperventilation at a steady level during the 30 days of exposure, since there was little or no change in arterial pH after 8 days. Such an overload is almost negligible compared with the $P_{I_{CO_2}}$ ($\Delta P_{A_{CO_2}}$ = 20%

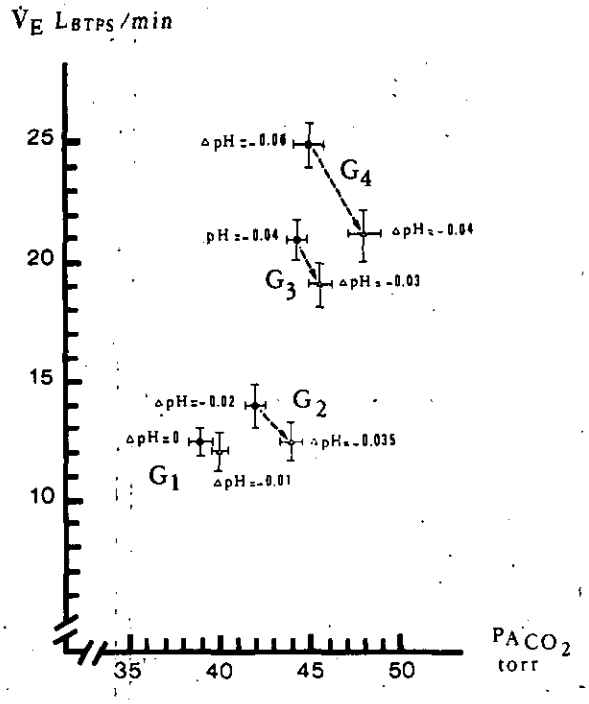

Fig. 7. Human minute expiratory volume ($\dot{V}_E$), alveolar CO_2 tension ($P_{A_{CO_2}}$) and pH decrease (ΔpH) mean values (±SD) after 2 h (o) and 24 h (Δ) at various $P_{I_{CO_2}}$ exposures; G_1, 6 subjects exposed to a $P_{I_{CO_2}}$ of 14 torr; G_2, 15 subjects exposed to a $P_{I_{CO_2}}$ of 21 torr; G_3, 15 subjects exposed to a $P_{I_{CO_2}}$ of 28 torr; G_4, 10 subjects exposed to a $P_{I_{CO_2}}$ of 32 torr.

$P_{I_{CO_2}}$), indicating that the organism was remarkably well protected by the hyperventilation; it also makes it possible to understand why such an exposure was so easily tolerated for one month. At a $P_{I_{CO_2}}$ of 28 torr, this overload reached 8 torr and was already critical, because it produced various signs of intolerance (headaches, stomach pains).

Finally, the effects of hyperventilation on $P_{A_{O_2}}$ should be mentioned. Indeed, $P_{A_{O_2}}$ increased significantly as a function of $P_{I_{CO_2}}$; from 10 torr at a $P_{I_{CO_2}}$ of 21 torr, it rose to 22 torr at a $P_{I_{CO_2}}$ of 28 torr. In a close, confined space, the $P_{I_{O_2}}$ could thus diminish somewhat without affecting the oxyhemoglobin saturation level.

Our results will now be compared with those obtained by Schaefer (1963) in a 42-day exposure to an $F_{I_{CO_2}}$ of 1.5%, which corresponds to a somewhat more moderate hypercapnia than that of our experiment at a $P_{I_{CO_2}}$ of 14 torr. Schaefer (1963) reported an alveolar CO_2 tension increase of 2.5 torr, a value well in line with that found in our experiment. As far as tidal volume and respiratory rate are concerned, he described on the one hand a progressive and continuous increase in V_T throughout the 42-day exposure period, which persisted even after 8 days of recovery. However, we never observed a similar trend during our experiments. Finally, it should be mentioned that in all of our experiments ($P_{I_{CO_2}}$ of 14, 21, 28, or 32 torr), $P_{A_{CO_2}}$ returned to the control value as early as the 24th h of the recovery period, irrespective of the duration and degree of hypercapnia. In addition, this is the result reported by Clark et al. (1971) after a 5-day exposure at a $P_{I_{CO_2}}$ of 30 torr. The transitory alveolar CO_2 tension increase in the presence of normal ventilation may have been due to a fast release of previously accumulated CO_2 from the body stores and a transitory decrease in the sensitivity of the centers to a P_{CO_2} stimulus. Schaefer (1963) reported an overload that persisted for another 8 days after the end of the exposure period and that was thought to be secondary to a slow and progressive delivery of CO_2 from body stores accumulated during the hypercapnic period. An approximate calculation from data published by Farhi (1964) showed that for an overload of a few torr, the amount of stored CO_2 was negligible compared with the metabolic CO_2 that was rejected.

Acid-base balance

At a $P_{I_{CO_2}}$ of 14 torr, the hypercapnia is very moderate ($\Delta P_{A_{CO_2}} = \Delta P_{a_{CO_2}} = 2.5$ torr) and causes only very mild changes in arterial pH (0.01 pH unit, on the average). The difficulties of detecting pH changes of such low amplitude with current measuring techniques should be emphasized; moreover, no change in arterial pH was noted in 3 of 6 subjects, despite an appreciable increase in $P_{a_{CO_2}}$. In the other 3 subjects, the phase of respiratory acidosis compensation had already started between the third and the eighth day, and acidosis seemed to have been completely compensated by approximately the 15th day of exposure. Under more moderate hypercapnia exposure to an $F_{I_{CO_2}}$ of 0.9%, Peck (1971) only observed a mild decrease in arterialized capillary blood pH by the second day of exposure. According to Pingree (quoted by Davies 1973) the arterial blood pH decreased, though it was mild and persisted during the 40 days of exposure. The respiratory acidosis was therefore very mild and hardly detectable during exposure to concentrations of $\leq 2\%$; this also explains why it was difficult to determine the period of compensated respiratory acidosis precisely. Finally, it appears that the findings of Schaefer, Nichols, and Carey (1964) relating to the amplitude of pH changes (0.06 pH unit) should be revised. Clark et al. (1971) also observed a pH change of such magnitude only during more hypercapnic exposures, such as to $P_{I_{CO_2}}$ of 28 and 32 torr. We also studied the contribution of the kidney to respiratory acidosis compensation. The results of the

study showed a slight increase in net acidity after 8 days of exposure, which corresponded to the increase in NH^+_4 ion excretion and titratable acidity.

In view of the low amplitude of the variations observed, one may wonder whether the net acidity increase corresponded to the renal process and came into play to compensate for an otherwise very mild respiratory acidosis, or whether there is any reason to consider the possible influence of other factors, such as for example diet, on the H^+ ion excretion level. It is difficult to answer this question because the diet was not standardized. During more severe hypercapnia as in the case of P_{ICO_2}'s of 28 and 32 torr, it has been shown that the renal response is important and limited to the first 24 h of exposure (Radziszewski et al. 1976). Even at a P_{ICO_2} of 21 torr, Glatte, Motsay, and Welch (1966) observed no changes in net acidity, while Gray et al. (1973) noticed a decrease in net acidity during the first two weeks of exposure to an F_{ICO_2} of 1% for 49 days followed by an increase for another two weeks and a further fall subsequently.

When analyzing all these results, it was found that during exposures to CO_2 concentrations $\leq 2\%$, the renal response, if any, was mild and occurred very late in comparison with effects observed during more acute hypercapnic exposures.

Metabolism and dead space studies

The increase in oxygen uptake (+ 10%) and CO_2 output (+ 10%) with no change in respiratory quotient may be explained by an increase in the work of the ventilatory muscles during hyperventilation.

The absence of significant changes in plasma cortisol level during exposure to a P_{ICO_2} of 14 torr demonstrated that the threshold of the adrenocortical activity was not reached, which rules out any hormonal stimulation of the metabolism. Moreover, it has been shown (Radziszewski 1974) that this threshold is only reached at a P_{ICO_2} of 32 torr.

During the first 23 days of exposure to an F_{ICO_2} of 1.5%, Schaefer et al. (1963) noticed a significant reduction in respiratory quotient as a result of a fall in $\dot{V}CO_2$ (20%), which they attributed to the accumulation of CO_2 in the various stores in the body; although this hypothesis cannot be completely ruled out, it alone does not appear to be able to explain such an important drop in $\dot{V}CO_2$.

The increase in physiological dead space observed at a P_{ICO_2} of 14 torr confirms the observations we made at a P_{ICO_2} of 21, 28, and 32 torr, and may be attributed to two facts: first, a rise in alveolar dead space, and second, an increase in anatomical dead space.

The simultaneous measurements of P_{ACO_2} and Pa_{CO_2} taken during our experiments included a total of 114 measurements that have shown that the $(a\text{-}A)CO_2$ difference is negligible in a healthy person at rest and does not rise during moderate hypercapnia, as is the case at a P_{ICO_2} of 14 torr. From a functional point of view, these results indicate that moderate hypercapnia does not affect the quality of pulmonary gas exchange and that changes in alveolar dead space are negligible.

Finally, it seems likely that the rise in physiological dead space observed during hypercapnia might be due solely to increased anatomical dead space. In this connection, two assumptions can be made: the first one deals with the direct effect of CO_2 on bronchiole tone, the second with changes in the caliber of the bronchi induced by hyperventilation. As far as the first hypothesis is concerned, the studies carried out by Nadel and Widdicombe (1962) have shown that carbon dioxide produces a bronchodilatation through direct action on the chemoreceptors in the mucosa and a bronchoconstriction through reflex action; the resulting increase in dead space is likely to be moderate, and this rise alone is not sufficient to explain

the changes observed. The second hypothesis seems more logical: that the rise in physiological dead space is mainly due to a bronchodilatation caused by a significant hyperventilation (Stein and Widdicombe 1975). Moreover, it should be noted that during the first 24 h of the recovery period, ventilation and physiological dead space simultaneously returned to control values despite a still elevated Pa_{CO_2}. This appears to support our analysis.

Plasma electrolytes

It should be specified that natremia changes (+ 1.5%) were within range of the measuring technique's accuracy, and therefore this result should be interpreted with great care.

As far as kaliemia is concerned, data from the literature are more homogeneous; indeed, hyperkaliemia was generally found during respiratory acidosis (Elkinton, Singer, Barker, and Clark 1955; Kilburn 1965; Reichart and Puchelle 1971). In the first analysis, the moderate hypokaliemia (6%) noticed at a $P_{I_{CO_2}}$ of 14 torr does not appear to be secondary to hypercapnia but to other factors inherent in prolonged confinement of periods exceeding 4 weeks. Yet the return to normocapnic conditions was marked by a fast correction of the hypokaliemia: this being so, it would be desirable to determine whether a moderate and prolonged hypercapnia, in contrast to acute hypercapnia, causes hypokaliemia. The significance of our results is not clear and needs further investigation. Yet it must be specified that Peck (1971), Messier, Heyder, and Schaefer (1971) and Gortner et al. (1971) also noted a kaliemia reduction during the first 30 days of exposure to an $F_{I_{CO_2}} < 1\%$, which appears to give support to our analysis.

Studies on the kinetics of Ca^{++}, Mg^{++}, and P(i) ion concentration in plasma showed a transitory increase in Ca^{++} only during the first 2 h of exposure and the recovery period. On the other hand, concentration changes were mild and not much affected by hypercapnia. Studying calcium metabolism is important because Schaefer et al. (1963) described considerable disturbance in this process, which caused a histopathological impairment, especially in the kidneys (Schaefer, Hasson, and Niemoeller 1961). Gray et al. (1973) also noticed a rise in plasma Ca^{++} concentration associated with a fall in the quantity excreted, a result that favors an increase in the reabsorption of this element.

Conclusions concerning calcium metabolism cannot be drawn from our results because in addition to plasma determinations, the total amount of the quantities ingested and eliminated every day ought to have been determined. Nevertheless, stress must be laid upon the fact that hypercapnia alone, as in the case of our experiment at a $P_{I_{CO_2}}$ of 14 torr, did not seem to produce changes in plasma Ca^{++} concentration. The question is then raised whether the trends described by Schaefer et al. (1963), Gray et al. (1973), and Schaefer (1976), and attributed to hypercapnia are not actually related to other factors peculiar to the life on board submarines such as for example total lack of sunlight, reduced body activity, drinking of demineralized water, etc.

Hematological parameters

The hematocrit reduction found at a $P_{I_{CO_2}}$ of 14 torr is caused to a great extent by a decrease in red blood cell count (10%) and to a lesser extent by a reduction in the mean red blood cell volume ($\simeq 4\%$). The red blood cell count decrease is in contrast to what Baker and Schaefer (1969) and Reichart and Puchelle (1971) noticed in animals exposed to hypercapnic conditions; it is also in contrast to what we noticed in man at a $P_{I_{CO_2}}$ of 28 and 32 torr, and it therefore seems unlikely that it is connected with hypercapnia. The RBC decrease may be due to the development of a mild anemia produced by prolonged confinement. In any case, it cannot be

attributed to blood withdrawal (150 ml in 45 days). The origin of the corresponding decrease in red blood cell volume is still unclear.

Adrenocortical activity

We studied the daily excretion pattern of the 17-ketosteroids, 17-hydroxycorticoids, and vannillyl-mandelic acid (VMA) during exposures at a $P_{I_{CO_2}}$ of 21, 28, and 32 torr. These determinations enabled us to set the adrenocortical activity stimulation threshold at a $P_{I_{CO_2}}$ of 32 torr. Indeed, during exposures to a $P_{I_{CO_2}}$ of 32 torr, we found a rise in the excretion of 17-ketosteroids ($+30\%$; $P > 0.001$) and in some subjects an increase in VMA excretion as high as 20% of the basic value. This threshold actually corresponds to an arterial pH reduction amounting to 0.06 of a pH unit. Taking these results into consideration, it seemed unlikely that a stimulation could be observed at a $P_{I_{CO_2}}$ of 14 torr. Yet Schaefer et al. (1964) noticed an adrenal activation in guinea pigs exposed to an $F_{I_{CO_2}}$ of 1.5% at the end of a 7-day period. We therefore carried out a determination to check whether the duration effect might not have influenced the adrenocortical activity. This assumption may be ruled out in humans, since no significant changes in plasma cortisol level were found.

Biorhythms

For the physiological parameters involved, the results showed that hypercapnia at a $P_{I_{CO_2}}$ of 14 torr was tolerated well. Moreover, shifting the watch schedules produced no biorhythm disturbances. When interpreting these results, it should be borne in mind that the subjects were relatively young men who seem to have adapted quite well to this new way of life. It is certain beyond doubt that the acrophases of the various variables did not shift with time (Guillerm et al. 1975).

Psychomotor testing

It must be noted that all psychomotor tests revealed the effect of training on performance speed and sometimes on the precision with which the test was performed. This is true for any long-duration experiment during which the same test is repeated several times, even when the procedure alone is exactly the same; as a matter of fact, it is even true when the testing equipment is changed each time to avoid any possible memorizing by the subject. In other words, the subject grows familiar with a given task and learns a method of working. Thus it is not possible to compare the experimental phase (under CO_2 exposure) directly with the two control phases (beginning and end of the experiment); it can only be determined whether the results were perturbed or modified as a function of time during the transition from one phase to another.

Finally, hypercapnia and confinement failed to induce any significant degradation in psychomotor performance.

Subjective symptoms

It seems likely that the fatigue felt by all the subjects at the end of the 45-day confinement period and characterized primarily by a sensation of "heavy legs" and a need for rest might be attributed to reduced body activity throughout the experiment. However, because similar trends have already been reported at the end of exposures of shorter duration at higher $P_{I_{CO_2}}$

levels, it might be advisable to assign the CO_2 factor a certain part in the development of fatigue. It should, however, be remembered that this subjective fatigue did not alter the psychosensorial performance of the 6 subjects.

Application to exposure limit

It is not easy to select a permissible CO_2 concentration limit for long submarine patrol missions. It would be desirable to approximate the concentrations found in the general environment, which are generally lower than or equal to 0.2% and are known by experience to cause no effects whatsoever. However, when the considerable increase in power and especially in the overall dimensions of the carbon dioxide removal facilities that attaining such a low CO_2 concentration would involve, on the one hand, and, on the other hand, the remarkable tolerance shown by subjects exposed to relatively high CO_2 concentrations during laboratory experiments are weighed, we arrive at a compromise between technical/military necessity and personnel tolerance.

The principal data to be taken into account are the CO_2 overload in alveolar air and hence in arterial blood (as noted earlier, $P_{A_{CO_2}} = Pa_{CO_2}$ in our experiments). Figure 8 shows that in

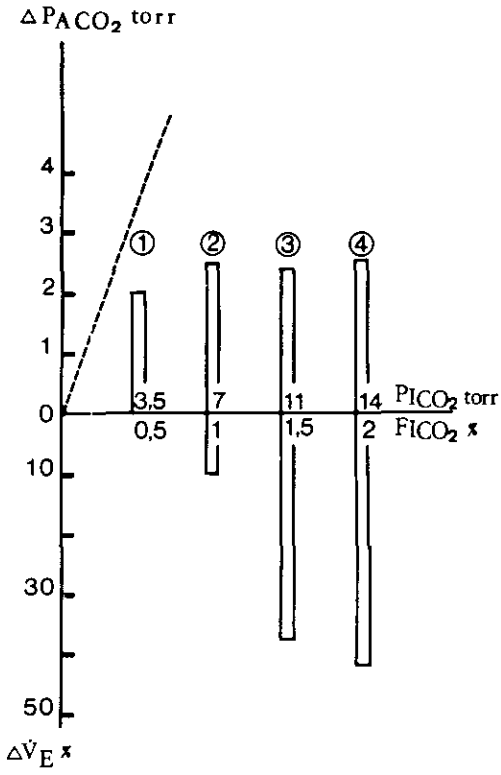

Fig. 8. Alveolar CO_2 tension and expiratory minute volume variations during human chronic hypercapnia experiments: (1) Davies, cited by Schaefer (1967); (2) Guillerm et al., unpublished data, CERTSM Report, 1957; (3) Schaefer (1963); (4) our data at a $P_{I_{CO_2}}$ of 14 torr. $P_{A_{CO_2}}$ overload is approximately the same between an $F_{I_{CO_2}}$ 0.5% and 2%; dotted line represents theoretical $P_{A_{CO_2}}$ overload without hyperventilation.

chronic hypercapnia, this overload does not vary very much (from 2 to 2.5 torr) for $F_{I_{CO_2}}$ values between 0.5 and 2%, because of the protection provided by the hyperventilation that grows gradually with $F_{I_{CO_2}}$. The overload only brings about a barely detectable respiratory acidosis ($\Delta pH < 0.01$) that is quickly compensated. Otherwise the overload causes no noticeable difficulties.

The second datum to be taken into consideration is the extent of hyperventilation: the 60% hyperventilation observed during exposure to an $F_{I_{CO_2}}$ of 2% is not desirable because of the metabolic cost involved. On the other hand, the hyperventilation cost of 1% ($\Delta \dot{V}_E = 10\%$) and at 0.5% [very mild hyperventilation, personal communication, Davies, 1976] is negligible. This clearly indicates that it does not matter much which value between 0.5 and 1% is selected; the overload and its effects will be the same for the organism. One would indeed have to lower the CO_2 level below 0.2% to do away with virtually any overload.

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Guillerm, R., and E. Radziszewski. 1979. Effets sur l'homme de 30 jours d'exposition a $P_{I_{CO_2}}$ 14 torr (2%): Applications aux limites de l'exposition. Undersea Biomed. Res. Sub. Suppl.: S91–S114.—*La fonction pulmonaire*, l'équilibre acido-basique, l'excretion rénale des électrolytes, l'hématologie, les biorythmes, et les fonctions psychomotrices ont été étudiés chez six hommes exposés pendant 30 jours à $P_{I_{CO_2}}$ de 14 torr ($F_{I_{CO_2}} = 0{,}02$) avec pré- et post-expositions en air. Les P_{CO_2} alvéolaire et artérielle son augmentés et sont restés constants pendant la période entière de l'exposition ($\Delta P_{A_{CO_2}} = \Delta P_{a_{CO_2}} = 2{,}5$ torr); l'augmentation du volume expiratoire minute ($\Delta V_E = 60\%$) est en rapport avec l'augmentation du volume tidal. La consommation d'oxygène et l'élimination de CO_2 sont augmentées de 10% à cause de la surcharge de travail ventilatoire. L'espace mort respiratoire est augmenté de 8% sans qu'une différence des P_{CO_2} alvéolaire-artérielle soit observée. L'acidose respiratoire est modeste ($\Delta pH \leq 0{,}01$), comme la réponse rénale. Sauf une diminution légère de potassium, aucune variation des électrolytes plasmatiques n'est observée. Le taux d'érythrocytes est diminué, indice de l'effet "confinement." L'adaptation à l'exercice est légèrement inhibée. Les résultats des tests électrobiologiques et psychomoteurs, comme les évaluations des biorythmes, ne font apparaître aucune variation. La discussion traite l'application de ces constatations aux limites de l'exposition au CO_2.

hypercapnie chronique
ventilation
tension alvéolaire de CO_2
pression artérielle de CO_2
espace mort respiratoire
équilibre acido-basique
électrolytes plasmatiques
électrolytes urinaires
hématologie
électrobiologie
tests psychomoteurs
biorythmes
limites de l'exposition à CO_2

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4. Respiratory Gas Exchange, Acid-Base Balance, and Electrolytes during and after Maximal Work Breathing 15 mm Hg $P_{I_{CO_2}}$

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Introduction

It is generally accepted on the basis of practical experience in submarines and other confined spaces that accumulation of CO_2 in the inspired air amounting to a partial pressure of 15 mm Hg is subjectively acceptable—if even noticeable—and compatible with ordinary physical and mental activities. Nevertheless, measurable changes in ventilation and alveolar P_{CO_2} have been reported by Lambertsen [1960] in resting subjects at 15 mm Hg P_{CO_2} and in light exercise by Froeb [1960]. Schaefer and his associates [1963] have described alterations in respiration, acid-base, and electrolyte balance in the course of acclimatization and de-acclimatization to an environment with a $P_{I_{CO_2}}$ of 11 mm Hg. Relatively little factual information exists, however, on the effects of CO_2 under conditions of strenuous exertion verging on the limits of work capacity as might be encountered in emergency situations in space operations, in submarines, or in diving activities. An excellent investigation by Menn, Sinclair, and Welch [1970] with inspired CO_2 tensions ranging from 8 to 30 mm Hg revealed a consistent and proportionate increase in ventilation, but reduced CO_2 output and respiratory exchange ratio (R.E.R.) in submaximal exercise. In exhausting exercise, with $P_{I_{CO_2}}$ 21 mm Hg ventilation was not significantly different from the controls, while maximal O_2 intake was only slightly less. But there was a highly significant reduction in CO_2 output. These authors concluded that strenuous exercise with exogenous hypercapnia leads to CO_2 retention, adding respiratory acidosis to the metabolic one, thus forcing the respiratory system to its limits.

The following experiments were designed to further explore the interaction of hypercapnia and exercise with a $P_{I_{CO_2}}$ of 15 mm Hg, which is the highest acceptable level for emergencies in spacecraft, by following the respiratory and circulatory responses to graded exercise including maximal work capacity and the alterations in acid-base balance, blood gases, and electrolytes at the breaking point and during recovery.

Methods and Procedures

The study consisted of two series of experiments. The first was focused primarily on exercise tolerance in terms of maximal aerobic power with and without added CO_2 and the course of respiratory and cardiovascular adjustments under increasing work loads. Twelve subjects participated in this series working on a bicycle ergometer at an initial brake load of 300 kpm/min at 50 rpm for the first three minutes. Subsequently the brake load was increased by 75 kpm/min every minute until the subject was unable to maintain the pedaling rhythm given by a metronome. Each subject was his own control

with one test on air and the other with a mixture producing a Pt_{CO_2} of 15 ± 2 mm Hg in random sequence. With the exception of the technician operating the gas supply, neither the subject nor the investigators monitoring the test were aware which gas was being administered. Both gases were supplied from pressure tanks through a large humidifying bottle and buffer bag with wide-bore tubing (i.d. 3.4 cm) to a low-resistance unidirectional breathing valve (Lloyd). The total resistance of the valve and collecting tubing was 2.5 cm H_2O at a flow rate of 5 l./sec. Heart rate and blood pressure were recorded each minute, and ventilation and gas exchange were derived from expired air collected at regular intervals in neoprene bags and analyzed immediately by the Scholander technique. With two exceptions, the subjects were not habitually active physically. Their mean age was 26.5 years, mean height 179 cm, mean weight 75.9 kg, and mean body surface area 1.93 m^2. Subjective sensations during tests with CO_2 elicited after both tests had been performed varied from no difference to a feeling of acute suffocation at the end point.

In the second series of tests on 10 subjects main attention was directed toward the interactions between respiratory gas exchange with arterial blood gases, acid-base balance, and electrolytes at peak performance and during 30 min of recovery. The exercise protocol was similar to the one followed in the first series, with the difference that an attempt was made to equalize the duration of exercise by imposing a handicap on the stronger subjects by increasing the brake load by 150 instead of 75 kpm/min during the first few minutes of the test so that the average duration to exhaustion was 14 min.

Prior to the exercise data were obtained at supine rest for 10 to 15 min after an indwelling Teflon catheter had been inserted into a brachial artery under local anesthesia. Blood was drawn simultaneously with respiratory measurements for blood gases and pH and the determination of sodium, chloride, potassium, calcium, phosphorus, total plasma protein, hemoglobin, cholesterol, and lactic dehydrogenase. The subject then mounted the bicycle and began the exercise program. Ventilation measurements were made during the last two minutes of exercise and in an uninterrupted sequence for the first seven minutes of recovery sitting on the bicycle. During the eighth minute the subject moved to an adjacent couch and expired air was collected in the 8–10th, 11–14th, 15–18th, 19–22nd, 23–26th, and 27–30th minutes. Arterial samples were drawn during the last minute of exercise, from 30–60 seconds after ceasing work, then in the 4th, 10th, 20th, and 30th minutes of recovery. Blood gases and pH were measured immediately with a Corning Model 16 electrode system, plasma bicarbonate and base deficit were derived according to Sigaard-Anderson whereby no correction was made for actual body temperature which was not measured. Analyses for calcium, phosphorus, total protein, cholesterol, and LDH were performed on a sequential auto analyzer (Technicon 12/30). Sodium, potassium, and chloride were measured with a four-channel electrolyte analyzer (Technicon). Hemoglobin determinations were made on samples at rest before exercise, in the first minute after and after 30 minutes using the cyanmethemoglobin method.

Results

I.

Table 1 presents circulatory data at three ascending work loads and at the end point. At all submaximal work loads the mean heart rate was consistently slightly higher in the runs with CO_2 than in the controls. However, the difference was not statistically significant. At the end point heart rate was always lower in the experimental tests than in the control, as if other than cardiovascular factors prevented the subjects from reaching their maximal frequencies. Systolic blood pressure was regularly higher on the average at all work

Table 1. Cardiovascular Parameters, Mean Values for 12 Subjects

	300 kpm/min		600 kpm/min		900 kpm/min		End point	
	Control	Exper.	Control	Exper.	Control	Exper.	Control	Exper.
Heart rate	111	114	128	131	152	155	185	180
Systolic blood pressure	143	150	159	167	181	188	204	211
Oxygen pulse	8.2	8.3	10.5	10.3	13.0	12.8	16.8	15.1

loads, including the maximal level with CO_2 without this being statistically significant. It was also noted that the O_2 pulse (product of stroke volume and arteriovenous O_2 difference) was less at end point with CO_2 than on air, while there was little difference under submaximal work conditions.

The respiratory data shown on Table 2 shows the expected excess ventilation caused by CO_2 at the lower and submaximal work loads, where the difference was 40 to 50% and statistically highly significant. At maximal work, however, the difference was only 2% and not significant.

Mean O_2 consumption was consistently slightly higher in the experimental runs at the intermediate work levels, possibly reflecting the increased energy cost of breathing. On the other hand, the significantly lower maximum O_2 uptake (−13%) is due to the fact that the subjects could not perform as much work under the effect of added CO_2. On the other hand, CO_2 elimination was consistently lower on the experimental mixture at comparable work levels, and the tendency for CO_2 loading is also apparent from the lower respiratory exchange ratios as seen on the last line of Table 2.

The hypothesis for this study had postulated on the basis of the alveolar equation (7) modified for CO_2 in the inspirate that in order to maintain the same P_{CO_2} and pH for a given CO_2 output with $P_{I_{CO_2}} = 15$ mm Hg, total ventilation would have to increase by more than 60%. The results in Table 3 show that the average increase in ventilation was actually only 48% at 300, 47% at 600, and 43% at 900 kpm/min, whereas at the end point ventilation was only 2% more on CO_2 than in the controls. The implications are that while a moderate degree of hypercapnia must be already present during submaximal exercise with CO_2, CO_2 loading must assume drastic proportions during maximal exertion where further increase in ventilation is no longer possible leading to acute respiratory acidosis at a point where metabolic acidosis is rapidly building up. The second series of experiments was to substantiate this contention.

Gas Exchange
II

As pointed out earlier, in the second series respiratory measurements were made at recumbent rest before exercise, during the

Table 2. Ventilation and Gas Exchange, Mean Values for 12 Subjects

	300 kpm/min		600 kpm/min		900 kpm/min		End point	
	Control	Exper.	Control	Exper.	Control	Exper.	Control	Exper.
V_I BTPS	27.67	41.04	40.0	58.7	62.66	89.45	139.4	142.2
V_{O_2} STPD	.89	.93	1.31	1.329	1.95	1.97	3.10	2.69
V_{CO_2} STPD	.84	.66	1.22	1.094	1.94	1.84	3.44	2.84
R.E.R.	.94	.71	.93	.82	.99	.94	1.11	1.06

Table 3. Ventilation and Respiratory Gas Exchange, Mean Values and Standard Deviations

	l./min. (BTPS)		l./min. (STPD)		l./min. (STPD)					
	Ventilation		O_2 *uptake*		CO_2 output		Resp. Exch. R.		Ventil. Equiv. for O_2	
$n = 10$	$\bar{c}$ CO_2	Air	$\bar{c}$ CO_2	Air	$\bar{c}$ CO_2	Air	$\bar{c}$ CO_2	Air	$\bar{c}$ CO_2	Air
Rest	9.23	9.23	.274	.291	.249	.243	.910	.835	33.7	31.7
	2.90	2.34	.032	.029	.050	.035	—	—	—	—
Exercise,	126.09	121.17	2.923	3.112	2.989	3.392	1.023	1.090	43.1	38.9
2nd last'	20.57	25.30	.305	.389	.475	.492	—	—	—	—
Exercise,	133.05	125.93	3.179	3.279	3.202	3.558	1.007	1.085	41.8	38.4
last'	18.61	23.38	.275	.432	.339	.479	—	—	—	—
Recovery,	117.04	109.14	2.116	2.217	2.483	2.790	1.173	1.258	55.3	49.2
1'	12.46	17.56	.285	.304	.271	.377	—	—	—	—
2–3'	82.52	61.95	.937	.902	1.301	1.339	1.388	1.484	88.1	68.7
	21.69	11.68	.152	.129	.287	.178	—	—	—	—
4–5'	53.85	38.06	.616	.629	.739	.764	1.120	1.215	87.4	60.5
	8.76	6.44	.092	.084	.144	.092	—	—	—	—
6–7'	48.81	34.67	.581	.616	.593	.660	1.021	1.071	84.0	63.8
	9.55	9.70	.113	.112	.113	.093	—	—	—	—
9–10'	43.36	26.39	.618	.632	.580	.589	.939	.967	70.0	41.8
	12.05	5.16	.116	.087	.151	.082	—	—	—	—
12–14'	30.47	18.58	.423	.432	.362	.373	.856	.863	72.0	43.0
	6.17	2.94	.055	.052	.085	.055	—	—	—	—
16–18'	24.96	15.76	.400	.395	.297	.307	.743	.777	74.9	39.9
	4.92	2.68	.075	.061	.065	.044	—	—	—	—
20–22'	20.65	13.30	.343	.373	.243	.273	.711	.732	60.2	35.7
	4.53	2.05	.064	.042	.062	.059	—	—	—	—
24–26'	18.90	12.82	.341	.364	.221	.243	.648	.669	55.4	35.3
	3.49	2.21	.052	.051	.045	.040	—	—	—	—
28–30'	17.40	11.25	.335	.338	.208	.217	.621	.642	51.9	33.2
	1.72	1.49	.055	.042	.016	.018	—	—	—	—

Note: All values given for "Rest" in Tables 2 through 6 were obtained breathing air.

last two minutes of maximal exercise and during recovery. Figure 1 shows O_2 intake in black with 15 mm Hg Pi_{CO_2} and cross-hatched for the controls on air. Consistent with the observations in the first series, oxygen consumption and maximum work was less with CO_2 in the last two minutes at work and during the first minute of recovery. For the following 30 min there was no appreciable difference and the cumulative O_2 consumption for this period was not significantly different being 14.9 l. with CO_2 and 15.3 l. on air. In ventilation also (Figure 2) there was not much difference between the experimental runs and the controls in the last two minutes at maximal work and the first minute of recovery. It will be noted that during that time ventilation was well over 100 l./min. But already in the 2 to 3 min, and for each sample period, ventilation was significantly greater with added CO_2, as more ventilatory reserve became available. This sequence of events is also reflected in the CO_2 output (Figure 3), which was significantly less (statistically) only during the last two minutes of exercise and the first minute of recovery. Thereafter the difference was consistently present over the 30 min but was no longer significant. The respiratory exchange ratio (R.E.R.) plotted in Figure 4 indicates that while under experimental and control conditions much more CO_2 was discharged than O_2 taken up (particularly during the first few minutes of recovery) the

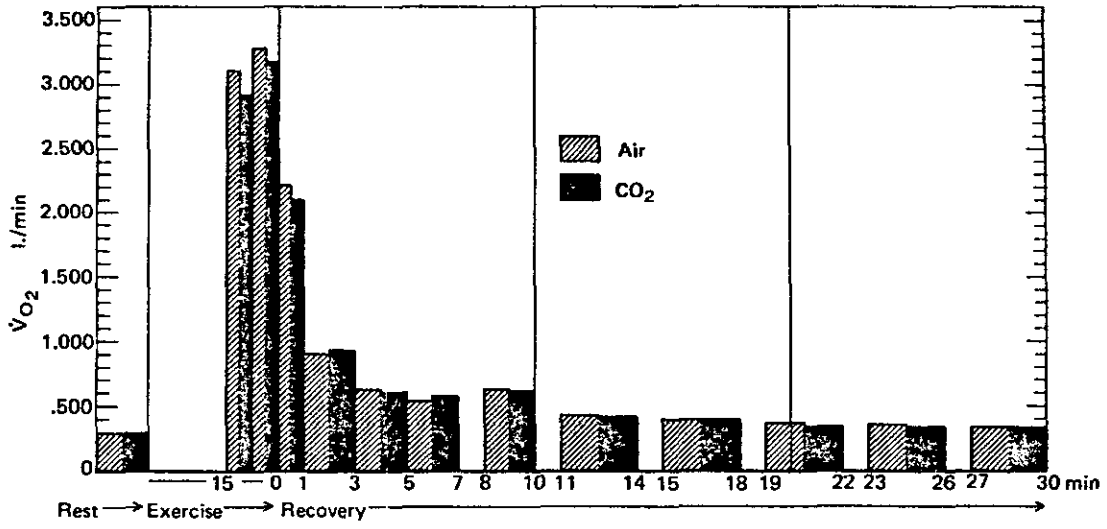

Fig. 1. Oxygen intake at rest before, during the last two minutes of exercise and for 30 r . recovery.

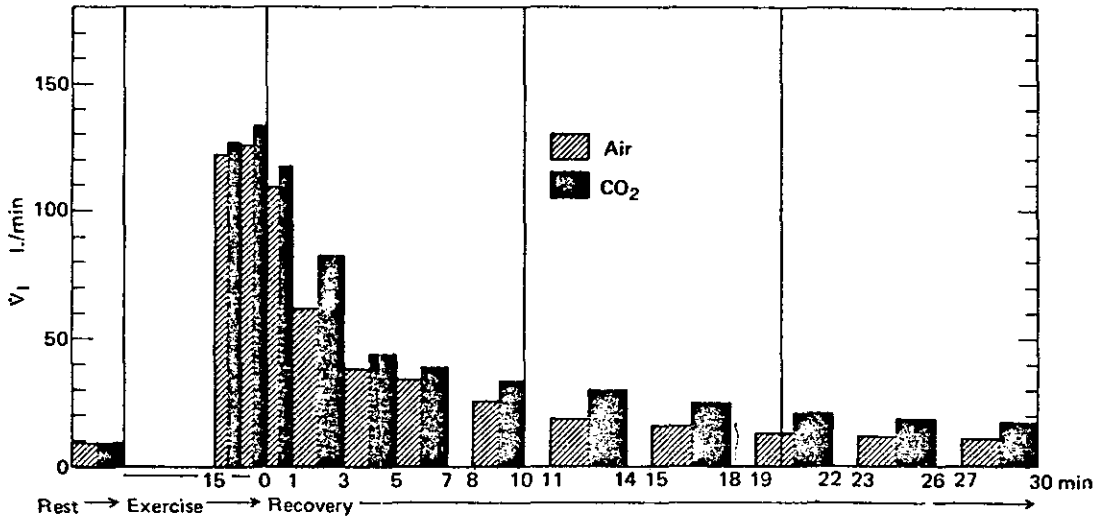

Fig. 2. The same as Figure 1 for ventilation.

inspired CO_2 had a distinctly depressing effect on its liberation from the body. The excess ventilation attributable to the relatively low partial pressure of CO_2 in the inspired air is perhaps best expressed in terms of specific ventilation or the ventilation equivalent for O_2 (Figure 5). The usual rise in specific ventilation after exhaustive exercise seen in our controls on air was greatly exaggerated by the inspired CO_2, and the difference was sustained throughout the entire recovery period.

Acid-Base Balance

The addition of small amounts of CO_2 to the inspired air also had a profound effect on the well known pattern in acid-base balance during and after vigorous exercise

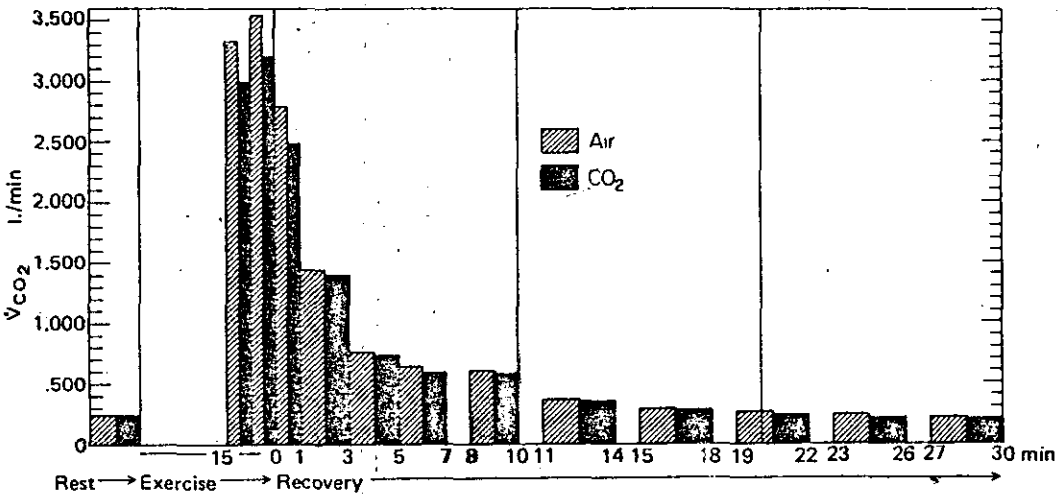

Fig. 3. The same as Figures 1 and 2 for carbon dioxide output.

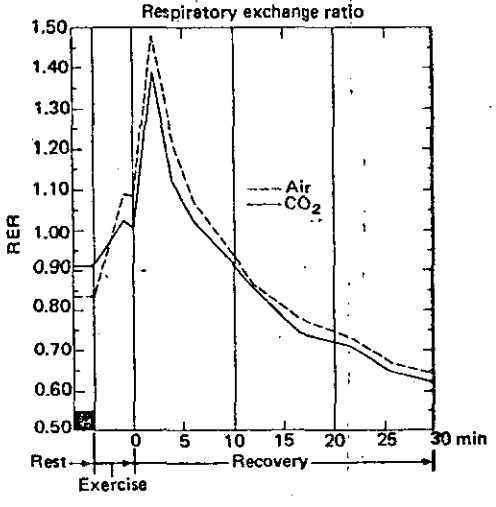

Fig. 4. The same as Figures 1 to 3 for the respiratory exchange ratio.

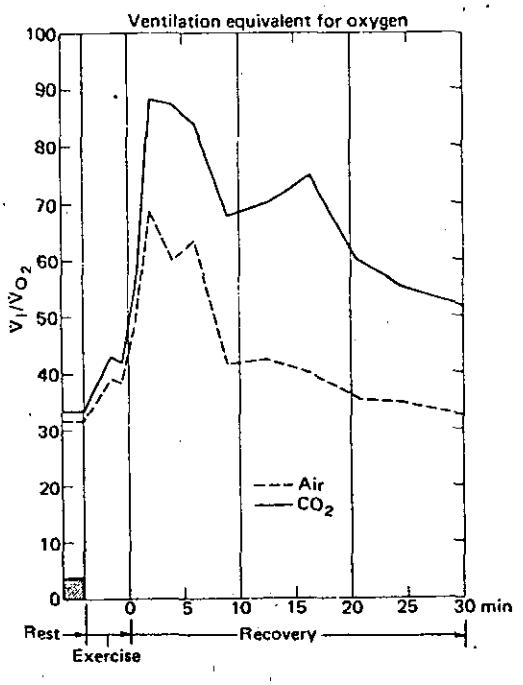

Fig. 5. The same as Figures 1 to 4 for the ventilation equivalent for oxygen.

(Figure 6). Whereas in the control runs arterial P_{CO_2} dropped to 30 mm Hg at the end of work and continued down to 26 mm Hg in the fourth minute of recovery, the course was different when CO_2 was added to the inspirate. Here arterial P_{CO_2} rose to 41 mm Hg in the last minute of exercise and dropped very little in the first minute after work, with a minimum of 33 mm Hg in the fourth minute of recovery (Table 4).

The observed fall in P_{CO_2} seen in the controls which signifies relative alveolar hyperventilation runs closely parallel to the sharp drop in bicarbonate during and continuing after exercise as an index of acid

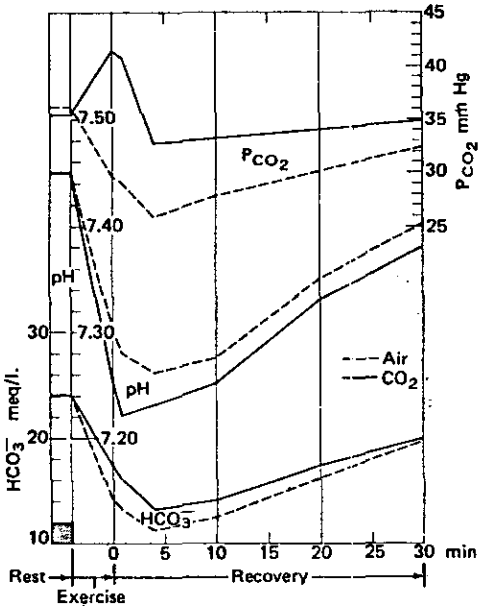

Fig. 6. Acid-base changes during and after exercise with and without 15 mm Hg $P_{I_{CO_2}}$.

metabolites accumulating in the blood. Apparently the partial respiratory compensation for metabolic acidosis is seriously jeopardized by the inspired CO_2 because ventilatory capacity is already overtaxed. In consequence we see a significantly lower pH with CO_2 than in the controls at the end of exercise and the difference increases in the first minute of recovery. Shortly thereafter the fall in pH is arrested, in spite of a continued loss of bicarbonate, when ventilation again begins to gain ground and reduces P_{CO_2}. The turn of the tide comes when the bicarbonate begins to increase, gradually restoring pH toward the initial value in the course of 30 min. It is noted that the bicarbonate was not reduced as much in the tests with CO_2 as in the controls. This could be attributed to the lower P_{CO_2} in the latter, following the CO_2 dissociation curve. To clarify this we have plotted base deficit, which is independent of P_{CO_2}, together with H^+ activity in Figure 7. This reveals two things. First, it confirms that the loss of buffer capacity due to the influx of fixed acid was slightly greater in the controls with added CO_2. Secondly, the tests with CO_2 show a significantly higher peak in H^+ activity in spite of a lesser metabolic acidosis, due to relative ventilatory insufficiency.

Arterial Oxygenation

In view of the fact that arterial P_{CO_2} was considerably reduced in the control tests (Figure 6) at the end of exercise, one would

Table 4. Acid-Base Balance, Mean Values and Standard Deviations

	pH		P_{CO_2} mm Hg		HCO_3 meq/l.		Δ Buffer base, meq/l.	
$n = 10$	c̄ CO_2	Air	c̄ CO_2	Air	c̄ CO_2	Air	c̄ CO_2	Air
Rest	7.449	7.447	35.5	36.2	23.8	24.2	0	0
	.024	.022	3.4	2.9	1.3	1.3	—	—
Exercise, last min	7.256	7.304	41.4	29.7	17.5	14.1	−10.2	−11.8
	.048	.049	4.1	5.2	1.6	2.0	2.3	1.8
Recovery	7.221	7.281	40.9	29.1	16.1	13.2	−12.2	−13.2
1′	.047	.049	4.1	3.5	1.9	2.0	2.8	2.4
4′	7.231	7.262	32.8	26.0	13.2	11.3	−14.1	−15.1
	.050	.058	2.3	3.3	1.9	1.7	2.9	2.2
10′	7.252	7.276	33.3	28.0	14.1	12.5	−12.8	−13.9
	.052	.051	2.6	1.7	2.4	1.4	3.5	2.3
20′	7.331	7.351	34.2	30.2	17.4	16.2	−7.9	−8.7
	.036	.040	2.5	2.6	2.5	2.2	3.1	2.2
30′	7.380	7.402	35.0	32.6	20.0	19.7	−5.2	−4.7
	.025	.021	2.3	2.6	2.0	2.2	2.1	2.3

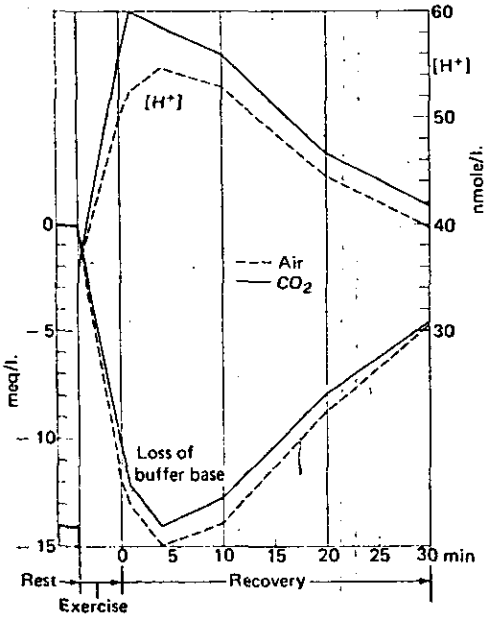

Fig. 7. Hydrogen ion activity and base deficit during and after exercise with and without 15 mm Hg P_{ICO_2}.

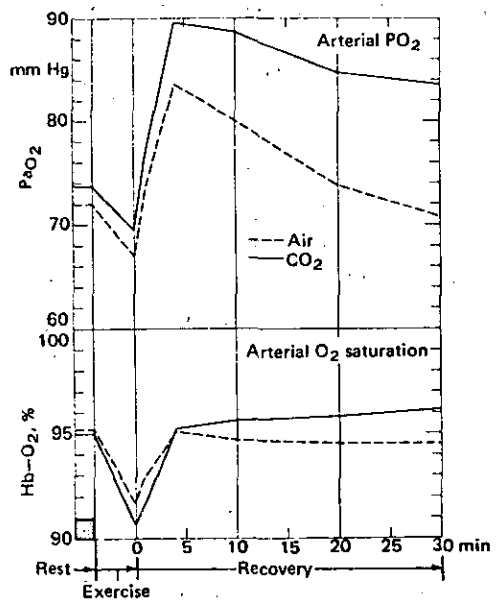

Fig. 8. Arterial O_2 tension and saturation during and after exercise with and without 15 mm Hg P_{ICO_2}.

expect arterial P_{O_2} to rise correspondingly at this point. Undoubtedly this was true for alveolar P_{O_2} which was not measured directly. This drop in arterial P_{O_2} (Figure 8) can be explained on the basis of an enlarged alveolar-arterial O_2 gradient described by others during maximal exercise (STAUB [1963], and WHIPP and WASSERMAN [1969]) and is attributed to limitations in diffusing capacity or physiological shunting with very low mixed venous O_2 tension. In view of the much higher arterial P_{CO_2} found in the group breathing CO_2, it is rather unexpected to see that P_{O_2} remained higher throughout than in the control group. This phenomenon is explained by displacement of some N_2 in the inspired gas by CO_2 and the associated hyperventilation (RAHN and FENN [1960]). It was also observed that arterial O_2 saturation was lower in the CO_2 group than in the controls while the opposite was true for P_{O_2}. This inversion reflects the reduced affinity of hemoglobin for oxygen due to the lower pH in the tests with added carbon dioxide.

Electrolytes

In examining the changes in plasma electrolyte concentration during these experiments (Table 5) it is apparent that all of them increased to some extent with a peak in the last minute of exercise and a gradual decline during the 30 min of recovery. The same is true of other constituents measured, including plasma protein and hemoglobin as shown in Table 6. Furthermore, there were no significant differences in any of these data between the experiments with added carbon dioxide and with air.

Generally speaking, the concentration of electrolytes and other blood constituents can change in two different ways. One of these is hemoconcentration due to loss of intravascular fluid volume as demonstrated during exercise by Kaltreider and Meneely [1940]. If the fluid loss consisted entirely of water, it would affect the concentration of all blood constituents equally and the absolute amount within the intravascular compartment would

Table 5. Electrolytes, Mean Values and Standard Deviations

	Na meq/l.		K meq/l.		Ca mg/100 ml		Cl meq/l.		P mg/100 ml	
$n = 10$	$\bar{c}$ CO_2	Air	$\bar{c}$ CO_2	Air	$\bar{c}$ CO_2	Air	$\bar{c}$ CO_2	Air	$\bar{c}$ CO_2	Air
Rest	139.5	139.7	3.70	3.77	9.47	9.42	103.1	104.3	2.87	3.23
	3.0	2.5	.35	.36	.46	.30	2.4	3.1	.51	.46
Exercise,	146.6	147.9	5.84	6.09	10.88	11.09	105.9	107.8	4.45	4.54
last min	5.2	2.6	.75	.64	.92	.71	2.6	4.2	.95	.77
Recovery,	145.1	146.9	4.85	5.05	10.80	11.12	104.6	106.8	4.62	4.63
1′	3.8	2.4	.58	.55	.82	.60	2.6	3.9	.90	.74
4′	142.0	143.3	3.50	3.56	10.32	10.45	102.0	103.3	4.35	4.43
	3.9	3.7	.36	.18	.67	.55	3.7	2.6	.96	.62
10′	139.6	141.4	3.69	3.70	10.10	10.14	101.2	102.8	4.19	4.17
	4.1	2.5	.18	.25	.46	.60	4.0	3.3	.92	.70
20′	139.8	140.7	3.63	3.66	9.70	9.89	102.1	103.9	3.74	3.73
	4.0	2.3	.22	.25	.46	.39	2.9	3.9	.82	.53
30′	140.1	140.5	3.71	3.67	9.56	9.77	103.9	104.8	3.32	3.19
	4.2	2.9	.23	.18	.40	.30	2.8	3.1	.53	.43

Table 6. Blood Constituents, Mean Values and Standard Deviations

	Plasma protein g/100 ml		Cholesterol, mg/ 100 ml		L.D.H. units		Hemoglobin, g/100 ml	
$n = 10$	$\bar{c}$ CO_2	Air	$\bar{c}$ CO_2	Air	$\bar{c}$ CO_2	Air	$\bar{c}$ CO_2	Air
Rest	6.79	6.99	175.5	173.0	99.7	105.9	15.60	16.0
	.36	.44	22.8	28.1	15.1	20.4	.86	.9
Exercise, last min	8.29	8.39	205.3	211.1	142.9	137.5	—	—
	.51	.40	30.0	29.6	43.4	32.6	—	—
Recovery,	8.21	8.45	210.0	208.9	126.4	124.6	17.85	18.2
1′	.47	.45	31.1	34.5	16.6	28.3	1.02	1.0
4′	8.16	8.42	206.8	213.9	125.4	126.0	—	—
	.43	.39	32.5	39.0	23.1	33.0	—	—
10′	7.96	8.21	202.6	204.9	118.5	117.0	—	—
	.34	.45	29.4	38.2	23.4	23.2	—	—
20′	7.38	7.53	186.2	191.6	111.2	110.4	—	—
	.45	.32	29.9	33.1	17.5	25.1	—	—
30′	7.09	7.18	178.6	182.9	100.5	102.5	15.85	16.2
	.38	.21	28.5	32.1	18.3	26.6	0.80	1.0

remain the same. On the other hand, an actual gain or loss of electrolytes by exchange with the extravascular compartments would probably affect each component differently depending upon concentration gradients and permeability factors. If the amount of fluid loss were known precisely, one could correct for hemoconcentration or dilution and reveal actual displacement of the electrolytes in or out of the bloodstream. Although no direct measurements of blood or plasma volume could be made in this study, two independent indices are available for gain or loss of blood water, namely plasma protein and hemoglobin, both of which do not readily traverse the capillary walls. Under this assumption changes in plasma fluid volume should be inversely proportional to changes in plasma protein and hemoglobin concentrations. It is thus possible to correct measured electrolyte concentrations to the concentration that would have been obtained

had there been no loss of fluid in an attempt to reveal true shifts in these elements. Figure 9 shows fractional changes in electrolytes derived from the data in Table 5. It is obvious that there are considerable differences in the magnitude of change. Whereas sodium and chloride apparently change very little, potassium and phosphorus increase by nearly 60%. When all electrolytes are corrected for hemoconcentration as described (Figure 10), sodium and chloride show an appreciable loss, as would be expected since they most readily follow water into and out of the extravascular compartment. There is also a minor loss of calcium, suggesting that more of it is retained by the capillaries. The gain in potassium at the end of exercise is much less than before correction for hemoconcentration but still amounts to 30% in the experimental group as well as the controls. Immediately after exercise potassium concentration falls precipitously and is 20% below the resting value in the fourth minute of recovery before gradually returning to the normal level. These extremely rapid changes

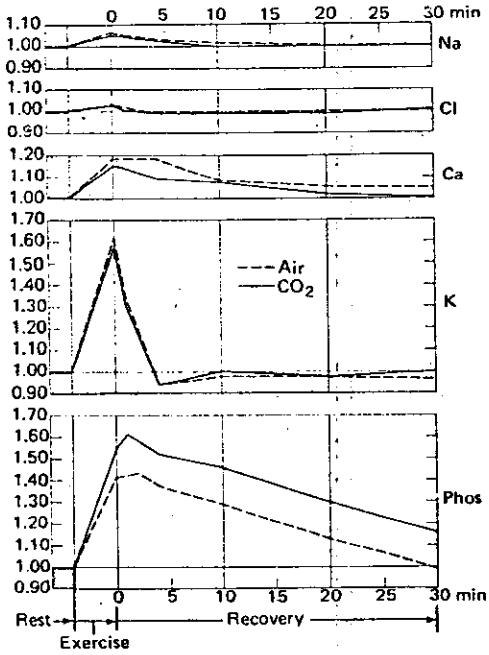

Fig. 9. Fractional changes in electrolyte concentrations (from Table 5).

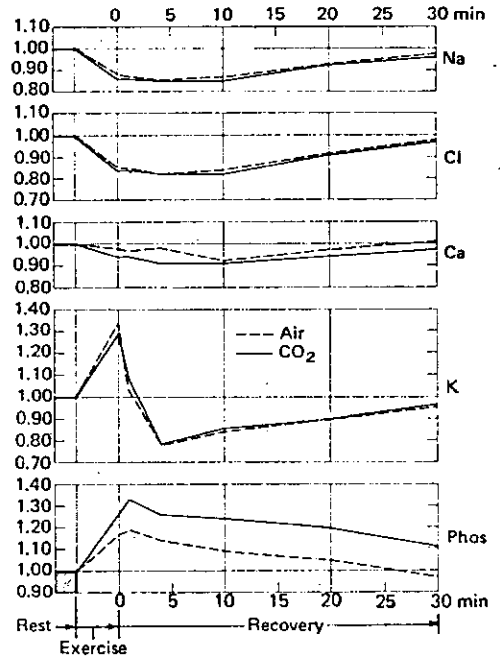

Fig. 10. The same as Figure 9 corrected for plasma fluid loss derived from changes in total plasma protein.

in potassium, commented upon previously by Laurell and Pernow [1966], are striking and deserve further study. Phosphorus also shows a 20 to 30% increase, but it does not reach its peak until after work has ceased with a slow return toward the control values.

Considerable attention has been given to the effects of exercise on serum cholesterol levels in the literature and possible mechanisms to explain the observed increase have been discussed (Kosiek and Klans [1968]). We also observed a 20% rise in cholesterol during exercise in our raw data, but there was practically no change when corrected for hemoconcentration (Figure 11). None of the organic or inorganic constituents of the blood that we measured showed any significant difference between the tests with added carbon dioxide and the controls on air.

Summary

An increase in the carbon dioxide content in the respiratory environment creating

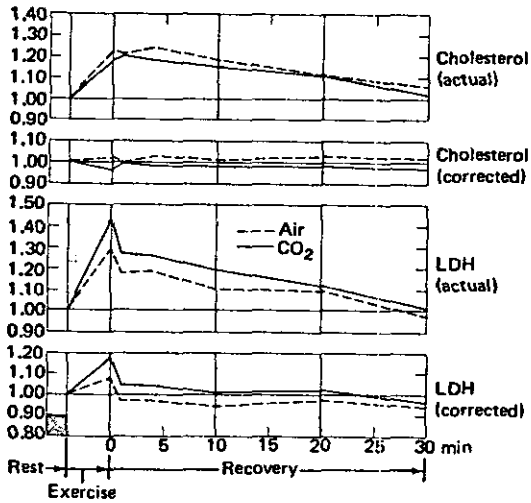

Fig. 11. Changes in cholesterol and lactic dehydrogenase concentrations actually measured and corrected for loss in plasma fluid.

a partial pressure of not more than 15 mm Hg is sufficient to jeopardize an individual's capacity for maximal exertion by impeding the respiratory discharge of CO_2 necessary to maintain homeostasis. It was demonstrated that there is a substantial rise in arterial P_{CO_2}, during maximal exercise breathing air contaminated with CO_2, whereas P_{CO_2} was consistently reduced without it. Consequently the metabolic acidosis generated by anaerobic processes in the muscles can no longer be attenuated by respiration, and the end point is precipitated by a critical rise in hydrogen concentration. No differences were seen in serum electrolytes, total plasma protein, hemoglobin, and other constituents between the tests with added carbon dioxide and the controls breathing air during and after exercise.

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Luft Discussion

NAHAS: During exercise the main source of energy substrates is fat. Do you have any measurements of free fatty acid and glycerol in your subjects? This is especially in reference to the fact that it would appear that during severe acidosis due to CO_2 there might be at one point an inhibition of the mobilization of free fatty acid which, of course, would contribute to the decrement in the performance.

LUFT: That's a very good point, Dr. Nahas. Unfortunately, we don't have any measurements on free fatty acids.

OTIS: You could say that this is an example of a case where the work of breathing is really a limiting factor, I think. Is that right?

LUFT: I think so. And if you watch the people doing the tests, or do them yourself, you would appreciate that. The breathing really becomes painful. Another observation may illustrate this: In exercising on the bicycle ergometer one inevitably falls into a breathing pattern closely related to the cadence of pedaling. Our subjects were pedaling at 50

rpm and when approaching their maximum work capacity with the CO_2 mixture; they were breathing at the same rate (50 rpm) to achieve a minute ventilation of close to 150 l./min with a tidal volume of 3 l. In spite of this, the dyspnea was such that several subjects attempted to increase their ventilation by breathing faster than they were pedaling. The only alternative was to double-up to a frequency of 100 rpm, which led to a marked drop in tidal volume and alveolar ventilation. This demonstrates, I believe, that the limits of ventilatory capacity were definitely exceeded.

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Reference may be made to this report as follows: K. E. Schaefer, Studies of Carbon Dioxide Toxicity: (1) Chronic CO_2 Toxicity in Submarine Medicine, MRL No. 181, 10, pp 156-176

OPERATIONAL APPLICATION

Experience of the German submarine service during World War II is cited to indicate that conclusions concerning habitability of submarines based on observation of peace-time operations do not necessarily apply to the war-time situation. Impairing effects of a submarine atmosphere containing 3% CO_2 and 15-17% O_2 on circulation, metabolism and attentiveness of submarine personnel during war patrols of several months duration are described. These results are attributed mainly to the depressing effect of 3% CO_2 which occurs during a prolonged exposure after an initial period of excitation has passed by. Even though it is anticipated that CO_2 concentration can be maintained at a low level in future submarines, the question remains as to whether toxicity will result from exposure for a month or more to CO_2 concentrations of less than 3%.

ABSTRACT

The historical development of the CO_2 problem in submarine medicine is given. Studies made on combat patrol by fleet type submarines with exposure to 3% CO_2 and 15-17% O_2 were compared with dockside and laboratory studies using 3% and 5% CO_2 with decreased O_2. In contrast to experiments of short duration, in which addition of CO_2 to low oxygen mixtures has a beneficial effect in alleviating the symptoms of oxygen lack, addition of CO_2 to low oxygen mixtures has an impairing effect under the conditions of prolonged exposure over days and weeks. It is shown that the basis of this different reaction is the biphasic effect of CO_2, that is, a period of excitation followed by depression. The necessity for establishing the time-concentration relationships for low concentrations of CO_2 was indicated.

History

Prior to World War II submarine operations did not impose extremely long submerged periods but anti-submarine warfare developments during the war brought a radical change. The experience of the German submarine service is pertinent to this matter. Figure 1 shows the proportion of submarine cruising time spent submerged during the years 1941-1944. Pointner noted that the submerged time rose from 10% to 60% in this period (1). Personal information indicates that the submerged time rose to levels as high as 80% during 1945. With this increasing proportion of submerged time the problem of chronic CO_2 toxicity became important.

In 1943 German submarines faced in the Atlantic a strong Allied anti-submarine defense. Their mean continuous daily submerged time was 13-16 hours. Table 1 shows an approximation of the weight required if sufficient canisters had been provided to absorb the CO_2 accumulated in the boat during a 50-day cruise under the 1943 conditions. The German U-Boats were normally supplied with 800 CO_2 absorbing canisters, which was 1300 less than the number calculated in Table 1 (from ref. 2); 1300 canisters would occupy considerable space and weigh 3-1/2 tons. In 1944 and 1945 the conditions were worse. Carrying more canisters meant carrying less food or less ammunition. As a consequence increased concentrations of CO_2, up to 3% and 4%, had to be tolerated for much longer periods than ever encountered before. Figure 2 was prepared from data collected by Pointner (1). It shows graphically the increase in CO_2 concentrations measured onboard German submarines during the years 1942 and 1943. The curves strikingly reflect the onset of strong anti-submarine measures in the second quarter of 1943 with a sharp increase in measured CO_2 concentrations. The increase of the CO_2 content in various types of submarines with various numbers of men aboard was calculated by Pointner under the assumption that no CO_2 absorbent was used and the average CO_2 exhalation amounts to 350 cc/min. (See Figure 3).

The technical equipment for the absorption of the CO_2 did not change on German submarines with the development of the war. According to the regulations the air conditioning system was supposed to be operated if the limit value of 2% CO_2 was exceeded. Then it was able to keep the CO_2 concentration approximately at that level. The machinery was noisy in its operation and for this reason frequently not used at all, thus adding to the difficulties of CO_2 absorption. The crews preferred dyspnea due to increased CO_2 to the risk of endangering the entire boat in order to maintain normal respiration. A demonstration of the 1943 conditions on operating submarines is given in Figure 4, based on Haldane gas analysis done by Haebisch during a patrol in the Atlantic (2). This

Table 1.- Estimation of CO_2 production, weight of alkali canisters needed for CO_2 adsorption for various periods of submergence on a German fleet type submarine

Air volume of boat 500 m^3. Crew 50 men.
Mean CO_2 exhalation per man and minute 350 cc.
CO_2 absorbing capacity of one alkali canister 400 liters
Weight of one canister 2.5 kg.

After	1	4	8	12	16	hours
Total CO_2 produced (liter)	1050	4200	8400	12600	16800	
CO_2 content in percent	0.21	0.84	1.68	2.52	3.36	
Alkali canisters needed for adsorption of all the CO_2		10.5	21	31.5	42	per day
		525	1050	1575	2100	for 50 days
Weight of these canisters in kg.		26.25	52.5	78.75	105	per day
		1312.5	2625	3937.5	5250	for 50 days

figure shows a characteristic curve of CO_2 and O_2 concentrations on a submarine when O_2 bottles were not used to replenish the depleted O_2. Figure 5 exhibits more clearly the relation of O_2 and CO_2 values measured with Haldane in submerged cruising of various lengths. Haebisch found the ratio of O_2 to CO_2 is 1:0.706 (2).

Observations were made during patrols on German boats comparable to the U. S. Fleet type submarine in 1943 and 1944 by Doctors Haebisch and Schaefer when conditions were those of daily recurring exposures to 3% CO_2 and 15-17% O_2 for periods of about 16 hours.

In 1944 and 1945 studies were reported from the U. S. Naval Medical Research Institute, Bethesda, Md., and the U.S. Naval Medical Research Laboratory, U.S. Naval Submarine Base, New London, Conn., which lasted for 72 and 68 hours respectively.

Investigations During Submarine Patrols (3% CO_2 and 16-17% O_2)

A. Circulatory System (K. E. Schaefer)(3)

1. Estimation of the Blood Flow to the Skin.

Rise of the skin temperature is associated with a considerable increase of the blood supply to the skin. The portion of the blood flowing to the peripheral vessels increases the temperature of the surface of the body and the blood is cooled at the same time. Therefore, the temperature of the whole blood as reflected by the rectal temperature is diminished, the difference between the temperature within the body and on its surface becomes less. This is shown by the decrease of the difference between the rectal and the mean skin temperature. According to Koenig (4), its reciprocal value can be used as an approximate measure of the quantity of blood present in the vessels of the skin.

The temperature of the skin was measured with a Buettner thermoelement (accuracy ± .10°C.). From values obtained at ten different places on the body surface the mean skin temperature was calculated according to Pfleiderer and Buettner (5). The rectal temperature was measured with a calibrated mercury thermometer. Skin temperature and rectal temperature were measured on six subjects several times during two patrols in the Atlantic and Baltic Seas during submergence and while surfaced. During submergence the skin temperature showed a rise in all cases and the rectal temperature a simultaneous drop in most of the subjects. The difference between rectal temperature and mean skin temperature was always less during submergence, thus indicating an increased blood supply to the skin. During submergence the CO_2 concentration in-

creased to 3 and 3.5% and the O_2 concentration decreased to 16 and 15%. The compartment temperature and humidity showed a small increase varying from 1-4°C. temperature (range 19-24°C.) and 5-10% relative humidity (range 70-90%). Since during submergence in the Atlantic the climatic index (Bradke and Liese) exceeded the upper limit of 4.5, it is obvious that the effect of increased CO_2 and the deficiency of O_2 were associated with hyperthermia effects of a slight degree.

With regard to the blood supply to the skin, all three factors (1) increased CO_2, (2) low O_2, and (3) increased temperature and humidity are effective in producing the same results. They all cause an increase of the blood supply to the peripheral vessels. The second series of investigations in the Baltic Sea was undertaken to eliminate a hyperthermia effect. The effective temperature of the compartment varied from 19° to 20° and the relative humidity of the air from 50% to 60%. Consequently in these cases only effects of the increased CO_2 and the decreased O_2 were present, but the changes in skin and rectal temperatures were the same.

2. Blood Pressure.

The record of the daily curves of the blood pressure during and after submergence during a 66-day patrol in the Atlantic showed that with an increasing CO_2 content and O_2 deficiency in the air there was a marked drop of the systolic blood pressure of six out of seven subjects (Figure 6). The course of the diastolic blood pressure was only partly parallel to the systolic blood pressure. In most of the cases it was slightly increased. As soon as the submarine surfaced and normal air was breathed a characteristic sharp rise of the blood pressure ensued; afterwards it dropped slowly. Consequently, the blood pressure was reduced during daylight hours when the boat remained submerged. Normally such a drop of the blood pressure is seen only during the night when the blood circulation is reduced to a minimum. Hence it follows that the rhythm of the blood pressure had changed as well.

Comparable investigations were made of the blood pressure curves during a cruise of three days in the Baltic Sea. During this cruise the boats submerged during the night; it was found that in three out of seven cases the systolic blood pressure decreased under the influence of an increased CO_2 content and an O_2 deficiency. The blood pressure of the remaining test subjects was either not changed at all or the systolic as well as the diastolic pressure was increased. There was a marked rise of the blood pressure of the test subjects on the first and second days, followed by a decrease on the third day. This is apparently connected with the time factor and it indicates that there was a change from the acute effect of CO_2

on the first days to the chronic effect of CO_2 during the two following days. This change is associated with a diminished sensitivity to CO_2 which according to the adaptability of the subjects ensues sooner or later, generally within three to four days.

3. Circulation Time

By measuring the time of the circulation with the decholine method, information is obtained on only the blood flow in that portion of the circulatory system which extends from the median cubital vein over the right part of the heart, the lungs, the left part of the heart up to the arteries of the tongue. The estimation of its value was made during the cruise of three days duration in the Baltic Sea. Values obtained from three subjects while breathing air were about 13 seconds, which correspond well with the average normal circulation time of 13 seconds reported by Tarr (6). Under the influence of increased CO_2 and decreased O_2, the blood circulation time is significantly shortened to 9 seconds (significant at .005 level) (Table 2).

4. Tests of the Regulation of the Circulatory System.

The circulatory response to exercise was studied with the subject in fresh air during surface operation and during submerged operation when the CO_2 was increased and the O_2 decreased. In Figures 7 and 8 the results of two tests are compared. Each test consisted of 25 knee bends performed by the same subject on successive days. Figure 7 shows the response when exposed to fresh air and Figure 8 shows the response of the same subject when exposed to CO_2 concentrations of 2.2-2.4% and O_2 concentrations of 17.3-17.6%. In fresh air after 3 minutes the systolic and diastolic blood pressure and pulse rate returned to their initial values. Under increased CO_2 and decreased O_2 the systolic blood pressure remained at its higher level for 6 minutes and in a second comparable test for 9 minutes. In addition, the increase of the pulse pressure in the first minute following the exercise was less than normal or did not appear at all. Repeated examinations of the same and of other subjects yielded the same results. This prolonged reaction indicates that the adaptability of the circulatory system to exertion was limited under the influence of prolonged exposure to moderately increased CO_2 and lowered O_2 concentrations. Under higher concentrations of CO_2 (3-3.5%) and O_2 concentrations as low as 16.0 to 15.0% similar observations of the reaction of the circulatory system were made and compared with tests made in normal air. The results of two of these tests are shown in Figures 9 and 10. In figure 9 it is demonstrated that (A) the systolic and diastolic blood pressure drop even when the subject is standing and the pulse rate is considerably increased, and (B) the reaction of the systolic and

Table 2.- Circulation time, blood pressure, pulse rate and respiratory frequency of three subjects during submergence and surfacing on a 3-day cruise in the Baltic Sea

Test person and date	Time	CO_2 %	O_2 %	Circulation time	Blood pressure	Pulse rate	Respiration frequency
STAHL							
22 Feb.	2300	0.8	19.3	13.8	105/58	54	14
23 Feb.	0530	3.5	15.9	9.0*	120/78	70	18
GLAESER							
22 Feb.	2330	0.9	19.2	13.0	106/70	72	18
23 Feb.	0600	3.5	15.9	9.1*	122/85	74	18
BARTELS							
22 Feb.	2345	0.9	19.2	13.2	125/85	68	16

* Differences in circulation time are significant at .005 level

diastolic blood pressure to exercise does not occur immediately but is delayed for about 5 minutes. Figure 10 shows an entire absence of response of blood pressure to exercise under similar conditions. Delay or absence of response of blood pressure to exercise was the important finding established while breathing CO_2 concentrations above 3% in submarines. The stress of the exercise performed in these tests under increased CO_2 and decreased O_2 produced a dyspnea which lasted for about 30 minutes.

Similar results were obtained in another test series. Four subjects were subjected to heavy work, clutching out the diesel engines by hand, which is normally done mechanically because of excessive exertion required. Work was performed during submergence at a CO_2 concentration of 2.6% and an O_2 content of 17.1%. In all cases only a small rise of the systolic blood pressure of about 20 mm. Hg immediately after exertion could be noted. No drop of the diastolic blood pressure could be found. Consequently there was only a slight increase of pulse pressure in contrast to what would normally be the case after exertion.

B. Influence of Watchstanding on the Bridge on Skin and Rectal Temperatures During a 66-day Patrol in the Atlantic. (7)

Skin temperature and rectal temperature were measured on two watch officers prior to and after their watch on the bridge and the following rewarming period. For two tests during a 4-hour watch at 7.5-8° temperature, wind 12-14 miles per hour, humidity 90-97% one subject showed a drop in mean skin temperature from 33° to 30.4°, in foot temperature from 32° to 23°, and in rectal temperature from 36.8° to 36.4°. The second subject showed similar results but with a lesser drop of skin and rectal temperatures. Figure 11 shows the results of one series of these measurements obtained during watch on the surface and the following rewarming period during submergence. The return to initial values of the foot temperature required about 15 hours. In other experiments, the rewarming period was 9-10 hours. Reports of studies conducted in climate chambers, employing healthy young subjects under normal air, indicate that a rewarming is expected to be completed in about 3-4 hours under the above mentioned temperature conditions. The delay of the rewarming process in the feet suggests a disturbance of heat regulations during the 66-day patrol with daily exposures to 3-3.5% CO_2 and 16-15% O_2.

C. O_2 Consumption and CO_2 Excretion.

During a patrol in the Atlantic, Doctor Haebisch (2) determined the O_2 consumption and CO_2 excretion on five subjects for a total of twenty-two determinations. He used a Haldane gas analysis apparatus, a 5-liter wet gas meter, and Douglas bags. The test con-

ditions and the climatic and atmospheric environment during this cruise were as follows:

The boat operated in the Northern Atlantic from 29 January until 3 March 1944. The daily period of submergence was as long as 17-21 hours. Oxygen consumption and carbon dioxide excretion of the subjects were determined about one hour before the first surfacing; that is, between 6:15 p.m. and 8:00 p.m. At that time the mean value of the CO_2 concentration in the submarine atmosphere was 3.5 vol. %. The O_2 concentration amounted to an average of 15.97 vol. % (at 37°C. 760 mm. Hg, the air being saturated with water vapor). The extreme values of the CO_2 concentration were 3.83 and 3.1 vol. %, those of the O_2 concentration 16.92 and 15.13 vol. %. At that time the temperature of the air aboard the submarine varied from 19° to 23.5°C. The barometric pressure aboard was above normal, varying from 758.3 to 817.5 mm. Hg, inasmuch as the measurements were made after prolonged submerged cruising. The humidity of the air was not measured, but it is certain that at that time the relative humidity exceeded 70%. No meal was taken during a four-hour period prior to the tests. The last previous meal consisted exclusively of carbohydrates. During the period preceding the tests, the test subjects had been sleeping or at least resting.

The Douglas bag method was employed for metabolic determinations. In order to accustom the subjects to the mouthpiece and its valve, the breathing was practiced for 10 minutes while the tap was left open. Thus, the tidal air was breathed into the room again. Then the air was exhaled into the Douglas bag for a period of exactly four minutes. A measured amount of air was taken from the bag for analysis and then by means of a precision gasometer of 5 liters capacity, the quantity of air remaining in it was determined. During the test a sample of air was taken from the atmosphere surrounding the test subjects and both samples were examined according to Haldane's method for determining the CO_2 and the O_2 content. Altogether twenty-two experiments were made on five healthy subjects between 20 and 21 years of age.

In comparison with predicted values based on height, weight and age, O_2 consumption was found to be decreased by 30% when a Respiratory Quotient (RQ) of 0.8 was assumed. The RQ was actually found to be 1.0 or more in 77% of the determinations. This increase of the RQ was primarily due to a decrease of O_2 consumption. In 77% of the determinations the CO_2 excretion was found to be increased.

D. Attentiveness (Burdon) Tests While Exposed to 3% CO_2 and 15-17% O_2 During Patrol.

Schaefer describes letter-canceling tests performed on sub-

marines with many subjects and, as far as possible, under the same conditions in normal air during surface cruising, and with various concentrations of CO_2 during submerged cruising (8). After the elimination of the training factor a considerable increase of the number of errors was seen in all tests done when there was increased CO_2 concentration. Figures 12 and 13 show the results of letter-canceling tests on two selected subjects (diesel and motor engineers) during a patrol while breathing air at the surface and after exposure to increased CO_2 concentrations and decreased O_2 concentration at the end of the submerged period. It can be seen that the number of errors made under these conditions is significantly increased (significant at .005 level Figure 12, and .01 level Figure 13). It was a characteristic feature of these tests under CO_2 that entire lines were omitted. This never occurred under atmospheric air conditions aboard the submarine among approximately 100 attentiveness tests.

The main results of the investigations carried out in submarines not equipped with snorkels during patrols of two months duration can be summarized as follows: Compared with values obtained on the surface breathing air, exposure to 3-3.5% CO_2 and 15-17% O_2 during submergence showed:

1. Evidence suggesting an increased blood supply to the skin (increase in skin temperature and decrease of rectal temperature).

2. Impaired response of the circulatory system to exercise.

3. Fall in blood pressure.

4. Decreased O_2 consumption.

5. Impaired attentiveness.

The fall in body temperature and the O_2 consumption seem to exhibit a depressing effect on the combination of 3% CO_2 and 15-17% O_2 on the heat regulatory system which is supported by a prolonged rewarming period during submergence after watch standing at surface operation. (7).

It has been found (7) that the rate of heat loss due to radiation is considerably increased during submergence in northern latitudes because of the high skin temperature (CO_2 effect) and the low wall temperature. (The wall temperature of the submarines is practically in equilibrium with the sea water temperature.) Under these conditions decreased heat production and increased heat loss form a vicious cycle.

According to Kleitman (9) efficiency of performance and the degree of alertness during the customary waking phase seem to conform to the rise and fall of the body temperature. Under the conditions found during submarine patrols this relation of fall of the body temperature and impaired performance was confirmed.

CO_2 Problem in Snorkels

The rapid advance of anti-submarine measures imposed the burden of a greatly increased proportion of submerged cruising time. Space and weight limitations made the current methods of CO_2 removal inadequate. The advent of the snorkel would appear to have solved this problem. But with steadily improving submarine detection methods by surface and aircraft the need for concealment in wartime will invalidate the snorkel to a degree directly relating to the concentration and effectiveness of enemy forces. Thus the historical cycle will have been completed in that the problem will once again become that of operating with inadequate ventilation through the snorkel. The experience of Doctor Marechaux who cruised to Java from France in 1944 in a snorkel equipped submarine is pertinent. He gave the following report:

"Adaptation to the prolonged exposure to CO_2 occurs indeed. At the beginning of submerged cruising (schnorchel cruising), which lasted for about 4 weeks, and during which the boat did not surface at all and fresh air was only supplied through the schnorchel, the entire crew suffered from a marked tachypnoea.

"This sign was particularly conspicuous shortly before the supply of fresh air, when there was a CO_2 concentration of 5.0 to 5.5% (measurement with 'Draegertopf'; Margin of error ± 0.1%) in the living compartments.

"The farther the adaptation had progressed the less was the number of breaths. After 2-1/2 weeks at the latest the normal frequency of breathing was regained, even when there were high concentrations of CO_2 in the air.

"I can confirm the observations of Schaefer regarding the disturbance of normal sleep and subsequent drowsiness or dullness during the waking hours.

"After about 2 weeks the state of somnolescence vanished, but other remarkable cerebral symptoms appeared.

"One of the engineers repeatedly dropped screw-drivers, wrenches, hammers, or other tools, which made much noise when they fell upon the deck plates. This noise can be detected and thus

cause the loss of the boat. The engineer concerned did not do this on purpose, nor was he clumsy (he later earned his living as a watchmaker), nor was he inexperienced, for it was not his first submarine cruise. The dull expression of his face was particularly remarkable. Later under normal air conditions ashore, this expression was never observed again.

"Two of the watch officers pulled themselves together every day whenever they were on duty at the periscope and sang although they were anything but musical, and under normal conditions could hardly be induced to sing.

"The submarine surgeon himself noticed queer ideas in his own mind.

"Under these named conditions the keenness of mind remained altered, and I am able to state at any rate that the process of thinking does not progress in normal paths."

The findings reported above, on regular fleet type submarines and snorkel submarines during patrols of several months duration under actual war conditions, demonstrate clearly the deleterious effect of prolonged exposure to 3-5% CO_2 and 15-17% O_2.

Confirmative evidence was obtained in dockside experiments in New London by Karlin and Curtis in 1945 (10). Under experimentally-produced similar conditions of exposure to 3% CO_2 and 17% O_2 for 68 hours, a definitely decreased capacity for physical work and indications of marked decrement in mental efficiency for all hands were noted in the New London report. The Harvard step-up test to measure physical fitness used in the New London study can be compared with the Schellong test used by Schaefer because in both the response of the circulatory system to exercise is measured.

In contrast, Consolazio, et al (11) reported in 1944, on the basis of laboratory (Bethesda) and dockside (New London) experiments that CO_2 up to 5% in combination with O_2 depletion to 13% did not impair the condition of personnel (72-hour exposure).

The studies done at New London in 1944 and 1945 appear to be in conflict with each other. Critical examination reveals that the conflict is more one of phraseology than of evidence. Although it is true that the men were not rendered incapable of effective action by 5% CO_2, it is also true that there is evidence of impairment by 3% CO_2 after 68 hours. The crucial point in both these studies is that neither was quite long enough to pass the initial excitation phase of CO_2 effect and did not reach the depression phase which usually becomes evident in man after 72 hours.

It should be emphasized that in submarines we have to deal with chronic CO_2 toxicity along with effects of prolonged exposure to low oxygen. Results obtained in experiments of short exposure to increased CO_2 and lowered O_2 concentrations cannot be applied to submarine conditions. An example will serve to demonstrate. It is well known that addition of CO_2 to low oxygen mixtures has in experiments of short duration a beneficial effect (12) in alleviating the symptoms of oxygen lack and preventing their occurrence. This effect of CO_2 is based on the stimulation of respiration and circulation which leads to an increase in tissue oxygen tension. From results of those experiments the impression might be gained that the submariner is relatively fortunate in that conditions giving rise to decreased O_2 lead to an increase of CO_2.

An increase in CO_2 to the level of 2-4% in the inspired air helps to maintain bloodpressure even during hyperventilation (13). But this is only true for a short exposure to CO_2 and low O_2. Actual measurements of blood pressure on board submarines during submergence (Figure 6) demonstrated that an increase in CO_2 to the level of 2-4% in the inspired air commensurate with a fall in O_2 concentrations to 16% produces a fall in blood pressure in six out of seven subjects. The results of investigations on board submarines can only be understood if one recognizes that 3% CO_2 shows a biphasic effect during a prolonged exposure. Stimulation in the first two or three days is followed by a depression which lasts during the whole exposure time. This is very clearly demonstrated in the decrease of the sensitivity of the respiratory center for CO_2 during prolonged exposure to 3% CO_2 (14). A beneficial effect of addition of 3% CO_2 to low O_2 mixture can therefore not be expected under the conditions of prolonged exposure.

The question might be raised whether an intermittent exposure to increased CO_2 concentrations, which is mostly encountered in submarines, would have effects different from those produced by continuous exposure to increased CO_2. If the time periods on air between the exposures to increased CO_2 are short, as was the case in German submarines cruising through the Bay of Biscay which was heavily patrolled by anti-submarine craft, the depressive phase of the CO_2 effect is produced even under intermittent exposure. The depressive phase of CO_2 once reached will hardly be reversed under intermittent exposure to CO_2. It takes from four to five days on fresh air to eliminate the depressive effects of CO_2. This was found in laboratory tests on humans (14) with continuous exposure to 3% CO_2 and 21% O_2 over periods up to 144 hours, followed by an intermittent 8-hour exposure to 3% CO_2 over a period of 192 hours. The depression state reached during the first part of the experiment with six days of continuous exposure to CO_2 did not change

during the second part of the experiment with eight days intermittent exposure to CO_2, in spite of relatively long time periods on air (16 hours per day) in between. A period of five days on air was required before the urine suddenly showed a very large output of CO_2 and at the same time the pulse rate, blood alkali reserve and the chronaxia returned to pretest levels. During the continuous and intermittent exposure to CO_2 pulse rate was lowered, blood alkali reserve was increased and the chronaxia prolonged. The CO_2 excretion in the urine was reduced to a minimum during the exposure to CO_2.

It should be mentioned that oxygen lack is usually not a decisive factor in submarines. The O_2 concentration found in submarines during submergence usually has a range of from 15-17%. Sixteen percent O_2 is equivalent to 6,500 feet altitude in terms of identity of alveolar gas composition. The alveolar O_2 tensions at 6,500 feet are above 70 mm. Hg (15) which is considered a threshold for the onset of changes in respiration. Adaptation to an altitude of 6,500 feet is easily acquired by the organism without any functional disturbances (16). In contrast to that, adaptation to 3% CO_2 does show definite changes in the functions of the organism (14). Chronic CO_2 toxicity (prolonged exposure of man and animals to increased CO_2 concentrations for periods up to several weeks) was until recently a neglected scientific field. It therefore seems necessary to present a summary of the recently published results of the investigations dealing with this subject.

Laboratory Experiments

In laboratory tests (Schaefer) with continuous exposure to 3% CO_2 and 21% O_2 over periods up to 144 hours followed by intermittent 8-hour exposures to 3% CO_2 over a period of 192 hours, it was established that CO_2 produces a decrease in the excitability of the respiratory center and an increase in the alkali reserve of the blood, mainly due to retention of alkali by the kidneys. Three percent CO_2 produces a biphasic reaction; that is, a period of excitation followed by depression, as demonstrated in subjective sensations, in tests of letter-canceling and hand steadiness, chronaxia measurements and changes in the EEG pattern (17),(18).

In the following discussion these studies concerning the influence of continuous exposure to 3% CO_2 for 4-6 days are referred to in more detail.

1. Subjective Sensations

After several prolonged exposures to 3% CO_2, subjects reported first a feeling of excitation, improved efficiency and verbal

associations, which can be designated as a state of euphoria. In the first and second night under 3% CO_2 the sleep was usually bad and the subjects experienced subsequently a state of depression and believed that their attentiveness and memory decreased. They felt in a state between sleep and wakefulness until the transition to air (17).

2. Letter-canceling Tests

Letter-canceling tests showed during the whole length of exposure to 3% CO_2 for five subjects a significant increase in the number of errors. The biphasic effect of CO_2 subjectively experienced was indicated in all the letter-canceling tests insofar as the number of errors was larger in the first two days, compared with the following days under CO_2 exposure. However, the difference proved to be statistically significant only in one case.

3. Hand Steadiness Tests

Similar results were obtained with hand steadiness tests. A significant increase in the number of errors was found in all tests under 3% CO_2. A difference in the acute and chronic effect of CO_2 was hinted in all tests, but was statistically significant in one case (17).

4. Chronaxia

Excitation time (chronaxia) was measured at the nerve point of the muscle brachioradialis on five subjects during six days exposure to 3% CO_2. Strength-duration curves were plotted and the chronaxia value obtained by extrapolation. During the first and most of the second day of the exposure period to 3% CO_2 the chronaxia and simultaneously the rheobase was found decreased, whereas from the third day on the chronaxia and the rheobase increased to twice its original value (17). It was concluded that the concurring changes of the rheobase and chronaxia during acute and chronic exposure to 3% CO_2 are due to an acceleration followed by a retardation of the processes underlying excitation of the nerves.

5. EEG

In spite of the individuality of the response to short exposures to CO_2, prolonged exposure to 3% CO_2 produced two uniform reactions. Within the first 24-hour exposure to 3% CO_2 6-cycle waves appeared. Generally these could not be observed on the succeeding days. They were considered as evidence of the excitability phase of the CO_2.

The depression phase of CO_2 was expressed in two findings: (a) the disappearance of the hypocapnea effect after three days exposure to 3% CO_2 (the hypocapnea effect consists of an increased occurrence of 6-cycle waves after transition from 3% CO_2 to normal air, which was not found with concentrations lower than 3% CO_2); and (b) the normal inhibitory effect of sensory stimuli on the brain action potentials disappeared after three days in 3% CO_2. This disappearance of the normal inhibitory effect of sensory stimuli develops parallel to a general decrease of the excitability of the respiratory center (18).

There is definite proof in numerous investigations of man and animals that adaptation takes place during prolonged exposure to 3% CO_2 (14),(17),(18),(19). The nature of this adaptation was revealed in physiological-pathological investigation of the endocrine glands of guinea pigs exposed continuously to 3% CO_2 over periods up to 17 days (20). The physiological investigations showed the following results:

1. During prolonged exposure to 3% CO_2 the adrenalin content of the adrenalin medulla decreased (extracts tested on the blood pressure of decerebrated cats).

2. The blood sugar level decreased during prolonged exposure to 3% CO_2. Morphological investigations on the same animals showed that (1) the chromaffin staining of the medulla cells decreases with exposure time to 3% CO_2; (2) a vacuolization of the medulla and the cortex takes place; (3) the zona reticularis enlarges with exposure time to 3% CO_2; (4) the exhaustive state of the adrenals after 17 days exposure to 3% CO_2 is developed after transitory phase of increased activity of the adrenals, which slowly decreases after five days of exposure to 3% CO_2. A biphasic effect of 3% CO_2 was found too in experiments with dogs (20). Adrenalin injections, during acute exposure to CO_2, produced a strong increase of the blood sugar level and a very small increase of the blood sugar level during chronic exposure to 3% CO_2.

Ferrosalt (20) had similar results under the same conditions. Klein (21) found a biphasic reaction in the basophil cells of the pituitary glands of guinea pigs during prolonged exposure to 3% CO_2. From these experiments referred to above, it seems evident that during prolonged continuous exposure of animals to 3% CO_2 the reaction chain--adrenal medulla, pituitary gland, adrenal cortex--is first stimulated and later impaired or exhausted due to a decrease in adrenalin release of the adrenalin medulla.

The question remains whether 3% CO_2 is the threshold for these effects on the endocrine glands. For short exposure 3% CO_2

was established as a threshold for distinct physiological effects. It seems doubtful whether this holds true for a prolonged exposure. Few experiments with prolonged exposure to concentrations lower than 3 % have been conducted except with animals, as far as we know. Dallwig, Kolls and Loevenhart (23) reported an increase of 8 to 10% in the erythrocyte count of dogs which had been exposed to 0.5 to 1.0% CO_2 in a respiration chamber for a period of a week. Miller (24) observed in dogs exposed to 1.5% CO_2 for one to four weeks a mild uncompensated acidosis with a decline in CO_2 combining power, and an increase in erythrocyte count and hemoglobin concentration after a variable latent period. These findings suggest that studies of prolonged exposure to CO_2 concentrations of 0.5% to 3% on humans and animals are urgently needed to determine the threshold of physiological effects of CO_2 under prolonged continuous exposure. Studies of this kind would be important on the other hand for establishing a CO_2 toxicity chart. There is some evidence that CO_2 effects show a time-concentration relationship. Klein (21) exposed guinea pigs to 30-60% CO_2 and in those animals which survived longer than ten minutes he observed changes of the pituitary gland similar to those obtained from much longer exposure to 3% CO_2. The apneustic respiratory pattern and the gasping previously reported by Barcroft (25) as well as Lucken and Timm (26) for short exposures to 35-60% CO_2 were confirmed when guinea pigs were exposed to 15-24% CO_2 for a longer time (19).

Existing standards of CO_2 toxicity would have to be evaluated in the light of proposed experiments with prolonged exposure to CO_2 concentrations lower than 3%. Operating forces may then be more exactly informed at what level of CO_2 concentration and after what exposure time the efficiency of submarine personnel is critically impaired.

If continuous low levels of CO_2 are found to have an impairing influence on physiological functions and performance, this finding is of importance in design of CO_2 removal equipment.

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Figure 1.- German World War II experience
Period of submerged cruising in percent of the total period at sea
for German submarines from 1940-1944 (Dr. Pointner)

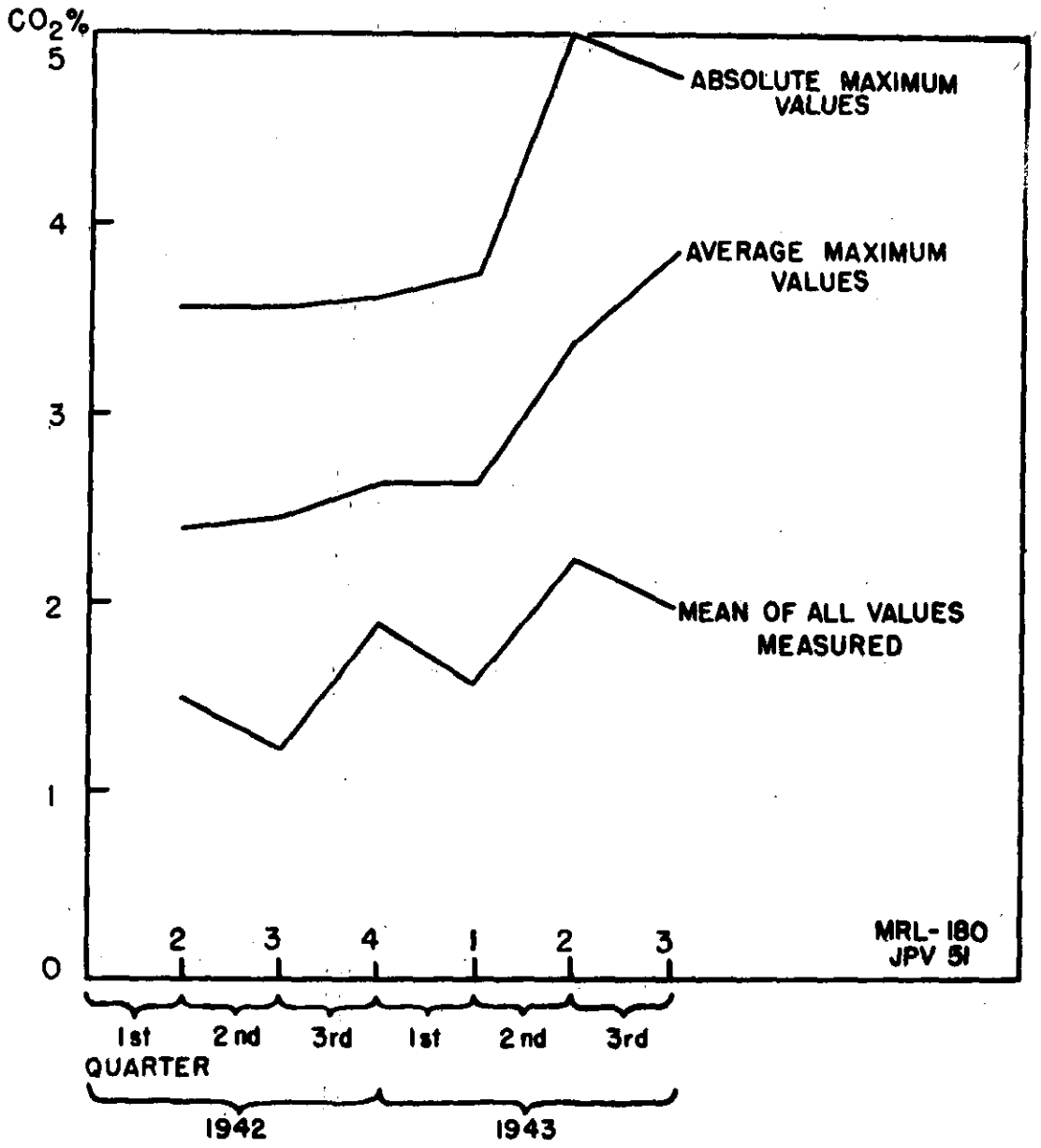

Figure 2.- CO_2 concentrations in vol. % measured on board German submarines during the years 1942-1943
(Instrument - Draegertopf)

(1) Mean of all values measured; (2) Average maximum values; (3) Absolute maximum values. (Dr. Pointner, 1943)

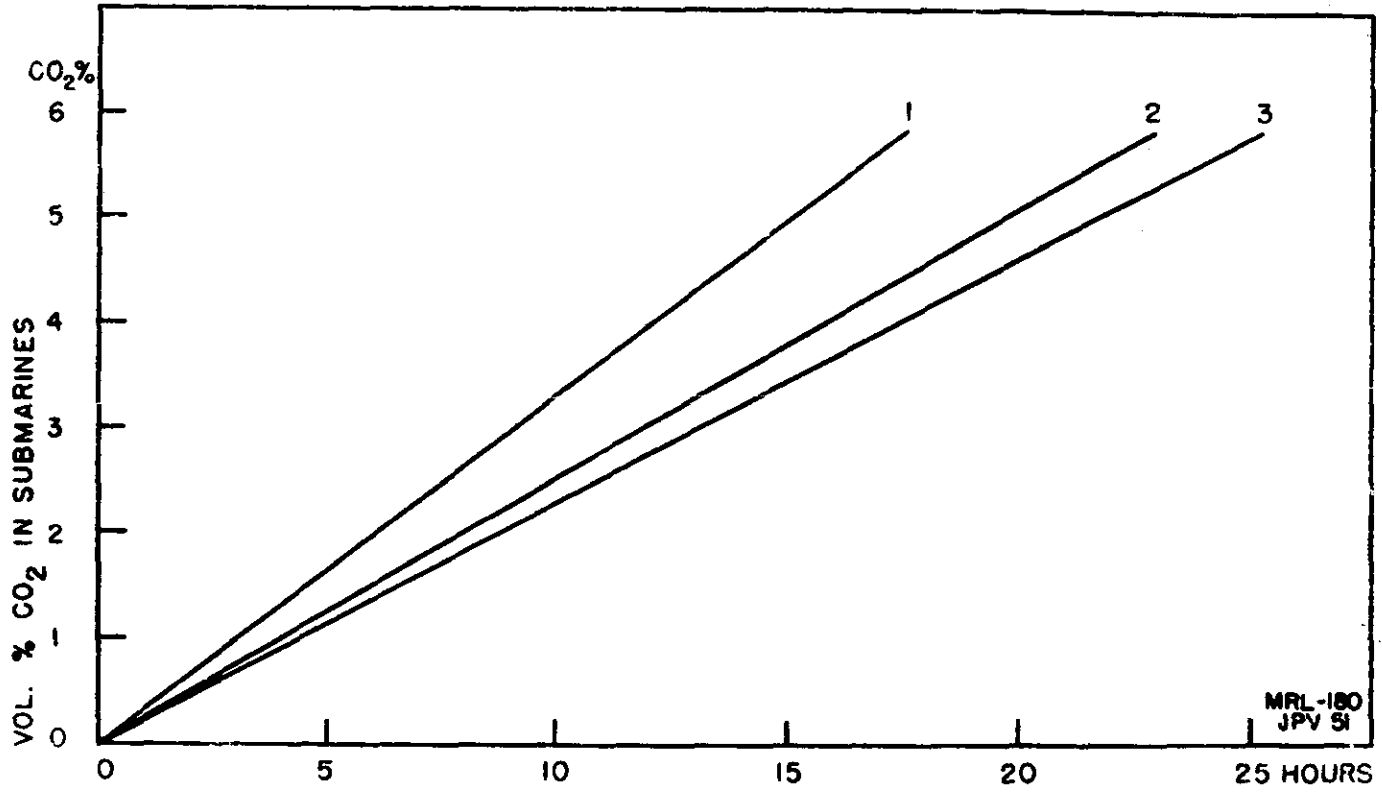

Figure 3.- Increase of CO_2 content in German submarine with submerged time

The abscissa shows the number of hours passed since the beginning of submerged cruising.
Ordinate: CO_2 content of the submarine air in vol. %. The numbered lines demonstrate:
(1) The increase of CO_2 on submarines of the type VII-B (270 m^3*, 45 men).
(2) The increase of CO_2 on submarines of the type VII-C (430 m^3, 55 men).
(3) The increase of CO_2 on submarines of the type IX-C (540 m^3, 65 men).

(Based on theoretical calculations 350 cc./min. was assumed as average CO_2 exhalation of a submariner during patrol)

* Data concerning volume of the boats refer to volume of air within the boats.

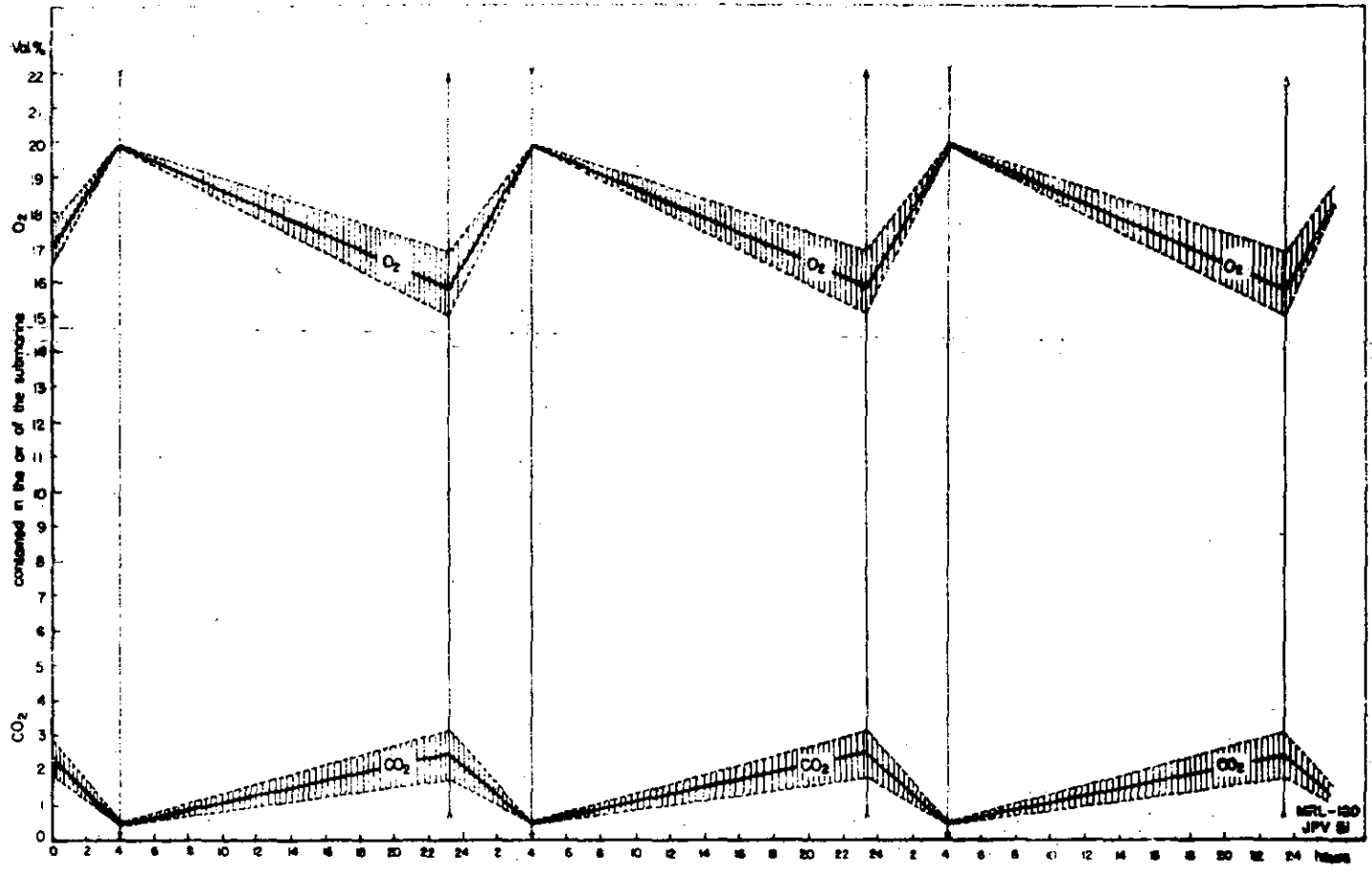

Figure 4.- CO_2 and O_2 concentrations measured at 2-hour intervals in a submarine for a period of 3 times 24 hours (Dr. Haebisch, 1943)

German submarine type VII-C (430 m^3, 55 men)

The lines and shaded areas indicate the extreme values including all values measured. The solid lines display the calculated mean values. The arrows pointing up show the instant of surfacing, those pointing down the instant of submerging.

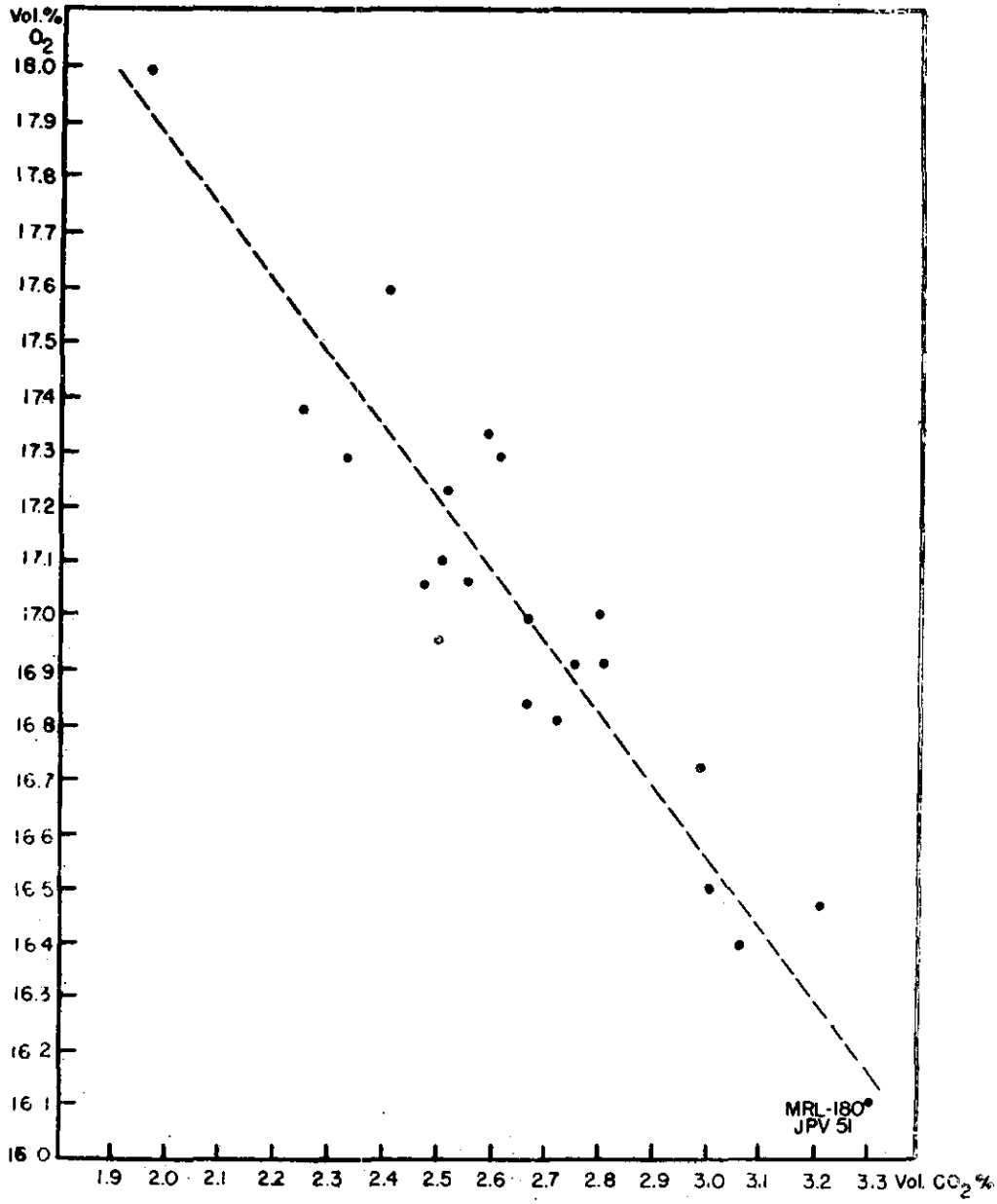

Figure 5.- Relation of CO_2 and O_2 content in submarine air during submerged cruising of various lengths
German submarine type VII-C (430 m^3, 55 men) Haldane gas analysis (Dr. Haebisch, 1943)
The broken line demonstrates the mean value of the proportion between CO_2 and O_2. The ratio of O_2 to CO_2 is 1:0.706.

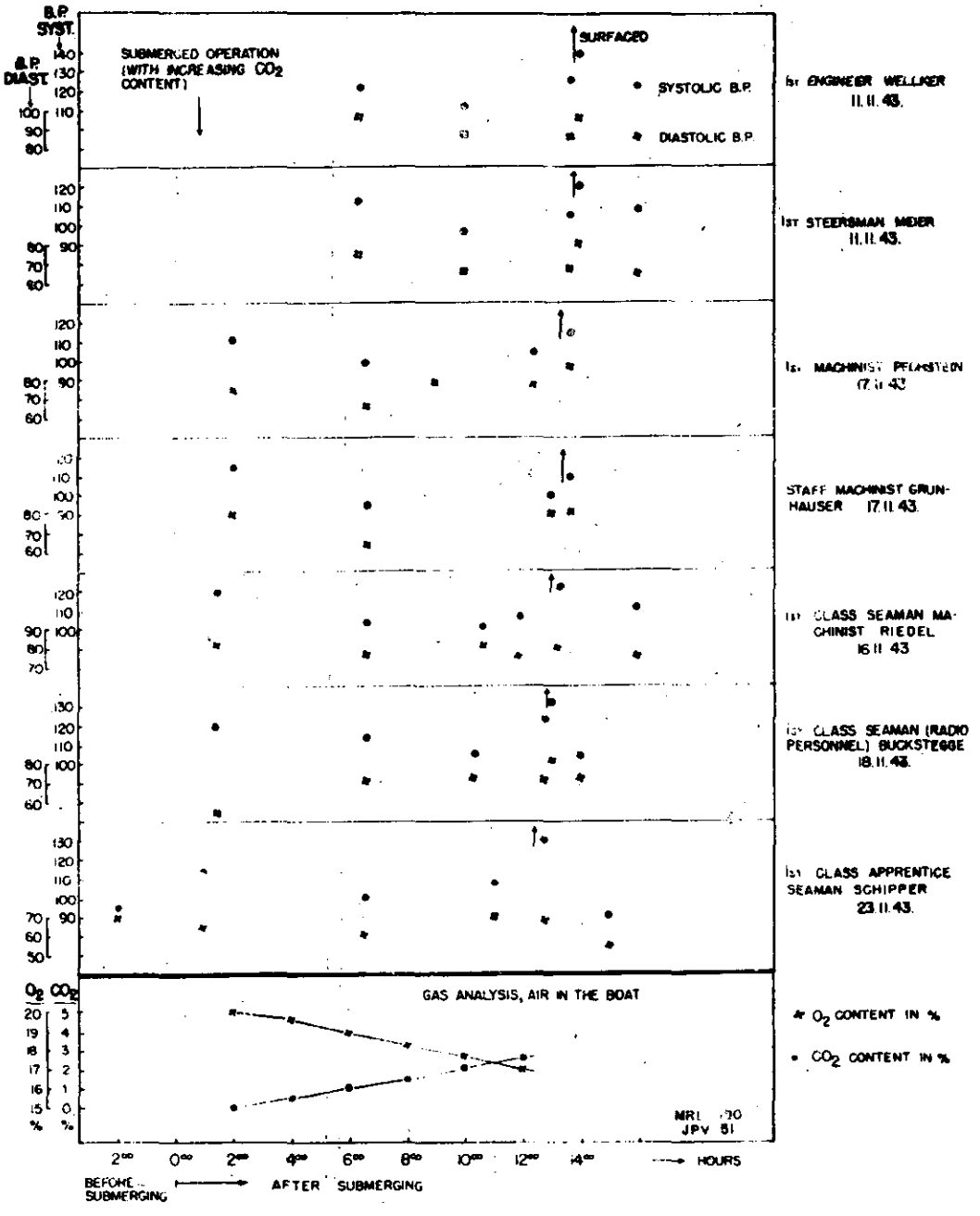

Figure 6.- The effect of prolonged exposure to increased CO_2 and decreased O_2 concentrations during submergence on the systolic and diastolic blood pressure of 7 subjects (Atlantic patrol Oct.-Nov. 1943 - German submarine type VII-C)

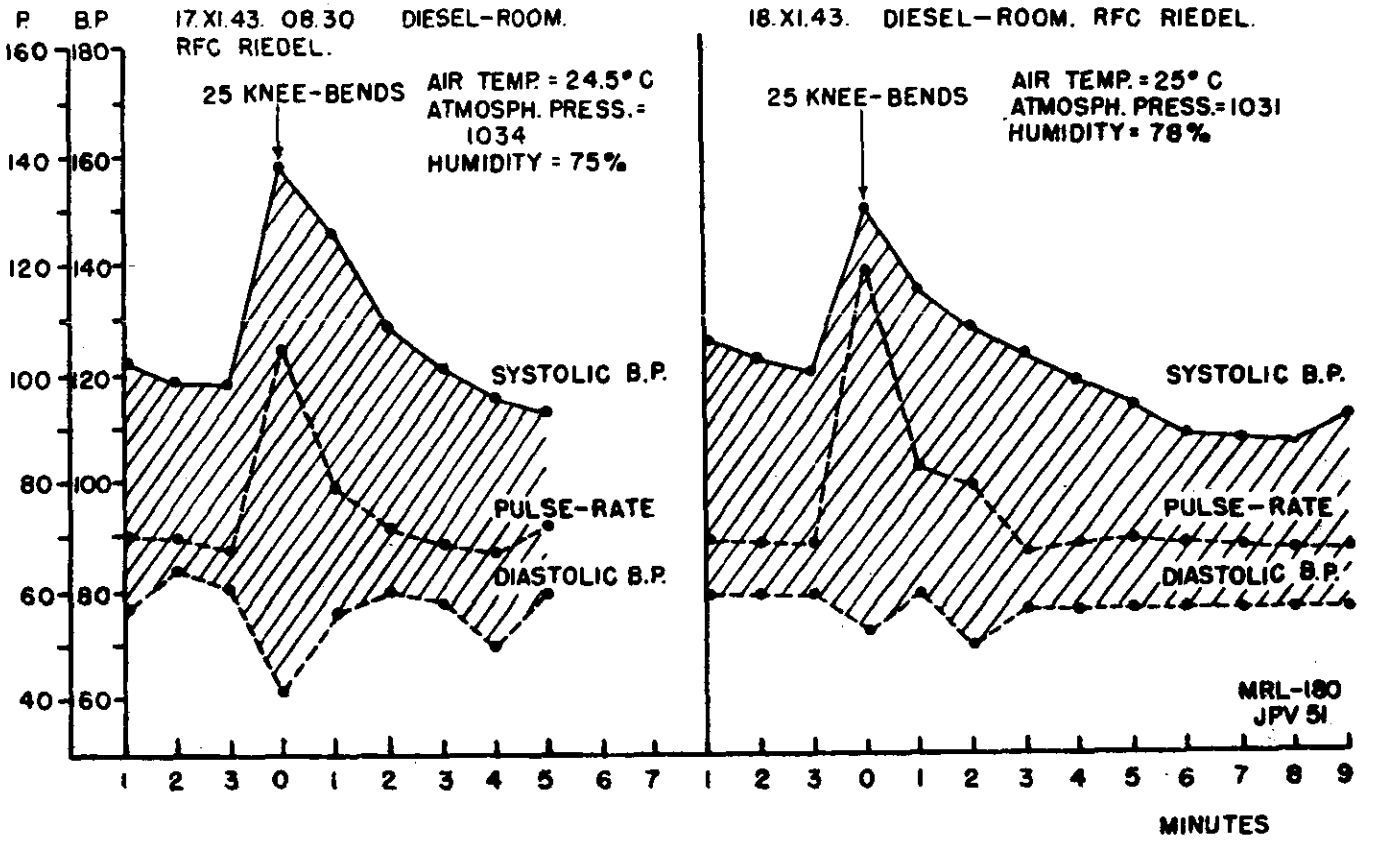

Figure 7.- Examination of the regulation of the blood circulation under fresh air on U-608

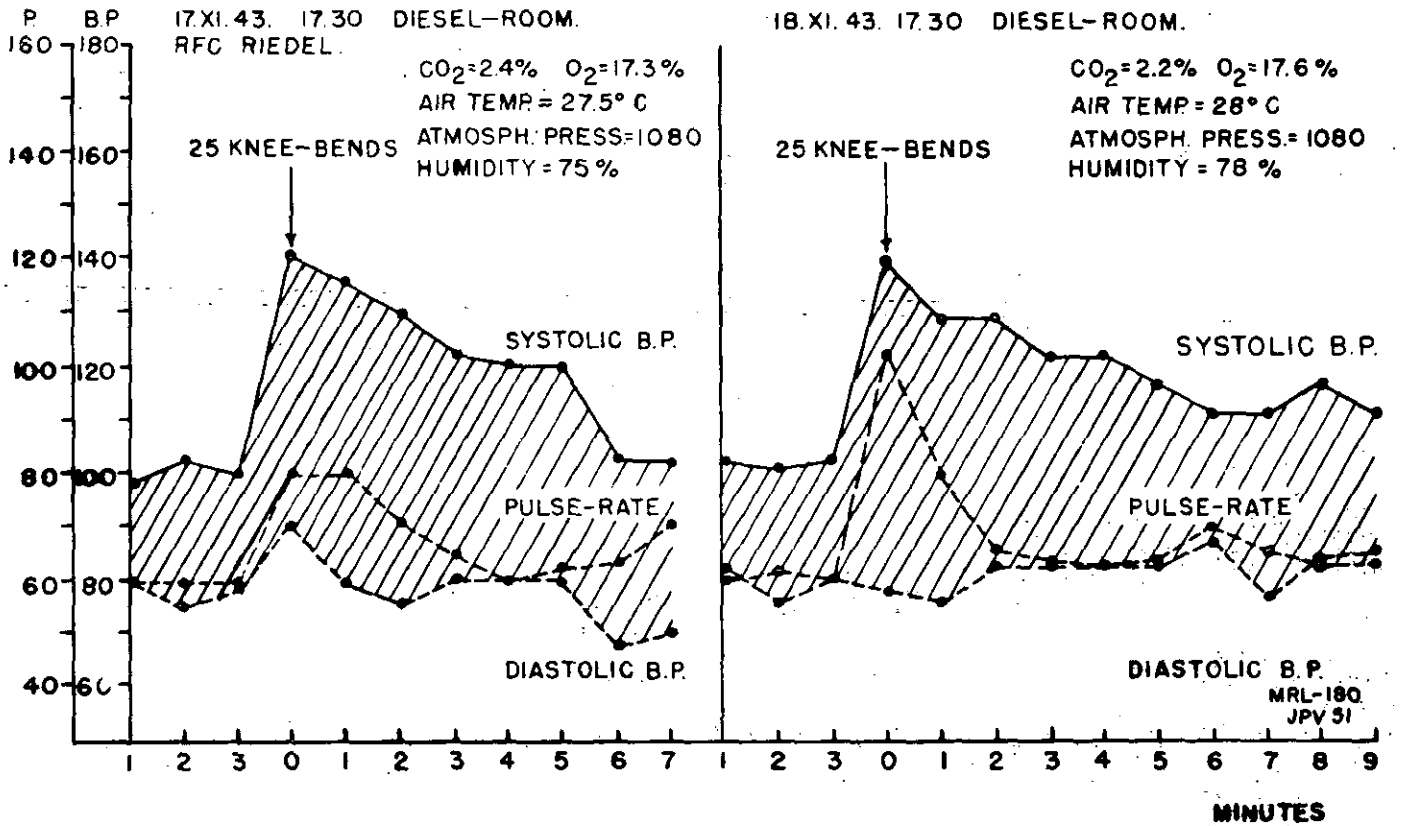

Figure 8.- Examination of the regulation of the blood circulation under 2.2% and 2.4% of CO_2 and 17.6% and 17.3% O_2 on U-668

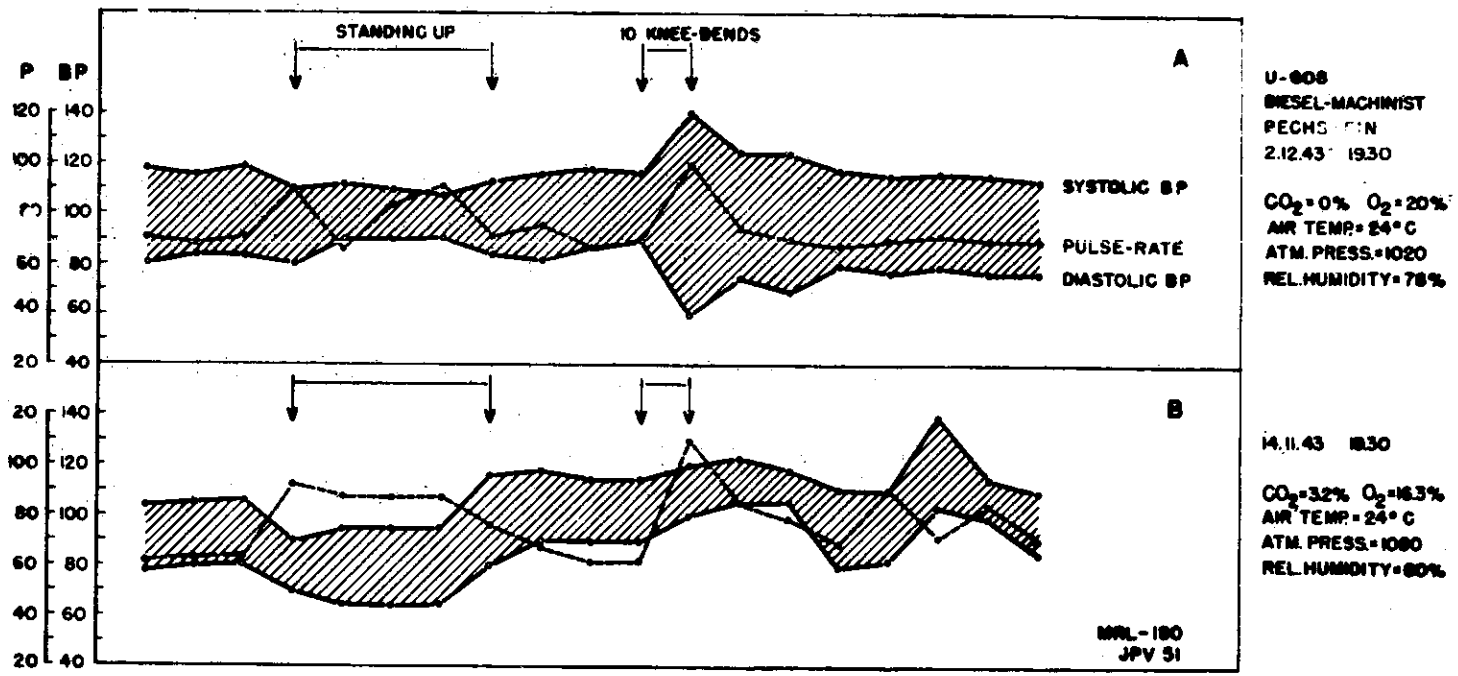

Figure 9.- Test of the circulatory system (after Schellong)
(A) Under normal air; (B) Under exposure to 3.5% CO_2 and 16.3% O_2 at the end of 15 hours submerged period during a patrol in the Atlantic (1943)

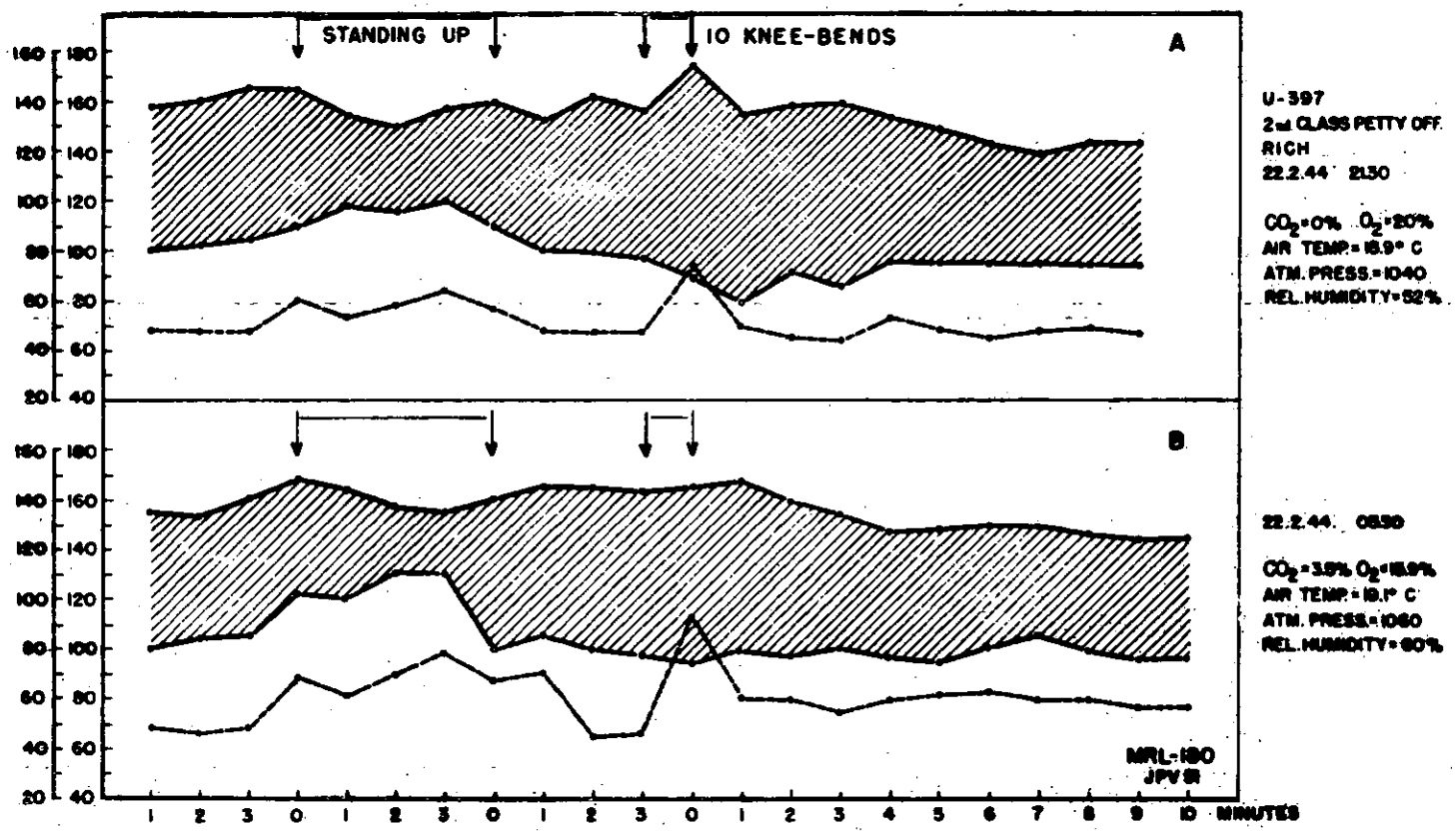

Figure 10.- Test of the circulatory system (after Schellong)
(A) Under normal air; (B) Under exposure to 3.5% CO_2 and 15.9% O_2 at the end of 15 hours submerged period during a patrol in the Baltic Sea (1944)

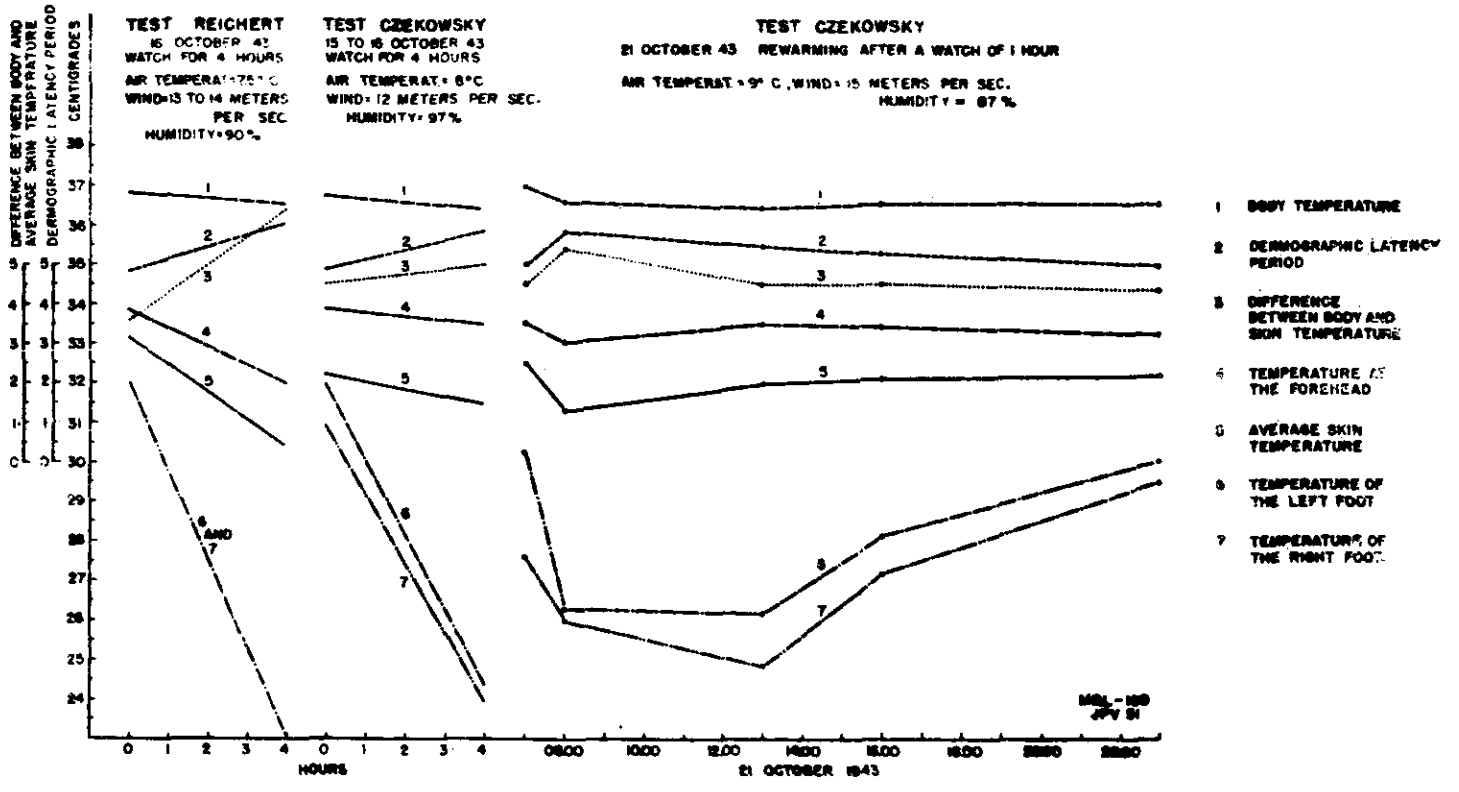

Figure 11.- Influence of watchstanding on skin and rectal temperature and dermographic latency period of 2 subjects during a 66 day patrol in the Atlantic with a German submarine type VII-C

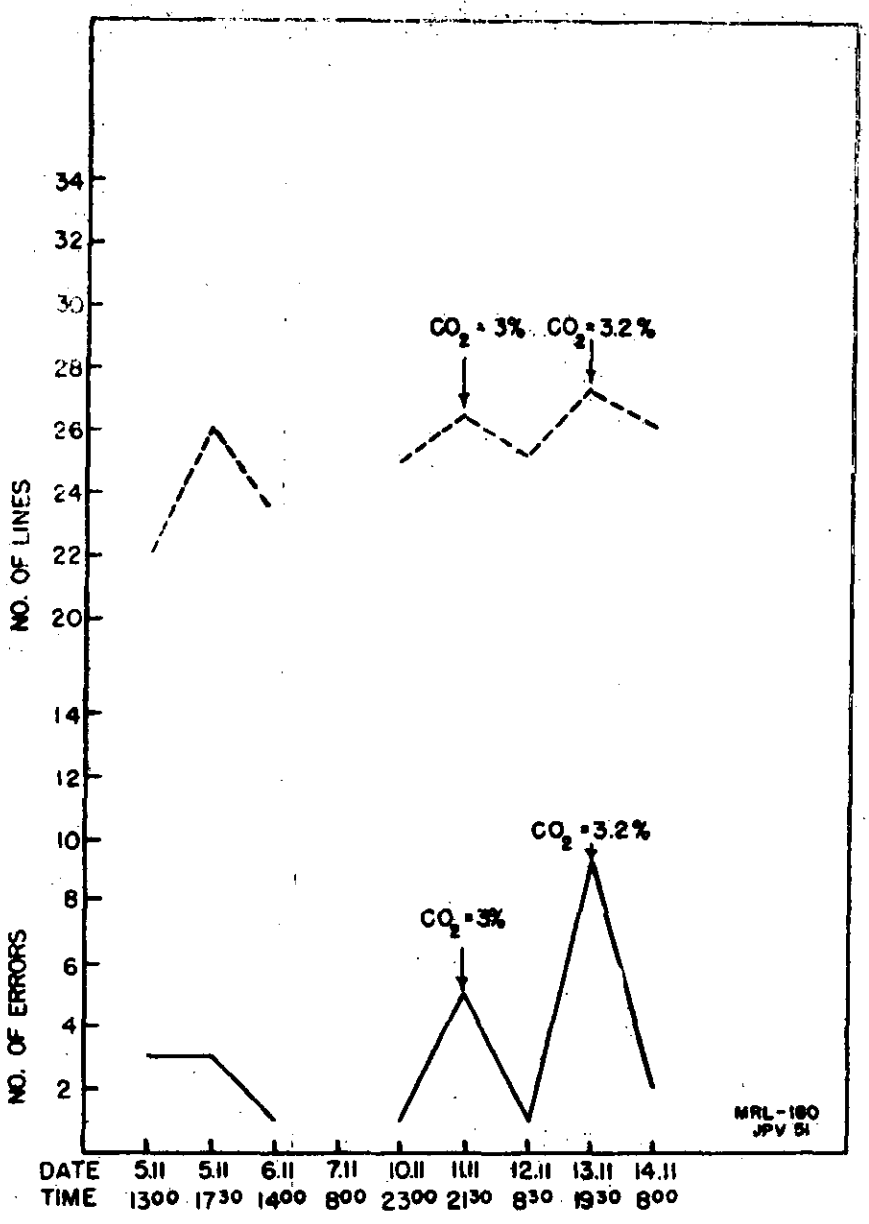

Figure 12.- Letter-canceling tests during combat patrol on German submarine type VII-C (1943) Subject: Diesel Engineer Pechstein
Influence of exposure to 3.2% CO_2 and 16.3% O_2 at the end of submerged time of about 15 hours

Dotted Line: Number of lines.
Straight Line: Number of errors made in the letter-canceling test.

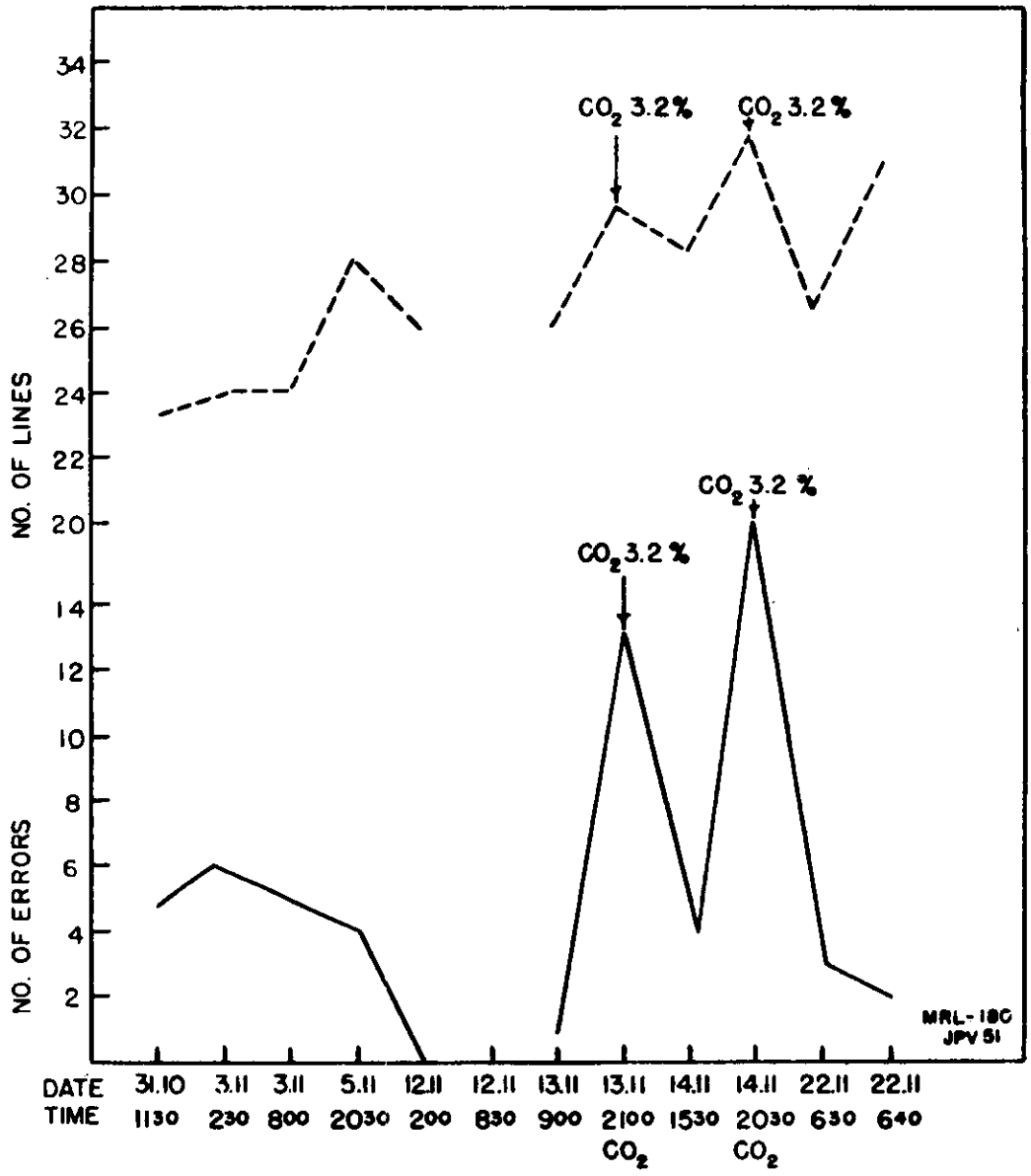

Figure 13.- Letter-canceling tests during combat patrol on German submarine type VII-C (1943) Subject: Electrician Gruenhaeuser

Influence of exposure to 3.2% CO_2 and 16.3% O_2 at the end of submerged time of about 15 hours

Dotted Line: Number of lines.
Straight Line: Number of errors made in the letter-canceling test.

SECTION 1. Patrol Studies

Physiological stresses related to hypercapnia during patrols on submarines

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Schaefer, K. E. 1979. Physiological stresses related to hypercapnia during patrols on submarines. Undersea Biomed. Res. Sub. Suppl.: S15–S47.—Physiological studies on hypercapnic effects carried out on 13 Polaris patrols are summarized. The average CO_2 concentrations ranged from 0.7–1% CO_2; CO_2 was identified as the only environmental contaminant of the submarine atmosphere that has a direct effect on respiration in the concentration range found in the submarine atmosphere. A comparison has been made of physiological effects produced during 42 days of exposure to 1.5% CO_2 during laboratory studies (L.S.) with those observed during 50 to 60 days of exposure to 0.7–1% CO_2 on patrols (P.S.). A close similarity was found in the effects on respiration and blood electrolytes under both conditions. Respiratory minute volume was elevated by 40–63% because of increased tidal volume. The physiological dead space increased 60%. Vital capacity showed a trend toward a decrease. Studies of acid-base balance carried out during patrols demonstrated cyclic changes in blood pH and bicarbonate; pH and blood bicarbonate fell during the first 17 days of exposure, rose during the subsequent 20 days, and decreased again after 40 days. These cycles cannot be explained on the basis of known renal regulations in CO_2-induced acidosis and were not found during exposure to 1.5% CO_2. The hypothesis is advanced that these changes in acid-base balance are caused by cycles in CO_2 uptake and release in bones. The time constants of the bone CO_2 stores fit the observed length of cycles in acid-base balance. Correlation with cycles of calcium metabolism provides further support for this hypothesis. Red cell electrolytes showed similar changes under 1.5% CO_2 (L.S.) and 0.7–1% CO_2 (P.S.). Red cell sodium increased and potassium decreased. Moreover, red cell calcium also increased under both conditions. The significance of these red cell electrolyte changes in regard to changes in permeability and active transport remains to be clarified. An increased gastric acidity was found during patrol (exposure to 0.8–0.95% CO_2). The changes observed during patrols disappeared during the recovery periods.

respiration
acid-base balance
CO_2 response
blood electrolytes

During the first 10 years after the advent of the nuclear-powered submarine, from 1953 to 1963, great strides were made in the improvement of submarine habitability and atmosphere

control. Contaminants in the submarine atmosphere were determined and threshold limit values were developed for a 90-day period. Experience showed that toxicological hazards were prevented by the existing atmosphere control system, and there were no significant, acute problems in health or disease related to prolonged confinement in the sealed environment of the nuclear-powered submarines (Ebersole 1960; Kinsey 1960; Schulte 1961, 1963; Schaefer 1964).

During the second decade, from 1963 to 1973, submarine medical officers wrote nearly 900 patrol reports, which contain a great deal of experience in preventive medicine (Wilken 1969; Tansey, Wilson, and Schaefer 1979). Moreover, medical officers carried out a large number of physiological studies during patrols.

There are two reasons to summarize these medical experiences and physiological studies at this time: (1) The program requiring naval medical officers to be aboard each patrol will not be continued, and any new programs to be developed will benefit from the summary of previous experiences. (2) The medical experiences and results of physiological studies gathered during the submarine patrols represent a genuine contribution to preventive medicine as it concerns the general public. They provide base-line data, not otherwise available, on healthy subjects exposed to a technological environment for prolonged periods of time.

Characteristics of patrol studies

Included in this report are the results of 13 patrol studies carried out by several naval medical corps officers.* The patrol studies had of necessity a limited scope to succeed at all. In some cases only one function was studied at one point of the patrol (20 days) and this was then compared with control conditions and a point during the recovery period. Such data do not lend themselves to publication but provide valuable information within the framework of the program on submarine studies.

The patrol studies were difficult to do because the control data had to be taken during the hectic time prior to going to sea, and the recovery data had to be obtained immediately after the patrol, when everybody wanted to go on leave. Moreover, during the patrol, the studies had to be fitted into the tight schedule of submarine operations. Despite these difficulties, careful collection of samples and meticulous performance of tests produced good data. The staff of the Environmental Physiology Branch spent a great deal of time and effort in the preparation of these studies and in particular in the analyses of the large number of blood and urine samples taken on patrol.

The patrol studies represent longitudinal studies, since the measurements were made prior to the patrol, during, and post-patrol. Even if the interval between exposure and recovery was sometimes several months, there were no problems in assessing physiological functions, such as respiratory function, because paired data were used.

During the 10 years of the existence of this program, sufficient material has been accumulated to warrant a summary report on the evaluation and interpretation of the submarine studies on hypercapnic effects.

*Braithwaite, Covington, Foster, Gortner, Gude, Harrison, Hughes, Kingsbury, McCluggage, Mendelson, Peck, Rodenbaugh, and Schwartz, in connection with the task titled "Effect of exposure to the total submarine atmosphere and various work rest schedules on physiological functions" assigned to the Environmental Physiology Branch of the Laboratory.

Methods used during patrols and in laboratory investigations

Conventional lung function tests during patrols were performed with a 9-liter Collins spirometer. Standard forced vital capacity maneuvers were performed three times and the highest value of the three trials was selected.

Measurements of physiological dead space aboard submarines (Gude and Schaefer 1969) were carried out as follows: after the subject accustomed himself to a two-way inspiration/expiration valve with a pliable rubber mouthpiece, a 100-liter Douglas bag was attached to collect any expired air over a 10-min period, during which the average respirations per minute were noted.

The volume of the expired air was measured with a dry gas meter and the expired air CO_2 concentration was determined with an infrared CO_2 analyzer (Beckman LB-1).

The 10-min volume of collected expired air was corrected to Body Temperature Pressure Saturated (BTPS) conditions, and the average tidal volume was determined by dividing the 10-min corrected expired volume by the total number of respirations over the 10-min period.

The actual blood pH values and the blood P_{CO_2} values were determined on arterialized capillary blood samples using an ultramicro pH/blood gas analyzer (113-S1, Instrumentation Laboratory, Inc.). Gambino (1959) has shown that arterialized capillary blood can be substituted for the arterial blood sample because it gives equivalent results.

Carbon dioxide tolerance curves were obtained during a patrol by Kingsbury in 1970; the results of that study are presented in this paper. Subjects were breathing ambient air or 5% CO_2 for 10 min through a respiratory valve. Expired air was collected in a Douglas bag during the last three minutes of breathing, and the volume was subsequently measured with a dry gas meter. End-tidal CO_2 was recorded with a Beckman Model LB1 CO_2 analyzer, tapping sample gas from near the mouthpiece. The CO_2 meter was calibrated immediately before measurement, using pure nitrogen for zero and 7.1% CO_2 for the calibration gas. Values of expired volumes were corrected to BTPS.

Blood gas analysis during patrol. Arterialized capillary samples were obtained by digital puncture of siliconized skin after a hand soak of five minutes in water at a temperature of 45°C (Peck 1971). All venous samples were collected in heparinized glass vacuum tubes. After measurements of pH, P_{CO_2}, and P_{O_2} were completed, venous samples were immediately centrifuged at 4000 rpm. The plasma was stored at − 15°C in capped syringes. The measurements of pH, P_{CO_2}, and P_{O_2} were made with an ultramicro pH/blood gas analyzer (Instrumentation Laboratory Model 113-SI). Blood bicarbonate values were calculated using a standard nomogram.

Collection and storage of plasma and red cell samples during patrols for subsequent analysis at the Laboratory. Venous samples were collected in 7-ml heparinized Vacutainers, spun down immediately, and separated anaerobically. The separated plasma and red cell fractions were then anaerobically transferred to fill a 2-ml test tube completely and frozen at −15°C. Twenty-four hour urine samples were collected, under oil, throughout the patrol and during control and recovery periods. At the end of each 24-h period, the urine volume was measured and a 10% aliquot of the samples was frozen at −15°C. No preservative was used. Analyses of pH and P_{CO_2} were made on a pH blood gas analyzer (I.L. 113-S1, Instrumentation Laboratory, Inc.), Na and K were analyzed on a flame photometer (I.L. 343, Instrumentation Laboratory, Inc.), and Cl with a chloridometer.

Fractional gastric analysis. Patrol samples were taken after 8 days, 23 days, and 54 days (Foster 1969). The fifth set of samples in the study was obtained during the post-patrol period one month after the exposure to elevated atmospheric CO_2 had ended.

All the gastric aspirate samples were taken from fasting subjects. To facilitate the procedure, before introducing a nasogastric tube, each man was given 10 ml of viscous xylocaine with which to gargle. Once the tube was in the stomach, a sample of the gastric content was collected over the next 30 to 45 min. A fractional gastric analysis was performed on 10 ml of the collected material after it had been filtered and the mucus removed. Free and total acidity determinations were made by titration using 0.1 normal NaOH, Topfer reagent (end point pH 2.9–4.0) and phenophthalein (end point pH 8.5). With this method, acid determinations are measured in degree units.

Data evaluation

The physiological functions that were studied undergo circadian cycles. Since many of the crew members were on different work schedules, it was difficult to take measurements of all subjects at the same time after awakening. If this is not taken into account, small but significant changes could be easily masked by circadian cycles, e.g., in acid-base balance studies.

For the statistical analysis, the paired *t*-test was used for a comparison of control data taken prior to the patrol with data obtained during and after patrol. Differences with $P \leq 0.05$ were considered significant.

The relevant variables in the submarine atmosphere

In studying the effect of prolonged exposure to the submarine atmosphere, we are dealing with a multi-factor problem and obviously cannot think in terms of a single-agent cause/effect relationship.

The contaminants in the submarine atmosphere that might affect respiration are listed in Table 1.

Carbon dioxide is the most important factor because it is present in a concentration that has a direct effect on respiration. In fact, it is the only contaminant that is generally on the average of twice that of the listed 90-day Threshold Limit Value (TLV) of 0.5% or 3.8 mmHg; this is so because of the limitations of the on-board scrubber system. All the other variables, such as CO, Freon 14, Freon 12, aerosols, and ions, are present in concentrations below the level at which effects on respiration can be expected (Motley and Kunzman 1958; Anderson and Ramskill 1960; Ramskill 1961; Rodenbaugh 1967; Maumus 1967; Harrison 1968).

Respiration was selected as a target function because of evidence indicating the CO_2 at the low levels found in submarines affects respiration. Another reason for emphasizing respiratory studies was given by the findings of Wilken (1969) showing that respiratory disease is the most prevalent internal medicine problem in submarine cases, followed closely by gastrointestinal diseases (Table 2). This determination was based on the number of sick days. Moreover, upper respiratory infections cause the greatest number of "sick calls," an evaluation category separate from "sick days." Frequently, between 70–90% of the crew made sick calls because of respiratory symptoms, according to Wilken's study.

Methods of presentation of results of physiological studies on submarines

Since CO_2 is the most important contaminant in the submarine atmosphere, amounting on the average to approximately 1% during the period in which most of these studies were carried

TABLE 1

LIMITS, OBSERVED VALUES, AND LEVELS OF ATMOSPHERIC CONTAMINANTS THAT AFFECT RESPIRATORY FUNCTION

Contaminant	90-day Limit TLVs	Frequently Observed Average Values	Levels at Which Respiratory Functions are Affected	Effect
CO_2	3.8 mmHg	6–7 mmHg	6–7 mmHg	Ventilation (Covington, cited in this paper); Dead Space (Gude and Schaefer 1969)
CO	25 ppm	20–30 ppm	500 ppm (Motley and Kunzman 1958)	Increase in Airway Resistance
Freon 114	200 ppm	10–25 ppm −54% Time 25–50 ppm −10% (Rodenbaugh 1967)	850–950 ppm for 1 h; case of bronchitis on submarine (Harrison 1968)	
Freon 12	200 ppm	Average 7 ppm (Rodenbaugh 1967)	No effect on respiration in observed range	
Aerosols	0.3 mg/liter	0.3–0.4 mg/liter (Ramskill 1961; Maumus 1967)	No effect on respiration in observed range	
Ions	—	Average concentration ≈ 600(+), 300 (−) ions/cc (occasional surges) (Ramskill 1961; Maumus 1967)	No effect on respiratory function in humans in observed range	(Schaefer, unpublished observations)

In the concentrations observed on nuclear-powered submarines, only CO_2 has a direct effect on respiratory function.

TABLE 2
GENERAL MEDICAL CASES RESULTING IN SICK DAYS ON PATROL

Condition	No. Cases	Total Sick Days
Respiratory	121	480
Gastrointestinal	119	197
Cardiovascular	9	45
Infectious Hepatitis	7	187
Infectious Mononucleosis	18	162
Influenza	74	160
All Other	53	251

Review of 360 patrols, 1963–1967 (Wilken 1969).

out, a comparison was made of the results of patrol studies and the effects of prolonged exposure to 1.5% CO_2 in 21% O_2 (a laboratory simulation study). There was rather close agreement between the effects of prolonged exposure to 1.5% CO_2 and those of the 1% CO_2 submarine atmosphere in regard to: (1) respiration; (2) acid-base balance; (3) electrolyte exchange; and (4) calcium metabolism.

RESULTS

Respiration

Table 3 shows a comparison of ventilatory changes measured under both conditions. Exposure to 1.5% CO_2 produced a consistent increase in respiratory minute volume of 39% and 37% in the two periods (1–24 days and 25–42 days), based on an increase in tidal volume (Schaefer, Hastings, Carey, and Nichols 1963a). Similar but somewhat larger increases in respiratory minute volume (40 and 52%) were observed during the corresponding periods of patrols, although the ambient CO_2 concentrations were lower (Covington data, cited in this paper).

During exposure to 1.5% CO_2, vital capacity showed a decreasing trend, which was more pronounced in the measurements obtained on a patrol after 2, 5, and 8 weeks. The physiological changes in respiratory functions observed during patrols returned to normal during the recovery period ashore.

In Table 4, results of physiological dead space determinations made under the two conditions are compared. Again, there is remarkably close agreement. An increase of about 60% in the physiological dead space was found under both conditions (Schaefer et al. 1963a; Gude and Schaefer 1969).

Figure 1 presents CO_2 tolerance curves obtained during patrol on six subjects who were exposed to an average CO_2 concentration of 1% CO_2. Tests were performed prior to the patrol and on two occasions during the patrol. Inhalation of 5% CO_2 during the patrol produced a significant elevation of both end-tidal CO_2 and minute ventilation compared to similar data obtained during the control period. The rise in end-tidal P_{CO_2} was relatively larger than that of ventilation, resulting in decreased slope of the CO_2 tolerance curve. These findings agree with those obtained during a laboratory experiment, in which subjects were exposed to 1.5% CO_2 for prolonged periods. Figure 2 shows a decreased slope of the average CO_2 tolerance curves

TABLE 3

EFFECT OF PROLONGED EXPOSURE TO 1.5% CO_2, 21% O_2 (LABORATORY) AND 0.8–1% CO_2 (PATROL) ON RESPIRATION

		Respiratory Minute Volume, Liters, BTPS	Percent Change	Respiratory Rate, breaths/min	Percent Change	Tidal Volume, Liters, BTPS	Percent Change	Vital Capacity, Liters, BTPS	Percent Change
				Exposure to 1.5% CO_2 (21% O_2)					
Control Period	Mean	5.32		9.8		0.603		4.56	
	SD	0.12		2.6		0.123		0.76	
	n	(20)		(20)		(20)		(20)	
On 1.5% CO_2	Mean	7.40	+39%	11.4*	+16%	0.704*	+17%	4.47	−2.0%
	SD	0.18		2.0		0.138		0.69	
1–23 Days	*n*	(20)		(20)		(20)		(20)	
24–42 Days	Mean	7.26	+37%	10.5	+ 7%	0.714	+18%	4.52	−1%
	SD	0.27		1.7		0.134		0.65	
	n	(20)		(20)				(20)	
				Exposure to 0.8–1.0% CO_2					
Control Period on Air	Mean	8.03		12.0		0.74		5.42	
	SD	0.40		0.3		0.04		0.37	
	n	(10)		(10)		(10)		(10)	
On 0.8–1% CO_2	Mean	11.22*	+40%	12.1	—	1.08	+48%	5.34	−1.5%
	SD	0.6		0.2		0.05		0.33	
14 Days	*n*	(10)		(10)		(10)		(10)	
35 Days	Mean	12.2*	+52%	11.5	−5.8%	1.16	+57%	5.25	−3.1%
	SD	0.8		0.3		0.06		0.32	
	n	(10)		(10)		(10)		(10)	
56 Days	Mean	13.1*	+63%	12.0	—	1.20*	+62%	5.31	−2.1%
	SD	0.8		0.2		0.05		0.23	
	n	(10)		(10)		(10)		(10)	

P <0.05 or better.

TABLE 4
EFFECT OF PROLONGED EXPOSURE TO 1.5% CO_2 AND 0.8–0.9% CO_2 ON PHYSIOLOGICAL DEAD SPACE

		% Change			% Change
Control period on Air $n = 10$	169±21		Control period on Air $n = 6$	206±24	
On 1.5% CO_2 in 21% O_2; 40 Days' Exposure $n = 9$	273±82	+62%*	On 0.9% CO_2 in 20–21% O_2; 20 Days' Exposure $n = 6$	367±49	+56%
4 Weeks' Recovery on Air $n = 8$	174±25	+ 3%*	8 Weeks' Recovery on Air = Control Period $n = 6$	216±40	
			On 0.8% CO_2 in 20–21% O_2 20 Days' Exposure**	369±42	+59%*

Values are means ± SD; *difference significant at 5% level or better;** exposure to 0.8% CO_2 during second patrol.

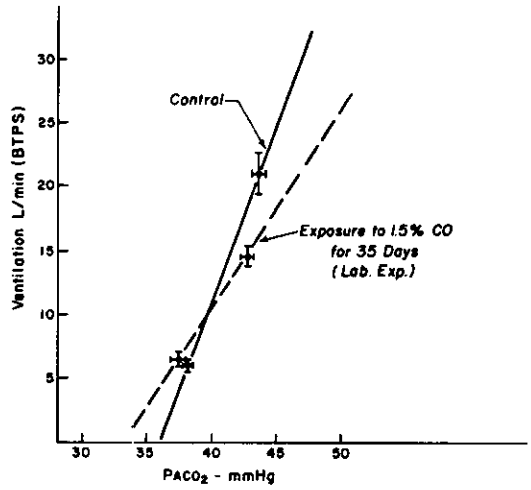

Fig. 1. Ventilation (BTPS) plotted against end-tidal P_{CO_2}. Decrease in slope of CO_2 tolerance curve obtained during patrol on 6 subjects after 14–18 days and 25–32 days of exposure to an average CO_2 concentration of 1% CO_2.

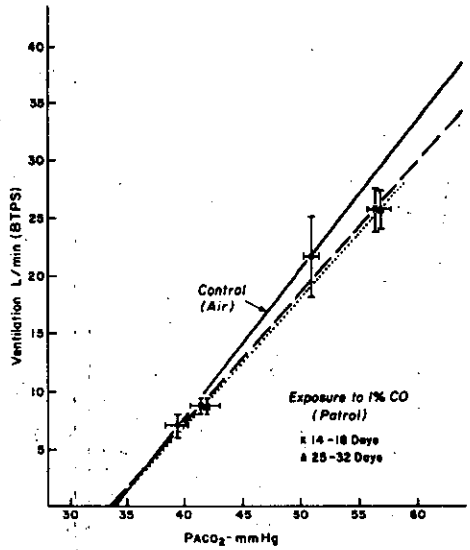

Fig. 2. Ventilation (BTPS) plotted against end-tidal P_{CO_2}. Decrease in slope of CO_2 tolerance curves after 35 days' exposure to 1.5% CO_2.

determined in 21 subjects after 35 days of exposure to 1.5% CO_2. However, this change is based mainly on a marked decline in ventilatory response; the end-tidal CO_2 tension changed very little.

Acid-base balance and electrolytes

Patrol studies carried out at a 1% CO_2 level demonstrated periods of a slight respiratory acidosis, indicated by slightly elevated P_{CO_2}, lowered pH, increased bicarbonate, and decreased plasma chloride (Gude and Schaefer 1969; Peck 1971; Gortner, Messier, Heyder, and Schaefer 1971; Messier, Heyder, Braithwaite, McCluggage, Peck, and Schaefer 1979), as well as periods of predominant metabolic acidosis, in which bicarbonate was lower.

The time course of pH changes in the arterialized capillary blood and in venous blood determined on 15 subjects during a 64-day patrol using an ultramicro pH blood analyzer (Instrumentation Laboratory Model 113-S1) (Peck 1971) is shown in Fig. 3, together with the P_{CO_2} level of the atmosphere. Because of the different watch schedules of the naval personnel involved in the studies, the samples were collected at times that varied greatly with regard to the length of the awake period (30 min to 24 h). To eliminate the known effects of circadian cycles on pH, the subjects were divided into two groups. In Group A, the blood samples were taken within four hours of awakening, and in Group B, longer than four hours after awakening. The measurements of pH in the arterialized capillary blood and in venous blood were made independent of each other on different blood samples. The time course of pH changes in arterialized capillary blood and venous blood correspond with each other, and so do those of the two subject groups. The pH falls during the first two weeks and subsequently rises to normal values. From the 42nd day on, another decline in pH occurs. Similar changes, shown in Fig. 4, were observed during the time course of plasma bicarbonate in arterialized capillary and venous blood. The significant decreases in bicarbonate during the third week and again during the seventh and eighth weeks of the patrol indicate the development of metabolic acidosis superimposed on the CO_2-induced respiratory acidosis. An increase in bicarbonate normally associated with a respiratory acidosis is observed during the first days of the patrol and after about four weeks.

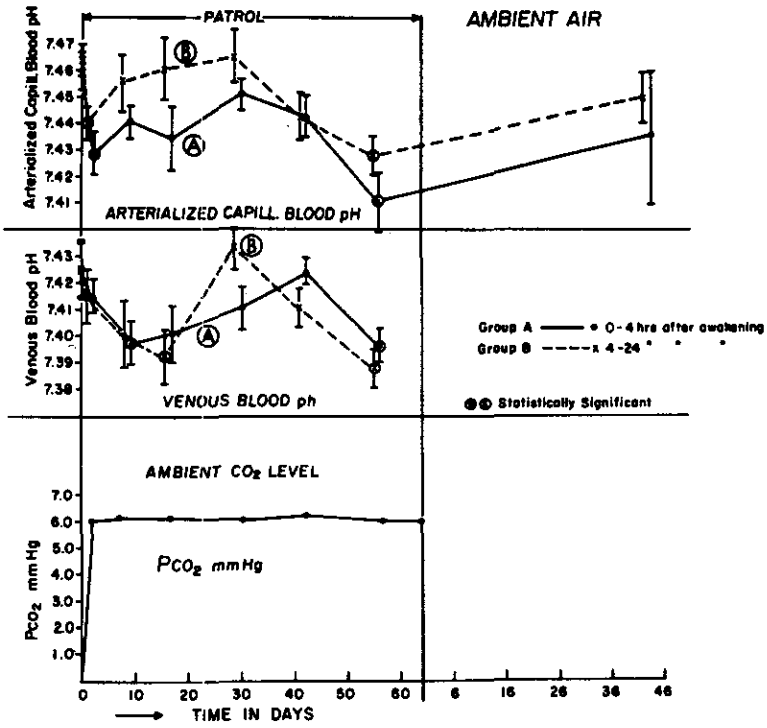

Fig. 3. Time course of pH in arterialized capillary and venous blood during patrol. Average ambient P_{CO_2} level 6 mmHg (Peck 1971: 15 subjects, two groups; group A: sample taken 0–4 h after awakening; B: samples taken 4–24 h after awakening).

Changes in blood CO_2 tension observed during patrol in arterialized and venous blood are presented in Fig. 5. Again, there are cyclic changes—an increase of about 2 mmHg during the first week, a subsequent fall of about 2 mmHg below control levels during the third week, followed by another rise and another fall. In other patrol studies in which a much more limited amount of data was obtained, a rise of about 4 mmHg P_{CO_2} in arterialized blood (10 subjects) was observed by Gude and Schaefer (1969) after 20 days of exposure to 1% CO_2. Schwartz (1969), using the Hackney-Collier CO_2 rebreathing method to estimate arterial P_{CO_2}, found an increase averaging 4 mmHg in eight subjects after 21 days' exposure to 1% CO_2; this agrees with the findings of Gude and Schaefer (1969). After 42 days of exposure to 1% CO_2, the estimated arterial blood P_{CO_2} was only 1.4 mmHg above control levels.

Data on pH, P_{CO_2}, and bicarbonate obtained in three patrol studies and two laboratory studies are shown in Fig. 6. The average ambient CO_2 ranged from 0.85%–1% CO_2 in the patrol studies and 1%–1.5% CO_2 in the laboratory simulation experiments. In all experiments, cyclic changes in pH are evident. The time periods of these cycles are about 20 days for the initial fall, subsequent rise, and second fall in pH. These three periods, which are also reflected in P_{CO_2} and bicarbonate, have been classified as a sequence of metabolic acidosis, respiratory acidosis, and metabolic acidosis. The longest experiment, of 90 days' duration, in which four subjects were exposed to 1% CO_2 (McDonnell 1971; Messier, Heyder, and Schaefer 1971) showed as many as four cycles of pH changes.

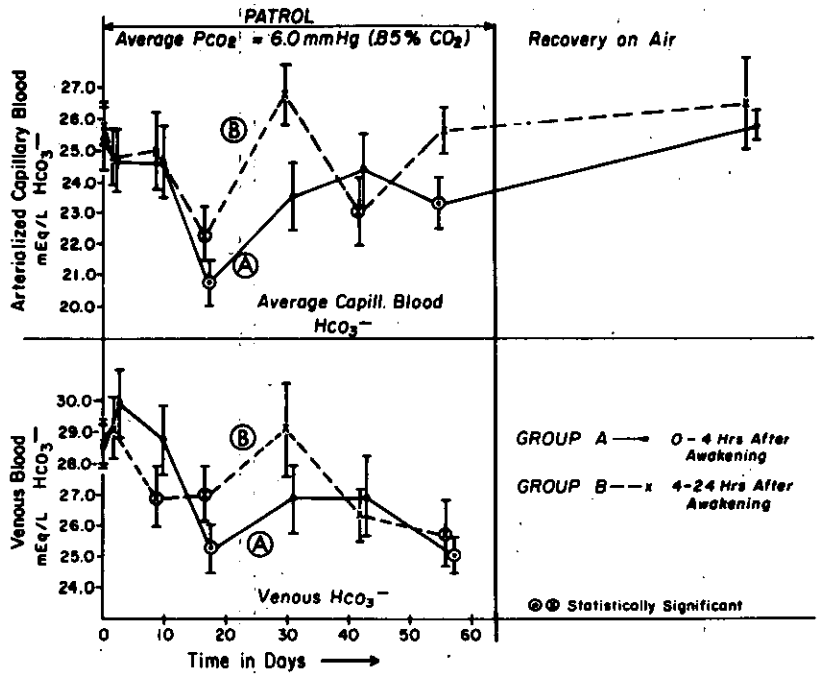

Fig. 4. Time course of bicarbonate in arterialized capillary blood and venous blood during patrol. Average ambient P_{CO_2} level = 6 mmHg: 15 subjects, two groups; group A, samples taken 0–4 h after awakening; B, 4–24 h after awakening (Peck 1971).

Data on plasma chloride collected on patrols are very limited. A significant decrease of plasma chloride during prolonged exposure to 0.9%–1% CO_2 on patrols was observed by Gortner et al. (1971) on Day 42, by Mendelson (cited by Gortner et al. (1971)) on Day 40, and by Messier et al. (1979) on Days 36 and 51. The fall in chloride occurs during the periods of respiratory acidosis and appears to correspond with the rise in bicarbonate.

In three of the studies that provided information on the acid-base status exhibited in Fig. 6, plasma calcium was measured. These data are exhibited in Fig. 7, together with those obtained during a patrol study by Gray, Morris, and Brooks (1973). In this figure, 20-day periods have been marked in the same manner as in Fig. 6. In most cases there is a fall of plasma calcium during the first 20 days, followed by a marked rise during the second 20-day period. The peaks of plasma calcium center around the 40th day, with the exception of one on Day 51. Between 40 and 60 days of exposure, there is again a decline in plasma calcium. The clearly pronounced cycles in plasma calcium follow the cycles in acid-base balance shown in Fig. 6.

Data on urinary excretion and urine volume collected in the same experiments are exhibited in Fig. 8. Cyclic changes in calcium excretion can be seen in every experiment, although the time periods do not correspond with each other in all cases. A more detailed presentation of data on urinary pH, titratable acidity, and calcium and phosphorus excretion collected during the 90-day experiment (1% CO_2) is given in Fig. 9. Cyclic pH changes occur in 20-day periods and correspond approximately to the cycles in calcium and phosphorus excretion. During the period in which the pH rises, urinary calcium and phosphorus excretion increase. Titratable acidity is higher during the first part of the experiment and lower during the second part and

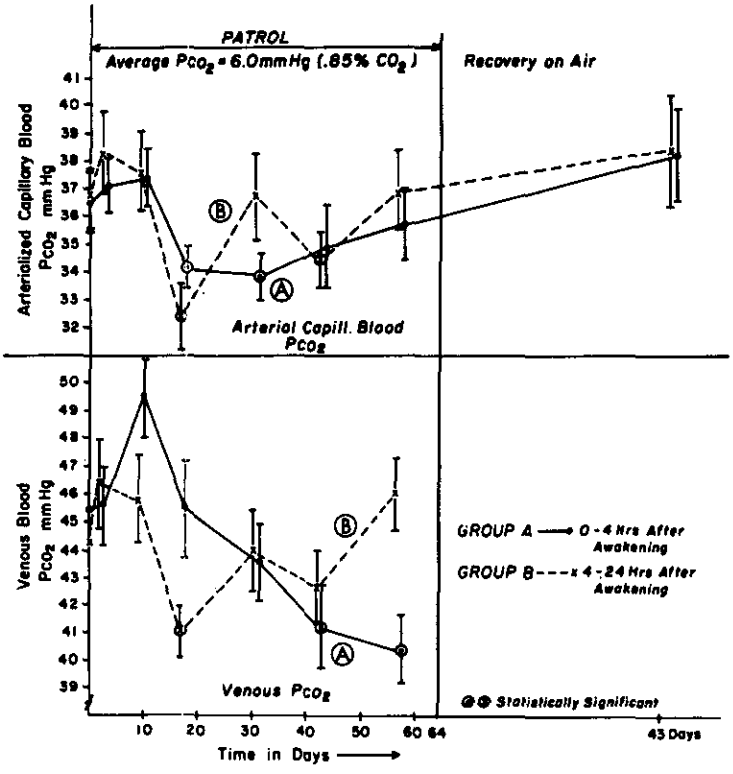

Fig. 5. Time course of CO_2 tension in arterialized capillary blood and venous blood during patrol. Average ambient P_{CO_2} level = 6 mmHg; 15 subjects, two groups; A, samples taken 0–4 h after awakening; B, 4–24 h after awakening.

does not show a clearly pronounced relationship to calcium excretion. However, in a British patrol experiment in which the ambient CO_2 level was 0.7% CO_2, a slight rise in calcium excretion at the 20th day of exposure was observed, which corresponded exactly with the rise in acid excretion shown in Fig. 10 (Gray et al. 1973). Data on urinary electrolyte excretion measured in the same experiment are plotted with the plasma calcium, magnesium, and phosphorus data collected simultaneously. Both plasma calcium and phosphorus show two peaks, on Day 5 and Day 40. Magnesium also exhibits an early peak on Day 5. However, there is no second peak on the 40th day. Urinary excretion of calcium, phosphorus, and magnesium do not reflect any of the peak plasma levels of these electrolytes. The findings of Gray et al. (1973) have been summarized and reproduced in this paper because they represent the most comprehensive published blood and urine data collected in human subjects exposed to low levels of CO_2 on patrols and correspond with findings on plasma, calcium, and phosphorus obtained in guinea pigs exposed to 1% CO_2 for 8 weeks, in which bone electrolytes were also measured (Schaefer, Pasquale, Messier, and Niemoeller 1979b). These findings will be discussed later.

Plasma electrolytes

Measurements of plasma Na concentrations during chronic low level hypercapnia produced equivocal results. During exposure to 1.5% CO_2, Schaefer, Nichols, and Carey (1963b) ob-

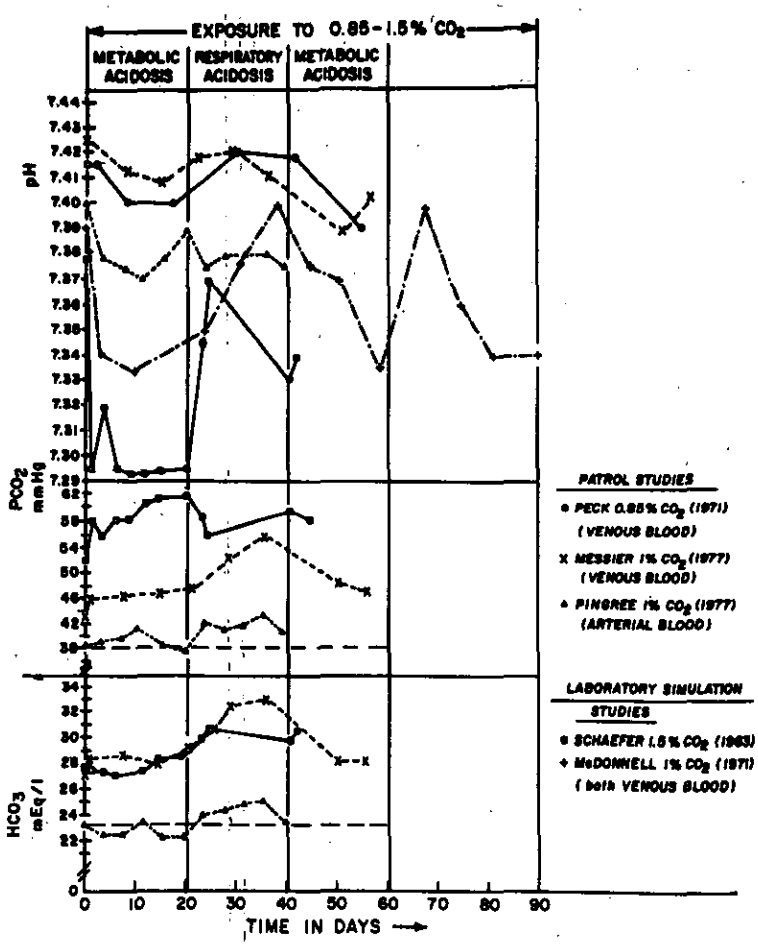

Fig. 6. Time course of pH, blood P_{CO_2} and bicarbonate during patrols (ambient CO_2 levels 0.85–1% CO_2) and during laboratory simulation tests in which subjects were exposed to 1.5% CO_2 for 43 days and 1% CO_2 for 90 days.

served an increase of 2 mEq during the first 24 days, and a subsequent return to control values. Messier et al. (1971) observed a decrease of 4 mEq during the first 24 days of exposure to 1% CO_2. In two patrol studies in which the combined CO_2 concentrations varied between 0.85–0.9% CO_2, a trend toward reduction in plasma Na values was seen (Peck 1971; Gortner et al. 1971). In another patrol study (Messier et al. 1979) an increase of plasma Na was observed.

Data on plasma K measured during laboratory and patrol studies are listed in Table 5. During exposure to 1.5% CO_2, plasma K content of the arterial blood showed a significant decrease. A decrease in plasma K was also observed during the first part of the McDonnell study and in three patrol studies in which plasma K was measured.

Red cell electrolytes

Red cell sodium increased and red cell potassium decreased both during exposure to 1.5% CO_2 and exposure to 1% CO_2 submarine atmosphere, as shown in Tables 6 and 7 (Schaefer, Nichols, and Carey 1964; Gortner et al. 1971; Messier et al. 1979). Similar changes occurred in

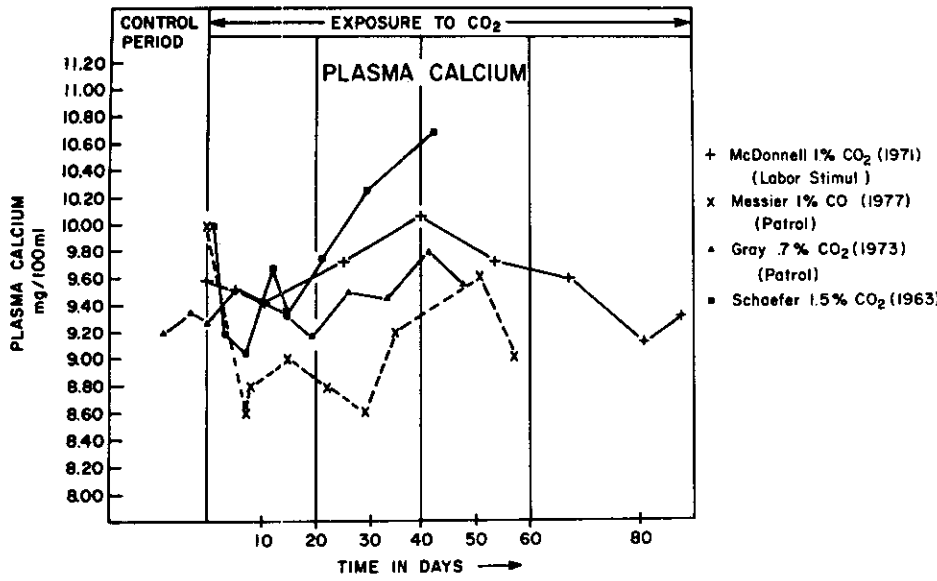

Fig. 7. Summary of plasma calcium data obtained during patrols with ambient CO_2 concentrations ranging from 0.7% CO_2 (Gray et al. 1973) to 1% CO_2 (Messier et al. 1979), and laboratory experiments with ambient CO_2 concentrations ranging from 1% CO_2 (McDonnell 1971) to 1.5% CO_2 (Schaefer 1963b).

red cell calcium during prolonged exposure to 1.5% CO_2 (laboratory experiment) and 1% CO_2 during patrols (Messier et al. 1979). In both cases there were increases in red cell calcium.

Saliva electrolytes

Studies by Hughes (1969) of salivary CO_2 and electrolyte excretion during exposure to a 1.2% CO_2 atmosphere on a patrol showed an increase of CO_2 content and corresponding decrease of chloride, while salivary flow rate remained at the control level. Calcium concentration decreased, which agrees with findings showing a decrease in serum calcium during three patrols (Messier et al. 1979) (Table 8). These saliva studies give additional evidence of the existence of a CO_2-induced acidosis on patrols.

Gastric secretion

Since many sailors complain during patrol about pyrosis symptoms, which are associated with increased gastric activity, a study was made of gastric acidity on five volunteer crew members during a patrol. All five subjects had above-normal total gastric acidity values during patrol compared with pre- or post-patrol levels (Table 9) (Foster 1969).

DISCUSSION

Respiration

The patrol study by Covington (cited in this paper) showed that prolonged exposure to CO_2 concentrations in the range of 0.85–1% CO_2 produces a continuous stimulation of respiration,

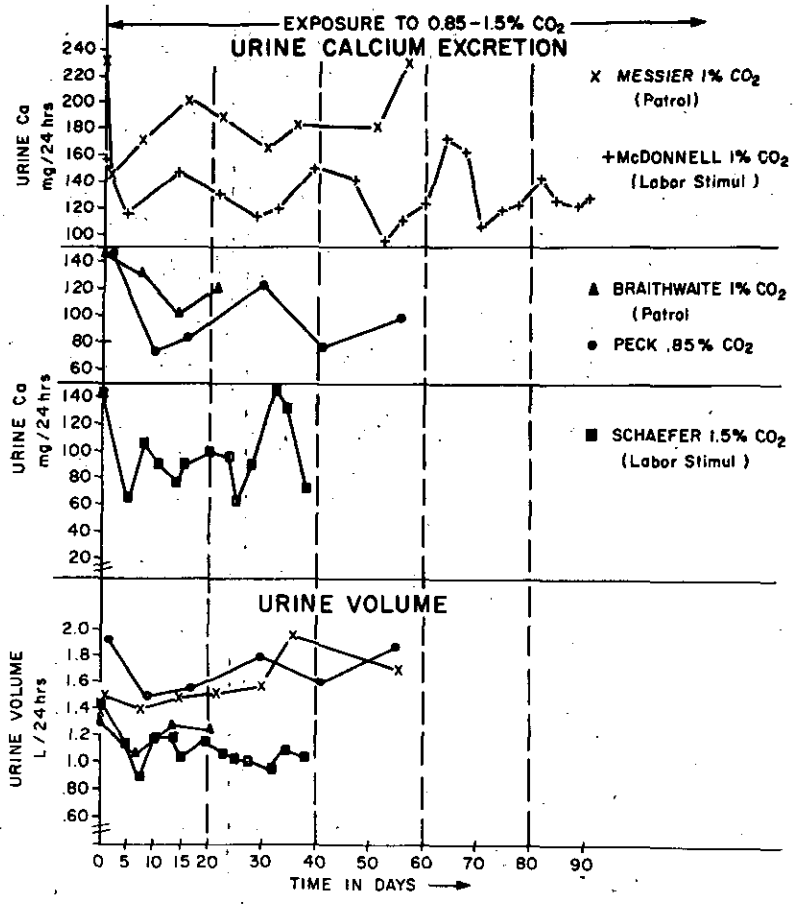

Fig. 8. Summary of urinary calcium excretion and urine volume data collected during patrols (ambient CO_2 levels 0.85%–1% CO_2) and laboratory experiments (ambient CO_2 concentrations 1% CO_2–1.5% CO_2).

demonstrated by the consistent increase in ventilation caused by an increased tidal volume throughout the exposure period.

In other patrol studies in which the ambient CO_2 concentration was 1%, a smaller increase in respiratory minute volume was observed (Pingree 1977; Kingsbury (cited in this paper)).

A summary of the effects of prolonged exposure to low CO_2 concentrations in the range of 0.8–2% CO_2 is presented in Table 10. The first two laboratory experiments with 2% and 1.5% CO_2 show very similar changes in end-tidal CO_2 tension ($P_{A_{CO_2}}$) and respiratory minute volume. Respiratory minute volume shows a modest decrease in the later part of the exposure period, while $P_{A_{CO_2}}$ remains essentially at the same level. In the three patrol studies listed, the ambient CO_2 concentrations ranged from 0.8–1% CO_2. A marked increase in ventilation was found during the first part of the exposure period in all three patrols, and was associated with very little or no decrease in $P_{A_{CO_2}}$. During the later portion of the patrol period, respiratory minute volume declined but remained above the control level in two studies; it fell 22% below control data in the study of Pingree (1977). However, the control respiratory minute volume reported by Pingree of 11.5 liter/min is much too high for resting conditions. It is therefore most likely that the subjects were not sufficiently trained and that they therefore

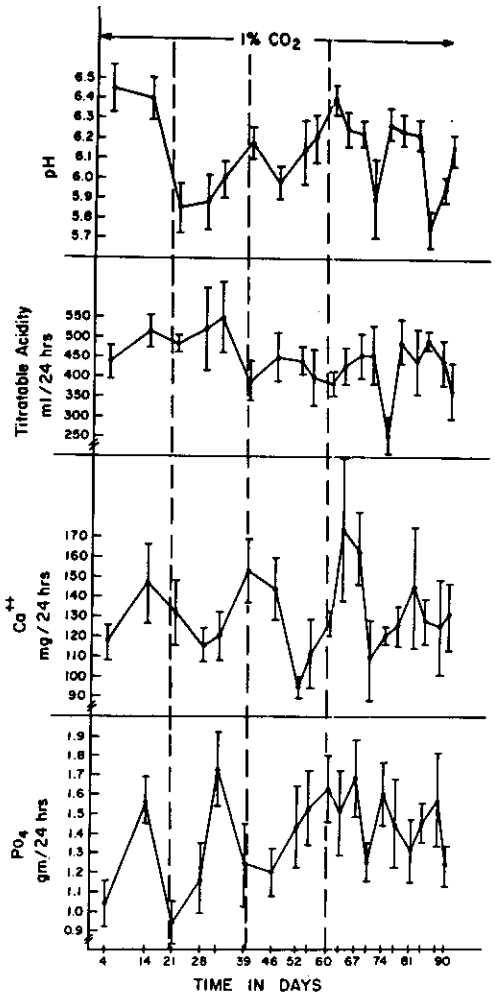

Fig. 9. Urine pH, titratable acidity, urine calcium, and phosphorus excretion during prolonged exposure to 1% CO_2 (4 subjects) (McDonnell 1971).

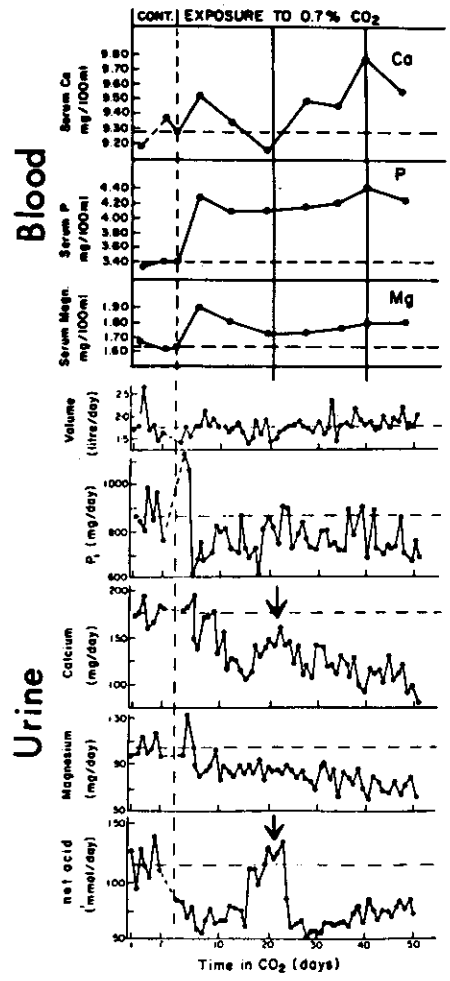

Fig. 10. Data on serum calcium, phosphorus and magnesium, and urinary calcium, magnesium, phosphorus, and acid excretion collected during prolonged exposure to 0.7% CO_2 on patrol (Gray et al. 1973).

hyperventilated. If one assumes a control respiratory minute volume of 8.0 liter/min, the decrease in the respiratory minute volume after the rise in the initial exposure period would bring the values down approximately to control values and not below. The importance of these studies (cited in Table 11) is the evidence for a continuous stimulation of respiration during long periods associated with such small increases in $P_{A_{CO_2}}$. In the later part of the studies, the hyperventilation effect declines. It seems to disappear altogether, according to the study of Pingree (1977). This agrees with findings in a recent British simulation study in which subjects were exposed for 36 days to 0.5% CO_2 and ventilation increased only during the first five days (Davies, Smith, Leitch, Morris, and Gray 1976). During exposure to the submarine atmosphere, factors other than CO_2 might increase ventilation. Aerosols and ions may interact with

TABLE 5

EFFECT OF PROLONGED EXPOSURE TO LOW LEVELS OF CO_2 ON PLASMA K CONCENTRATIONS

Experiment (Schaefer), $n=10$; arterial blood, on 1.5% CO_2	K, mEq/liter mean ± SEM 4.77±1.5	Patrol (Messier), $n=7$; venous blood, on 1% CO_2	K, mEq/liter means ± SEM 4.3±0.07	Patrol (Peck); $n=15$; venous blood, on 0.85% CO_2	K, mEq/liter means ± SEM 5.9±0.08	Patrol (Gortner), $n=12$; venous blood, on 0.9% CO_2	K, mEq/liter mean ± SEM 3.9±0.0	Experiment (McDonnell), $n=4$; venous blood, on 1% CO_2	K, mEq/liter means ± SEM 4.2±0.1
35–41 days	4.41 ±0.37*	Day 7	4.4 ±0.09	Day 2	3.9 ±0.07	Day 7	3.6 ±0.12*	Days 1–24 (16)	3.81 ±0.1*
Recovery on Air (9 days)	4.08 ±0.24*	Day 8	4.1 ±0.12	Day 9	3.7 ±0.07	Day 21	3.8 ±0.16	Days 25–45 (12)	4.0 ±0.1
		Day 15	4.1 ±0.19	Day 17	3.4 ±0.10*	Day 42	3.8 ±0.17	Days 49–90 (20)	4.2 ±0.1
Recovery on Air (4 Weeks)	4.32 ±0.37*	Day 22	3.9 ±0.06*	Day 30	3.8 ±0.04	Day 63 + *Recovery* 3 days on air	3.9 ±0.24	Post exposure Recovery 1–25 Days	
		Day 29	3.7 ±0.07*	Day 56	3.7 ±0.08				4.2 ±0.2
		Day 30	3.7 ±0.07*						
		Day 51	4.0 ±0.08*						
		Day 57	3.8 ±0.06*						

*Difference significant at the 5% level or better; control periods on air.

TABLE 6
EFFECT OF PROLONGED EXPOSURE TO 1.5% CO_2, 21% O_2 ON PLASMA AND RED CELL Na AND K CONCENTRATIONS

		Plasma		Red Cells	
		Na, mEq/liter	K, mEq/liter	Na, mEq/liter	K, mEq/liter
Control Period on Air	Mean	141.4	4.77	13.5	86.0
	SD	±2.9	±0.15	±4.5	±4.5
	n	(9)	(10)	(10)	(10)
On 1.5% CO_2 35–41 Days	Mean	141.2	4.41*	21.6*	78.9*
	SD	±0.6	±0.37	±4.8	±4.4
	n	(10)	(10)	(9)	(9)
8–9 Days Recovery on Air	Mean	140.0	4.08*	24.4*	76.2*
	SD	±1.4	±0.24	±4.9	±4.7
	n	(8)	(9)	(8)	(9)
4 Weeks Recovery on Air	Mean	142.0	4.32*	12.8	79.9*
	SD	±4.1	±0.37	±6.9	±4.2
	n	(10)	(10)	(8)	(10)

*Difference significant at the 5% level or better. Data from Schaefer et al. 1964.

TABLE 7
EFFECT OF PROLONGED EXPOSURE TO 1% CO_2 DURING PATROL ON Red CELL Na AND K CONCENTRATIONS

		Plasma		Red Cells	
		Na, mEq/liter	K, mEq/liter	Na, mEq/liter	K, mEq/liter
Control Period on Air	Mean	131.2	4.3	11.1	72.2
	SEM	1.5	0.07	0.2	1.3
	n	(7)	(7)	(7)	(7)
On 1% CO_2 8 Days	Mean	136.3*	4.1	17.4*	67.1*
	SEM	0.9	0.12	1.5	1.7
	n	(10)	(10)	(10)	(10)
22 Days	Mean	137.3*	3.9*	16.0*	68.1*
	SEM	2.1	0.06	1.1	0.5
	n	(10)	(10)	(10)	(10)
36 Days	Mean	136.0*	3.7*	19.8*	65.1*
	SEM	0.7	0.08	0.8	0.7
	n	(9)	(9)	(9)	(9)
51 Days	Mean	136.9*	3.8*	17.5*	67.5*
	SEM	0.4	0.06	0.7	0.6
	n	(10)	(10)	(10)	(10)

*Difference significant at the 5% level or better. Data from Messier et al. 1979.

TABLE 8
ANALYSIS OF SALIVARY COMPONENTS DURING AN FBM PATROL

	Flow, ml/5 min	CO_2, vol%	Na^+, mEq/liter	K^+, mEq/liter	Ca^+, mg/100 ml	P_i, mg/100 ml	Cl^-, mEq/liter
Pre-patrol	4.7	55.87	24.85	18.95	4.7	10.71	37.76
	0.49	6.73	2.73	0.99	0.22	0.41	4.02
6th week of patrol	4.6	66.13	22.8	19.63	4.23	14.83	30.91
	0.34	7.63	3.44	1.07	0.33	1.81	3.32

Values are means, with SEMs below; $n = 10$. Data derived from Hughes 1969.

CO_2. This would explain the fact that in the study of Covington, a lower concentration of CO_2 (0.8–1%) produced a higher increase in ventilation (Table 3) than exposure to 1.5% CO_2, and showed an even further increase in the later part of the patrol.

Guillerm and Radziszewski (1979), in their excellent study on the effects of prolonged exposure to 2% CO_2 for 30 days, have shown an immediate decrease in CO_2-induced hyperventilation in the period between 2 and 24 h of exposure. They observed a similar decline in hyperventilation during exposure to 3% and 4% CO_2, which was associated with a slight increase in $P_{A_{CO_2}}$. The authors could demonstrate that this initial decline could not have been caused by changes in $P_{A_{CO_2}}$ and arterial pH. Alterations in cerebrospinal fluid pH and peripheral chemoreceptor activity could also be excluded. It was concluded that this early alteration of hyperventilation might be related to a decrease in the respiratory center sensitivity to the P_{CO_2} stimulus. The data published by Guillerm and Radziszewski (1979) showed a second and more pronounced attenuation of the CO_2-induced hyperventilation between the 8th and 15th day of exposure to 2% CO_2, a finding to which the authors made no reference. This decline in respiratory minute volume occurred after a compensation of the acidosis was reached on Day

TABLE 9
EFFECT OF PROLONGED EXPOSURE TO 1% CO_2 ON GASTRIC SECRETION DURING PATROL

Condition	Total Acid, Degrees
Control Period on Air	41.2±3.3
On 1.0% CO_2 for 8 Days	54.2±6.4
23 Days	57.4±11.7
54 Days	64.0±13.4
Post-Patrol 4 Weeks Recovery on Air	32.2±6.1

Values are means ± SEM; $n = 5$. Data derived from Foster 1969.

TABLE 10
EFFECT OF EXPOSURE TO LOW CO_2 CONCENTRATIONS ON $P_{A_{CO_2}}$ AND RESPIRATORY MINUTE VOLUME

Ambient CO_2, %	Duration, Days	n	Control $P_{A_{CO_2}}$, mmHg	CO_2 Exposure, $\Delta P_{A_{CO_2}}$	CO_2 Exposure, $\Delta P_{A_{CO_2}}$	Control Respiratory Minute Volume, BTPS	CO_2 Exposure Respiratory Minute Volume, %	CO_2 Exposure Respiratory Minute Volume, %	References
						Laboratory			
2%	30	6	37.8	1–9 Days +2.5	10–30 Days +2.5	7.8 liter/min	1–9 Days +38%	10–30 Days +30%	Guillerm and Radziszewski (1979)
1.5%	42	20	37.8	1–24 Days +2.4	25–42 Days +2.1	6.1 liter/min	1–24 Days +39%	25–42 Days +37%	Schaefer et al. (1963a)
						Patrol			
0.8–1%	56	10	—	14 Days —	35 Days —	8.03 liter/min	14 Days +40%	35 Days +52%	Covington, cited in Schaefer (1978)
1%	50	5	40.6	14–18 Days —	25–30 Days —	7.5 liter/min	14–18 Days +16%	25–32 Days +9%	Kingsbury, cited in Schaefer (1978)
1%	44	15	38.2	1–4 Days +0.4	16–44 Days +3.1	11.5	1–4 Days +33%	16–44 Days −22%	Pingree (1977)

TABLE 11
SUMMARY OF PHYSIOLOGICAL EFFECTS OF PROLONGED EXPOSURE TO 1% CO_2 IN 20–21% O_2 ON SUBMARINE PATROLS

Respiration	Increase in respiratory minute volume (+40–60%); Increase in tidal volume (+40–60%); Increase in physiological dead space (+50–60%); Decrease in vital capacity (−3%)	Covington 1968 Gude and Schaefer 1969
Acid-Base balance	Respiratory acidosis; Increase in P_{CO_2} and decrease in pH for different periods	Messier et al. 1979; Schwartz 1969; Gortner et al. 1971; Peck 1971
Electrolytes	Decrease of plasma chloride related to acidosis; Red cell Na increase, K decrease Saliva: Increase in CO_2, decrease in Cl	Messier et al. 1979; Mendelson 1969; Hughes 1969
Gastric acid secretion	Increase in total gastric acid (5 subjects) throughout patrol	Foster 1969
Calcium-Phosphorus metabolism	Decrease in plasma calcium; Decrease in urine calcium; Decrease in urine magnesium	Messier et al. 1979
	Red cell calcium increase during patrol	Messier et al. 1979; Braithwaite 1972

15. It is therefore most likely that this second attenuation of the CO_2-induced hyperventilation was related to the compensation of the respiratory acidosis associated with plasma bicarbonate increase (Torino, Goldring, and Heinemann 1974).

In the other hypercapnia studies listed in Table 11, no measurements were made at 2 h of exposure. Consequently, no comparison can be made with the data on 2% CO_2 with regard to the early changes in respiratory minute volume. However, the second decline of the CO_2-induced hyperventilation after 2–4 weeks of exposure is pronounced in all the other studies, with the exception of that of Covington. It should be pointed out that all acid-base balance studies performed during low level chronic hypercapnia showed a phase of compensatory respiratory acidosis during the time in which this later decline in respiratory minute volume was observed (Fig. 6). This supports the conclusion that acid-base changes caused the decreases in ventilation during the later part of the exposure.

The increase in physiological dead space found during patrols agrees with the changes observed during exposure to 1.5% CO_2 (Schaefer et al. 1963a) and seems to indicate a dilating effect of CO_2 on the airways. The significance of these findings can only be assessed through regular pulmonary function studies of submariners in a longitudinal health study.

The observations of Sonnenburg (1965) on the effect of submarine air on ciliary mucus transport should be mentioned. During a routine patrol of an FBM submarine, he measured the ciliary mucus activity in freshly prepared frog esophagus strips exposed to "submarine air" and "surface air." The latter was brought aboard the submarine in cylinders. Results

showed a definite decrement in ciliary activity in those tissues exposed to submarine air. The author suggested that activity of (+)ions, in association with CO_2 and aerosols, might account for these results. Air ions have been measured in FBM submarines and are in general no different from those of the natural atmosphere. Average concentrations for positive and negative ions are less than 1,000/cc, considerably lower than concentrations measured in conventional fleet-type submarines (Schaefer 1961b). Occasionally, ion surges occur and higher concentrations are reached (Ramskill 1961; Maumus 1967). Interaction of aerosols and ions may result in a shift of the spectrum of ions (Schaefer and Dougherty 1961). Respiratory functions were measured in our laboratory in human subjects exposed to (+) and (−) ion concentrations observed on submarines. No effects were observed. However, further studies on the combined effects of aerosols, ions, and low levels of CO_2 would be required to see whether aerosols and ions in the submarine atmosphere interact with ambient CO_2 and influence respiration.

Verzar (1962) has pointed out that condensation nuclei (aerosols) in the closed-space atmosphere might play a role by concentrating toxic trace substances, e.g., organic substances containing acid material, causing them to exceed effective threshold levels. This could occur in the ambient air or in the respiratory tract during normal respiration and could have effects on respiration.

In another study of pulmonary functions carried out by Rodenbaugh (1967) on 135 members of a Polaris crew on patrol, six crew members were found to have definitely abnormal pulmonary functions and several more were borderline cases, as indicated by reduced maximal expiratory flow rates and 1-, 2-, and 3-s vital capacity data. Smokers had significantly lower maximal flow rates than non-smokers.

Rodenbaugh (1967) attempted to compare the 2.5% incidence of abnormal lung functions in his submarine crew with that of an industrial population of males below the age of 40 years; the latter incidence was reported to be 0.5%. However, further studies would be required to establish whether there is a greater incidence of abnormal pulmonary functions in submariners during patrols.

Acid-base balance and electrolytes

The cyclic changes in blood pH, bicarbonate, and P_{CO_2} observed during patrols involving prolonged exposure to 0.85%–1% CO_2 and during laboratory simulation experiments with ambient CO_2 levels of 1.0 to 1.5% CO_2 (Fig. 6) are significant findings. They demonstrate a new phenomenon that has not been described previously. The time course of pH, bicarbonate, and P_{CO_2} shown in Fig. 6 shows alterations between a metabolic acidosis during the first 15–20 days, followed by a respiratory acidosis (20–40 days) and a subsequent metabolic acidosis during the period between 40 and 60 days.

Moreover, Gray et al. (1973) observed cyclic changes in urinary net acid excretion and ammonia excretion during 7 weeks of exposure to 0.7% CO_2 on a submarine. Under these conditions, similar to those reported in this paper, net acid and NH_4 excretion decreased during the first two weeks; this was followed by a rise to control levels that lasted for 10 days (up to Day 24) and a subsequent fall, with no further change, until the end of the exposure.

From what is known about renal regulation during CO_2-induced respiratory acidosis, one would expect that an increased acid load would be met with an increased net acid and ammonia excretion. Recent studies on the mechanism of urinary acidification (Rector 1974) indicate that H^+ secretion plays a major role in both bicarbonate reabsorption and formation of titratable acid and ammonia. For each hydrogen ion excreted in the urine through titratable

acid and NH_4, a newly formed bicarbonate is added to renal venous blood. The fall in blood bicarbonate observed during the first 17 days of exposure to 0.85% CO_2 (Fig. 3) and the failure of the kidney to respond with an increased acid and NH_4 excretion to the acid load during the first two weeks of exposure to 0.7% CO_2 (Gray et al. 1973) indicate that renal defense mechanisms known to operate against respiratory acidosis induced by higher CO_2 concentrations are not brought into play immediately under lower CO_2 concentrations. The rise in blood bicarbonate and the increase in net acid and NH_4 excretion occur, however, after a delay of nearly three weeks. What caused this delay?

Acid-base balance, CO_2 storage, and calcium homeostasis

I am trying to show that this delayed renal response in low level chronic hypercapnia is related to the dominant role of bone buffering in the regulation of acid balance, in particular to the processes of bone CO_2 storage and associated bone calcium changes.

Data on blood calcium obtained during prolonged exposure to 0.70–1.5% CO_2 (Fig. 7) show cycles of 14–20 days, which mirror those for pH exhibited in Fig. 6. Except for an initial peak in the first few days of exposure, plasma calcium falls during the first three weeks and then rises during the period between 20 and 40 days. Urinary calcium excretion is definitely reduced during the first 20-day period in all cases and subsequently shows an increase that may vary in length (Fig. 8). The cycles of increased urinary calcium excretion do not correspond to the peaks of blood calcium but are shifted to a later time that may be related to the interaction of parathyroid hormone and calcitonin, which raise and decrease the threshold of urinary calcium excretion, respectively (Peacock, Robertson, and Nordin 1969; Crumb, Martinez-Muldonado, Eknoyan, and Suki 1974).

The activity of parathyroid hormone and calcitonin was measured in two patrol studies in which the ambient CO_2 concentration was 1% CO_2 (Messier et al. 1979). In one of these studies, a tendency towards an increase was observed after two and three weeks, but the differences were not statistically significant. In the second study, no trends in parathyroid hormone activity (PTH) were observed. No significant changes in calcitonin levels were found; however, it should be remembered that the tests carried out at the Endocrine Laboratory of Mass. General Hospital had about a 15% variability. Under these conditions it is difficult to establish statistically whether minor but physiologically significant increases in PTH activity or calcitonin occurred. Increased levels of PTH have been found to decrease bicarbonate reabsorption and to produce a systematic acidosis (Crumb et al. 1974). Such a condition may have played a role in the development of the acidosis observed during the first three weeks of exposure to increased CO_2 levels.

The CO_2-induced decreases in urinary calcium excretion during the first 2–3 weeks of exposure were in most cases associated with a decrease of serum calcium. This is in agreement with earlier findings of Schaefer and his group (1963b) at a 1.5% CO_2 level. It has been suggested that these changes in calcium metabolism during adaptation to CO_2 mark the deposition of CO_2 in bones (Schaefer et al. 1963b) and that bones play an important role in acid-base regulation. More recent studies carried out by Bursaux and Poyart (1974) have given further support to this view. It was found that bone has a rapidly exchangeable pool of bicarbonate, amounting to about 30% of the total bone CO_2, which equilibrates in a rather short time with the level of CO_2 in the blood. In good agreement with the findings of Bursaux are data obtained by Pellegrino and Biltz (1965) showing that in patients with uremia, 37% of the carbonate of the bones was lost. Furthermore, 5% of the total calcium was used for the buffering of hydrogen ion acidosis.

During exposure to low CO_2 concentrations (between 0.7–1.5% CO_2), the acid load seems so small that the threshold of the kidney's regulation is not reached. The bone apparently is the first line of defense under these conditions. However, the bone's defense is static compared to the dynamic defense of the kidney, and it depends on the capacity of its CO_2 stores, which amounts to 110 liters for a 70-kg man or 80% of total body CO_2 stores (Rahn 1962). When capacity is reached, it can be assumed that CO_2 is released from the bone after about three weeks, in accordance with the long time-constants of the bone CO_2 store (Freeman and Fenn 1953). A CO_2 flood coming out of the bone would then represent an acid load large enough to turn on the kidney regulation and cause an increased net acid excretion, associated with an increased bicarbonate retention. This could result in a phase of respiratory acidosis lasting from about 20 days to 35 days, which corresponds to the increase in bicarbonate found (Fig. 6). Subsequently, the cycle repeats itself. The second phase of CO_2 storage in the bones, requiring about 20 days, would end at about 55 days and would coincide approximately with the end of the present patrol exposure period. There are probably a number of other factors that may influence the periods of bone CO_2 storage and release and therefore the phase of metabolic and respiratory acidosis. More investigations about the time sequence of these cycles in acid-base balance during prolonged exposure to low levels of CO_2 need to be carried out.

Additional evidence supporting the hypothesis that bone CO_2 storage and release cause cyclic changes in kidney function and acid-base balance is found in observations made during intermittent exposure to CO_2 (Schaefer et al. 1979). Intermittent exposure to increasing CO_2, rising at a constant rate from 0.0 to 3.0% within a period of 15 h, followed by a 9-h period of air breathing for six days, produced a transient filling and emptying of CO_2 stores within a 5-day period, and led to normal alveolar CO_2 levels and gas exchange data on the sixth day. CO_2 accumulated over a 4-day period and was eliminated through an increased urinary H^+ ion excretion, which was associated with an increased urinary calcium excretion on the fourth and fifth days.

The subject in this study was on a liquid diet to obtain balance data on minerals and to ensure that the hydroxyproline excretion would not be influenced by changes in diet. Hydroxyproline excretion remained at the control level throughout the exposure period, indicating that bone resorption based on parathyroid stimulation was not involved in the calcium flood associated with the CO_2 release. The findings of this experiment provide a model for the explanation of the cyclic changes in acid-base balance found during a patrol.

The exposure periods of 60 days on submarines and of 90 days in a laboratory simulation experiment with 1% CO_2 (Messier et al. 1971) were long enough to accommodate cycles of CO_2 uptake and release in the bone. Based on the limited amount of data available on acid-base balance and calcium metabolism during exposure to low levels of CO_2, the approximate time frame for the periods of CO_2 uptake would be 15–25 days, and for the period of CO_2 release, 10–15 days. If only a few blood samples are drawn, which was the case in most of the patrol studies, one might have either a hypocalcemia or hypercalcemia, depending on the period of the cycle during which the samples were taken. This may explain the difference in Gray, Lampert, and Morris's findings of hypocalcemia in the first submarine study (1969), where only a few samples were taken, and cycles of slight hypocalcemia followed by hypercalcemia in the second British submarine study (1973), with exposure to 0.7% CO_2, in which weekly blood samples were obtained (Fig. 10).

There is another biological model, hibernation, in which acidosis and cyclic changes in hyper- and hypocalcemia seem to occur simultaneously. Riedesel (1960), commenting on the contradictatory literature reports of hypocalcemia and hypercalcemia observed during hiber-

nation, suggested that the calcium level may cycle during long-term hibernation and that the data may have been gathered at different points of the cycle.

Confirmatory evidence for the existence of cycles in bone CO_2 uptake and release has recently been obtained from prolonged exposure of guinea pigs to 1% CO_2 (Schaefer et al. 1979). It has been known for some time that the CO_2 store in the bone contains at least two major fractions: 1) carbonate comprising approximately 60–70% of the total CO_2 content and probably located in the lattice of bone crystals; and 2) bicarbonate, accounting for 30% of the total bone CO_2 stores, which seem to be located in the hydration shell of the hydroxyapatitic crystals and appear to be easily exchangeable. Poyart, Freminet, and Bursaux (1975b) determined, in constant infusion experiments using ^{14}C bicarbonate, that approximately 50% of the ^{14}C activity was lost upon heating. Based on their in-vitro studies, Poyart, Bursaux, and Freminet (1975a) concluded that this heat-labile CO_2 fraction may be considered to make up half of the bone bicarbonate pool. We determined both CO_2 fractions, the dry bone CO_2 content (carbonate) and the heat-labile CO_2, which is the difference between fresh bone and dry bone CO_2 content (bicarbonate), in guinea pigs exposed up to 8 weeks to 1% CO_2.

During the first two weeks of exposure, the bicarbonate fraction increased while the carbonate fraction showed a slight decrease. During the third and fourth week, the carbonate fraction rose markedly and bicarbonate fell to control levels; at six and eight weeks carbonate remained at the level attained at four weeks. However, the bicarbonate fraction rose once again. The rapid uptake of CO_2 into the fast exchangeable bone CO_2 fractions (bicarbonate) during the first phase provides support for the Poyart theory (1975a). The hypothesis states that gaseous CO_2 hydrates with bone water to form carbonic acid, which then dissociates into one HCO_3^- and one H^+ ion

$$CO_2 + H_2O \rightarrow H_2CO_3 \rightarrow HCO_3^- + H^+ \qquad (1)$$

The hydrogen ion is taken up by available carbonate ions in the form of bicarbonate. The decrease in the carbonate fraction, which is associated with a fall in bone calcium and phosphorus during the first week of exposure, indicates the participation of a fraction of the carbonate pool (calcium-phosphate-carbonate complex). During the subsequent period of three and four weeks, reversal takes place; the carbonate fraction increase is associated with a rise in bone calcium and phosphorus. The bicarbonate fraction, on the other hand, declines. Heat-labile CO_2 fell 20 mM/kg, which corresponds to 40 mM/kg of bicarbonate, during this period. If the CO_2 exchange follows the reaction

$$2HCO_3 \rightarrow CO_2 + H_2O + CO_3^= \qquad (2)$$

and 20 mM/kg appear in the form of carbonate, the other 20 mM/kg must have been released as gaseous CO_2 into the extracellular space and blood. It is postulated that this internally released CO_2 provided the stimulus for the activation of the renal bicarbonate reabsorption process, resulting in the phase of respiratory acidosis.

Figure 11 presents in a schematic form the time course of cycles in bone buffering, changes in bone CO_2 fractions, and related calcium-phosphorus exchanges, based on animal experiments. The cyclic changes in acid-base balance found in human studies during exposure to

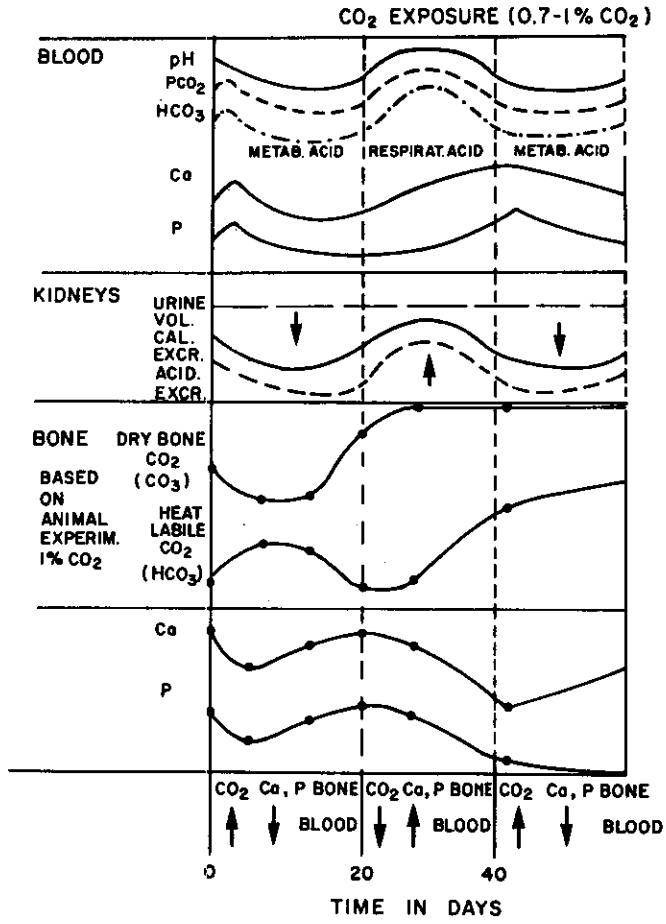

Fig. 11. Cycles in acid-base balance, bone buffering, and renal regulation during prolonged exposure to 0.7%–1% CO_2. Schema is based on data obtained in studies on effects of chronic hypercapnia carried out during patrols and in laboratory experiments. Time course of bone CO_2 and bone calcium and phosphorus is based on animal experiments in which guinea pigs were exposed to 1% CO_2 for 8 weeks (Schaefer et al. 1979b).

0.7%–1.5% CO_2 have been related to cyclic changes in CO_2 and calcium uptake and release by the bones.

The submarine environment contains a number of other factors besides CO_2 that can influence calcium metabolism. Davies and Morris (in this supplement) discuss some of these: the effects of CO_2; reduction in skin synthesis of Vitamin D due to the absence of sunlight; limitations of physical activity; absence of significant trace materials caused by using distilled water; and altered diet habits. They found no evidence that altered dietary habits or distilled water had effects on urinary calcium of the magnitude seen in patrol results. However, a high protein intake in the submariner's diet (120 grams) could cause, according to Johnson, Alcantara, and Linkswiler (1970) and Walker and Linkswiler (1972), an increased urinary calcium

excretion, contrary to the findings obtained in submarine patrols. Moreover, reduced physical activity was found to increase renal calcium excretion in the presence of an ambient CO_2 level of 4% CO_2 (Giannetta and Castleberry 1974). Davies and Morris (1979) obtained unequivocal evidence for the CO_2-induced reduction in urinary calcium excretion in recent chamber studies. After an increased calcium output associated with bed rest on air, they raised the ambient CO_2 level to 0.5% and found a simultaneous reduction in renal calcium excretion. The differences in the results of these two studies are probably related to the difference in the effects of higher and lower CO_2 concentrations on calcium metabolism (summarized by Schaefer (1976)). Exposure to higher CO_2 concentrations results in a continuous hypercalcemia and increased urinary calcium excretion (Schaefer, Hasson, and Niemoeller 1961; Stanmeyer, King, Scofield, and Colby 1962; Heyder 1972).

The significance of the CO_2-induced fall in calcium excretion in the first three weeks of patrol studies is strengthened by findings that reduced physical activity and high protein intake alone cause opposite effects. Davies and Morris (1979) observed a significant decrease in the measured circulating blood levels of 25-hydroxy Vitamin D (25 HCC), indicating a state of hypovitaminosis D, in naval personnel between the beginning and end of a patrol. These authors point out that in their most recent unpublished studies, evidence was obtained showing that fecal excretion of calcium increased, during a 5-week exposure to 0.5% CO_2 and isolation, to a level commensurate with the reduction of 25 HCC levels. The net result of the exposure to the submarine environment with raised ambient CO_2 and artificial light appears therefore to be calcium loss due to increased fecal calcium excretion. These authors concluded that CO_2 contributes to the reduction in urinary calcium excretion during the early part of a patrol and to Vitamin D loss during the later part of a patrol. However, the interaction of CO_2 and Vitamin D hypovitaminosis cannot explain the cycles in calcium excretion reported in this paper; these cycles can only be explained by bone CO_2 uptake and release and associated calcium changes. These cycles in both blood calcium and urinary calcium excretion were not recognized by Davies et al. (1976) and Gray et al. (1973), although they were expressed in the data in their studies.

The theory advanced for the interpretation of the cycles in acid-base balance observed during prolonged exposure to low levels of CO_2 does not fit easily in the framework of accepted concepts of acid-base balance. The major contributions to the understanding of CO_2-induced changes in acid-base balance made by Schwartz and his co-workers (Polak, Haynie, Gordon, Hayes, and Schwartz 1961; Schwartz et al. 1965; van Ypersele, Brasseur, DeConincok 1966) deal only with the effects of high concentrations of CO_2, which cause a rapid and significant renal response. Little attention has been given to the effects of prolonged exposure to low CO_2 concentrations on acid-base balance. In an article on "Concepts of Triple Tolerance to CO_2," (Schaefer 1961a), I have previously pointed to the large differences in the effects of high and low concentrations on the rate of acclimatization. It requires 3–5 days to reach a compensation in pH during exposure to CO_2 concentrations of 3% and above, and much longer times during exposure to lower CO_2 concentrations (Schaefer 1961a). More recent animal studies of prolonged exposure to low CO_2 concentrations have demonstrated that renal reabsorption of bicarbonate, indicated by standard bicarbonate values, becomes less and less effective (Schaefer, Niemoeller, Messier, Heyder, and Spencer 1971). As a matter of fact, during exposure of guinea pigs to 1% CO_2, standard bicarbonate remained below control values for four weeks, indicating a metabolic acidosis (Schaefer et al. 1979).

Figure 12 presents a summary of available data on the rate of acclimatization to chronic hypercapnia based on the time to reach a maximal compensation of pH (arterial or venous blood). The more recent results of Clark, Sinclair, and Welch (1971) and Guillerm and Radzis-

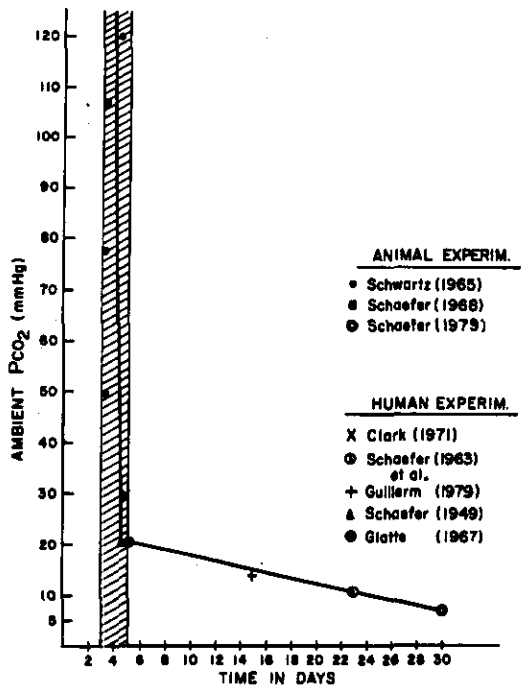

Fig. 12. Time to reach maximal compensation of blood pH during prolonged exposure to different ambient CO_2 tensions. Animal and human experiments.

zewski (1979) are included. There is obviously a systematic difference in the response to levels of CO_2 of 3% and above, compared with that at lower CO_2 concentrations. In the former conditions, the renal regulation (bicarbonte reabsorption) is fully active, while in the latter it becomes less effective and bone buffering, which has a slow time constant, seems to become the dominant factor (Schaefer 1976). This brings up the question of the role of CO_2 stores. In the present concept of gas stores (Farhi 1964), the level of P_{CO_2} in blood or tissue is the determining factor for uptake of CO_2. Guillerm and Radziszewski (in this supplement) have pointed out that on the basis of approximate calculations from data published by Farhi (1964), an overload of a few mmHg of P_{CO_2} is negligible compared with the metabolic CO_2 that is rejected and eliminated. However, it should be pointed out that there are metabolic processes involved in bone CO_2 uptake that clearly are not dependent on P_{CO_2}; the best example is the increase in bone CO_2 that occurs with aging (Poyart et al. 1975a).

Guillerm and Radziszewski (1979) did provide additional data showing opposite effects of higher and lower CO_2 concentrations on blood potassium levels and hematocrits, which are increased during exposure to higher CO_2 concentrations and decreased by lower CO_2 concentrations. This agrees with our observations during exposure to low CO_2 concentrations on patrols (Table 5).

There is a close similarity in the red cell changes observed during exposure to 1.5% CO_2 and those found during exposure to 0.7–1.0% CO_2 on patrols. Under both conditions, red cell sodium increased while red cell potassium decreased. Moreover, red cell calcium increased (Messier et al. 1979). The significance of these changes in relation to a possible inhibition of active transport and red cell permeability needs to be clarified.

Gastric acidity

CO_2 has been shown to be a stimulator of gastric acid secretion in man (Tenney and Naitove 1960; Blakemore and Wolfson 1962). Moreover, gastric secretion was found to increase in dogs during chronic hypercapnia (Phil, Pohl, Dickens, and Glotzer 1967).

Findings of an increased gastric acidity observed during prolonged exposure to 0.80%–0.95% CO_2 are in agreement with the reported effects of acute and chronic hypercapnia on gastric acid secretion and should be taken into consideration in evaluating symptoms of pyrosis. The latter show a rather high incidence during patrols, second only to the incidence of complaints about respiratory symptoms (Table 2).

In view of the established increased incidence of peptic ulcer disease in patients with chronic emphysema and CO_2 retention (Latts, Cummins, and Zieve 1956; Ridgen 1961), it is interesting to note that the incidence of the onset of acute peptic ulcer disease occurring during Polaris submarine patrols has been very low (Wilken 1969).

A *summary of changes in respiration*, acid-base balance, electrolytes, and calcium metabolism observed during patrols is presented in Table 11.

The results of physiological studies on patrols demonstrate that there is stress on the respiratory system and gastrointestinal system. Incidence of diseases of the respiratory system and gastrointestinal system rank highest in the list of general medical cases in the medical officers' reports (Wilken 1969). Any association of the targets of physiological stress and incidence of disease with the dominant factor in the submarine atmosphere, CO_2, would be strengthened if a decrease in the CO_2 level produced by improved atmosphere control were reflected in a decreased incidence of disease.

This is indeed the case, and these data are presented in Table 12. The incidence of respiratory disease and gastrointestinal disease in the two periods, 1963–1967 and 1967–1973, decreased by 62% and 50%, respectively, simultaneously with a decrease in the level of CO_2 in the submarine atmosphere. Other atmospheric contaminants such as CO and aerosols also

TABLE 12
MEDICAL CASES RESULTING IN SICK DAYS ON PATROL

	1963–1967				1968–1973					
Number of patrols	360				525					
Man-Patrols (140 men/crew)	50,400				73,500					
Average CO_2 concentration during patrols	——				Approximate Decrease −33%					
	Cases		Sick Days		Cases		Sick Days		Cases	Sick Days
1) Respiratory diseases	121	13.9%	480	13.1%	64	7.9%	214	7.8%	−6%	−5.3%
2) Gastrointestinal diseases	139	16.0%	462	12.6%	91	11.2%	237	8.6%	−4.8%	−4.0%

Data for 1963–1967 from Wilken 1969; 1968–1973 data from Tansey et al. 1979.

decreased markedly over this period. During this 10-year period, the CO_2 concentration in the submarine atmosphere decreased approximately 33% (Tansey et al. 1979).

The validity of the observed relationship between decrease in CO_2 concentrations and decrease in incidence of disease can be questioned on the basis of impressions that different standards of medical reporting were used during the 10-year period. On the other hand, no evidence can be marshalled to prove definitely that the observed relationship did not exist. This relationship, between reduction of pollution and decrease in the incidence of sickness, pertains to a healthy population (age range 20–40).

Fallacy of using standard normal clinical values as a reference in long-term exposure studies

Most standard textbook normal values are given for the purpose of differentiating from clearly defined acute pathological conditions. They are not useful for the comparison of subtle changes induced by chronic exposure to different environmental conditions, such as the submarine atmosphere. Moreover, they do not give ranges with respect to circadian cycles. The cyclic changes in acid-base balance, blood pH, bicarbonate, and P_{CO_2} described in this paper fall within the range of normal clinical values. This shows that significant trends, such as those of acid-base balance indicating certain aspects of chronic CO_2 toxicity, are clearly expressed over time (horizontally) within the (vertical) range of so-called normal clinical values.

Outlook for future studies

Evaluation of the medical officers' patrol reports with regard to the prevalence of symptoms pointed to the respiratory system and gastric intestinal system as target organs. Specific physiological studies demonstrated that these two systems were the targets of stress effects produced by prolonged exposure to 0.7–1% CO_2. These stress effects disappeared during the recovery period after the patrols. Whether or not chronic stress effects accumulate over time will be one of the factors determined in the proposed Longitudinal Health Study of Submariners. This should include, in addition to general screening, function studies that are sufficiently sensitive to detect residuals of chronic stress effects.

It is suggested that a special project be instituted in which the three basic elements in submarine medicine: (1) patrol reports; (2) in-patrol studies and pre- and post-patrol studies; and (3) longitudinal health study results are coordinated and the results of the three areas evaluated within the overall framework of preventive aspects of submarine medicine.

These patrol studies, covering a period of 10 years, could not have been carried out without the dedicated assistance and support provided by the staff of the Physiology Branch to the Medical Officers in planning, training, and outfitting the patrols. The analysis of blood and urine samples and data evaluation were also done by the Staff of the Physiology Branch. The following current and former members of the Physiology Branch contributed greatly to the success of this overall program: Charles Carey, James Dougherty, Jr., Arthur A. Messier, Michael Jacey, Elly Heyder, and Carolyn Morgan.

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Schaefer, K. E. 1979. Stress physiologique et hypercapnie chez l'équipage de sous-marins. Undersea Biomed. Res. Sub. Suppl.: S15–S47.—Nous résumons les résultats d'études sur la physiologie des effets hypercapniques observés pendant 13 voyages en sous-marins du type "Polaris". Les concentrations moyennes de CO_2 se situaient entre 0,7 et 1%. CO_2 est l'unique contaminant atmosphérique à bord du sous-marin qui puisse avoir une influence directe sur la respiration dans les

concentrations observées. Nous avons comparé les effets physiologiques produits pendant 42 journées d'exposition à CO_2 (1,5%) au laboratoire à ceux observés pendant les voyages de 50–60 jours. Les effets sur la respiration se ressemblent, comme aussi les effets sur les électrolytes sanguins. La ventilation minute a augmenté de 40–63% à cause de l'augmentation du volume tidale. L'espace mort respiratoire est augmenté de 60%, la capacité vitale légèrement diminuée. Des altérations cycliques de l'équilibre acido-basique ont été observées aussi. Le pH et le taux de bicarbonate sanguin sont diminués pendant les premiers 17 jours d'exposition, sont augmentés pendant les 20 jours suivants, et puis sont diminués de nouveau après 40 jours d'exposition. Ces cycles ne se laissent point expliquer par les connaissances actuelles sur la régulation rénale de l'acidose à CO_2, et ne sont pas observés pendant les expositions expérimentales à 1,5% CO_2. Ces altérations de l'équilibre acido-basique sont peut-être provoquées par des cycles osseux de captation et de libération de CO_2. Les durées des cycles osseux de CO_2 coincident avec celles de l'équilibre acido-basique. La corrélation avec les cycles du métabolisme du calcium est étroite. Des altérations semblables (augmentation du sodium, diminution du potassium) des électrolytes érythrocytaires ont été observées au laboratoire comme chez les sous-mariniers. Le calcium érythrocytaire se trouve aussi augmenté da chez les deux groupes. La signification de ces altérations électrolytiques n'est pas encore bien compris. Une augmentation de l'acidité gastrique s'observe aussi chez les sous-mariniers. Toutes les alterations observées pendant les voyages sont revenues aux valeurs normales pendant les périodes de repos.

respiration
équilibre acido-basique
réponse au CO_2
électrolytes sanguins

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Calcium phosphorus metabolism in man during acclimatization to carbon dioxide

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SCHAEFER, K. E., G. NICHOLS, JR., AND C. R. CAREY. *Calcium phosphorus metabolism in man during acclimatization to carbon dioxide.* J. Appl. Physiol. 18(6): 1079–1084. 1963.—The calcium phosphorus metabolism was studied in 20 subjects who were exposed for 42 days to 1.5% CO_2. Plasma calcium mirrored the changes of the pH, showing a decrease during the first 23 days of exposure, a return to initial levels during the latter part of exposure, a marked rise above control values during the 8–9 day recovery period following exposure, and a return to normal values after 4 weeks of recovery. Changes in plasma calcium were found to correspond to changes in pulmonary CO_2 excretion indicating a significant role of bone CO_2 stores in acclimatization and deacclimatization of carbon dioxide. Plasma inorganic phosphorus was elevated throughout the exposure period and recovery period. At the end of the exposure period to CO_2 red cell calcium had increased and red cell phosphorus had decreased. After 9 days, as well as after 4 weeks, of recovery on air the calcium content of the red cells continued to increase and the inorganic phosphorus values remained lowered.

chronic respiratory acidosis chronic hypercapnia

SINCE CHANGES IN CALCIUM and phosphate metabolism have been observed in association with chronic metabolic acidosis, it seemed desirable to include studies of the balance and metabolism of these two ions as part of the over-all study of the effects on man of prolonged exposure to low concentrations of carbon dioxide in the inspired air. Interest in these two ions was further stimulated by the observation of plaques of hypercalcification in the fingernails of submarine crew members who had been subjected to increased CO_2 concentrations in the atmosphere because of long submerged cruises during World War II (5).

Therefore, in addition to the observations of other physiological variables reported in the communications of these studies, measurements of the urinary excretion and whole blood and plasma concentrations of Ca and P were made at various intervals in the 20 subjects who were exposed to 1.5% CO_2 in the atmosphere for 42 days. The data obtained and their relation to changes reported elsewhere form the subject of this communication.

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METHODS

Blood. The experimental design has been described elsewhere by Schaefer et al. (9). In ten subjects arterial blood samples were drawn anaerobically during periods prior to exposure to CO_2, between the 35th and 41st day of exposure to 1.5% CO_2, after 8 to 9 days of recovery on air, and 1 month or more postexposure. Venous blood samples were collected at more frequent intervals on all 20 subjects. Blood pH was measured with a Beckman model pH meter and corrected for temperature (8) and for glycolysis (9)

Blood CO_2 and O_2 contents were determined with the Van Slyke apparatus. Inorganic phosphorus in blood, plasma, and serum was measured by the method of Fiske and Subbarow as modified by Roe and Whitmore (7). Calcium in blood, serum, and urine was determined according to the method of Clark and Collip (1), a modification of the procedure of Kramer and Tisdall. Serum protein was measured using the method of Wolfson et al. (12).

Blood and plasma water was determined by the weight change of 0.3-ml samples after drying for 24 hr at 105 C.

RESULTS

Calcium and inorganic phosphorus in arterial and venous blood. Concentrations in whole arterial blood and plasma of calcium and inorganic phosphorus are presented in Table 1, together with calculated values for the red cells.

Whole blood calcium tended to increase during exposure to CO_2 and rose significantly during both recovery periods. In contrast, whole blood phosphorus decreased during both exposure and recovery. The

TABLE 1. *Effect of prolonged exposure to 1.5% CO_2 on red cells and plasma calcium and phosphorus (arterial blood)*

		Measured Values							Calculated Values		
		Whole blood				Plasma			Red cells		
		H_2O, g/liter blood	mmoles/liter blood		Hematocrit	H_2O, g/liter plasma	mmoles/liter plasma		H_2O, g/liter red cells	mmoles/liter red cells	
			Ca	P			Ca	P		Ca	PO_4
Control period on air	Mean	828	1.22	1.37	45.4	925	2.46	1.22	710	.14	1.65
	SD	8	.10	.21	2.3	3	.19	.25	11	.06	.63
	N	10	10	8	10	10	10	10	10	4	7
35–41 Days on 1.5% CO_2	Mean	818	1.48	1.15	44.0	926	2.55	1.25	682	.36	1.06
	SD	7	.36	.36	2.3	4	.11	.20	15	.11	.76
	N	10	10	6	10	10	10	7	10	4	6
8–9 Days recovery on air	Mean	822	1.62*	1.06†	43.9	922	2.75†	1.15	693	.63*	.98*
	SD	7	.32	.10	2.7	6	.18	.11	23	.40	.17
	N	9	10	10	9	9	10	9	9	5	9
4 Weeks recovery on air	Mean	823	1.95†	1.16*	43.5	924	2.51	1.27	692	1.16†	1.0*
	SD	12	.16	.10	2.3	5	.18	.11	24	.45	.3
	N	10	9	10	10	10	10	10	10	9	10

* Differences from controls statistically significant at the 5% level. † Differences from controls statistically significant at the 1% level and better.

reduction of inorganic phosphorus was statistically significant in two recovery periods.

Plasma, calcium, and phosphorus changed little with the exception of the 8- to 9-day recovery period during which plasma calcium rose significantly. The calculated data on red cell calcium and red cell phosphorus indicate changes which correspond with those of the measured whole blood values—an increase in red cell calcium and decrease in red cell phosphorus. As has been noted, the red cells lost water during exposure to CO_2 and even after 4 weeks of recovery on air the water content remained below normal. Plasma water, however, apparently did not change.

Since the arterial plasma calcium and phosphorus values were determined only once during the 42 days of exposure to CO_2, the time course of these changes in arterial blood could not be obtained from these data. However, venous blood samples were collected at regular intervals throughout the experiment and the calcium and phosphorus concentrations observed in the venous plasma have been plotted together with pH in Fig. 1.

The pH was decreased during the first 23 days of exposure and then returned to initial levels, thus indicating two distinct phases during the CO_2 exposure; namely, a phase of uncompensated followed by a phase of compensated respiratory acidosis. (This conclusion is further supported by the pattern of urinary pH (Fig. 2) and bicarbonate excretion reported elsewhere.) It can be seen that the inorganic phosphorus concentration increased during the CO_2 exposure, reaching the highest values during the first 13 days of exposure when a very mild uncompensated acidosis was present. The values then returned to the normal range as the compensated phase of acidosis developed.

Plasma calcium concentration followed pH, being lower during the first 23 days of exposure and returning to control values during the second phase of compensated respiratory acidosis. The highest plasma calcium concentrations were reached in *subjects 1–10* in the first days of recovery on air at a time when the pH rose and the CO_2 excretion reached the first peak. On the 8th and 9th day of recovery on air a second even higher peak of CO_2 excretion was observed. Unfortunately, at this time plasma calcium data were obtained only from *subjects 11–20*. However, these showed an extraordinary increase in plasma calcium. These data are plotted together with the results of other samples obtained from this group of subjects at infrequent intervals in Fig. 1. Since the values of both groups are in good agreement it seems justified to conclude that *subjects 1–10* probably had a similar increase in plasma calcium at the 8th day of recovery. It is noteworthy that pH also fell at this time.

The arterial whole blood and plasma calcium samples of *group 1–10* were obtained during several days of the recovery period. They were significantly elevated but somewhat lower than the venous plasma values of *group 11–20* obtained on the 8th day of recovery when the second peak in CO_2 elimination through the lungs occurred (9).

A statistical evaluation of data obtained from venous plasma is given in Table 2; pH, HCO_3 content, and plasma water values are included for comparison. The pH is significantly decreased (.06 pH units) during the first 23 days of exposure and returned to initial levels during the second "compensated" phase. Bicarbonate

content is elevated throughout the exposure period as well as during the 9-day recovery period on air following exposure. The fall in plasma calcium during the first phase was statistically significant, as was the increase in plasma calcium noted during the 9-day recovery period on air. The inorganic phosphorus values rise during the CO$_2$ exposure to CO$_2$ and remain elevated during the whole recovery period of 4 weeks. Plasma water values did not change throughout the experiment. Calcium phosphate products were slightly increased during exposure to 1.5% CO$_2$ and during the recovery periods (Table 3).

Urinary excretion of calcium and inorganic phosphorus. Average values of urine volume, pH, inorganic phosphorus, and calcium excretion obtained from 20 subjects are shown in Fig. 2. The urine volume was lower throughout the experiment than during the control period. The two phases of uncompensated and compensated respiratory acidosis are reflected in the changes of the urinary pH. Excretion of inorganic phosphorus increased markedly during the 1st and 2nd day of exposure to 1.5% CO$_2$, after which it decreased, reaching the lowest point at the beginning of the compensatory phase of respiratory acidosis after 25 days. On the 8th day of recovery on air a sudden fall of the otherwise rather stable level of inorganic phosphorus excretion was noted with subsequent return to normal.

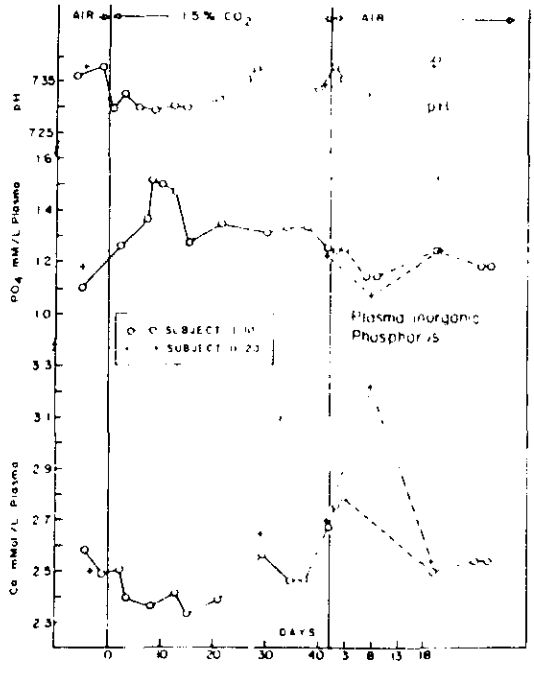

FIG. 1. Effect of exposure of *subjects 1 to 10* and *subjects 11 to 20* to 1.5% CO$_2$ for 42 days on venous plasma pH, inorganic phosphorus, and calcium.

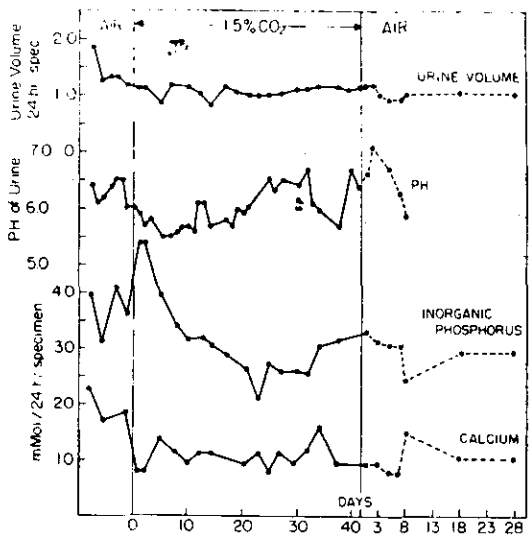

FIG. 2. Effect of exposure of *subjects 1 to 10* to 1.5% CO$_2$ for 42 days on urine volume, pH, and urinary excretion of inorganic phosphorus and calcium.

Urinary calcium decreased sharply during the first 2 days of CO$_2$ exposure and remained lower than control values throughout the exposure period. On the 8th day of recovery on air a significant rise in urinary calcium occurred which corresponds with the increased plasma calcium concentration at this time.

A statistical evaluation of the data is given in Table 4 based on values of the same ten subjects from whom the blood data of Tables 1 and 2 were obtained.

The urinary phosphorus excretion decreased significantly during the second phase of CO$_2$ exposure and remained at this lower level through the recovery period. Urinary calcium excretion fell significantly during the first days of CO$_2$ exposure and continued to be significantly smaller during the rest of the experiment.

DISCUSSION

Exposure to 1.5% CO$_2$ produced a slow rise in red cell calcium content which became significant during the 9-day recovery period and was still present after a 4-week recovery period. Red cell inorganic phosphorus content changed in exactly the opposite way. If these changes were indicative purely of a movement of calcium into and phosphorus out of the cells, an increase in plasma phosphorus and a decrease in plasma calcium should have occurred. The few measurements of inorganic phosphorus in arterial plasma showed a tendency towards an increase in concentration at the end of the exposure period and again at the end of the recovery period; however, the arterial plasma calcium concentration did not decrease throughout the experimental period.

In the more numerous samples of venous plasma an

increase of inorganic phosphorus was clearly shown both during exposure to CO_2 and during recovery. Thus an outward movement of inorganic phosphorus from cells into plasma can be considered to have occurred.

Plasma calcium decreased significantly only during the first 23 days of exposure during which no arterial samples were collected and no data on cell calcium are available. During the second phase of the exposure period as well as during the recovery period, during which the red cell calcium was found to be increased, the plasma calcium was either normal or elevated. Thus the mechanisms involved in changes in red cell calcium content would appear to differ from those controlling phosphate content and to be more complex than a simple shift of this ion between cell and plasma.

Associated with the increase in calcium and decrease in phosphorus a slight dehydration of the red cells occurred, which was still present after 4 weeks.

Changes in the rate of urinary calcium excretion cannot be considered responsible for changes in plasma calcium level since the former is reduced during the exposure to CO_2 as well as during the recovery period. This reduction in calcium excretion probably represents an adjustment to the reduced food intake present during the exposure and recovery period. It therefore might be more reasonable to consider the data obtained after 3 weeks recovery as control values. If this is done, calcium excretion remained practically constant throughout the CO_2 exposure and recovery periods with the exception of two peaks. The peak on the 8th day of recovery coincided with the marked rise in plasma calcium, and another increase in calcium excretion corresponded to the secondary fall in urinary pH after 34 days of exposure to 1.5% CO_2. However, on the latter occasion the plasma calcium was low.

TABLE 2. *Effect of prolonged exposure to 1.5% CO_2 on venous plasma, pH, bicarbonate, water, calcium, and phosphorus*

		pH	HCO_3, mmoles/liter	H_2O, g/liter	Calcium mmoles/liter	Phosphorus, mmoles/liter	Ca × P, mg/100 ml
9 Day control period on air	Mean	7.37	26.9	921	2.52	1.10	34.4
	SD	.06	1.7	8	.24	.16	
	N	10	9	10	10	10	
1–23 Days on 1.5% CO_2	Mean	7.31*	28.7*	921	2.39*	1.40	41.6
	SD	.01	1.8	7	.09	.11	
	N	10	10	10	10	10	
24–42 Days on 1.5% CO_2	Mean	7.36	29.1*	924	2.53	1.29	40.6
	SD	.04	1.2	4	.11	.16	
	N	10	10	10	10	10	
9 Day recovery period on air	Mean	7.37	29.1*	923	2.75*	1.23	42.0
	SD	.01	.6	9	.16	.11	
	N	10	10	10	10	10	
4 Week recovery period on air	Mean	7.41*	27.0	924	2.53	1.26	39.7
	SD	.03	1.0	5	.13	.11	
	N	9	9	10	10	10	

* Differences from controls statistically significant at the 5% level.

TABLE 3. *Effect of prolonged exposure to 1.5% CO_2 on venous plasma calcium and phosphorus of a second group of subjects (11–20)*

		Calcium	Phosphorus	Ca × P, mg/100 ml
9 Day control period on air	Mean	2.49	1.18	36.4
	SD	.06	.17	
	N	9	10	
28 Days exposure to 1.5% CO_2	Mean	2.66		
	SD	.21		
	N	10		
41 Days exposure to 1.5% CO_2	Mean	2.69	1.21	40.4
	SD	.21	.11	
	N	9	6	
8 Days recovery on air	Mean	3.32*	1.09	44.6
	SD	.24	.17	
	N	9	10	
4 Weeks recovery on air	Mean	2.59	1.25	40.2
	SD	.15	.10	
	N	10	10	

* Differences from controls statistically significant at the 5% level.

The significant increase in urinary phosphorus excretion during the first 2 days of CO_2 exposure indicated an immediate change in phosphorus metabolism in a direction which would tend to help compensate for the rather slight acidosis. This was in contrast to the lack of response in chloride excretion under the same conditions. If the data obtained after 3 weeks of recovery are used as controls, phosphorus excretion appeared to be increased during most of the period of uncompensated respiratory acidosis (1–23 days) and decreased during the compensated phase of respiratory acidosis (24–42 days). The difference between these two periods is statistically significant.

The biphasic pattern displayed by the phosphorus excretion during exposure to CO_2 is in keeping with the well-known role of phosphorus in the acidification of urine. However, in the recovery period on air this relationship no longer appeared to hold. Thus, on the 8th day of recovery there was a sharp fall in P excretion at a time when urinary pH also decreased. At this time, phosphate excretion seemed, rather, to reflect the decrease in plasma phosphate concentration.

The plasma calcium changes mirrored the alterations of pH which were associated with the CO_2 exchange during the uncompensated and compensated phase of CO_2 exposure and during the recovery period. The astonishingly long period of CO_2 retention (23 days), which was required before CO_2 stores reached equilibrium and normal CO_2 excretion began, was probably related to a slow increase in bone CO_2, since Freeman

TABLE 4. *Effect of prolonged exposure to 1.5% CO_2 on urinary pH and urinary excretion of calcium and inorganic phosphorus (subjects 1–10)*

		Urinary Vol. 24 hr Specimens	Urine pH	Urine Calcium, mmoles/ 24 hr Specimens	Urine Inorganic Phosphorus, mmoles/ 24 hr Specimens	Ratio, Calcium/ Phosphate
9 Day control period on air	Mean	1.43	6.31	19.4	35.3	.55
	SD	.27	.27	5.6	4.9	
	N	10	10	10	10	
1–23 Days exposure to 1.5% CO_2	Mean	1.08*	5.87*	11.0*	33.0	.33
	SD	.12	.18	1.8	6.4	
	N	10	10	10	10	
24–42 Days exposure to 1.5% CO_2	Mean	1.09*	6.16	10.9*	27.7*	.39
	SD	.16	.14	2.6	4.0	
	N	10	10	10	10	
9 Day recovery on air	Mean	.95*	6.45	10.0*	30.0†	.30
	SD	.17	.15	2.6	4.0	
	N	10	10	10	10	
4 Weeks recovery on air	Mean	1.17*		10.8*	29.1	.37
	SD	.05		2.5	12.2	
	N	10		10	10	

* Differences from controls statistically significant at the 1% level and better. † Differences from controls statistically significant at the 5% level.

and Fenn (2) have shown that it takes 6–28 days to increase the bone CO_2 in rats exposed to 10% CO_2. The significant decrease in plasma calcium during this period of CO_2 retention suggests that calcium was deposited in the skeleton together with CO_2. During the compensated phase a new equilibrium was seemingly established between blood and bone calcium, since the former returned to control values for this period. The rise in plasma calcium on the 8th day of recovery on air, which occurred at the same time as the second peak in CO_2 excretion, suggests a simultaneous release of calcium and CO_2 from bone. It is noteworthy that this large quantity of CO_2 was completely eliminated via the lungs (the urine carbon dioxide excretion decreased during this period (Fig. 2)), while the total of 6.63 mmoles of calcium, which was added to the extracellular compartment was quantitatively eliminated in the urine (Fig. 2).

It would appear that this transfer of calcium into the blood, together with the transient drop in pH, provided appropriate conditions for an increased calcium uptake by the red cells—a process not reversed after 3–4 weeks of recovery on air. The causes of these shifts in Ca distribution cannot be ascertained from these data. Although evidence of increased parathyroid gland activity has been found in guinea pigs during chronic exposure to 15% CO_2 (9), no such evidence was apparent in the men reported here. Indeed the plasma Ca concentration was low or normal and the phosphorus high during the period of CO_2 exposure. The only time that possible evidence of parathyroid stimulation could be found was in the first few days of recovery on air when plasma Ca increased and P declined. However, the decrease in renal phosphate excretion and increase in calcium excretion which occurred simultaneously do not fit with such an hypothesis (6).

The question might be raised whether seasonal fluctuations of calcium and phosphorus levels in the blood had an influence on the results of these experiments. The study was carried out during the months January to March. At this season a slight decrease of the plasma phosphorus values would be expected (3). However, the opposite was found, suggesting that seasonal changes did not affect the alterations produced by exposure to CO_2.

Data on caloric intake and nitrogen balance obtained in this experiment have been reported elsewhere. Food intake decreased 24% during the first 3 weeks of CO_2 exposure and continued to fall very slightly thereafter. The small changes observed in nitrogen excretion corresponded to the changes in calculated protein intake. The subjects maintained their body weight in spite of the reduction in food intake, which has been explained with a CO_2-induced water retention.

The subjects carried out their routine chores such as cleaning detail and watch standing, simulating operational conditions during their confinement aboard a submarine and went, once or twice a week, through a short strenuous exercise (Harvard step-up tests). A marked reduction in physical activity was thereby prevented. It is unlikely that the various phases noted in calcium and phosphorus metabolism were influenced by the change in dietary intake since the latter occurred, to a significant degree, only during the first 3 weeks of exposure.

Finally, the mechanisms involved in the increase in red cell calcium and decrease in inorganic phosphorus, together with a dehydration, need clarification which cannot be supplied from available information. It is interesting, as Netter (4) has pointed out on the basis of Seelich's experiments (11), that the surface tension of biological membranes has an inverse relationship to hydration—the higher the water content, the smaller the surface tension. He further emphasizes that calcium ions increase the surface tension due to their dehydration effects. Thus the effects of calcium ions on the biological membranes appear to be similar to the effect of a narcosis; namely, a hardening of the surface due to dehydration and increase of surface tension (4). How these phenomena are related to the changes induced by chronic exposure to low concentrations of CO_2 in the inspired air remains an unanswered question.

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Acid-base balance and blood and urine electrolytes of man during acclimatization to CO_2

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Acid-base balance and blood and urine electrolytes of man during acclimatization to CO_2

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SCHAEFER, K. E., G. NICHOLS, JR., AND C. R. CAREY. *Acid-base balance and blood and urine electrolytes of man during acclimatization to CO_2.* J. Appl. Physiol. 19(1): 48–58. 1964.—Acid-base balance regulation and changes in electrolyte metabolism have been studied in 20 subjects exposed to 1.5% CO_2 over a period of 42 days with control periods preceding and subsequent to exposure. During exposure to CO_2 a slight uncompensated respiratory acidosis was present during the first 23 days followed by a compensated respiratory acidosis. Deacclimatization was incomplete, even after 4 weeks of recovery on air. Arterial CO_2 tension increased 5 mm Hg during exposure and remained at this elevated level during the first 9 days of recovery on air. In chronic respiratory acidosis the concentration of chloride in the red cells and in plasma remains practically normal, indicating that the chloride shift does not operate. Cation exchange was observed under these conditions. Sodium increased while potassium showed an approximately equivalent decrease. Sodium and potassium balance studies indicated that only sodium exhibits a pattern paralleling the two phases of acid-base balance regulation, retention being followed by increased excretion. Body weight was maintained throughout the experiment in spite of a 24–30% reduction in food intake.

mild respiratory acidosis and compensation 1.5% CO_2 exposure and recovery arterial pCO_2, chloride shift, and cation exchange sodium and potassium excretion sodium potassium and nitrogen balance acid-base regulation in chronic hypercapnia time course in acid-base regulations during chronic exposure to low concentration of CO_2 acclimatization and deacclimatization to low concentration of CO_2

CHANGES IN ACID-BASE and electrolyte balance under conditions of respiratory acidosis have been extensively studied. The over-all pattern of response to this condition has been well defined by Peters and Van Slyke (16), Henderson (11), and Pitts (17).

As part of a general study concerning the acclimatization of man to low concentrations of CO_2 in the inspired air, it was of great interest to determine whether these regulatory mechanisms are called into play during prolonged exposure to atmospheres containing as little as 1.5% CO_2. If such were the case, a study of the time required for the development of these homeostatic responses would be important.

The data reported here indicate that respiratory acidosis (although of a very mild degree) develops soon after the beginning of exposure to 1.5% CO_2. This suffices to set into motion many of the compensatory mechanisms which have been described. Of particular interest is the long time interval required for the development of sufficiently large shifts in electrolyte balance to result in compensation of the acidosis under these conditions.

METHODS

The experimental design has been described in detail in the first paper of this series (28). A schematic representation showing the time and number of samples taken during the five experimental periods is given in Table 1.

Blood. In ten subjects arterial blood samples were drawn anaerobically during *periods A, C, D,* and *E.* Venous blood samples were collected about twice weekly on all 20 subjects.

The pH determinations were made at room temperature with a Beckman model G pH meter using an anaerobic sample chamber model no. 40313, and corrected to body temperature according to Rosenthal (20). The blood samples were collected in heparinized syringes and immediately stored in ice water. No chemical was added to prevent glycolysis because of a number of other biochemical determinations to be carried out on the same blood specimens.

Collection and transfer of the blood samples from the submarine to the laboratory and subsequent measurements required 1½ hr. Although blood samples were stored in ice water, additional correction factors for glycolysis had to be determined in a series of studies simulating these experimental conditions. Blood samples

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were drawn from ten subjects and one portion of the blood was immediately centrifuged at 37 C. pH was measured at 37 C on whole blood and plasma with an Epsco blood analyzer using a Sanz electrode and a Beckman model G pH meter. The latter instrument had been employed in the original experiment. The second portion of the blood was stored in ice water for 60 min. After this period whole blood was rewarmed for 20 min to 37 or 27 C and another portion was centrifuged at 37 and 27 C. pH measurements were then repeated on whole blood and plasma. Body temperature of the subjects was measured at the time the blood samples were taken and the obtained pH values on whole blood and plasma were corrected for temperature according to Rosenthal (20) using 0.0147 units per degree change in temperature. Results are listed in Table 2.

Findings obtained at 37 C in the absence of temperature effects on pH measurements gave supporting evidence for the glycolysis effect (−.04 pH) and glass-electrode effect of red cells (−.01 pH) measured at room temperature, simulating the original experimental conditions. Determinations made with the more accurate Epsco blood analyzer were in accord with those of the older Beckman instrument. Consequently, .043 and .01 = .053 pH units (Epsco) were added to the measured pH values of whole blood corrected to body temperature, 2.09 vol % to the measured CO_2 content and .54 vol % to the measured O_2 content. The pH values are in good agreement with data obtained by Severinghaus on glycolysis effects in whole blood stored for 1 hr and plasma-whole blood pH differences due to effects of red cells on glass electrodes (33).

Plasma pH of venous blood was only corrected to body temperature, which had been determined shortly before the collecting of samples. No correction of the measured plasma CO_2 content was necessary (Table 2).

Blood CO_2 and O_2 content were determined manometrically by the methods of Van Slyke et al. (39). Sodium and potassium in blood, plasma, urine, and feces were determined according to Chaney (5) using the Beckman flame photometer. Plasma, blood, and urine chloride were estimated by the method of Schales and Schales (30). Blood and plasma water content were determined by drying 0.5-ml samples for 24 hr at 105 C until the weight was constant. The hematocrit was determined by centrifuging the blood at 3,000 rev/min for 25 min and corrected for "trapped" plasma according to the method of Chaplin and Mollison (6). Electrolyte concentrations in red cells were calculated from the values found in blood and plasma using the corrected

TABLE 1. *Data on acid-base balance and electrolyte exchange during prolonged exposure to 1.5% CO_2 in submarine*

EXPERIMENTAL PERIODS		AIR	1.5% CO_2 IN 21% O_2		AIR	AIR
		A	B	C	D	E
Physiological Variables	Number of Sample Collections	9 Days Control on Air	1–23 Days Uncompensated Respiratory Acidosis	24–42 Days Compensated Phase of Respiratory Acidosis	1–9 Days Recovery on Air	4 Weeks Recovery on Air
ARTERIAL WHOLE BLOOD	4					
pH						
pCO_2						
RED CELL						
HCO_3						
Na						
K						
Cl						
H_2O						
VENOUS PLASMA	19					
pH						
HCO_3						
Na						
K						
Cl						
H_2O						
URINE VOLUME	60 Collections on 10 Subjects Each on Separate Days					
pH						
HCO_3						
Na						
K						
Cl						
PO_4						
NITROGEN						
FAECES	Pooled 4 (2–3 Days)					
NITROGEN						
Na						
K						
WEIGHT	Daily 60 Measurements	NO CHANGE				

● = Samples; — = control levels; ↓ ↑ = changes from control symbols.

TABLE 2. *Changes in pH, CO_2 content, and O_2 content produced in whole blood and plasma after 1 hr storage in ice water and 20 min rewarming to 37 and 27 C*

	N	Whole Blood	Plasma	Diff. in pH of Plasma and Whole Blood	
				After collection of blood	After 60 min storage + 20 min rewarming
		I. At 37 C			
ΔpH Epsco	10	−.044 ± .013	+.013 ± .012	.010 ± .009	.054 ± .010
pH meter, Beckman model G	10	−.04 ± .01	*	*	.05 ± .02
		II. At 27 C†			
ΔpH Epsco	10	−.043 ± .009	+.008 ± .008	.010 ± .007	.053 ± .009
pH meter, Beckman model G	10	−.04 ± .01	*	*	.05 ± .02
ΔCO_2 vol. %	6	−2.09 ± .47	−.20 ± .09		
ΔO_2 vol. %	6	−.54 ± .05			

* Differences in plasma pH within limits of analytical error of the Beckman instrument (model G). † After correction of values to body temperature using .0147 pH units per degree temperature difference for whole blood and true plasma.

hematocrit. Arterial CO_2 tension was computed from the pH values and CO_2 content measured in whole blood at room temperature using the appropriate serum pK′ values for carbonic acid and solubility coefficients for CO_2 in plasma and corrected to body temperature as outlined in more detail elsewhere (28). Carbon dioxide tension of the plasma was calculated by substituting measured values of CO_2 content and pH in the Henderson-Hasselbalch equation. Dissolved carbon dioxide in red cells was calculated from the CO_2 tension and solubility coefficient of carbon dioxide in red cells (38), assuming that pCO_2 in red cells and plasma is the same. Bicarbonate concentrations in plasma and red cells were estimated as the difference between total CO_2 content and dissolved CO_2. The daily food intake was approximated from detailed questionnaires filled out daily throughout the experiment by the subjects.[2] Standard-size portions were served and typical servings were analyzed in the laboratory. The daily intakes of calories: carbohydrate, fat, and protein, as well as Na and K, were calculated for each subject from standard tables of food composition. In the four phases of the experimental program feces were collected for two to three consecutive days from each subject as follows: *a*) during the control period, *b*) near the end of CO_2 exposure, *c*) during a recovery period of 8–9 days on air following CO_2 exposure, and *d*) after approximately 4 weeks of recovery. The samples were pooled for each individual and analyzed for Na, K, and N content. Thus, the external balance of sodium, potassium, and nitrogen could be estimated for the important periods of the experiment.

RESULTS

For an easier evaluation of the voluminous material, a summary chart (Table 1) has been prepared which shows the changes of the various parameters investigated during the five different experimental periods.

Blood electrolytes. Data on the distribution of carbon dioxide in plasma and red cells (Table 3) show that, during the period of 8–9 days recovery on air (*period D*) following exposure to 1.5% CO_2, arterial pCO_2 and plasma and red cell bicarbonate remained approximately at the elevated level attained during CO_2 exposure due to release of previously accumulated CO_2 from CO_2 stores with different time constants (28). Changes in blood, plasma, and red cell electrolytes (Table 4) follow a similar pattern. In whole blood and red cells an increase in sodium and commensurate decrease in potassium was observed during *periods C* and *D*. Plasma potassium content was found decreased in the four experimental periods, following the control period. Plasma water, sodium, and chloride did not change significantly throughout the experiment. The slight reduction in hematocrit measured during exposure to 1.5% CO_2 (*C*) and the following recovery periods (*D*, *E*) corresponded to slight decreases in red blood count and hemoglobin content of the same subjects (Table 5).

In Fig. 1 the bicarbonate content of arterial and venous plasma is plotted against the pH showing the acid-base pattern during and after prolonged exposure to 1.5% CO_2. Figure 2 and Table 6 exhibit venous plasma electrolyte values for the same ten subjects from whom the data on arterial red cell and plasma composition were obtained. Venous pH values, measured at more frequent intervals than those of arterial blood, show during exposure to 1.5% CO_2 *1*) a period of lowered pH lasting from 1–23 days followed by *2*) a period in which the pH returned approximately to initial levels. The changes in venous pH did correspond with similar changes found in urinary and pulmonary CO_2 excretion (28). Thus, two phases of an uncompensated (*period B*) and a compensated respiratory acidosis (*period C*) were differentiated. Venous plasma sodium, potassium, chloride, and water did not show any consistent and significant changes except a transitory increase in plasma sodium during *period B* and a marked rise in plasma water during the 1st day of recovery on air.

Table 7 presents data on chloride distribution in blood,

[2] The procedure of obtaining diet records, as well as a sample questionnaire, have been deposited as Document number 7730 with the ADI Auxiliary Publications Project, Photoduplication Service, Library of Congress, Washington 25, D.C. A copy may be secured by citing the Document number and by remitting $1.25 for photoprints, or $1.25 for 35-mm microfilm. Advance payment is required. Make checks or money order payable to: Chief, Photoduplication Service, Library of Congress.

TABLE 3. *Effect of exposure to 1.5% CO_2 over a period of 42 days on distribution of CO_2 in blood and plasma*

Plasma				Red Cell	
HCO_3, mmoles/liter	H_2CO_3, mmoles/liter	pH	pCO_2, mm Hg	HCO_3, mmoles/liter	H_2CO_3, mmoles/liter
Control period on air, 10 subjects					
24.1 ± 2.3	1.21 ± 0.06	7.38 ± 0.03	39.4 ± 1.7	13.8 ± 1.9	0.99 ± 0.05
35–41 Days on 1.5% CO_2, 10 subjects					
26.1* ± 2.0	1.38* ± 0.13	7.35* ± 0.03	44.9* ± 4.1	15.4* ± 1.18	1.12* ± 0.11
8–9 Days recovery on air, 9 subjects					
25.1 ± 2.2	1.30* ± 0.11	7.37 ± 0.04	43.9* ± 3.9	15.3 ± 1.14	1.10* ± 0.10
4 Weeks recovery on air, 8 subjects					
23.6 ± 1.4	1.17 ± 0.03	7.41* ± 0.02	38.3 ± 0.9	14.0 ± 0.97	0.96 ± 0.02

Values are means ± SD. * Statistically significant difference from control value at the 5% level and better.

TABLE 4. *Effect of prolonged exposure to 1.5% CO_2 on red cells and plasma electrolytes (arterial blood)*

Measured Values									Calculated Values			
Whole blood					Plasma				Red cells			
H_2O, g/l. blood	Na, mEq/l. blood	K, mEq/l. blood	Cl, mEq/l. blood	Hct	H_2O, g/l. plasma	Na, mEq/l. plasma	K, mEq/l. plasma	Cl, mEq/l. plasma	H_2O, g/l. red cells	Na, mEq/l. red cells	K, mEq/l. red cells	Cl, mEq/l. red cells
Control period on air												
828	84.0	41.6	80.9	45.4	925	141.4	4.77	102.5	710	13.5	86.0	55.8
±8	±1.8	±2.2	±2.7	±2.3	±3	±2.9	±.15	±4.6	±11	±4.5	±4.5	±8.6
(10)	(10)	(10)	(7)	(10)	(10)	(9)	(10)	(9)	(10)	(10)	(10)	(7)
35–41 Days on 1.5% CO_2												
818	88.4*	37.0*	80.6	44.0	926	141.2	4.41†	98.6	682	21.6*	78.9*	58.3
±7	±1.0	±2.6	±1.0	±2.3	±4	±0.6	±0.37	±1.6	±15	±4.8	±4.4	±1.8
(10)	(9)	(9)	(4)	(10)	(10)	(10)	(10)	(4)	(10)	(9)	(9)	(4)
8–9 Days recovery on air												
822	89.2*	35.6*	80.2	43.9	922	140.0	4.08*	98.6	693	24.4*	76.2*	56.9
±7	±0.91	±1.2	±4.4	±2.7	±6	±1.4	±.24	±5.3	±23	±7.9	±4.7	±14.3
(9)	(9)	(9)	(8)	(9)	(9)	(8)	(9)	(8)	(9)	(8)	(9)	(8)
4 Weeks recovery on air												
823	84.6	37.26	81.4	43.5	923	142.0	4.32*	99.4	692	12.8	79.9†	58.8
±12	±1.9	±2.1	±4.46	±2.3	±5	±4.1	±0.37	±6.06	±24	±6.9	±4.2	±1.61
(10)	(10)	(10)	(5)	(10)	(10)	(10)	(10)	(5)	(10)	(8)	(10)	(5)

Values are means ± SD. Numbers in parentheses represent number of subjects. * Differences from controls statistically significant at the 1% level and better. † Differences from controls statistically significant at the 5% level.

plasma, and red cells of venous blood obtained from a second group of ten subjects from whom no arterial blood data were collected. Again no significant changes in chloride content of red cells and plasma were noted during exposure to CO_2.

Electrolyte changes in urine. Mean values for urine pH, total CO_2, and bicarbonate obtained from 20 subjects at frequent intervals during the experiment are plotted in Fig. 3. Total CO_2 and bicarbonate changes correspond very closely. During the first 20 days of CO_2 exposure the pH fell below the initial levels and bicarbonate excretion was very low. From the 20th day on, an increase in pH was noted which was paralleled by a marked rise in bicarbonate excretion. During the last 10 days of CO_2 exposure pH and bicarbonate fell again but reached a high level once more during the last 2 days of exposure. This unexpected change apparently was not the result of analytical error. After 2 days' recovery on air, pH and bicarbonate reached their highest values, returning to normal after 7 days of recovery.

Urine volume and sodium, potassium, and chloride excretion in the urine of the same subjects are displayed in Fig. 4. The two phases during CO_2 exposure, which were marked in the bicarbonate excretion of the urine, are also reflected in sodium excretion which was significantly lower during *period B* of the CO_2 exposure than during the control period. During *period C*, the sodium content of the urine rose again without reaching its initial level. Compared with the control values, urine volume decreased during the experimental periods, sug-

TABLE 5. *Effect of prolonged exposure to 1.5% CO_2 on red cell count and hemoglobin*

	RBC	Hb
Control on air	4.91±0.47	13.80±0.63
28 Days on 1.5% CO_2	4.70±0.47	12.90*±0.8
35–41 Days on 1.5% CO_2	4.75±0.36	13.7±0.98
8–9 Days recovery on air	4.80±0.17	13.27±0.58
4 Weeks recovery on air	4.40*±0.25	12.7†±0.46

Values are means ± SD for ten subjects. * Differences statistically significant at the 1% level and better. † Differences statistically significant at the 5% level.

gesting a water retention. Both potassium and chloride excretion were reduced throughout exposure to CO_2 and had not returned to normal after 4 weeks on air. A statistical evaluation of urine volume and pH and urinary excretion of inorganic phosphorus, sodium, potassium, and chloride is given in Table 8. In order to allow a comparison of the urine data with the blood data of Tables 3, 4, and 6, the material of Table 8 was compiled from the same ten subjects.

Caloric intake and sodium potassium and nitrogen balance. The caloric as well as the sodium and potassium intake was significantly higher during the control period than during the experimental periods (Table 9). The main reduction occurred during the first 8 days of exposure to CO_2. From there on the caloric consumption continued to fall slightly but steadily. In spite of a decreased food intake, the body weight of the subjects remained constant, presumably because of water retention.

The reduced sodium and potassium intake associated with the decreased food intake must be taken into account in an evaluation of changes in Na and K excretion. Sodium potassium and nitrogen balances are shown in Fig. 5. Intakes are plotted downward from the zero lines; urinary output (diagonally lined) and feces output (black) are superimposed on intake. During the control period both Na and K balances were slightly negative. During the period of uncompensated respiratory acidosis (*B*), there was sodium retention (positive balance), while the potassium balance remained slightly negative.[3] During the compensated phase of respiratory acidosis (*C*) and during the first 8–9 days of recovery, the sodium excretion was again higher than the intake while the potassium balance remained unchanged.

The nitrogen balance is shown in Fig. 5. Urinary and fecal excretion and the calculated protein breakdown (Table 10) decreased during *periods B, C,* and *D*. These reductions are in keeping with the changes in calculated protein intake and seem to support the validity of food intake calculation based on daily questionnaires.

[3] During the first 23 days of exposure to CO_2 no feces determination of Na, K, and N were made. Since the changes during the whole experiment were, however, so small that they could not affect the balance, the Na, K, and N values of the exposure period from the 23rd to 42nd day have been assumed not to differ markedly from the first 23 days of exposure and were used for calculation of the balance during this period.

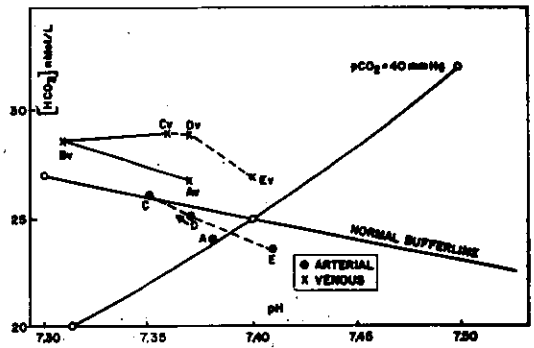

FIG. 1. Acid-base path during prolonged exposure to 1.5% CO_2.

DISCUSSION

Exposure to 1.5% CO_2 for 42 days produces a slight, but significant, uncompensated respiratory acidosis which lasts for the first 23 days—as indicated in a fall of extracellular pH (0.06 pH units), a decrease in urine pH and bicarbonate excretion, and a parallel reduction in pulmonary CO_2 excretion (28). From the 24th to the 42nd day of CO_2 exposure the respiratory acidosis is compensated. Blood pH returns to approximately control levels, urinary pH rises, and bicarbonate excretion in the urine is markedly increased. Pulmonary CO_2 excretion has also returned to normal levels (28). This pattern of response agrees well with results of chronic CO_2 exposure in animals (22). It is important to note that it takes 23 days to reach this compensation, which under 3% CO_2 is usually reached after 3 to 5 days (21). This delayed response in the acclimatization to 1.5% CO_2 has its counterpart in a delayed deacclimatization after transition to air. During a recovery period of 9 days on air the elevated blood CO_2 content and tension remained virtually unchanged in spite of increased CO_2 excretion in the urine and expired air. These unexpected findings raise the question whether the mechanisms involved in acclimatization to low concentrations of carbon dioxide are different from those known to play a role during acute hypercapnia.

Extrarenal effects of chronic respiratory acidosis. The chloride shift between plasma and red cells which occurs when blood is exposed to higher CO_2 tensions does not appear to operate under conditions of chronic respiratory acidosis. This confirms the usual findings in emphysematous subjects (18). The plasma chloride content did not decrease nor did the calculated red cell chloride increase significantly throughout the exposure to CO_2 (Table 4). These data obtained on arterial blood correspond with those of venous blood from a second group of subjects (Table 7). Indeed, venous plasma chloride was slightly elevated during CO_2 exposure (Table 6).

It should be noted that the blood and plasma values reported here are in good agreement with data reported by Singer (35), although the calculated red cell data are somewhat higher due to differences in hematocrit.

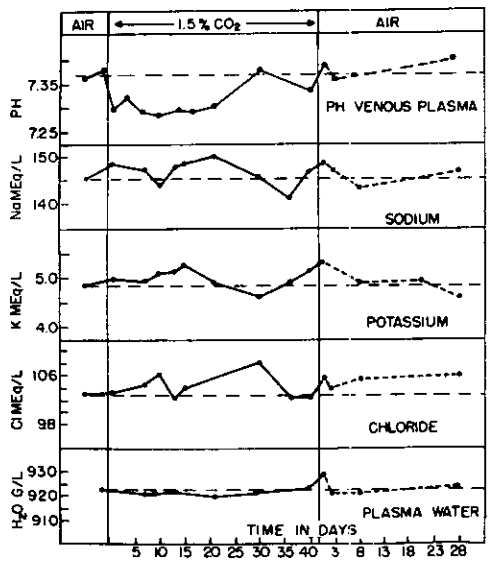

FIG. 2. Effect of prolonged exposure to 1.5% CO_2 on plasma electrolytes (venous blood).

Control values of blood sodium and potassium measured in our subjects also corresponded to the lower ranges reported by Sunderman and Boerner (36). Plasma sodium and potassium appear to be within the ranges of average to maximum, and by comparison red cell sodium and potassium are slightly lower than the minimum values given by these workers.

During CO_2 exposure, as well as during 8–9 days recovery on air after CO_2, an increase of sodium in the red cells and a concurrent reduction in cell potassium was observed which, during the 8–9 days period on air, amounted to 10.9 mEq/liter and 9.5 mEq/liter, respectively. This seems to suggest a nearly equivalent exchange of sodium and potassium in the red cells with sodium entering and potassium leaving the cells during the recovery period on air following CO_2 exposure. If this is so, one might expect that the plasma sodium and potassium values would reflect this exchange. However, arterial plasma sodium does not change and arterial plasma potassium decreased rather than increased. Thus, the plasma electrolytes are influenced by processes other than red cell plasma exchange such as reduced intake and changes in distribution between extracellular fluids and other tissues (14, 32). In addition, the increased alkali reabsorption of the renal tubuli known to occur in respiratory acidosis should lead to increases in body content of sodium and potassium which, in the case of this experiment, might compensate for a decreased potassium and sodium intake. Increases in red cell sodium commensurate with a transient decrease in red cell potassium, after 24 hr of exposure, were also found in skin divers with CO_2 retention (25) and in patients with respiratory acidosis combined with decompensation and congestive heart failure (4). Moreover, guinea pigs exposed to 15% CO_2 for prolonged periods also exhibited this red cell cation shift (15), which appears to be a regular mechanism under conditions of chronic respiratory acidosis. The significance of this mechanism is not clear and needs further investigation.

The acid-base path during prolonged exposure to 1.5% CO_2 was plotted in the pH-bicarbonate diagram for arterial and venous blood since arterial blood samples were not collected during *period B*. Data obtained from the more frequent venous samples show the typical picture of a compensated respiratory acidosis. Renal compensation produced a metabolic alkalosis as indicated in the 2.0 mmoles/liter of extra fixed base (graphically estimated) in the venous blood at point Cv. This condition is maintained during the subsequent 9-day recovery period on air (Dv). A slight respiratory alkalosis is present after 4 weeks' recovery (E, Ev).

Relative anion deficit in the plasma has been reported during acute exposures to high concentrations of CO_2 (1, 3). It was therefore of interest to calculate the sum of anion and cation equivalents for the various periods of these experiments in which the CO_2 level in the in-

TABLE 6. *Effect of prolonged exposure to 1.5% CO_2 on venous plasma electrolytes in ten subjects*

pH	HCO_3, mmoles/l.	Na, mEq/l.	K, mEq/l.	Cl, mEq/l.	H_2O, g/l.
9-Day control period on air					
7.37 ± .06	26.9 ± 1.4	145.2 ± 2.3	4.9 ± 0.4	103.1 ± 3.4	921 ± 8
1–23 Days on 1.5% CO_2					
7.31† ± .01	28.7† ± 0.5	147.9* ± 0.7	5.1 ± 0.7	105.6 ± 0.6	921 ± 7
24–42 Days on 1.5% CO_2					
7.36 ± .04	29.1† ± 0.6	145.2 ± 1.8	4.9 ± 0.2	104.5 ± 2.7	924 ± 4
9-Day recovery period on air					
7.37 ± .01	29.1† ± 0.8	145.7 ± 2.0	5.1 ± 0.3	105.1 ± 1.8	924 ± 9
4-Week recovery period on air					
7.40 ± .03	27.0 ± 1.0	144.4 ± 1.3	4.8 ± 0.1	106.2 ± 6.6	924 ± 5

Values are means ± SD. * Differences from controls statistically significant at the 1% level and better. † Differences from controls statistically significant at the 5% level.

TABLE 7. *Effect of prolonged exposure to 1.5% CO_2 on chloride distribution in red cells and plasma of venous blood**

	Whole Blood		Plasma	Red Cells
	Cl, mEq/l. blood	Hct	Cl, mEq/l. plasma	Cl, mEq/l. red cells
Control period on air	80.3 ±2.7 (9)	46.0 ±2.0 (10)	97.7 ±2.6 (10)	59.4 ±5.4 (9)
35–42 Days on 1.5% CO_2	81.6 ±1.5 (10)	47.6 ±1.5 (10)	102.8 ±1.5 (10)	58.5 ±3.3 (10)
8–9 Days recovery on air	79.2 3.5 (9)	47.3 1.4 (9)	103.0 2.2 (9)	54.2 6.9 (9)

Values are means ± SD. Numbers in parentheses represent number of subjects. * Subjects 11–20.

spired air was low, but the period of exposure was very long. The data, expressed as milliequivalents per liter of plasma water, for venous plasma are shown in Table 11 for each period. Values for Na, K, Cl, HCO'_3^-, Ca, and P represent means of many measurements. The Ca and P values have been taken from another communication in this series (29) while Mg values were taken from the literature (9). Equivalence for inorganic P was calculated from the titration curve of phosphoric acid at the pH of the plasma for each period. The remaining negative charges needed to produce electroneutrality before exposure to CO_2 have been arbitrarily assigned to "protein and others." Thus, the difference between the sum of the positive and negative charges during the control period is zero (last column, Table 11). As can be seen from this table, if the assumption is made that the anionic equivalence (negative charge) of the proteins and others does not change with exposure to CO_2, a relative excess of anions develops which persists even after 4 weeks recovery on air.

Arrhenius' dissociation theory demands that electroneutrality exist at all times in dilute solutions of electrolytes such as plasma and, therefore, some explanation of this phenomenon must be sought. The possibility exists that plasma Mg concentration (not measured) decreased or some unmeasured anion (organic or inorganic) increased. However, a far simpler (and probably correct) explanation would be that the total anionic equivalence assigned to proteins was not fixed but decreased with prolonged exposure to CO_2. Two pieces of evidence favor this view. First, a small but persistent decrease in red blood count and hemoglobin was noted in these subjects during and after exposure to CO_2. This decrease was greatest after 4 weeks on air following CO_2 exposure—corresponding to the period of greatest "anion excess," calculated as shown. Second, the anionic equivalence of the protein present might have been expected to be lower during these periods while exposed to CO_2 when the pCO_2 of the blood was slightly elevated because of small shifts in pH (intra- and extracellularly) toward the acid side. (It should be noted that in these

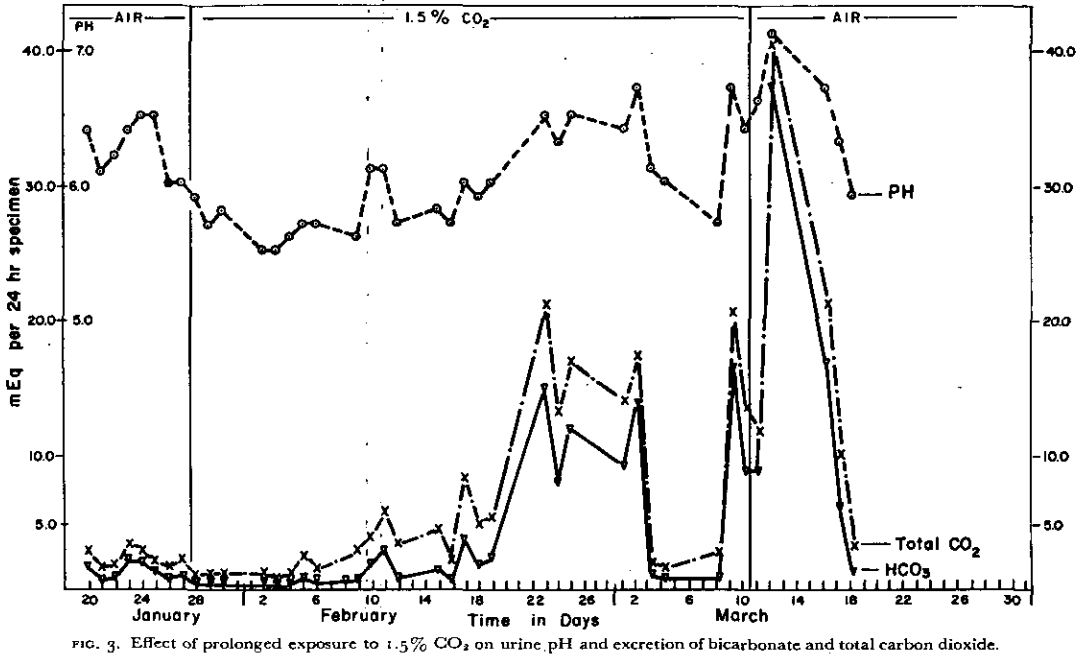

FIG. 3. Effect of prolonged exposure to 1.5% CO_2 on urine pH and excretion of bicarbonate and total carbon dioxide.

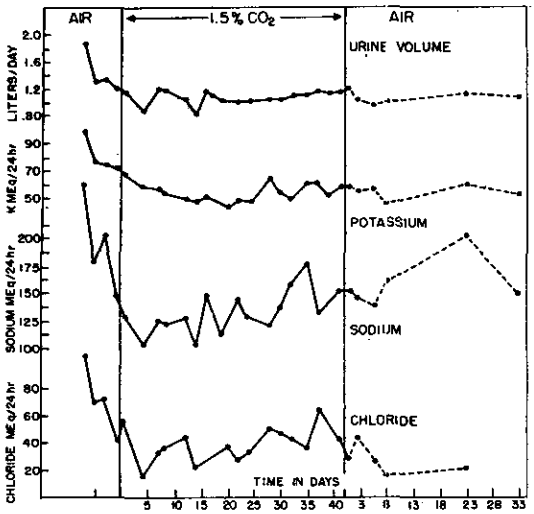

FIG. 4. Effect of prolonged exposure to 1.5% CO_2 on urine volume and excretion of Na, K, and Cl.

experiments plasma electrolyte composition and pH are influenced by red cell protein-buffer effects since the plasma was in equilibrium with the red cells in vivo before the withdrawal and separation of the blood.)

Renal effects of chronic respiratory acidosis. The values for daily urinary excretion of sodium potassium and phosphorus are in the ranges of normal values listed by Shohl (34). However, the urinary chloride values are somewhat lower than those reported as normal for adult persons in the literature (36). Since it is well known that excretion of chloride in the urine varies greatly with diet, intake of sodium chloride, and body activity, the lower urine chloride values reported here may be related to reduced food intake and reduced body activity associated with the confinement of 60 days.

The pH and CO_2 contents of the urine reflect, like a mirror, changes in blood pH in the phases of uncompensated and compensated respiratory acidosis. Even the unexplained drops in pH and urinary CO_2 excretion during the second phase of respiratory acidosis, which may represent a cyclic response, are reflected in the blood pH values (Fig. 2).

The increased elimination of carbon dioxide, during the first 9 days of recovery on air, must have been a manifestation of delivery of CO_2 from the various stores in the body equilibrated with the higher CO_2 tension during exposure. If this hypothesis is accepted then the increased blood CO_2 tension, as well as alveolar CO_2 tension, which remained throughout the recovery period of 9 days at the level attained during exposure, can be considered to reflect the CO_2 tension with which body stores were in equilibrium at the end of the exposure period. These observations on CO_2 tension in blood and alveoli and CO_2 elimination from the body support the concept of multiple CO_2 stores in the body with slow and fast equilibrium times suggested by Vance and Fowler (37) and Farhi and Rahn (8). However, evidence from this experiment indicates that there are three CO_2 stores with different time constants. After transition to air, following 42 days of exposure to 1.5% CO_2, pulmonary CO_2 excretion shows a peak on the 1st day and urinary CO_2 excretion on the 2nd day. On the 8th and 9th day another peak in pulmonary CO_2 is noted which is associated with a blood calcium tide (29), suggesting that this slowest CO_2 store is located in the bones. Furthermore, recent experiments carried out with guinea pigs exposed to 15% CO_2 for periods up to 7 days showed that various tissues have different CO_2 dissociation curves (27) and different electrolyte exchange under CO_2 exposure (15, 26). Similar data were obtained in rats exposed to 25% CO_2 for several days (13)—observations consistent with the thesis proposed. Respiratory adaptation (28) probably contributes to the maintenance of elevated blood and alveolar CO_2 tensions after transition to air in spite of increased CO_2 elimination. During exposure to CO_2 a respiratory pattern develops consisting of an increased tidal volume and reduced respiratory rate which continues after transition

TABLE 8. *Effect of exposure to 1.5% CO_2 over a period of 42 days on urinary excretion of electrolytes in ten subjects*

Urinary Vol., liters/24 hr	pH	CO_2, mEq/24-hr Specimens	Urine Cl., mEq/24-hr Specimens	Urine Na, mEq/24-hr Specimens	Urine K, mEq/24-hr Specimens	Inorganic P, mEq/24-hr Specimens
9-Day control period on air						
1.43 ± .27	6.31 ± .27	1.98 ± .93	72.0 ± 16.4	195.1 ± 28.6	78.15 ± 6.8	60.8 ± 8.5
1–23 Days on 1.5% CO_2,						
1.08* ± .12	5.87* ± .18	3.28 ± 1.64	34.1* ± 8.1	125.5* ± 15.6	52.4* ± 2.9	59.7 ± 12.3
24–42 Days on 1.5% CO_2,						
1.09* ± .16	6.16 ± .14	7.96† ± 7.0	45.2* ± 11.7	145.3* ± 19.1	56.7* ± 3.5	48.8* ± 6.8
9-Day recovery on air						
.950* ± .17	6.45 ± .15	21.0† ± 22.0	29.2* ± 6.2	151.9* ± 26.2	54.3* ± 6.6	51.6† ± 7.0
4-Week recovery period on air						
1.17† ± .05			23.9* ± 6.3‡	176.5 ± 44.0	57.5* ± 12.0	50.1 ± 21.0

Values are means ± SD. * Statistically significant difference from control value at the 1% level and better. † Statistically significant difference from control value at the 5% level. ‡ Exception: 4 subjects.

TABLE 9. *Effect of prolonged exposure to 1.5% CO_2 on body weight, daily caloric consumption, and Na, K, and protein intake*

Control Period on Air	Exposure to 1.5% CO_2 for: 1–23 Days	24–42 Days	9 Days Recovery on Air
Body wt., lb			
162±19.4	162±24.2	162.2±21.7	162.0±20.8
Cal/day			
2,772±322	2,103*±330	1,977*±174	1,918*±204
Na intake/day, g			
4.24±1.55	3.27*±.64	2.94*±1.41	2.76*±1.19
K intake/day, g			
3.39±.97	2.58*±.90	2.35*±.83	2.55*±.94
Protein intake/day, g			
101±9.4	70*±8	65*±8	62*±10

Values are means ± SD for 23 subjects. * Differences from controls statistically significant at the 1% level.

back to air. This respiratory pattern alone is able to produce higher alveolar and blood CO_2 tensions (23). Moreover, the demonstration of a marked arterial alveolar P_{CO_2} difference (28) during the compensatory phase of exposure to 1.5% CO_2 and at the end of the 9-day recovery period attests to the presence of an alveolar dead space with its effect of raising arterial P_{CO_2}.

Although urinary chloride excretion is known to increase in acute respiratory acidosis no increase in chloride excretion during the period of uncompensated respiratory acidosis was found. On the contrary, the chloride excretion was reduced and remained low throughout the experiment. This suggests that changes in chloride metabolism do not participate in the renal compensation of chronic respiratory acidosis induced by 1.5% CO_2.

Balance studies. The average caloric intake of 2,772 cal, estimated on the basis of questionnaires, lies between a value of 2,400 cal/man day reported by Behnke (2) for submarine personnel in the temperate zone and 3,800 cal/man day found by Schulte (31) on a submarine patrol in the Arctic. Our data appear therefore to be in the expected range.

According to sodium and potassium balance studies only sodium participated in the acid-base balance regulation during this prolonged exposure to 1.5% CO_2. This was indicated by the sodium retention during the uncompensated phase of respiratory acidosis and a negative balance of this ion during the phases of compensated respiratory acidosis and the first 9 days of recovery on air. The balance studies also reveal that the reduced chloride excretion throughout the experimental period was probably an adjustment to the reduced food intake.

Similarly, a reduced inorganic phosphorus excretion would also be expected. However, during the period of respiratory acidosis (1–23 days) the excretion of phosphorus was about the same as during the control period. Thus phosphorus balance during this period can be assumed to have been negative. The significant reduction in phosphorus excretion during the period of compensatory respiratory acidosis (24–42 days) and the biphasic pattern displayed by the phosphorus excretion (the

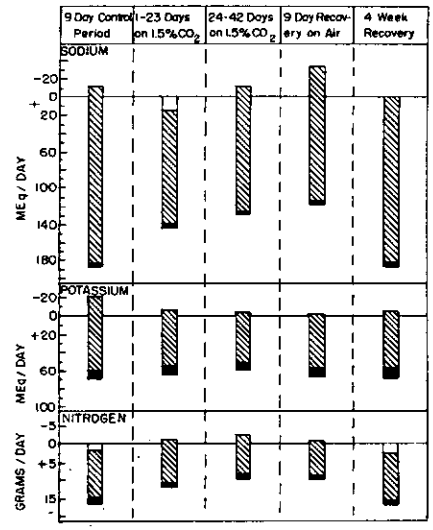

FIG. 5. Effect of prolonged exposure to 1.5% CO_2 on Na, K, and N balance.

TABLE 10. *Nitrogen excretion in urine and feces during exposure to 1.5% CO_2 over a period of 42 days*

	Control	27–31 Days on 1.5% CO_2	Recovery on Air 6–10 Days	Recovery on Air 4 Weeks
Urine nitrogen excretion, g/day	13.98±2.5 (23)	10.64*±2.2 (23)	9.86*±2.2 (23)	12.86±6.6 (16)
	Control	27–29 Days on 1.5% CO_2	Recovery on Air 6–8 Days	Recovery on Air 22–24 Days
Feces nitrogen excretion, g/day	1.09±0.48 (17)	0.91±0.43 (19)	0.68†±0.29 (12)	0.68±0.28 (8)
Protein breakdown, g/day	94.2	72.2	65.8	84.6

Values are means ± SD. * Differences from controls statistically significant at the 1% level. † Differences from controls statistically significant at the 5% level.

mirror image of sodium excretion) during the exposure to CO_2 is in line with the well-known role of phosphorus in the acidification of the urine.

Food intake decreased 24% during the first 3 weeks of CO_2 exposure (uncompensated respiratory acidosis) and continued to fall slightly, 4.8% during the subsequent 3 weeks of compensatory respiratory acidosis and 2% during the 9-day recovery period on air. Since the main reduction of food intake occurred during the 1st week of CO_2 exposure it appears most reasonable to attribute this more acute change to a CO_2 effect. The subsequent continuous slight decline of food intake may

TABLE 11. *Effect of prolonged exposure to 1.5% CO_2 on cations and anions in venous plasma*

Cations					Anions					Diff., Anions-Cations
Na	K	Ca	Mg	Total	HCO_3	Cl	Protein & others	PO_4	Total	
9-Day control period on air										
157.7	5.28	2.73	1.5	167.2	29.1	111.9	24.1	2.12	167.2	
1–23 Days on 1.5% CO_2										
160.6	5.51	2.59	1.5	170.2	31.2	114.6	24.1	2.58	172.5	2.3
24–42 Days on 1.5% CO_2										
157.2	5.30	2.73	1.5	166.7	31.5	113.1	24.1	2.48	171.2	4.5
9-Day recovery period on air										
157.7	5.53	2.98	1.5	167.7	31.5	113.8	24.1	2.39	171.8	4.1
4-Week recovery period on air										
156.3	5.17	2.73	1.5	165.7	29.2	115.0	24.1	2.56	170.9	5.2

Values are expressed in mEq/liter H_2O. Calculations of mEq/liter inorganic phosphorus are based on the method of Levinskas cited by W. F. Neuman and M. W. Neuman in *The Chemical Dynamics of Bone Mineral*. Chicago: Univ. of Chicago Press, 1958, p. 22.

be considered as an adjustment to a reduced activity imposed by the long confinement, although the subjects went through a short strenuous exercise once or twice a week. If one would assume that the decrease in food intake is only related to the confinement, it would represent a condition of semistarvation similar to those extensively studied by Keys and co-workers (12). However, a comparison of our data with the results obtained in the semistarvation experiments involving a 55% reduction in food intake shows some significant differences. The urinary excretion increases significantly under conditions of semistarvation while the opposite was found under CO_2 exposure. Furthermore, a decrease in serum bicarbonate was reported in most cases of semistarvation and fasting (cited in ref. 12) in contrast to the elevation of serum bicarbonate found in our experiment. The most important difference is the maintenance of body weight during prolonged exposure to CO_2 in spite of a 24–30% reduction in food intake which seems most reasonable to have been due to water retention.

During chronic exposure to 3% CO_2 for 4–5 days Pointner (19) noticed water retention in dogs, and Schaefer in man (21). Furthermore, guinea pigs exposed to 15% CO_2 for 7 days also showed significant water retention (in preparation).

The slight decrease in hematocrit found during exposure to 1.5% CO_2 and during the recovery period was also observed in separate determinations of red cell blood counts and hemoglobin. This is in line with previous findings of hemoglobin reduction in chronic respiratory acidosis (10, 18).

The data of this study show clearly the differences which exist between pH and pCO_2 homeostasis. After the pH has returned to normal, pCO_2 was still elevated 5 mm Hg. The significance of these findings in relation to amine buffer therapy of chronic respiratory acidosis have been discussed elsewhere (24).

We express our appreciation to Dr. A. Baird Hastings for critically reading the manuscript and making important suggestions. The assistance of Miss C. M. Oliver of Harvard University in making the calculations of daily food intake composition is gratefully acknowledged. We are indebted to Andrea Thelin and Michael J. Jacey for statistical analysis of data.

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CO_2-induced kidney calcification

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Schaefer, K. E., S. M. Pasquale, A. A. Messier, and H. Niemoeller. 1979. CO_2-induced kidney calcification. Undersea Biomed. Res. Sub. Suppl.: S143–S153.—Light microscopic examination of kidney tissue of guinea pigs exposed to 1.5% CO_2, 21% O_2, and balance N_2 for periods as long as 42 days and of rats exposed to the same CO_2 concentrations for up to 91 days showed that the incidence of focal kidney calcification increased with length of exposure. Calcification occurred primarily in the tubules of the renal cortex. Another group of guinea pigs were exposed to 1% CO_2, 21% O_2, and the balance N_2 for periods up to six weeks and were later killed at regular intervals, together with control animals of the same litter. In the exposed animals, arterial P_{CO_2} was elevated by 3–4 mmHg and hydrogen ions by about 4 nmol/liter. The standard bicarbonate level was lowered by 1–1.5 mmol, indicating a lack of renal reabsorption of bicarbonate (HCO_3), which in turn placed greater stress on the bone buffer system and apparently caused bone calcium and phosphorus mobilization. Bone calcium and phosphorus levels exhibited a cyclic decrease, which resulted in cyclic hypercalcemia and hyperphosphatemia, after one week and six weeks of exposure to 1% CO_2. Kidney calcium content increased significantly after two weeks of exposure (27%) and remained at this elevated level during subsequent exposures between the third and sixth weeks. These findings indicate that once the kidney calcification process has started, kidney mineralization is independent of fluctuations in the blood calcium level. A rise in plasma phosphate level that occurred after one day of exposure could have been a precipitating factor in the calcification process. The small but consistent increases in ionized calcium during a 4-week exposure to 1% CO_2 may have stimulated the parathyroid, causing an increased blood calcium level that was independent of the two calcium tides in the blood associated with marked bone calcium loss.

chronic CO_2 toxicity
calcium and phosphorus metabolism
metabolic acidosis
kidney calcification

Chronic CO_2 studies in men exposed to 1.5% CO_2 for prolonged periods demonstrated changes in calcium and phosphorus metabolism that appeared to be associated with storage and release of CO_2 from the bones (Schaefer, Nichols, and Carey 1963). One of the main findings of histopathological investigations of animals exposed to 3% and higher CO_2 concentrations was kidney calcification (Meesen 1948; Zinck 1949). In subsequent combined physiological and histopathological studies of guinea pigs exposed to 15% CO_2 for prolonged periods,

significant renal calcification was observed, consisting of interstitial calcium deposits in the renal medulla, and calcium deposits in the tubules and in the basement membranes of the renal cortex (Schaefer, Hasson, and Niemoeller 1961). Significant changes in calcium metabolism observed in American and British submarine patrol studies (Gray, Morris, and Brooks 1973; Messier, Heyder, Braithwaite, McCluggage, Peck, and Schaefer 1979) focused attention on the need for further exploration of the relationship between CO_2-induced changes in calcium metabolism and kidney calcification during prolonged exposure to low levels of CO_2 (in the range between 1% and 1.5%). Results of such studies are presented in this report.

MATERIALS AND METHODS

Experiments were carried out with mature male guinea pigs of the Hartley strain, weighing between 400 and 600 grams (g), and mature male rats, between 75 and 120 days of age, from the Harvard Biological Laboratory and from the Charles River Laboratory. In the first series of experiments carried out in 1961, guinea pigs and rats were exposed to 1.5% CO_2, 21% O_2, and the balance N_2. The gas mixtures were obtained by mixing 100% CO_2, supplied from a bank of cylinders charged to 1800 psi, with air delivered to the gas inlet from high-pressure oxygen cylinders. Animals were killed at different periods of exposure to 1.5% CO_2 and tissues were examined with the light microscope. The exposure chambers used in this series had a water-cooled temperature control system and a closed-circuit air ventilation system that continuously circulated chamber air through silicagel containers. Under these conditions, the temperature in the exposure chambers was kept at 25.6 ± 1.1°C and the humidity between 65 and 75%. Ammonia vapor was absorbed by boric acid spread on the floor of the cages. The carbon dioxide level in the chambers was continuously monitored with a Beckman infrared CO_2 meter, and the oxygen content with a Beckman E 2 Oxygen Analyzer. An automatic gas sampling device switched from one exposure chamber to another every 20 min, and recordings were made of gas concentrations.

In the second series of experiments, guinea pigs were exposed to 1% CO_2, 21% O_2, and the balance N_2 in commercially built environmental control chambers with automatic temperature and humidity controls. The environmental temperature was kept at 25.6 ± 1.1°C, and the humidity between 65 and 75%. The gas mixtures were prepared by mixing proportional amounts of CO_2 to air; oxygen was added from a high-pressure cylinder. The air within the chamber was recirculated 12 times a minute. With this fast and large turnover of chamber air, mixing of CO_2 and air was nearly instantaneous. The carbon dioxide concentration in the chamber was continuously monitored with a Beckman infrared CO_2 analyzer, and the oxygen content was sampled intermittently with a Beckman O_2 analyzer. The CO_2 concentrations were kept at 1% within limits of ± 0.1%, and the oxygen concentrations at 21% ± 0.5%. Ammonia vapor was absorbed by boric acid placed in the chamber. The chamber was opened each morning for a period of 3–5 min to fill the water and food containers and to remove urine and feces.

Litter mates of the animals exposed to CO_2 were kept in a second environmental chamber under identical environmental conditions, except that the ambient air was free of CO_2. From the first to the fourth week of exposure, six animals were killed weekly, together with 3–4 control animals. After six weeks of exposure to 1% CO_2, the same procedure was used. During the period of six weeks, the weight of both control and exposed animals increased in the same fashion (Fig. 2). For blood gas studies, 8 control animals were usually used to obtain enough arterial blood samples in which the oxygen partial pressure was above 50 mmHg, the criterion set in our laboratory for acceptable values.

Prior to blood sampling, the animals received 40 mg pentobarbital/kg body weight (wt) subcutaneously and were returned to the CO_2 exposure chamber. The anesthesia was usually effective after approximately 5 min, at which time the animals were taken out of the exposure chamber and placed immediately under a mask, through which they breathed the same CO_2 gas mixtures to which they had been exposed. Blood samples were drawn from the abdominal aorta. Blood pH and P_{CO_2} were determined with an Instrumentation Laboratory blood gas and pH analyzing system. The femurs of both legs were removed and rapidly cleaned and stripped free of adhering tissues and bone marrow. Compact bone specimens (between 200–300 mg) were kept on ice for determination of total CO_2 content and bone electrolytes. The time between procurement and analysis of the fresh samples did not exceed two hours. Paired specimens were oven-dried to constant weight at 150°C for 18 h before analysis.

Bone and kidney calcium were determined with an atomic absorption spectrometer. For calcium determination both bone and kidney samples were dry-ashed at 650°C for 24 h. Appropriate dilutions with 3 N hydrochloric acid were used for analysis; recovery was assessed by adding known amounts of calcium.

Phosphorus of bone samples was measured on acid digests of bone. Bone samples were dissolved in 6 N hydrochloric acid, and the appropriate dilution was analyzed according to a method modified from that of Fiske and Subbarow (1925).

In a separate preliminary experiment, guinea pigs of the Hartley strain weighing between 400 and 600 grams were exposed to 1% CO_2 for 4 weeks. Acid-base parameters and blood electrolytes were measured, using the methods listed above. However, bone specimens were not analyzed. Ionized calcium was determined using an Orion Model 99-20 sensor calcium flow-through system connected to an Orion Model 801 Digital pH/mV meter for determination of serum ionized calcium. Blood samples for the measurement of ionized calcium were withdrawn by syringe and quickly injected to fill completely a Vacutainer containing no anticoagulant.

Tissue specimens (kidneys) from the first group of experimental animals were fixed in buffered formalin, embedded in paraffin, sectioned and routinely stained with hematoxylin and eosin. In certain cases Masson stain was also used. A card was prepared for each animal on which the results of the histological examination of the various organs were entered. After this, another evaluation was made comparing the findings of individual organs in a whole experimental series. The principal histological changes were graded from 1 to 3 and charted. In the second experimental series, no histopathological investigation of the kidneys was performed. All statistical comparisons of physiological data were done by Student's *t*-test.

RESULTS

Table 1 shows the results of histopathological studies of the kidney carried out in guinea pigs and rats exposed to 1.5% CO_2 for prolonged periods. No significant changes were observed in kidney morphology, except in renal calcification. Incidence of focal and tubular kidney calcifications increased with the duration of exposure in both guinea pigs and rats. During the first two weeks of exposure to 1.5% CO_2, focal kidney calcification was not observed.

Data on blood P_{CO_2}, hydrogen ion concentration, and standard bicarbonate in guinea pigs exposed to 1% CO_2, 21% O_2, and balance N_2 for up to six weeks and those of control animals are shown in Fig. 1. These acid-base parameters did not change in the control animals; however, in the exposed animals Pa_{CO_2} was persistently elevated by 3–4 mmHg and was statistically different from that of controls after 3 and 4 weeks of exposure. Hydrogen ion concentrations of the exposed animals were on the average about 3–4 nmols higher (statisti-

TABLE 1
EFFECT OF PROLONGED EXPOSURE TO 1.5% CO_2 ON KIDNEY MORPHOLOGY OF GUINEA PIGS AND RATS

Conditions	No. of Animals	Focal Calcification, Incidence	Grade
		Guinea Pigs	
Controls	5	0	0
(1.5% CO_2 in 21% O_2)			
1–25 days	6	33%	1
35–42 days	6	66%	1
Recovery on Air			
27 days after			
42 days of exposure	6	66%	1–2
		Rats	
Controls	5	0	0
(1.5% CO_2 in 21% O_2)			
1–15 days	5	0	0
35 days	6	50%	1.0
91 days	5	100%	2.0

cally significant after 1, 2, and 4 weeks). Standard bicarbonate was 1–1.5 mmol lower in exposed animals (statistically significant after 1, 2, and 4 weeks).

Figure 2 shows changes in body weight and in the calcium content of bone, kidney, and plasma in animals exposed for six weeks to 1% CO_2 and in control animals. Body weight increases were virtually the same in control and exposed groups. Bone calcium content in control animals remained at the same level. Animals exposed to 1% CO_2 showed a significant initial fall of bone calcium at the end of one week, followed by a rise to near normal levels after three weeks and a subsequent greater decrease after six weeks of exposure. Blood calcium reflects the changes in bone calcium, rising when bone calcium falls. Blood calcium in control animals tended to be lower than that in exposed animals, and remained at the same level throughout exposure. The kidney calcium content did not change in control animals; however, in the exposed animals it rose slightly after one week and continued to increase after two and three weeks, at which time the kidney calcium content was 27% above control level.

Carbon dioxide-induced alterations in phosphorus metabolism are shown in Fig. 3. Changes in phosphorous levels in bone and blood mirrored those in calcium metabolism. In addition to the phases related to bone phosphorous changes, plasma phosphorus showed a significant increase after the first day of exposure.

Table 2 shows data on ionized calcium measured in a separate experiment in which guinea pigs were exposed to 1% CO_2 for 4 weeks. A slight acidosis occurred, shown by the small increase in H^+ ion concentration. Ionized calcium tended to increase but the changes were not statistically significant.

DISCUSSION

Light microscopic histopathological investigations were carried out in 1961 by Dr. Niemoel-

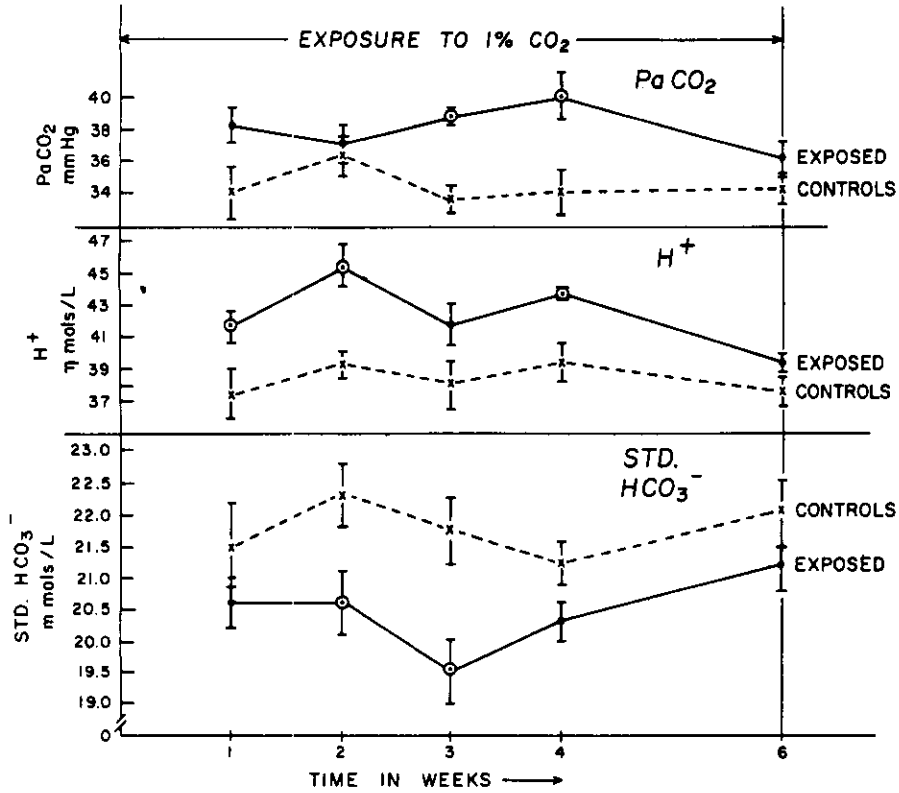

Fig. 1. Effect of prolonged exposure to 1% CO_2 on arterial P_{CO_2} (Pa_{CO_2}), hydrogen ion concentrations (H^+), and standard bicarbonate. Data represent means ± SEM. Significantly different from controls at the 5% level or better. Each exposed group consisted of 6 animals; each control group (litter mates of exposed guinea pigs) consisted of 7–8 animals in blood gas studies.

ler at the Department of Pathology, Yale University, as part of a larger CO_2 project. Guinea pigs and rats exposed for prolonged periods to 1.5% CO_2 showed focal tubular calcification that increased with the length of exposure. The pattern of renal calcification observed during prolonged exposure to 1.5% CO_2 was similar to that seen during exposure to higher CO_2 concentrations (Schaefer et al. 1961). The types of calcification included interstitial deposits, which were generally confined to the medulla, intratubular deposits, and, occasionally, calcification in the tubular basement membranes in the cortex and medulla close to the corticomedullary junction. The pattern of CO_2-induced renal calcification reported here is consistent with that observed under other conditions, e.g., magnesium deficiency, where calcification was reported usually to occur within the lumen of the renal tubules at the junction between the medulla and cortex (Schneeberg and Morrison 1965; Meyer and Forbes 1967; Hamuro, Shino, and Suzuoki 1970).

Prolonged exposure to 1% CO_2 produced a metabolic acidosis, indicated by the increase in H^+ associated with a fall in standard bicarbonate. This indicates that the kidney does not respond to the CO_2-induced acidosis by increasing renal bicarbonate reabsorption, which is the typical response in hypercapnia caused by higher CO_2 concentrations (Schwartz, Brackett, and Cohen 1965). The acidosis produced by prolonged exposure to 1% CO_2 should therefore be considered a predominantly metabolic acidosis. Under these conditions, kidney-calcium

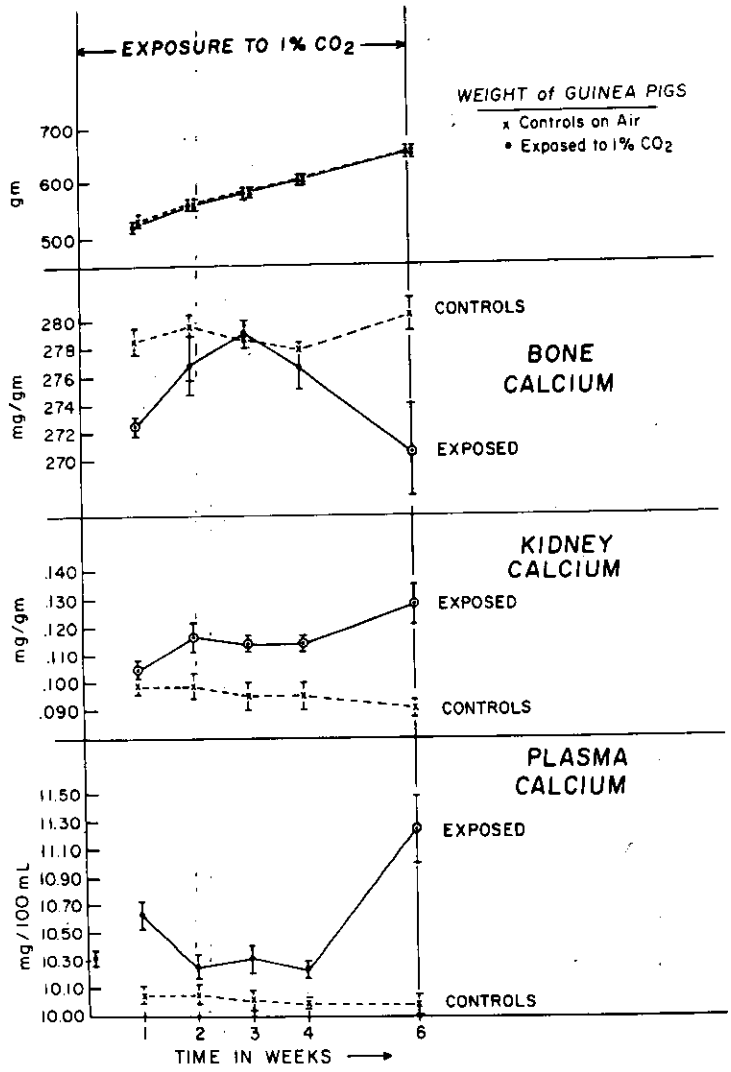

Fig. 2. Effect of prolonged exposure to 1% CO_2 on body weight, bone calcium, kidney calcium, and plasma calcium in guinea pigs. Data represent means ± SEM. ⊙ = significantly different from controls at the 5% level or better. Each experimental group consisted of 6 animals, each control group of 3–4 animals.

content increased significantly after the second week of exposure. Since a 25% rise in kidney calcium content has been accepted as evidence of kidney calcification (Britton and Stokstad 1970), the elevation of kidney calcium found under conditions of 1% CO_2 is evidence of kidney calcification.

Two causes of CO_2-induced kidney calcification have to be considered: (1) hypercalcemia produced by CO_2-induced bone calcium mobilization, with or without involvement of parathyroid hormone stimulation, and (2) hyperphosphatemia. Carbon dioxide uptake in the bones was found to be associated with loss of bone calcium and phosphorus in rats exposed to 8% CO_2 for periods of 2, 4, and 6 weeks (Claudon, Reichart, Bolot, Berstein, and Sabliere 1976). Freeman and Fenn (1953) exposed rats to 10% CO_2 for periods of from 6 to 28 days.

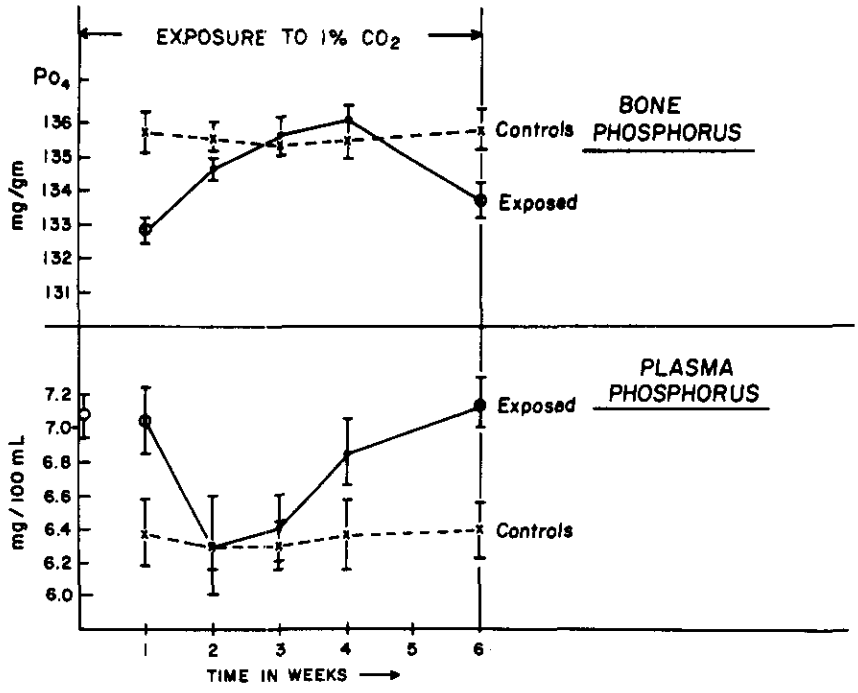

Fig. 3. Effect of prolonged exposure to 1% CO_2 on bone and plasma phosphorus. Data represent means ± SEM. ⊙ = significantly different from controls at the 5% level or better. Experimental groups = 6 animals, control groups, 3–4 animals each.

Their bone calcium data did not show any significant loss of bone calcium. This may have been due to the fact that existing cycles in bone calcium were masked by summarizing all the data during the 4-week period. We have demonstrated the existence of cycles in bone calcium in rats exposed to 15% CO_2 for 7 days (Pasquale and Schaefer 1977). There is sufficient evidence in rats and guinea pigs exposed to different CO_2 concentrations that CO_2 uptake in bone is associated with calcium loss during specific phases of CO_2 binding in the bone.

The time course of CO_2 uptake in bones during exposure to 1% CO_2 has been determined by indirect titrimetry and the results have been reported elsewhere (Schaefer, Pasquale, and Messier 1976). The bicarbonate fraction of bone CO_2 showed two phases of significant increases during the first and sixth week of exposure; these increases coincided with periods of bone calcium and phosphorus loss (Fig. 2). Bone calcium mobilization leads to hypercalcemia (Fig. 2), which could cause kidney calcification just as it does in hypercalcemia produced by administration of parathyroid hormone (Cohn, Bowden, and Eller 1967). These authors demonstrated that the kidney is a target organ for parathyroid hormone action, because calcium accumulation occurred only in the kidneys and not in the liver or heart. Analysis of the calcium content of heart tissues from guinea pigs exposed up to 4 weeks to 1% CO_2 did not show any increase in calcium. These preliminary findings suggest that the kidney calcification seen during exposure to 1% CO_2 may involve the parathyroid hormone. Although ionized calcium showed only small increases that were not statistically significant during 4 weeks of exposure to 1% CO_2 (Table 2), this small rise may have stimulated the parathyroid gland. The fact that plasma calcium remains continuously elevated in animals exposed to 1% CO_2, independent of the two episodes of calcium flux out of the bone that occurred at one and six weeks,

TABLE 2

EFFECT OF EXPOSURE OF GUINEA PIGS FOR 4 WEEKS TO 1% CO_2 ON ACID-BASE PARAMETERS AND IONIZED CALCIUM

	H^+, nmol/liter	Pa_{CO_2}, mmHg	Ionized Calcium, mg %
		Control	
$\overline{X}$	37.1	35.9	5.0
SE	0.9	2.3	0.10
n	10.0	10.0	10.0
		Exposure to 1% CO_2	
1 Day, $\overline{X}$	39.4	37.6	5.1
SE	1.9	2.6	0.11
n	6.0	6.0	6.00
1 Week, $\overline{X}$	40.9*	37.8	5.2
SE	1.3	1.7	0.10
n	8.0	8.0	8.0
2 Weeks, $\overline{X}$	40.7*	37.2	5.0
SE	1.6	2.4	0.09
n	5.0	5.0	5.0
3 Weeks, $\overline{X}$	41.7*	38.9	5.3
SE	1.6	0.11	0.13
n	5.0	5.0	5.0
4 Weeks, $\overline{X}$	40.9*	38.9	5.0
SE	1.8	1.9	0.13
n	6.0	6.0	6.0

* = Significant at 0.05 level.

also seems to support the notion that a stimulation of the parathyroid gland existed throughout the 1% CO_2 exposure. Moreover, PTH may have been the cause of the acidosis observed during prolonged exposure to 1% CO_2. The decreased standard bicarbonate level indicates a failure of the kidney to reabsorb bicarbonate. PTH has been found to decrease bicarbonate reabsorption and to produce a systemic acidosis (Crumb, Martinez-Muldonado, Eknoyan, and Suki 1974). The same authors reported that hypercalcemia causes an increased bicarbonate reabsorption, but this effect can be suppressed by increased levels of PTH. The fact that elevated blood calcium levels found during prolonged exposure to 1% CO_2 failed to produce an increase in bicarbonate reabsorption gives further support to the notion of increased PTH activity under these conditions.

These findings, which suggest that small elevations of P_{CO_2} produced by prolonged exposure to 1% CO_2 may cause sustained increases in PTH activity and lead to a systemic acidosis, may increase our understanding of the mechanisms underlying the development of the systemic acidosis associated with primary and secondary hyperparathyroidism seen in the clinic (Muldowney, Freaney, and McGeeney 1968; Siddiqui and Wilson 1972).

In studies of magnesium deficiency, a sudden increase in plasma phosphate has been named as a factor precipitating kidney calcification (Hamuro et al. 1970). The initial increase in

TABLE 3

EFFECT OF PROLONGED EXPOSURE TO 15% CO_2 IN 21% O_2, BALANCE N_2 ON ACID-BASE PARAMETERS AND KIDNEY CALCIUM CONTENT

	pH	P_{CO_2}, mmHg	Kidney Calcium, mg/g (wet weight)	Blood Calcium, mg/100 ml
			Control	
$\bar{X}$	7.369	37.7	0.115	11.25
SE	0.013	0.9	0.009	0.08
n	8.0	8.0	8.0	8.0
			Exposure to 15% CO_2	
1 Hour, $\bar{X}$	7.078*	106.8*		—
SE	0.022	2.18		
n	6.0	6.0		
6 Hours, $\bar{X}$	7.085*	110.2*	0.124	11.75*
SE	0.025	2.1	0.002	0.08
n	6.0	6.0	6.0	6.0
1 Day, $\bar{X}$	7.088*	104.5*	0.125	11.78*
SE	0.047	5.8	0.008	0.08
n	6.0	6.0	6.0	6.0
3 Days, $\bar{X}$	7.178*	122.0	0.135*	12.44*
SE	0.021	8.9	0.002	0.08
n	6.0	6.0	6.0	6.0
7 Days, $\bar{X}$	7.230*	123.0*	0.169*	13.30*
SE	0.012	9.0	0.010	0.05
n	6.0	6.0	6.0	6.0

pH and P_{CO_2} data were corrected to body temperature; *significantly different from controls at the 5% level or better.

plasma phosphate occurred after the first day of exposure. Bone phosphorus data were not obtained at this point and the basis of the rise in plasma phosphorus on Day 1 of the exposure to 1% CO_2 cannot be explained on the basis of the available data. After one week of exposure to 1% CO_2, plasma phosphate was still elevated, which correlated with bone phosphorus loss. The early rise in plasma phosphorus might have contributed to kidney calcification, and the initial precipitation of calcification might have been sufficient to maintain the process. It has been pointed out that once kidney calcification has been started, mineralization becomes progressive because the solubility product for calcium is always exceeded in the serum (Ryke 1973).

Previous histopathological investigations of the kidney under conditions of chronic hypercapnia were carried out under higher CO_2 concentrations (3% CO_2 and above) without concomitant analysis of kidney calcium content (Meesen 1948; Zinck 1949; Schaefer et al. 1961). Since the most extensive histopathological investigations of kidney calcification were made in guinea pigs during exposure to 15% CO_2 (Schaefer et al. 1961), which served as a reference point, we repeated this experiment and measured kidney calcium content; these data are presented in Table 3. After 3 days of exposure, kidney calcium content was significantly elevated, and it rose by 47% on the 7th day of exposure to 15% CO_2. Blood calcium was

significantly increased throughout the exposure period. These data underline the significance of kidney calcification in chronic hypercapnia caused by different levels of CO_2 concentration.

To put the findings reported here into perspective, it has to be emphasized that exposure of guinea pigs and rats to CO_2 concentrations ranging from 1–20% for periods up to 6 months (1.5% CO_2) and 72 days (15% CO_2) did not produce any severe tissue damage and post-mortem examination of the animals did not show any untoward effects. As a matter of fact, there is a paucity of histopathological effects in chronic CO_2 poisoning, which contrasts favorably with the histopathology observed in other environmental stress conditions, e.g., chronic hypoxia (Schaefer, Niemoeller, Messier, Heyder, and Spencer 1971). The problems encountered in chronic CO_2 poisoning are primarily related to the adaptation of acid-base regulation.

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Schaefer, K. E., S. M. Pasquale, A. A. Messier, and H. Niemoeller. 1979. Calcification rénale provoquée par CO_2. Undersea Biomed. Res. Sub. Suppl.: S143–S153.—Des foyers de calcification rénale sont observés chez des cobayes après 42 jours d'exposition à 1,5% CO_2 (21% O_2, reste N_2), et chez des rats exposés pendant 91 jours. L'incidence des anomalies est en rapport directe avec la durée de l'exposition. La calcification se localise surtout au niveau des tubules du cortex rénal. Les cobayes sont exposés pendant des périodes jusqu'à 6 semaines et sont ensuite sacrifiés avec des témoins de la même portée. Chez les animaux exposés, P_{CO_2} artériel est augmenté de 3–4 mmHg, et les ions d'hydrogène de 4 nmol/liter. Le bicarbonate standard est réduit de 1–1,5 mmol, ce qui trahit une réabsorption rénale de bicarbonate (HCO_3) compromise. Ceci fait travailler d'avantage le système de tamponnage osseux, et parait provoquer la mobilisation du calcium et du phosphore osseux. Des baisses cycliques des deux minéraux sont observées après une et six semaines, et provoquent des hypercalcémies et des hyperphosphatémies cycliques. Une augmentation significative du calcium rénal est observée après deux semaines d'exposition; la concentration ne diminue pas pendant les semaines suivantes. Ces résultats montrent que la minéralization rénale ne dépend pas des variations calcémiques, une fois les processus rénaux commencés. Une augmentation immédiate de la phosphatémie après un jour d'exposition aurait pu jouer un role décisif. Les augmentations menues mais constantes de calcium ionisé pendant quatre semaines d'exposition à CO_2 (1%) peuvent avoir abouti à une stimulation des parathyroides, qui aurait maintenue une calcémie accrue pendant la période d'exposition; cette calcémie serait indépendente de la calcémie élevée associée à la libération du calcium des os.

toxicité chronique de CO_2
métabolisme du calcium
métabolisme du phosphore
acidose métabolique
calcification rénale

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Phasic changes in bone CO_2 fractions, calcium, and phosphorus during chronic hypercapnia

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SCHAEFER, KARL E., STEPHEN PASQUALE, ARTHUR A. MESSIER, AND MICHAEL SHEA. *Phasic changes in bone CO_2 fractions, calcium, and phosphorus during chronic hypercapnia.* J. Appl. Physiol.: Respirat. Environ. Exercise Physiol. 48(5): 802–811, 1980.—The bone CO_2 buffering system and bone calcium and phosphorus were studied in guinea pigs exposed to 1% CO_2 for periods up to 8 wk and killed at weekly intervals together with control animals of the same age. Measurements were made of arterial CO_2 tension, pH, standard bicarbonate, and bone Ca and P. Heat-stabile bone CO_2 (carbonate) was determined as dry bone CO_2 and heat-labile bone CO_2 (bicarbonate) as Δ wet-dry bone CO_2. During the first 3–4 wk of exposure to 1% CO_2, a systemic acidosis was found as indicated in a lowered pH, increased arterial CO_2 tension, and decreased standard bicarbonate. The acidosis subsided during the last 4 wk of exposure. Phasic changes in bone bicarbonate were observed as shown in immediate rise lasting for 2 wk followed by a 2-wk decline and second rise after 6 and 8 wk. Bone carbonate exhibited the opposite change during the first 4 wk and thereafter remained stable at an elevated level. Bone Ca and P fell in association with increasing bone bicarbonate and rose with increasing bone carbonate.

acid-base balance

PROLONGED EXPOSURE OF MEN to 1.5% CO_2 for 42 days has been found to result in a phase of uncompensated respiratory acidosis lasting for about 3 wk followed by a compensatory respiratory acidosis (38). This long time period required to reach a compensation during exposure to 1.5% CO_2 is in marked contrast to the 4- to 5-day periods needed to accomplish maximal compensation in chronic hypercapnia induced by exposure to CO_2 concentrations of 3–15% CO_2. More recent studies of the effects of prolonged exposure to lower CO_2 concentrations (0.85–2% CO_2) have provided additional evidence showing longer time periods for maximal compensation of the CO_2-induced acidosis as judged by blood pH and bicarbonate measurements. During a 30-day exposure of men to 2% CO_2, Guillerm and Radziszewski (16) observed maximal compensation of the acidosis after 2 wk. In American and British submarine patrol studies in which the ambient CO_2 levels were kept between 0.8 and 1% CO_2, maximal compensation of the CO_2-induced respiratory acidosis was reached after 3–4 wk (22, 28, 37).

If one plots the time required for maximal compensation of CO_2-induced acidosis, which has been reported in the literature on prolonged exposure to different CO_2 concentrations, against arterial or venous CO_2 tensions measured, one obtains a graph that exhibits a systematic difference in response to levels of 3% CO_2 and above (time for compensation remains the same) compared with that at lower levels where the time periods required for compensation increase with decreased ambient CO_2 concentrations. Renal regulation (bicarbonate reabsorption) is fully active during exposure to higher CO_2 concentrations and becomes less and less effective during exposure to lower CO_2 concentrations. Under the latter conditions bone buffering, which has a slow time constant, becomes the dominant factor.

Evidence for an initial transient failure in the activation of renal bicarbonate reabsorption is indicated in findings showing that blood bicarbonate did not rise during the first 3 wk of exposure to 1.5 and 1% CO_2 (22, 38). However, during the subsequent period between 3 and 6 wk blood bicarbonate did increase. The reported phases in acid-base balance during chronic low-level hypercapnia were found to be reflected in calcium homeostasis, inasmuch as blood calcium levels mirrored the pH changes and urine calcium changes also exhibited related alterations (37, 38).

It has been suggested in an earlier study on calcium metabolism during exposure to 1.5% CO_2 that the initial 3-wk period of decline in blood calcium corresponding to the decrease in blood pH marks a period of deposition of CO_2 in bones and that bones play an important part in acid-base regulation during low-level chronic hypercapnia (38). Recent submarine studies have given further support to this hypothesis and demonstrated the need to carry out animal experiments with prolonged exposure to 1% CO_2, in which acid-base parameters, bone CO_2 exchange, and bone calcium and phosphorus could be measured simultaneously.

Bone comprises about 80% of the total CO_2 storage capacity of the body (13, 33) and is also known to be a major reservoir for electrolytes such as calcium, phosphorus, potassium, and sodium. Although the role of bone in the maintenance of mineral and acid-base homeostasis has been demonstrated (24, 27), little information is available in the literature about CO_2 exchange during hypercapnia and other acid-base balance changes. The earlier studies carried out under condition of chronic hypercapnia, such as those of Freeman and Fenn (13)

and Nichols (25), were limited to the measurement of dried bone CO_2 stores, which represent only fixed carbonates. However, it has been shown by Buchanan and Nakao (4), Neuman and Mulyran (23), and Poyart et al. (31) that the CO_2 stores in bone contain at least two major fractions: *1*) carbonate comprising approximately 60–70% of the total CO_2 content, probably located in the lattice of bone crystals, and *2*) bicarbonate assumed to be located in the hydration shell of the hydroxyapatite crystals. This fraction is considered to be easily exchangeable with blood CO_2.

Poyart et al. (32) determined in constant-infusion experiments using [^{14}C]bicarbonate that approximately 50% of the ^{14}C activity was lost upon heating. Based on their in vitro studies, Poyart et al. (31) concluded that this heat-labile CO_2 fraction may be considered as half of the bone bicarbonate pool, which accounts for 30% of the total bone CO_2 store.

The bone carbonate fraction does not seem to respond to acute hypercapnia. Freeman and Fenn (13) did not find any changes in rats exposed for 5–6 h at 10% CO_2. However, Bursaux and Poyart (5) demonstrated changes in total fresh bone CO_2 in response to acute hypocapnia and hypercapnia. We recently obtained CO_2-titration curves in rats during acute 1-h exposure to different CO_2 concentrations ranging from 1 to 15% CO_2. By use of a modified titration technique for the determination of the CO_2 content in fresh and dried paired bone samples, a linear relationship was found between arterial CO_2 tension (Pa_{CO_2}) and the increment in fresh bone CO_2 content (bicarbonate fraction); the dry bone CO_2 content (bone carbonate) did not change (26).

The responses of carbonate and bicarbonate CO_2 fractions to chronic hypercapnia have not been determined. It was one of the main purposes of the present investigation to clarify their role in adaptation to CO_2 and to document relationships of bone CO_2 uptake to calcium and phosphorus metabolism under conditions in which the established Pa_{CO_2}-dependent bone bicarbonate uptake could not play a significant role because of the minimal increase in Pa_{CO_2} during exposure to 1% CO_2.

METHODS

Mature male guinea pigs were exposed to 1% CO_2-21% O_2-balance N_2 in commercially built environmental control chambers with automatic temperature and humidity controls. The environmental temperature was kept at 25.6 ± 1.1°C and the humidity between 65 and 75%. The gas mixtures were prepared by mixing proportional amounts of CO_2 to air; O_2 was added from a high-pressure cylinder. The air within the chamber was recirculated 12 times/min. With this fast and large turnover of chamber air, mixing of CO_2 and air was nearly instantaneous. The CO_2 concentration in the chamber was continuously monitored with a Beckman O_2 analyzer. The CO_2 concentrations were kept at 1% (within the limits of ±0.1%) and the O_2 concentrations at 21% (±0.5%). Ammonia vapor was absorbed by boric acid placed in the chamber. The chamber was opened each morning for a period of 3–5 min to fill the water and food containers and to remove the urine and feces.

Animals of the same age and weight as those exposed to CO_2 were kept in a second environmental chamber under identical environmental conditions except that the ambient air was free of CO_2. From the 1st to 4th wk of exposure, six experimental animals and three or four control animals were killed weekly. After 6 and 8 wk of exposure to 1% CO_2 and after an 8-week recovery period, the same procedure was used. The weight of both control and exposed animals corresponded closely. To avoid changes due to circadian cycles the animals were always killed between 9 and 10 A.M.

Prior to blood sampling, the animals received pentobarbital sodium, 40 mg/kg body wt intraperitoneally, and were returned to the CO_2 exposure chamber. The anesthesia was usually effective after 5 min; the animals were then taken out of the exposure chamber and immediately placed under a mask through which they continued to breathe the same CO_2 gas mixtures to which they had been exposed. Blood samples were drawn from the abdominal aorta. Blood pH and CO_2 partial pressure were determined with an Instrumentation Laboratory blood gas and pH analyzing system. For blood gas studies, usually eight control animals were used to obtain a significant number of arterial blood samples in which O_2 partial pressure was above 50 Torr, a criteria set in our laboratory for acceptable values in anesthetized animals. The femurs of both legs were removed and rapidly cleaned and stripped free of adhering tissues and bone marrow. Specimens of compact bone between 200 and 300 mg were kept on ice for determination of total CO_2 content and bone electrolytes. The time between procurement and analysis of the fresh samples did not exceed 2 h. Preliminary studies had shown that such a time delay did not produce significant changes in CO_2 measurements. Paired specimens were oven-dried to constant weight at 150°C for 18 h before analysis. Total CO_2 content of fresh and dry bone was determined by indirect titration with a modification of the method of Bursaux and Poyart (5), which resulted in a greater accuracy (26).

The dry bone CO_2 content or heat-stabile fraction is subsequently referred to as the carbonate CO_2 fraction. The difference between wet and dry bone CO_2 content represents the heat-labile CO_2 fraction. According to Poyart et al. (31) this bone CO_2 fraction corresponds to 50% of the rapidly exchangeable bicarbonate pool in the bone. Bicarbonate in the blood was calculated using the Henderson-Hasselbalch equation and a pK of 6.1. The volume of the extracellular fluid of the bone samples was assumed to be equal to the chloride space and calculated by the formula of Hastings and Eichelberger (17). A Donnan factor of 0.98 was used for the calculation of extracellular chloride concentration (21). The volume of intracellular water was obtained by subtracting the extracellular water from the total tissue water. The concentration of HCO_3 in extracellular water was calculated from the values of plasma water divided by a Donnan factor of 0.99 (21).

Bone and blood calcium were determined with an atomic absorption spectrometer. For calcium determination both bone samples were dry ashed at 650°C for 24 h. Approximate dilutions with 3 N hydrochloric acid were

used for analysis. Recovery was assessed by adding known amounts of calcium.

Measurement of phosphorus in bone samples was made in acid digests of bone. Bone samples were dissolved in 6 N hydrochloric acid, and appropriate dilutions were analyzed according to a modified method of Fiske and SubbaRow (12). Bone chloride was determined with the Atomic Absorption spectrometer. All statistical comparisons were done by Student's t test.

RESULTS

Data on body weight, arterial carbon dioxide tension (Pa_{CO_2}), arterial oxygen tension (Pa_{O_2}), pH, and standard bicarbonate of guinea pigs exposed to 1% CO_2 and control animals are presented in Table 1. CO_2 exposure did not affect the regular increase of body weight with time.

Pa_{CO_2} was found to be persistently elevated by 3–4 Torr in the exposed animals and statistically different from controls after 3 and 4 wk of exposure. Average Pa_{O_2} values ranged from 51 to 71 Torr. pH fell by about 0.03–0.04 pH units (statistically significant after 1, 2, and 4 wk). Standard bicarbonate was found to be 1–1.5 mM lower in the exposed animals (statistically significant after 2–3 wk of exposure).

Figure 1 shows the changes in CO_2 content of fresh bone and dry bone (heat-stabile CO_2 fraction), the difference between fresh and dry bone CO_2 content (heat-labile CO_2 fraction), and the water content of bone in exposed and control animals.

During the period of 8 wk, the CO_2 content of fresh bone increased in control animals by 21 mmol/kg. Since bone CO_2 content is known to increase with age, the observed rise in bone CO_2 of control animals is considered to represent the effect of age. The CO_2-exposed animals by contrast showed an increase of 111 mmol/kg. Subtracting the age-related increase in bone CO_2 content leaves 90 mmol/kg, which is associated with the very small increase in blood CO_2 tension.

After 8 wk of recovery following 8 wk of exposure, the fresh bone CO_2 content was still elevated by 40 mmol/kg when compared with the bone CO_2 content of the control animals. However, after 2 wk of recovery following 4 wk of exposure to 1% CO_2, bone CO_2 content was not statistically different from control levels.

The dry bone CO_2 content in control animals showed an initial rise that seemed to have become stabilized after 4 wk. During the first 2 wk of exposure to 1% CO_2, the dry bone CO_2 content declined below that of control animals; but it rose rather steeply during the 3rd and 4th wk and remained stable during the subsequent 4 wk of exposure. After 8 wk of recovery following 8 wk of exposure, the dry bone CO_2 values were still elevated above those of control animals.

The bone water increased significantly during the 2 wk of exposure, declined during the 4th wk when the heat-labile CO_2 content was at a low value, and remained during the last 4 wk of exposure below the level of control animals. After 8 wk of recovery, the bone water content returned to the control level.

Measurements of bone tissue water, bone chloride, serum water, and chloride are shown in Table 2. Levels of bone chloride were generally lower during exposure to 1% CO_2 as compared with control animals. There were no significant differences in serum water and serum chloride between controls and experimental animals. The extracellular water compartment of bone calculated on the basis of chloride space was found to be consistently less in animals exposed to 1% CO_2 as compared with control animals. The intracellular water increased during the first 3 wk and returned subsequently to control levels after 6 wk of exposure to 1% CO_2.

The bicarbonate levels in extracellular fluid and extracellular fluid compartment of the bone were calculated.

TABLE 1. *Effect of prolonged exposure of guinea pigs in an environmental chamber to 1% CO_2 on weight and acid-base parameters: comparison with control animals*

Time	Exposed to 1% CO_2					Control Animals				
	Wt, g	P_{CO_2}, Torr	P_{O_2}, Torr	pH, units	Std HCO_3^-, mM	Wt, g	P_{CO_2}, Torr	P_{O_2}, Torr	pH, units	Std HCO_3^-, mM
1 wk	521 ± 7 (8)	37.6 ± 1.3 (8)	64.6 ± 12.5 (8)	7.381 ± 0.009* (8)	20.6 ± 0.4 (8)	537 ± 8 (8)	34.0 ± 1.6 (8)	65.2 ± 4.4 (8)	7.429 ± 0.016 (8)	21.5 ± 0.7 (8)
2 wk	560 ± 4 (5)	37.2 ± 2.4 (5)	55.3 ± 10.0 (5)	7.342 ± 0.014* (5)	20.6 ± 0.4 (5)	568 ± 5 (7)	36.4 ± 1.2 (7)	66.1 ± 3.0 (7)	7.405 ± 0.008 (7)	22.3 ± 0.5 (7)
3 wk	577 ± 6 (5)	38.9 ± 0.4* (5)	56.6 ± 12.0 (5)	7.380 ± 0.013 (5)	19.5 ± 0.5* (5)	584 ± 3 (7)	33.6 ± 0.8 (7)	71.1 ± 4.3 (7)	7.422 ± 0.019 (7)	21.7 ± 0.5 (7)
4 wk	607 ± 5 (6)	40.9 ± 1.7* (6)	58.3 ± 8.3 (6)	7.358 ± 0.003* (6)	20.3 ± 0.3 (6)	602 ± 5 (7)	34.0 ± 1.5 (7)	61.3 ± 3.8 (7)	7.406 ± 0.017 (7)	20.9 ± 0.4 (7)
6 wk	655 ± 7 (5)	36.1 ± 1.0 (5)	71.3 ± 3.5 (5)	7.405 ± 0.004 (5)	21.1 ± 0.4 (5)	662 ± 5 (7)	34.2 ± 0.9 (7)	62.2 ± 4.6 (7)	7.424 ± 0.012 (7)	21.9 ± 0.3 (7)
8 wk	813 ± 12 (6)	39.2 ± 0.7 (6)	55.6 ± 0.5 (6)	7.377 ± 0.018 (6)	22.4 ± 0.7 (6)	819 ± 12 (6)	37.0 ± 0.8 (6)	52.0 ± 2.5 (6)	7.392 ± 0.013 (6)	22.0 ± 0.7 (6)
Recovery on air										
4 wk on 1% CO_2 + 2 wk on air	790 ± 10 (6)	34.0 ± 2.0 (6)	67.5 ± 4.0 (6)	7.371 ± 0.029 (6)	20.0 ± 1.1 (6)					
8 wk on 1% CO_2	913 ± 13 (6)	39.5 ± 1.7	52.6 ± 2.0	7.395 ± 0.013	21.7 ± 0.6	918 ± 11 (6)	38.2 ± 0.8 (6)	54.0 ± 3.0 (6)	7.396 ± 0.012 (6)	21.9 ± 0.5 (6)

Values are means ± SE; no. of animals given in parentheses. * Statistically significantly different from controls at the 0.5% level and better.

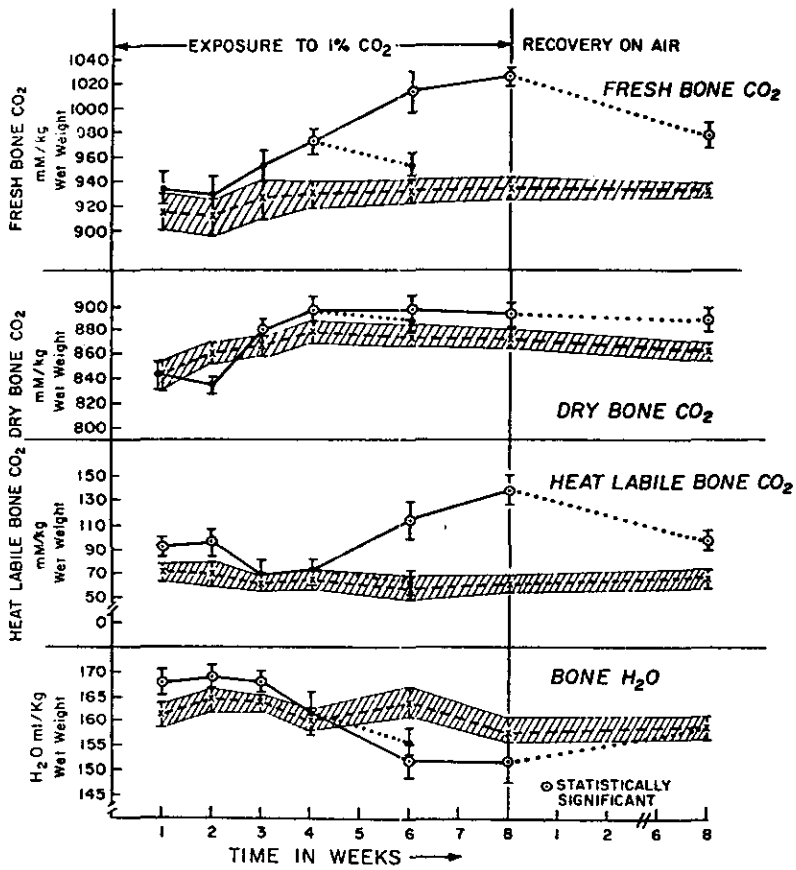

FIG. 1. Effect of prolonged exposure to 1% CO_2 on total bone CO_2 content of fresh bone, dry bone, difference between fresh bone and dry bone CO_2 content (heat-labile CO_2), and bone H_2O content. Data represents means and SE, in mmol/kg wet wt. Exposed animals ——; control animals ----; recovery following exposure ·····. Statistically significantly different from controls at 5% level and better. Each group of exposed animals consisted of 6 animals, each control group (littermates of the exposed guinea pigs) of 3–4 animals.

TABLE 2. *Effect of prolonged exposure to 1% CO_2 on extracellular and intracellular fluid compartments and extracellular bicarbonate*

Time	Bone H_2O, g/kg wet bone	Bone Cl, meq/kg wet bone	Serum H_2O, g/kg	Serum Cl, mmol/kg	Total $H_2O_{(e)}$, g extracellular fluid per kg wet bone	Total $H_2O_{(i)}$, g/ cellular H_2O per kg wet bone	$HCO_{3(e)}$, meq/kg extracellular H_2O	$HCO_{3(i)}$, meq/kg ex tracel lular bone H_2O
Controls (n = 4)								
1 wk	161 ± 2	16.6 ± 0.6	930.5 ± 19	102.8 ± 0.6	145 ± 4.5	15.0 ± 2.8	23.4	3.4
2 wk	163.0 ± 1.7	17.0 ± 0.4	915 ± 20	103.8 ± 1.2	149 ± 3.0	15.8 ± 1.4	22.4	3.3
3 wk	162 ± 1.8	17.7 ± 0.6	929 ± 16	109.5 ± 1.4	152.3 ± 5.0	11.0 ± 4.3	22.3	3.2
4 wk	161 ± 1.21	16.7 ± 0.4	928 ± 25	103.9 ± 1.6	145.8 ± 3.6	15.3 ± 4.1	22.5	3.4
6 wk	163 ± 3	17.1 ± 0.5	928 ± 28	102.3 ± 1.0	150 ± 5	12.0 ± 3.3	23.6	3.6
8 wk	159 ± 2	17.2 ± 0.6	929 ± 30	102.3 ± 0.4	153.5 ± 4	11.5 ± 3.0	23.7	3.9
Exposure to 1% CO_2 (n = 6)								
1 wk	168.8 ± 2*	14.66 ± 0.9	933 ± 28	104.0 ± 0.5	129.0 ± 7.9	41.6 ± 7.3*	23.5	3.0
2 wk	169.3 ± 1.8*	14.1 ± 0.8	932 ± 35	103.0 ± 0.8	124.0 ± 5.0*	44.0 ± 6.4*	21.1	3.0
3 wk	168.0 ± 1.5*	15.1 ± 0.5*	931 ± 21	102.0 ± 0.3	125.0 ± 4.7*	40.1 ± 5.8*	24.0	3.1
4 wk	162.8 ± 4.0	14.4 ± 0.5*	927 ± 19	101.8 ± 0.7	122.0 ± 4.1*	41.3 ± 4.2*	23.9	2.9
6 wk	151.5 ± 4*	15.1 ± 0.4*	927 ± 18	106.2 ± 0.3	128.0 ± 3.4*	23.0 ± 5.0	23.9	3.0
8 wk	152.1 ± 2*	15.1 ± 0.4*	926 ± 25	102.5 ± 0.5	133.0 ± 3.0*	18.3 ± 4.0	24.1	3.1

Values are means ± SE; *n*, no. of animals. * Statistically significantly different from controls at the 5% level and better.

As shown in Table 2, the extracellular bicarbonate concentration in bone is very small and does not play a role in the measured changes of the bone CO_2 fractions.

Calcium content of bone and blood in exposed and control animals is depicted in Fig. 2. After 1 and 6 wk of exposure, bone calcium content exhibited a sharp drop that corresponded with the rapid increase in CO_2 uptake of the heat-labile CO_2 fraction. During the rise of the heat-stabile CO_2 fraction, bone calcium content rose again. The bone calcium loss was reflected in a blood

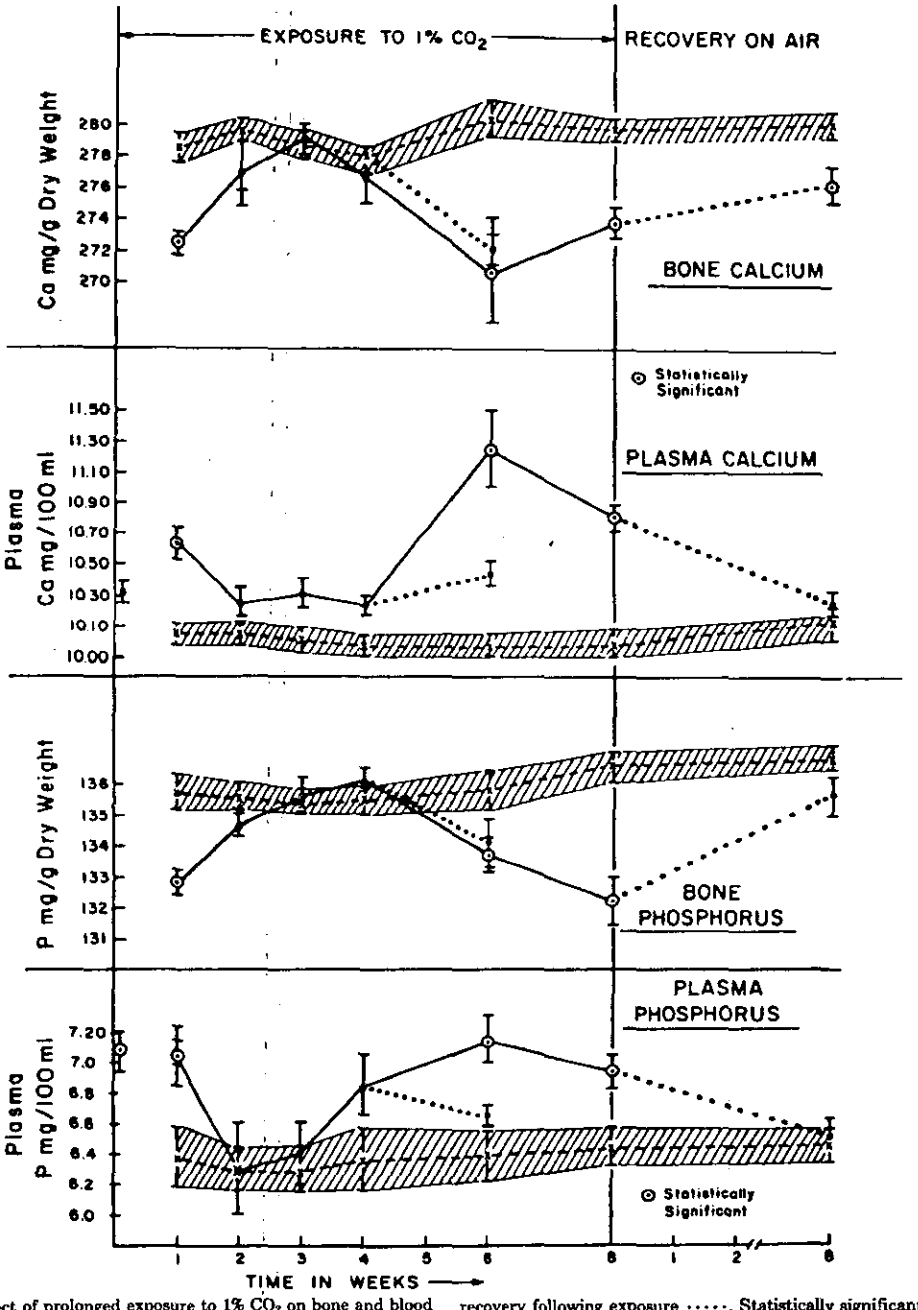

FIG. 2. Effect of prolonged exposure to 1% CO_2 on bone and blood calcium and bone and blood phosphorus. Data represent means and SE, in mg/g dry wt. Exposed animals ——; control animals ----; recovery following exposure ·····. Statistically significantly different from controls at 5% level and better. Each group of exposed animals consisted of 6 animals, each control group of 3–4 animals.

calcium tide. It should be noted that the blood level of exposed animals was at all times higher than those of control animals. At the end of 8 wk of exposure, bone calcium was significantly lower than that of control animals. After 8 wk of recovery on air, the bone calcium content was still statistically different from control levels.

Bone and blood phosphorus changes showed the same pattern as bone and blood calcium (Fig. 2).

To summarize the effects of prolonged exposure to 1% CO_2 on bone CO_2 fractions and calcium and phosphorus, the differences between control animals and experimental animals were calculated in milliequivalents per kilogram of wet bone and listed in Table 3.

The first 2 wk of exposure can be characterized as a phase of initial bone bicarbonate uptake and carbonate decline. During this period there is a maximum loss of calcium and phosphorus at 1 wk of exposure. During the 3rd and 4th wk bicarbonate uptake is reduced and carbonate uptake is increased. This phase exhibits a minimum change in bone calcium and phosphorus at 3 wk. During the period of 6 and 8 wk a large bicarbonate uptake occurs while the carbonate level remains stable. Increased losses in calcium and phosphorus are associated with this large bicarbonate uptake.

These data clearly demonstrate the existence of three different phases in the observed changes of bone CO_2 fractions and of bone calcium and phosphorus.

DISCUSSION

Throughout this experiment lasting for a total of 112 days, weights of control and experimental animals compared closely with each other indicating a lack of gross health effects attributable to CO_2.

During the first 4 wk of exposure to 1% CO_2 the Pa_{CO_2} level was found to be significantly elevated at 3 and 4 wk and the pH decreased at 1, 2, and 4 wk. Moreover, a slightly depressed standard bicarbonate level existed during this period, indicating that the kidney failed to increase bicarbonate reabsorption in response to this low-level hypercapnia.

During the subsequent period of 6 and 8 wk of exposure to CO_2, the acid-base parameters showed no significant differences from controls. Standard bicarbonate increased, reaching control levels. Based on these findings one can divide the acid-base status of the animals exposed to 1% CO_2 into two phases. First, an acidosis existed during the first 4 wk of exposure associated with a depressed renal bicarbonate reabsorption, which may be classified as metabolic acidosis. Second, a period (6 and 8 wk of exposure) in which the pH returned to near control levels and the kidney began to reabsorb bicarbonate at a limited scale. This second phase appears to be similar to a compensated respiratory acidosis, although it was not preceded by a typical respiratory acidosis. The data on fresh and dry bone CO_2 content we obtained in control animals are similar to those reported by Poyart et al. (31) on rats. Bone calcium content of 278.7 mg/g dry wt measured in guinea pigs is in close agreement with the average value of 270 mg/g dry wt reported by Easthoe and Easthoe (11) for this species The results of bone chloride, phosphorus, and calcium determinations in rats made by Levitin et al. (19) are also similar to those observed in this experiment.

TABLE 3. *Phasic changes in bone calcium, phosphorus, carbonate, and bicarbonate produced by prolonged exposure of guinea pigs to 1% CO_2*

Exposure to 1% CO_2	ΔCa, meq/kg wet bone	ΔP, meq/kg wet bone	ΔCO_3^{2-}, meq/kg wet bone	ΔHeat-Labile CO_2, meq/kg wet bone	ΔHCO_3^-, meq/kg wet bone	Phases
1 wk	−390	−260	0	+21	+42	*I* (initial HCO_3^- uptake; CO_3^{2-} decline)
2 wk	−200	−30	−15	+25	+50	
3 wk	−30	−5	+13	+10	+20	*II* (CHO_3^- uptake reduced; CO_3^{2-} uptake increased)
4 wk	−196	−50	+32	+9	+18	
6 wk	−320	−100	+23	+62	+124	*III* (large HCO_3^- uptake; CO_3^{2-} remains stable)
8 wk	−148	−180	+30	+66	+132	

Differences between experimental animals and littermate controls.

Bone CO_2 Fractions

Total bone CO_2 content in fresh tissue was slightly above control values during the first 3 wk of exposure and rose significantly and continuously at 4, 6, and 8 wk of exposure (Fig. 1). This late rise in bone CO_2 is surprising. With such a small increase of Pa_{CO_2}, consisting of a few Torr, one would expect that an equilibrium of bone CO_2 uptake would have been reached at an early stage, e.g., after 1–2 wk, if the bone CO_2 exchange would be solely dependent on Pa_{CO_2}. These findings suggest that different mechanisms must be involved in the CO_2 accumulation during the 4- to 8-wk period of exposure to 1% CO_2, be it incorporation of CO_2 into the osseous tissue structure or chemical substitution. Similar observations were made by Reichart et al. (35), who measured CO_2 uptake in the whole body and in different organs such as liver, muscle, and bone in rats exposed to 8% CO_2 for 2, 4, 6, and 8 wk. They observed that whole-body CO_2 content and bone CO_2 content were still increasing after 8 wk of exposure, whereas the CO_2 content of liver and muscle had reached an equilibrium. The authors could not explain the disparity in the CO_2 uptake of different organs. Brown and Michel (3), who studied whole-body CO_2 exchange in rats during chronic hypercapnia (10% CO_2), also found that the CO_2 uptake did not reach an equilibrium within 6 wk of exposure. To our knowledge there is no information in the literature that would provide an explanation for the observed continuous rise of whole-body CO_2 and bone CO_2 content in chronic hypercapnia.

The major rise in total bone CO_2 content during the period of 4–8 wk of exposure to 1% CO_2 is due to the increase in the bicarbonate fraction since the carbonate fraction remains stable from 4 wk on through the remainder of the exposure period. Inasmuch as extracellular bicarbonate did not change during exposure to 1% CO_2 (Table 2), it could not have contributed to the large accumulation of total bone CO_2 in form of bicarbonate observed during the later periods of 6 and 8 wk of exposure.

Extracellular water was found to be reduced throughout the whole 8-wk exposure period. The observed shrinkage of the extracellular bone water compartment might have contributed to limit the role of extracellular bicarbonate in bone CO_2 uptake. Intracellular water was found increased during the first 4 wk of exposure to 1% CO_2 and returned to control levels at 6 and 8 wk of exposure. The movement of intracellular water marks two periods with different forms of bone CO_2 uptake. It is concluded from our experiments with 1% CO_2 that the large increase in bone bicarbonate after 6 and 8 wk of exposure must be based on an accumulation of bone bicarbonate not in equilibrium with the extracellular space and not dependent on Pa_{CO_2}. Similar observations were made by Reichart et al. (35).

Possible Mechanisms Involved in Phases of CO_2 Exchange in Chronic Hypercapnia

Three phases of CO_2 exchange in bone have been demonstrated (Table 3).

Phase I. Bone CO_2 uptake during the first 2 wk of exposure was limited to the bicarbonate fraction and was associated with an influx of water. At the same time, the carbonate fraction declined simultaneously with a loss in bone calcium and phosphorus. A decrease in bone carbonate was also observed by Nichols (25) in rats during the first 5 h of exposure to 24% CO_2. Findings of this first phase of CO_2 uptake in the bone provided confirming evidence for the theory proposed by Poyart et al. (31) that gaseous CO_2 hydrates with bone water to form carbonic acid, which dissociates into one HCO_3^- and one H^+ ion as follows

$$CO_2 + H_2O \rightarrow H_2CO_3 \rightarrow HCO_3^- + H^+ \qquad (1)$$

The H^+ ion is most probably located at the surface of the bone crystal structure to be able to participate rapidly in bicarbonate formation. It is probably taken up by the available carbonate fraction resulting in a fall in bone calcium and bone phosphorus.

$$H^+ + CaCO_3 \rightarrow HCO_3^- \rightarrow Ca^{2+} \qquad (2)$$

The influx of H_2O into the bone also fits this scheme well.

Phase II. During the subsequent period of 3 and 4 wk of exposure (*phase II*), a reversal takes place. The carbonate fraction increases in association with a rise in bone calcium and bone phosphorus. Conversely, the bicarbonate fraction decreases in conjunction with a decrease in bone water.

It has been pointed out that the process of CO_2 binding into the bone is dependent on Pa_{CO_2} and time, which involves a saturation mechanism (31). Under 1% CO_2, the saturation of the rapidly exchangeable pool of bone CO_2 is apparently accomplished within 2 wk, after which dehydration and loss of heat-labile CO_2 occurs. Heat-labile CO_2 fell by 15 mmol/kg during this period, corresponding to 30 mmol/kg reduction of bicarbonate. If the CO_2 exchange followed the reaction given in *Eq. 3* and 15 mmol/kg appeared in the form of carbonate as measured, then the other 15 mmol/kg must have been released as gaseous CO_2 into the extracellular space and blood.

$$2HCO_3^- \rightarrow CO_2 + CO_3^{2-} + H_2O \qquad (3)$$

Bone carbonate attains an equilibrium after 3–4 wk of exposure following transformation of part of the originally accumulated bicarbonate stores into carbonate. The increase of 22 mmol/kg corresponds to about 2.6% of the total carbonate pool. This process seems to be associated with the release of CO_2 in gaseous form as indicated in a rise in Pa_{CO_2} concomitant with the outflow of excess bone water accumulated during the first 2 wk of CO_2 loading. The release of CO_2 from the bone could by itself not have caused an increase in Pa_{CO_2}, unless other factors came into play at the same time. It has been theorized, that CO_2 released from the bones could trigger an activation of the renal bicarbonate reabsorption mechanism leading to an increase in blood bicarbonate and consequently to a compensation of the acidosis (37). Moreover, a reduction in the CO_2-induced hyperventilation has been found during the compensatory phase of respiratory acidosis in chronic hypercapnia induced in human subjects during prolonged exposure to 0.8–2% CO_2 (37). Of the three factors described, the first one consisting of the bone CO_2 exchange process underlying CO_2 release from the bone has been demonstrated in this experiment. The activation of renal bicarbonate reabsorption begins at 4 wk of exposure to 1% CO_2, since standard bicarbonate is increased from this time on for the rest of the exposure period. Ventilation was not measured in these animals, but it can be assumed that it follows the pattern observed in human studies.

Phase III. The second rise of the bone bicarbonate fraction after 6 and 8 wk of exposure to 1% CO_2 (*phase III*) was apparently based on a process that differs from the first increase in bone bicarbonate (*phase I*). Bone water does not change, nor does the carbonate fraction. After 8 wk of exposure, the heat-labile form of CO_2 has increased by 66 mmol/kg, corresponding to 132 mmol/kg, or 92% of the total bicarbonate pool originally present. This was a significantly larger increase than that observed during the first 2 wk and is out of proportion to any Pa_{CO_2}-dependent mechanism. It would seem to require a membrane and an active pump mechanism to accumulate so much CO_2 in the form of bicarbonate. Further investigations are necessary to clarify the nature of this process. The process of CO_2 binding under these circumstances probably involved deeper layers in the bone. It seems to correspond with the increased CO_2 binding found to occur during aging (31, 32, 42). This aging effect is also associated with loss of bone water Poyart et al. (31) have suggested that the increased CO_2 binding in aging may be related to bicarbonate formation from a CO_2 fraction located deeper in the apatite crystals The lowered levels of bone calcium and phosphorus found after 6 and 8 wk of exposure to 1% CO_2 support the argument that the calcium-phosphate-carbonate complex in the bone gives up carbonate for the formation of bicarbonate, and calcium and phosphorus are released as a consequence. Bicarbonate formed under these circumstances may not belong to a rapidly exchangeable CO_2 fraction of the bone, since 8 wk of recovery on air following 8 wk of exposure was not sufficient to let either the carbonate fraction or the bicarbonate fraction return to control levels. Therefore, the loss of bone calcium and phosphorus still existed at this time.

These findings suggest the existence of two carbonate

fractions involved in fast and slow exchangeable CO_2 pools in the bone as well as the presence of two bicarbonate fractions.

Application of Animal Study Results to Acid-Base Balance Studies of Chronic Hypercapnia in Men

The phasic changes in bone CO_2 uptake and their effects on acid-base balance in guinea pigs during prolonged exposure to 1% CO_2 can give a clue to the understanding of the cyclic changes in acid-base balance found in human subjects exposed to 0.7–1% CO_2 for prolonged periods in submarine patrols (14, 15, 22, 28, 36, 37). The dominant feature of the acid-base changes under these conditions was a metabolic acidosis during the first 3 wk of exposure, indicated by either no change or a decrease in blood bicarbonate commensurate with a slight increase in Pa_{CO_2} and H^+. During the 4th and 5th wk, however, blood bicarbonate and Pa_{CO_2} increased. During the second period (4–6 wk) acid-base status appeared as a compensated respiratory acidosis. The well-known renal response to hypercapnia observed during exposure to higher CO_2 concentrations consists of an increased acid secretion and renal bicarbonate reabsorption resulting in an increased blood bicarbonate (2, 7, 29, 34, 43). This response does not occur during the first 3 wk but develops during the subsequent 4th and 5th wk. The theory has been advanced that the stimulus for activation of renal bicarbonate reabsorption occurring after 3 wk of exposure to low levels of CO_2 on submarines may come from a larger acid load involving the release of CO_2 from the bone after the capacity of the rapidly exchangeable CO_2 stores has been reached (37). The results of this study supply evidence in support of this theory by showing that the fast exchangeable pool of bone CO_2 is indeed saturated during the first 2 wk, and that a decrease of the bicarbonate fraction with a release of CO_2 in the blood occurs during the subsequent period.

To bring this important point out more clearly a diagram depicting the phasic changes in bone carbonate and bicarbonate and their relationship to Pa_{CO_2} caused by prolonged exposure to 1% CO_2 is presented in Fig. 3. The differences between experimental and control animals have been averaged for 2-wk periods. Individual data points have been presented in Tables 1 and 3 and Figs 1 and 2.

Bone Calcium and Phosphorus

A significant loss in bone calcium and phosphorus was found in association with the increase of the bicarbonate bone CO_2 fraction after 1 and 6 wk of exposure to 1% CO_2. Bone calcium and phosphorus showed an increase commensurate with the rise in the bone carbonate fraction. These results demonstrate that phasic alterations in bone calcium and phosphorus are related to specific phases of CO_2 binding in the bone involving the bicarbonate and carbonate CO_2 fractions. Loss of bone calcium and phosphorus has also been observed in chronic hypercapnia in rats exposed to 8% CO_2 for periods of 2, 4, and 6 wk (8). The decrease in calcium observed under these conditions was more pronounced after 6 wk of exposure as compared to 4 wk and 2 wk of exposure; this finding is in line with our observations. The sampling

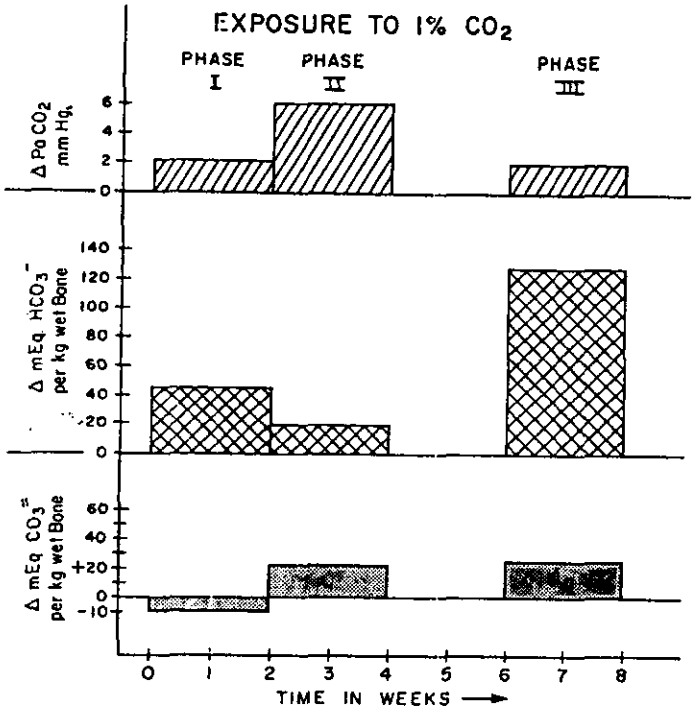

FIG. 3. Diagram showing differences in Pa_{CO_2}, bone HCO_3^-, and $CO_3^{=}$ between animals exposed to 1% CO_2 and control animals. Data are averaged for 2-wk periods.

eriods, however, were not frequent enough to detect hases in bone calcium similar to those observed in our tudy. Leon (18) exposed rats to 1% CO_2 for 28 days and ound small decreases in bone carbonate and bone calium, which were not statistically significant.

Based on our findings of phases in bone calcium and *hosphorus exchange* it is concluded that the length of he exposure period to CO_2 will determine whether bone alcium and phosphorus is decreased or increased. Levin et al. (19) observed, in rats exposed for 24 h to 8% CO_2, a statistically significant fall in bone phosphorus nd a slight decline of bone calcium. Rats exposed to 10% CO_2 for 11 days showed a slight increase in bone calcium, vhich was, however, not statistically significant (6).

The Role of Parathyroid Gland

The cyclic changes in blood calcium and phosphorus re of such a nature that they can be expected to influnce the endocrine balance of parathyroid hormone and alcitonin. In addition, bone calcium mobilization and esultant hypercalcemia (Fig. 2) was also found to be ssociated with the kidney calcification reported elsevhere (40). Kidney calcification was also demonstrated istologically in guinea pigs and rats exposed to 1.5% CO_2 or extended periods of time (40).

Administration of parathyroid hormone has been ound to cause kidney calcification but did not change he calcium content in the heart and liver (9). Analysis of the calcium content in heart tissue of guinea pigs exposed from 1 to 4 wk to 1% CO_2 did not show an ncrease in calcium. These findings suggest that the kidney calcification seen during exposure to 1% CO_2 may nvolve parathyroid hormone (PTH). The fact that plasma calcium in animals exposed to 1% CO_2 remains continuously elevated independent of the two episodes of calcium flux out of the bone at 1 and 6 wk also seems o support the argument that a stimulation of the parathyroid gland existed during exposure to 1% CO_2.

Recent studies on PTH and CO_2 effects on kidney calcium metabolism further strengthen the argument for a CO_2-induced increase in PTH activity. Borle et al. (1) found that PTH produced intramitochondrial calcification in kidney cells. CO_2 alone appears to have the opposite effect of PTH. In isolated rat kidney cells *exposure to 20% CO_2 depressed* all cellular calcium pools and total cell calcium (41). However, CO_2 has been shown to increase PTH effects as measured by ^{45}Ca release from fetal bones (6, 20).

Parathyroid hormone stimulation may have been the cause of the acidosis observed during prolonged exposure to 1% CO_2. The decrease in standard bicarbonate indicates a failure of the kidney to reabsorb bicarbonate. PTH has been found to decrease bicarbonate reabsorption and to produce a systemic acidosis (10). Crumb et al. (10) *also reported that hypercalcemia* caused an increased bicarbonate reabsorption, but this effect could be suppressed by increased levels of PTH. Although PTH activity was not measured in this study, there is indirect evidence suggesting that PTH activity was indeed increased during exposure to 1% CO_2. The elevated blood calcium found in the study failed to produce an increase in bicarbonate reabsorption during the first 4 wk of exposure; this suggests that it was associated with increased PTH activity.

This study produced provocative findings showing that bone calcium and phosphorus were significantly lower than control values after 8 wk of exposure to 1% CO_2, indicating a demineralization of bone, which in the case of bone calcium was not alleviated by a recovery period on air for 8 wk. Such a demineralization caused by a small increase of P_{aCO_2} points also to a CO_2-induced hyperparathyroid state.

These findings may also stimulate some research into the clinical significance of slightly increased P_{aCO_2} levels *in hyperparathyroid states.*

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The opinions and assertions contained herein are the private ones of the authors and are not be construed as officially reflecting the view of the Navy Department, the Naval Submarine Medical Research Laboratory, or the Naval service at large.

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COMPARISON OF PHYSIOLOGICAL RESPONSES OF NORMAL MAN TO EXERCISE IN AIR AND IN ACUTE AND CHRONIC HYPERCAPNIA

R. D. Sinclair, J. M. Clark, and B. E. Welch

The results of studies on acute and chronic hypercapnia have shown that the healthy man at rest can tolerate an ambient P_{CO_2} of up to 30 mmHg without signs or severe symptoms of incapacitating physiological changes (4, 8, 13). However, this information does not completely answer the question of just what CO_2 exposures are tolerable for humans living in the artificial environment of habitats or vehicles used in underwater and space exploration. It must be assumed that individuals thus exposed will very likely be required to perform tasks calling for increased muscular work. Therefore, defining the interactions between the normal physiological responses to exercise and hypercapnia and the influence of these interactions on CO_2-tolerance limits in man is an important challenge in environmental research.

Exercise During Hypercapnia—The Problem

During acute hypercapnia man, even at rest, is in an environment unfavorable to metabolic CO_2 elimination (14), and he must therefore increase minute ventilation ($\dot{V}_E$) in response to elevated Pa_{CO_2}, and $[H^+]$. Thus, the basic physiological responses that adequately eliminate the CO_2 produced by the body during exercise in air are less effective when exercise is done in a high CO_2 atmosphere. Consequently, Pa_{CO_2} and $[H^+]$ increase progressively in proportion to elevations of inspired PI_{CO_2} (13). Although ventilation is not usually considered to be a limiting factor in man's capacity for doing heavy or maximal exercise in air (1, 20), exercise during hypercapnia places excessive demands upon ventilation that may in turn limit exercise capacity. Furthermore, the normally high incidence of premature ventricular contractions in man performing exercise in air (14) and cardiac arrhythmias while he breathes high concentrations of CO_2 (7–14% at ambient pressure) at rest (17) raise an important question: Is there a possible interaction of these combined stressors on rhythmicity of the heart?

Theoretically, during chronic exposure to CO_2 with its concomitant physiological adapta-

TABLE I

EXERCISE DURING EXPOSURE TO HYPERCAPNIA

Subjects	Ambient P_{CO_2} (mmHg)	Workload[a]	Duration (min)	Source
6	8	L	180	Krasnogor *et al.* (11)
7	21[b]	L	60	Glatte *et al.* (8)
4	21[b]	L–M–H	45	Sinclair *et al.* (this study)
8	8–30	M–H–Max	20–30	Menn *et al.* (14)
7 (dog)	15–60	M	15	Sinclair *et al.* (18)
4	16	Max	—	Finkelstein *et al.* (6)
2	21 (15–35)[b]	M	—	Schaefer (15)
32	7–35	L	10	Froeb (7)
11	35	H	2	Hickam *et al.* (9)
3	(7–45)	M–H	10	Asmussen and Nielsen (2)
3	(15–45)	M–H	12	Craig (5)

[a] Classified as low (L), moderate (M), heavy (H), and maximum (Max).
[b] Acute (hours) and chronic (days) exposure.

tions—e.g., increased body buffering of $[H^+]$, slightly abated $\dot{V}_E$ (3, 8), and readjustment of hormonal activity (16, 17, 21)—man might be somewhat better able to do exercise than he is during acute exposure to the same P_{CO_2}. This possibility has been the basis for studies of responses to exercise during prolonged hypercapnia.

Previous Studies Concerning Exercise During Hypercapnia

Table I summarizes a limited number of studies reported in the literature (2, 5–9, 11, 14, 15, 18) that provide data on exercise tolerance during exposure to CO_2, and shows the approximate degree of work performed, its duration, and the ambient P_{CO_2} during the exercise. The ambient P_{CO_2} values shown in parentheses indicate that CO_2-response curves were obtained during steady-state exercise; second footnote denotes the studies that were made during both acute and chronic exposure to CO_2 (21 mmHg in all cases). Man was the experimental subject in these studies; the single exception was a dog experiment, which was performed to extend the ambient P_{CO_2} to 60 mmHg—a P_{CO_2} level to which man has not been exposed during exercise. One can see from the data that heavy work has been done for relatively long periods in both 21 and 30 mmHg of ambient P_{CO_2}, and maximum exercise has been done in 16 and 21 mmHg. The table also shows that the highest ambient P_{CO_2} breathed by man during heavy exercise was 45 mmHg for 12 min.

The first five studies listed in the table were performed at the USAF School of Aerospace Medicine as a series of related experiments performed specifically to define the levels of CO_2 exposure that man can tolerate. These studies included measurements of ventilation, gas exchange, pH of the blood, and blood gases, in addition to cardiac monitoring.

The remaining studies listed in the table are from other laboratories and, with the exception of the work by Schaefer (15) and Finkelstein *et al.* (6), were not specifically designed to answer questions regarding tolerance levels for exposure to CO_2. Most of these studies concentrated on ventilation and gas exchange measurements, and omitted arterial acid–base and electrocardiographic data.

Graded Exercise in Acute and Chronic Exposure to Hypercapnia—21 mmHg P_{CO_2}

Methods

The present investigation involved four young male subjects in excellent physical condition, who performed three levels of work (low, moderate, and heavy). The work was done in air and during acute (1 hr) and chronic (15–20 days) exposure to an atmosphere containing 21 mmHg ambient P_{CO_2}. While in a supine position, the subjects performed 45 min of continuous steady state exercise on a bicycle ergometer. They breathed air or CO_2-enriched air directly from the environmental room using a modified Otis-McKerrow low-resistance valve. The expired air was directed to a 600-L Tissot spirometer. Two runs, 5 hr apart, were performed by the same subject on each experimental day in order to minimize the total number of arterial catheterizations. The data used to construct the curves in Figs. 1–4 represent measurements obtained

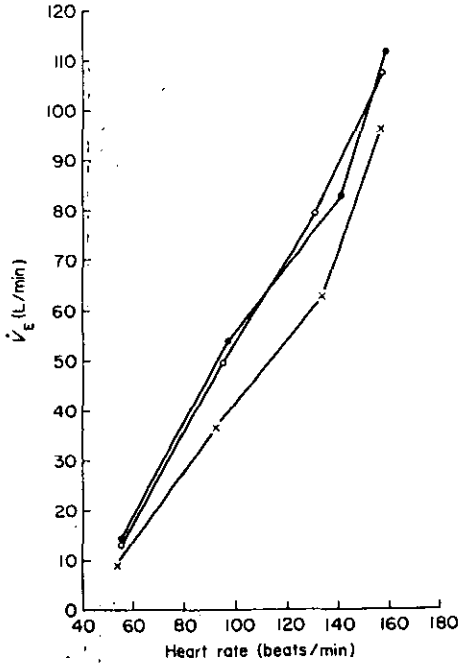

FIG. 1. Effect of graded exercise upon respiratory minute volume in air (×) and in acute (●) and chronic (○) exposure to hypercapnia (21 mmHg). $\dot{V}_E$ values are corrected to BTPS conditions.

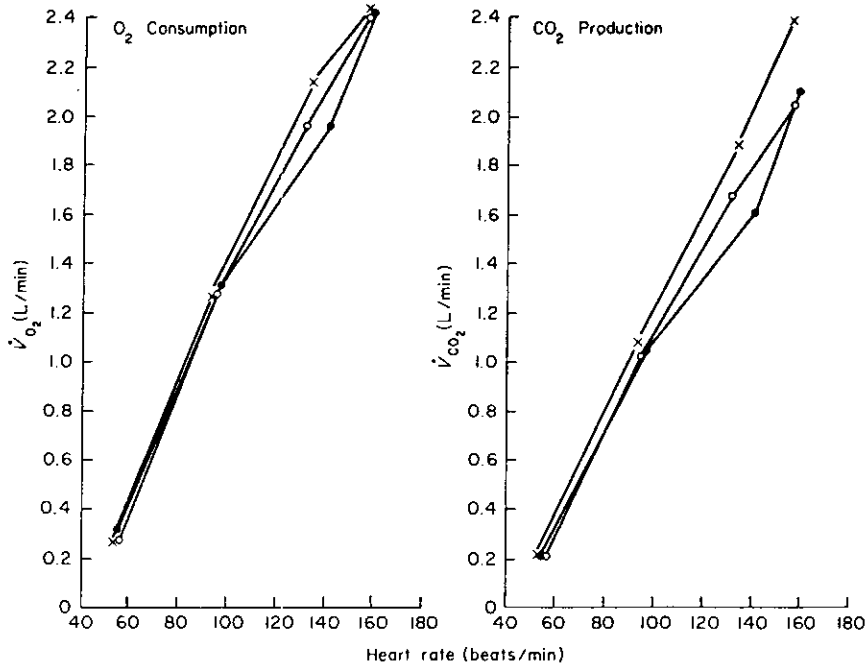

FIG. 2. Effect of graded exercise on respiratory gas exchange in air (×) and in acute (●) and chronic (○) hypercapnia. $\dot{V}_{O_2}$ and $\dot{V}_{CO_2}$ values were corrected to STPD conditions.

between the 12th and 15th minute of exercise. Analysis of variance was used to test the data, which are considered significant when $P < 0.05$.

RESULTS

In Figs. 1–4, the experimental data are plotted against the mean heart rate (HR) responses to exercise rather than against work loads. This method of plotting data is justified because of the highly significant linear correlation between exercise work load and cardiac rate (1, 20). The present study shows that this linear relationship also holds for exercise during acute and chronic CO_2 exposure. Each resting and exercise point on the graphs shown in Figs. 1–4 represents the mean of 12 and 4 individual measurements, respectively.

The effects of graded exercise on $\dot{V}_E$ both in air and CO_2-enriched air are illustrated in Fig. 1. The parallelism of the ventilation curves during exercise agrees with the results of work done by Asmussen and Nielsen (2) and Craig (5). These investigators found that the effect of CO_2 on hyperpnea during exercise, for a limited number of P_{CO_2} and work load combinations, approximates a simple addition of increments produced by the action of each stressor acting independently. However, the difference between $\dot{V}_E$ in air and in CO_2 at rest was approximately doubled at the low work load, and appeared to remain constant at higher work loads. The average $\dot{V}_E$ at similar work levels was essentially equal both in acute and chronic hyper-

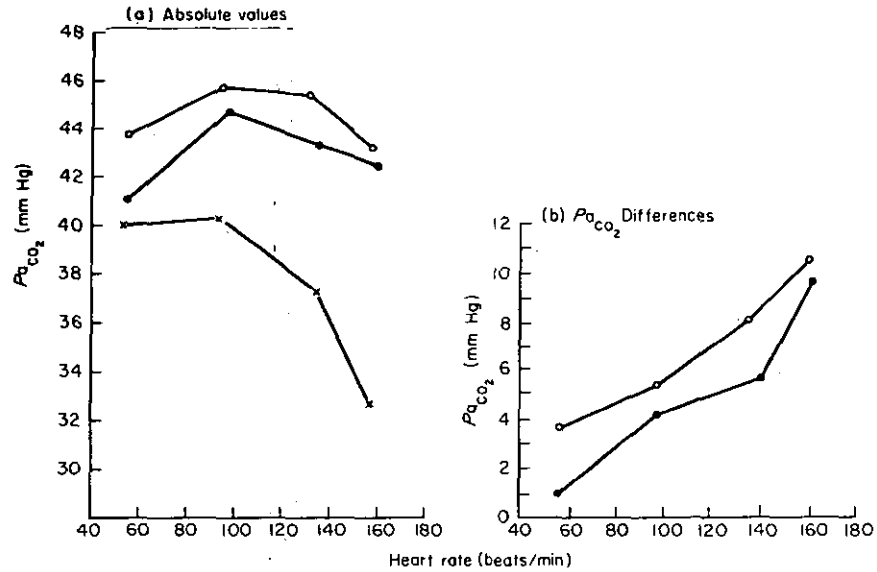

FIG. 3. Effect of graded exercise upon P_{aCO_2} in air (×) and in acute (●) and chronic (○) hypercapnia. Blood gases were temperature corrected. P_{aCO_2} differences refer to the difference between the absolute P_{aCO_2} values in acute or chronic hypercapnia and the corresponding P_{aCO_2} values during air breathing for rest and at each level of work.

capnia; the air curve was approximately 15 L/min lower at each work load. The difference among the three curves is considered highly significant ($P < 0.001$).

The changes in $\dot{V}_E$ with progressive exercise in each experimental condition resulted from changes in both respiratory rate and tidal volume, the former becoming relatively more important with increasing work load. Comparison of the respiratory patterns under similar work loads in both acute and chronic hypercapnia showed that tidal volume was higher and rate lower in chronic hypercapnia.

The finding that there was little difference between the average $\dot{V}_E$ at similar work loads in acute and chronic CO_2 conditions is in contrast to the finding of Schaefer (15). His data for one subject showed that the ventilatory response to exercise during acute hypercapnia was reduced when exercise was done after 8 days of exposure to 21 mmHg ambient P_{CO_2}. The individual data from the present study reveal that one of our four subjects showed a response similar to that described by Schaefer, but the ventilatory responses of the other three were not clearly different in acute and chronic hypercapnia.

The effects of graded exercise on gas exchange in air and in CO_2 are shown in Fig. 2. The oxygen uptake ($\dot{V}_{O_2}$) curves are essentially linear, and the mean values vary little from one another at the same work load in the different experimental conditions. There is no significant difference between the curves. Krasnogor *et al.* (11), Glatte *et al.* (8), and Menn *et al.* (14) likewise found no differences in $\dot{V}_{O_2}$ whether exercise was performed in air or CO_2-enriched air environments. In contrast, Finkelstein *et al.* (6) reported a 12% decrease in maximum $\dot{V}_{O_2}$ with exercise in an environment containing 16 mmHg inspired P_{CO_2} (PI_{CO_2}). However, they did not indicate whether the degree of exercise performed in CO_2 and in air was the same.

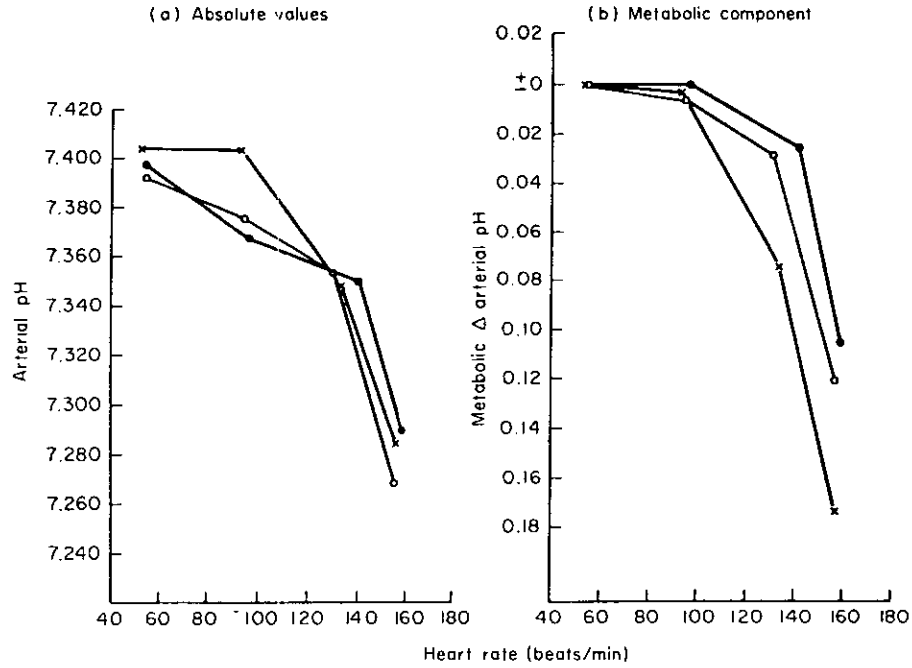

FIG. 4. Effect of graded exercise upon arterial pH in air (×) and in acute (●) and chronic (○) hypercapnia The pH values were temperature corrected. The *metabolic component* was calculated by subtracting the respiratory component from the total change in pH. The relationship between change in P_{CO_2} and pH has a slope of −0.0075 pH units/1.0 mmHg increase in Pa_{CO_2} (12).

The mean values for $\dot{V}_{O_2}$ (L/min) and HR (beats/min) for the three experimental conditions at low, moderate, and heavy work loads were 1.281/95, 2.018/135, and 2.411/158, respectively. The average resting HR was 55 ± 6 beats/min, which reflects the excellent physical condition of the subjects and the absence of excitement prior to exercise.

Increases in CO_2 production ($\dot{V}_{CO_2}$) were also progressive as the work load under all three experimental conditions increased. The curves are significantly different ($P < 0.025$), with the $\dot{V}_{CO_2}$ curves for acute and chronic CO_2 exposure falling below the air curve. This finding agrees with those of Menn *et al.* (14) and Finkelstein *et al.* (6), who observed a CO_2 retention (decreased $\dot{V}_{CO_2}$) during exercise in hypercapnia that could not be explained by a decrease in metabolism.

Figure 3 shows a comparison of changes in Pa_{CO_2} during exercise in air and in acute and chronic hypercapnia. During air breathing, Pa_{CO_2} values showed essentially no change from the state of rest to the low work load, and then proceeded to decrease progressively with exercise to reach a low value of 32.5 mmHg at the highest work load (7.5 mmHg lower than the resting control value). During exercise at the low work load in acute and chronic hypercapnia, Pa_{CO_2} increased by 3.6 and 2.0 mmHg, respectively, and then decreased progressively to values at the highest work load that were near the mean resting control in both experimental conditions. With all work loads, the changes in Pa_{CO_2} from the resting value were smaller in prolonged than in acute hypercapnia.

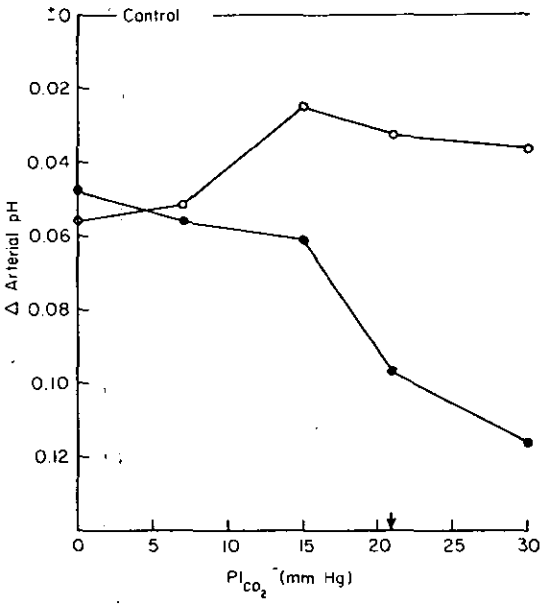

FIG. 5. Contribution of metabolic acidosis to changes in arterial pH with exercise in progressive hypercapnia (after Menn *et al.* [14]). Subjects exercised on a bicycle ergometer in upright position for 30-min periods in air and in four levels of ambient P_{CO_2} on different days. The metabolic acidosis component was calculated as described in legend for Fig. 4. The nearly identical heavy work loads in the Menn *et al.* and the present studies were performed during the same acute exposure to 21 mmHg P_{CO_2} (note arrow on abscissa). (○) Metabolic acidosis; (●) respiratory acidosis. PI_{CO_2} = 0, 8, 15, 21, 30 mmHg.

Although the Pa_{CO_2} changes were small during exercise in hypercapnia, the differences between the mean Pa_{CO_2} during acute or chronic CO_2 exposure and the corresponding Pa_{CO_2} values during air breathing increased progressively with higher work loads (Fig. 3). The differences in Pa_{CO_2} curves were highly significant ($P < 0.001$).

The changes in arterial pH during exercise in hypercapnia are shown in Fig. 4. The decreases in pH below resting control values were also progressive with increasing work loads, and were similar in magnitude at each work load under the three experimental conditions, despite the concomitant changes in Pa_{CO_2} shown in Fig. 3. The metabolic acidosis component of the pH changes was greatest during air breathing, smallest in acute hypercapnia, and intermediate in chronic hypercapnia—thus explaining the similarity in the pH values under the heavy work load for all three experimental conditions, despite quite dissimilar Pa_{CO_2} values.

Figure 5 is based on data drom the study of Menn *et al.* (14), and illustrates the contribution of metabolic acidosis to changes in arterial pH at the end of 30-min periods of heavy exercise in graded levels of hypercapnia. Each point on the graph represents the mean of seven individual measurements. The curves show that the metabolic component of the observed change in pH was considerably less with exercise in the higher levels of PI_{CO_2} than it was with exercise in air. In the Menn *et al.* study, the metabolic acidosis resulting from exercise performed during acute exposure to 21 mmHg P_{CO_2} was about 58% of that resulting from exercise in air. At a

comparably high level of exercise in the present study, the metabolic component of the change in arterial pH during acute hypercapnia was about 60% of that found during air breathing.

The only symptoms reported by our subjects during exercise in hypercapnia were occasional mild headaches and awareness of increased respiratory effort when the work load was heavy. The symptoms of air hunger and intercostal muscle pain reported by Menn *et al.* (14) in their subjects, during exercise at a heavy work load in 30 mmHg PI_{CO_2}, and at maximum exercise in 21 mmHg PI_{CO_2}, were not experienced by our subjects. Neither were the occasional premature ventricular contractions reported by Menn *et al.* (14) observed in our subjects.

Discussion and Conclusions

Analysis of the quantitative data in Figs. 1–4 indicates that some of the normal responses to graded exercise in air were significantly modified by the simultaneously imposed stress of exposure to an ambient P_{CO_2} of 21 mmHg. Of particular note was the retention of CO_2 as work increased, as indicated by a significant decrease in $\dot{V}_{CO_2}$ and increase in Pa_{CO_2}. These observations agree with the results of Menn *et al.* (14), which demonstrated progressive CO_2 retention both with submaximal and maximal exercise in increasing levels of hypercapnia. Finkelstein *et al.* (6) also reported decreased $\dot{V}_{CO_2}$ with maximum exercise during acute exposure to 16 mmHg PI_{CO_2}. Retention of CO_2 in exercise during exposure to hypercapnia indicates that alveolar ventilation does not increase sufficiently to compensate for its reduced effectiveness in CO_2 elimination.

The finding of reduced metabolic acidosis in response to heavy exercise in CO_2, as compared to that in air, may reflect decreased production of organic acids. This could be caused by a decrease in the requirement for energy obtained from anaerobic metabolism or by changes in enzyme activity. The former could be explained by improved perfusion of blood through the skeletal muscles during hypercapnia, which permits more rapid adjustment of the circulation to the demand for O_2 in the early exercise period. In support of an enzymic effect, Hughes *et al.* (10) showed that, during light exercise and voluntary hyperventilation in air (which lowered the Pa_{CO_2} to 27 mmHg), the blood lactate rose by 1.3 mmoles/L. However, no increase in lactate occurred if the Pa_{CO_2} was kept constant by the addition of CO_2 to the inspired air. Takeshita (19) likewise found that the rise in blood lactate owing to hypoxia at rest— which is in part the result of alkalemia due to hyperventilation—could be prevented by adding CO_2 to the inspired gas to keep the blood P_{CO_2} constant.

The present study demonstrates that an ambient atmosphere containing a CO_2 tension of 21 mmHg is well tolerated by a subject who is resting or engaging in strenuous steady state exercise. This general conclusion is applicable whether the CO_2 exposure is acute or chronic. In agreement with the previous reports, however, this study shows that exercise during exposure to increased ambient P_{CO_2} caused CO_2 retention and a concomitant elevation of Pa_{CO_2}. Similar interactions between the stresses of exercise and hypercapnia will become limiting at higher levels of inspired P_{CO_2}. Determination of these tolerance limits will require quantitative studies of larger groups of subjects performing graded exercise during exposure to progressively greater pressures of ambient CO_2.

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THE "CARBON DIOXIDE RESPONSE CURVE" FOR CHRONIC HYPERCAPNIA IN MAN*

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RESPIRATORY failure is usually complicated by a rising blood carbon dioxide tension (pCO_2) and, as a consequence, carbonic acid and hydrogen ion concentration increase in the body fluids. Acutely, the resulting acidosis is partially offset through the body buffers that raise the concentration of bicarbonate. Subsequently, defense of blood pH is strengthened by the generation of new bicarbonate by the kidney. This renal compensation, although much slower than the acute buffering process, is a great deal more effective in protecting blood pH.

The wide scatter of acid-base patterns reported in chronic pulmonary insufficiency, ranging from alkalosis to severe acidosis, has given ground to different views on the efficiency of the renal mechanisms.[1-7] Some suggest that full renal compensation should occur, at least up to pCO_2's of 70 mm. of mercury,[4,5,7-11] whereas others believe that hydrogen ion concentration is not returned to normal, without defining, however, the degree of the acidosis that should be expected for a given pCO_2.[12]

This question is of importance for the appraisal of the acid-base status of patients suffering from chronic lung disease. Confronted with such a case, the physician finds it difficult to decide what, in the acid-base pattern, should be attributed to hypercapnia and what is a reflection of complicating metabolic factors.[13] Knowledge of the acid-base response normally elicited by a given level of pCO_2 should allow detection and quantification of complicating acid-base disturbances and should lead, therefore, to an appropriate therapy.[13]

The recent delineation, by Schwartz et al.,[14] of the pattern of adaptation to chronic hypercapnia in the dog has provided a new approach to this problem. Unfortunately, up to now, similar data have not become available in normal man. Therefore, as an alternative approach, the acid-base status of 420 patients suffering from various degrees of chronic lung insufficiency has been reviewed. The relevance of the relations described to the normal response to chronic hypercapnia in man is evaluated in the light of the probable incidence of complicating acid-base disturbances.

METHODS

A total of 781 acid-base measurements were obtained in 420 patients over a five-year period. Both ambulatory (12 per cent) and hospitalized patients were studied; they had been referred for evaluation or treatment of chronic lung disease. No selection was made among them. The age ranged from thirty-one to eighty-five years, with a mean of fifty-eight and two-tenths years. Complete data were obtained in two thirds of the patients (281). Among them, 65 per cent were under active treatment, including oxygen, bronchodilator agents, cardiotonic steroids and diuretics, and 9 per cent had some evidence of moderate renal insufficiency (creatinine ranging between 1.1 and 1.8 mg. per 100 ml.) secondary to cardiac failure.

Samples of heparinized blood were obtained from the brachial artery through a Cournand needle. All analyses were done in duplicate. The blood pH was determined promptly, at 37.5°C., with a Radiometer glass electrode and a Radiometer IV potentiometer. Plasma total carbon dioxide content was measured by the method of van Slyke and Neill,[15] and oxyhemoglobin saturations by that of Zylstra.[16]

Blood pCO_2 and plasma bicarbonate were calculated from the Henderson–Hasselbalch equation. According to Severinghaus, pK'a of carbonic acid has been assumed to vary with pH.[17] A carbon dioxide solubility coefficient of 0.03044 has been used.

Statistical analyses were done by standard methods.[18]

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Results

In the present population, pCO_2 ranged from 39 to 77 mm. of mercury. The results were grouped according to increasing degrees of hypercapnia, each group encompassing a 2-mm. pCO_2 interval. Table 1 gives for each group the number of observations, the number of patients and the average values, plus or minus standard error (±S.E.), for blood hydrogen ion concentration [H^+], plasma bicarbonate concentration [HCO_3^-] and blood oxygen saturation. Average results for the group whose pCO_2 ranges from 39 to 41 mm. of mercury are in close agreement with previously published values for normal man.[19]

Hydrogen Ion Concentration

Figure 1 shows the relation observed between pCO_2 and hydrogen ion concentration [H^+]. It can be seen that the latter increases in direct proportion to the rise in the former. The calculated weighted regression line represented in Figure 1 has a slope of 0.30 and an intercept of 26.8. By statistical analysis (F test), it was shown that the sum of individual deviations from this line were not significantly different from 0. It is therefore apparent that the relation between hydrogen ion and carbon dioxide tension is linear.

The scatter of the data around every mean hydrogen ion concentration can be evaluated from the S.E. given in Table 1. As discussed below, this spread is probably due to the inclusion of patients whose acid-base pattern has been further distorted by superimposed acid-base disturbances. The incidence of alkalotic ([H^+] ≤ 35.7 or pH ≥ 7.45) and normal (42.7 ≥ [H^+] > 35.7 or 7.45 > pH ≥ 7.37) hydrogen ion concentrations is given in Table 2. As higher pCO_2's are reached the incidence of normal values for hydrogen ion decreases.

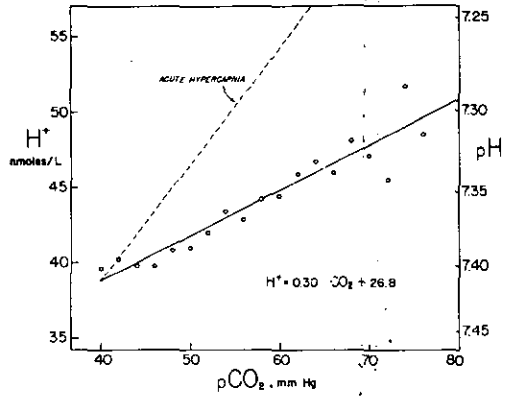

FIGURE 1. *Relation between Blood Hydrogen Ion Concentration (H^+) and pCO_2 in a Population of 420 Patients with Chronic Lung Disease.*

Results of 781 determinations of the acid-base status were grouped according to increasing degrees of hypercapnia, each group encompassing a 2-mm. pCO_2 interval. Each point represents the mean value for a given group. The solid line drawn through the points is the weighted regression line calculated from individual values. The dotted line represents the mean hydrogen ion response observed in human volunteers during acute hypercapnia.[19]

TABLE 1. *Summary of Blood Acid-Base and Oxygen Values in 420 Patients Suffering from Chronic Pulmonary Disease.*

pCO_2	No. of Observations	No. of Patients	Hydrogen Ion Concentration*	Bicarbonate Concentration*	Oxygen Saturation*
mm. Hg.			*nEq./liter*	*mEq./liter*	%
39.0–40.9	44	44	39.6±1.7	25.1±1.3	95.5± 2.0
41.0–42.9	55	52	40.2±1.8	26.0±1.3	93.5± 3.1
43.0–44.9	74	66	39.8±2.8	27.6±2.2	89.6± 7.9
45.0–46.9	91	73	39.8±3.9	28.7±2.8	87.3± 7.0
47.0–48.9	79	70	40.8±3.4	29.4±2.5	85.6± 8.5
49.0–50.9	68	60	41.0±3.6	30.3±2.8	84.3±10.1
51.0–52.9	74	59	42.0±4.2	30.9±3.2	84.7± 7.9
53.0–54.9	63	58	43.4±3.6	30.9±2.7	81.8± 7.9
55.0–56.9	45	40	42.9±4.1	32.4±3.2	79.0±12.0
57.0–58.9	38	33	44.2±4.9	32.6±3.4	75.4±13.7
59.0–60.9	44	35	44.4±4.2	33.6±3.3	74.6±10.9
61.0–62.9	32	26	45.9±5.0	33.8±3.5	72.6±14.4
63.0–64.9	18	16	46.7±4.5	33.9±3.1	72.9±11.6
65.0–66.9	11	8	46.0±3.3	35.5±2.7	67.6±14.3
67.0–68.9	18	16	48.1±6.2	35.2±4.3	68.0±17.0
69.0–70.9	7	6	47.1±3.3	36.8±2.4	74.7±20.6
71.0–72.9	7	7	45.5±2.3	38.9±2.2	71.9±18.5
73.0–74.9	9	9	51.7±8.6	35.9±5.7	61.0±16.7
75.0–76.9	4	3	48.5±1.5	38.5±1.3	81.5±15.6

*±S.E.

Plasma Bicarbonate Concentration

Figure 2 presents the pattern of bicarbonate response to increasing degrees of hypercapnia. In contrast with the linear rise of hydrogen ion concentration, bicarbonate concentration increases in a curvilinear fashion as pCO_2 rises. Through appropriate substitutions in the Henderson–Hasselbalch equation, it can be shown that, since the regression of hydrogen ion concentration on pCO_2 is linear, the relation between plasma bicarbonate and pCO_2 is best described by a hyperbola whose equation is

$$[HCO_3^-] = \frac{24.69\ pCO_2}{0.30\ pCO_2 + 26.8}.$$ *

Blood Oxygen Saturation

The average oxygen saturation for each group is given in Table 1. It can be seen that percentage saturation decreases progressively as respiratory insufficiency proceeds.

Discussion

A new approach to the evaluation of the acid-base status of patients with pulmonary insufficiency has

*The Henderson–Hasselbalch equation can be rewritten as $[H^+] = \frac{K\alpha pCO_2}{[HCO_3^-]}$, where K is the dissociation constant of carbonic acid (8.11×10^{-7}) and α the solubility coefficient of carbon dioxide in plasma (0.03044 at a temperature of 37.5°C.). If $[H^+]$ is expressed as a function of pCO_2, $[HCO_3^-] = \frac{24.69\ pCO_2}{0.30\ pCO_2 + 26.8}$. It should be noted that in the calculation of pCO_2 it has been assumed that pK' varies as a function of pH (as described above under Methods). Although such a variation slightly distorts the described hyperbolic curve, the error introduced is so small that it has been disregarded.

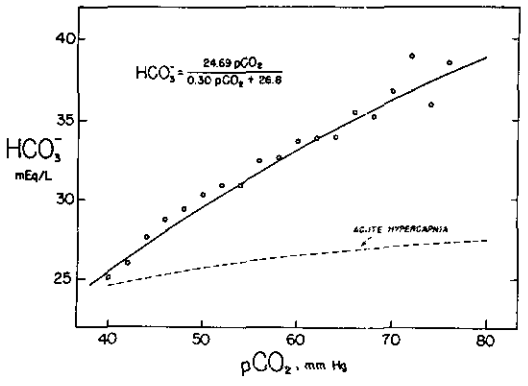

FIGURE 2. *Relation between Plasma Bicarbonate Concentration (HCO_3^-) and pCO_2 in a Population of 420 Patients with Chronic Lung Disease.*

Each point represents the average of all plasma bicarbonate concentrations observed in individual groups encompassing a 2-mm. pCO_2 interval. The solid hyperbolic curve was calculated from the weighted regression of blood hydrogen ion concentration on pCO_2 (Fig. 1) by appropriate substitutions in the Henderson–Hasselbalch equation. The dotted line represents the mean bicarbonate response curve observed in human volunteers during acute hypercapnia.[19]

recently evolved from experimental studies describing quantitatively the response of the normal organism exposed to a wide range of carbon dioxide tensions. It was shown that in the dog, plasma bicarbonate concentration rose in a curvilinear fashion as pCO_2 was acutely increased, whereas hydrogen ion concentration was linearly related to pCO_2.[20] These studies were subsequently extended to normal human volunteers.[19] An analogous curvilinear rise in plasma bicarbonate concentration was observed in response to stepwise increments in carbon dioxide tension. The relation between hydrogen ion concentration and pCO_2 was also found to be linear, every millimeter increase in pCO_2 raising the hydrogen ion concentration by 0.77 nM per liter, a value identical to that observed in the dog. In these acute studies the acid-base pattern was determined only by the characteristics of the body buffers. In chronic hypercapnia, however, additional bicarbonate is generated by the kidney so that the overall acid-base picture is considerably modified. In a subsequent set of experiments, Schwartz et al.[14] allowed dogs to achieve maximum renal compensation at different levels of pCO_2. In this way, a pattern representative of the normal response to chronic hypercapnia was defined. Here, again, plasma bicarbonate rose in a curvilinear fashion but, at every level of pCO_2, the increment exceeded largely that reported in the acute experiments. Despite this renal compensation, however, pH never returned to control levels. The relation between hydrogen ion concentration and pCO_2 was still highly linear although every millimeter rise in the latter elicited an augmentation in the former of only 0.32 nM per liter – less than half the value observed in acute hypercapnia. From these studies, Schwartz et al. defined statistically significance bands within which, for a given pCO_2, blood hydrogen ion and plasma bicarbonate concentrations were expected to fall with a probability of 95 per cent.

TABLE 2. *Incidence of Normal or Alkalotic Hydrogen ion Concentration in Patients with Chronic Lung Disease.*

pCO_2 *mm. Hg.*	PERCENTAGE OF TOTAL OBSERVATIONS/GROUP	
	$[H^+] \leq 35.7$ nM/liter $pH \geq 7.45$	*35.7 nM/liter $< [H^+] \leq 42.7$ nM/liter $7.45 > pH \geq 7.37$*
39.0–40.9	2	93
41.0–42.9	0	96
43.0–44.9	10	82
45.0–46.9	7	71
47.0–48.9	9	67
49.0–50.9	6	68
51.0–52.9	3	55
53.0–54.9	2	46
55.0–56.9	0	53
57.0–58.9	0	55
59.0–60.9	2	36
61.0–62.9	0	25
63.0–64.9	0	6
65.0–66.9	0	18
67.0–68.9	0	17
69.0–70.9	0	0
> 71	0	5

Whether the pattern of adaptation to chronic hypercapnia would be the same in man as in the dog is still a matter of speculation since long-term observations on hypercapnia in normal volunteers have not been feasible up till now. We therefore attempted, in the present study, to delineate the acid-base response of man to chronic hypercapnia by reviewing the acid-base status of patients suffering from pulmonary disease. The present data show that in a large unselected population of such patients, mean plasma bicarbonate concentration rises in a curvilinear fashion as pCO_2 increases from normal values to 77 mm. of mercury. Despite this increment, however, hydrogen ion concentration increases linearly with pCO_2, rising 0.3 nM per liter for every millimeter increment in pCO_2 – a value closely similar to that reported in dogs chronically adapted to high carbon dioxide tensions. The relevance of these relations to man's normal response to chronic hypercapnia depends on how these patients' acid-base status had been further distorted by added disturbances.

During the natural course of pulmonary disease, the normal pattern of adaptation to hypercapnia is likely to be disrupted by some superimposed acid-base disturbances. In an unselected group of patients such as ours the exact incidence of these complications is not known. If superimposed alkalosis and acidosis occurred with the same frequency and severity, the described overall relations might be taken as representative of man's normal response to chronic hypercapnia. Alternatively, if either of these two disturbances prevails, the influence of a systematic bias will have to be considered. A review of the likely causes of acid-base disturbances

suggests that, if any bias exists, it is more likely to shift the mean response curves to the alkaline rather than to the acid side. Sources of complicating alkalosis are multiple. Superimposed respiratory alkalosis is not uncommon since patients with mild hypercapnia transiently hyperventilate during arterial puncture. Many patients with chronic pulmonary disease suffer from cor pulmonale and are therefore likely to be treated with diuretics and a low-salt diet, a condition known to induce hypochloremia and metabolic alkalosis.[21,22] Similarly, a chloride-restricted diet may be expected to delay renal adaptation to a therapeutically induced lowering of pCO_2 and lead, therefore, to the so-called posthypercapneic alkalosis.[23-25] In addition, in salt-restricted patients, any other causes of chloride loss such as gastric suction or vomiting are likely to result in sustained metabolic alkalosis.[26]

In contrast with metabolic alkalosis, the frequency of complicating metabolic acidosis seems to be very low: treatment of lung insufficiency with ammonium chloride and carbonic anhydrase inhibitors is extremely uncommon in our hospital, whereas none of the other causes of metabolic acidosis, such as diarrhea, diabetic ketosis and renal insufficiency, are likely to be systematically associated with chronic pulmonary disease. Superimposed acute respiratory acidosis, on the other hand, whether secondary to an exacerbation of pre-existing lung disease or to a drug-induced depression of the respiratory center, is probably much more frequent. However, in contrast with metabolic alkalosis, which persists as long as chloride intake is restricted, superimposed acute respiratory acidosis is short-lived as a distorting factor since renal adaptive mechanisms are immediately set into motion and provide maximum adaptation within a few days.*

These considerations suggest that, if any bias exists in this population, it will probably tend to increase both blood pH and plasma bicarbonate concentration for any given pCO_2 and, as a consequence, exaggerate the degree of renal compensation. The present finding that despite maximal renal compensation hydrogen ion concentration increases in proportion to the degree of hypercapnia is therefore even more striking. It suggests that in man, just as in the dog,[14,25,27] the kidney normally fails to return the hydrogen ion concentration — that is, the pH — to control values. Thus, in uncomplicated situations, acidosis appears to be the natural companion of hypercapnia.

It should not be inferred, however, that an "acid" pH (that is, one below 7.37) is necessarily associated with any degree of hypercapnia. The width of the accepted normal pH range is such that, despite an increase above control levels, the hydrogen ion concentration of a moderately hypercapneic patient may still fall within normal limits. If a mean increase of 0.3 nM per liter per millimeter of pCO_2 is assumed, it can readily be calculated that a patient starting at a "low normal" value of 35.7 nM per liter (pH = 7.45) at a pCO_2 of 40 mm. of mercury will still have a "high normal" value of 41.7 nM per liter (pH = 7.38) at a pCO_2 of 60 mm. of mercury. Thus, in a certain number of patients, the increase in hydrogen ion concentration elicited by a rise in pCO_2 will be overlooked.

The incidence, however, of such apparently normal values in the presence of an elevated pCO_2 should be inversely proportional to the degree of hypercapnia. It was indeed calculated from the original data of Schwartz et al.[12] that 75 per cent of the dogs with a pCO_2 of 50 mm. of mercury were expected to have a hydrogen ion concentration falling within the accepted normal range. This percentage fell to 15 per cent for a pCO_2 of 60 mm. and to less than 1 per cent for one of 70 mm. of mercury.† The finding, therefore, of apparently normal hydrogen ion values in patients with mild hypercapnia otherwise free of superimposed metabolic alkalosis should not be taken as evidence against the suggestion that hypercapnia is always associated with an increase in hydrogen ion concentration. At a normal pCO_2, these subjects would be expected to have a hydrogen ion concentration falling in the lower part of the normal range. The widespread belief that up to pCO_2's of 70 mm. of mercury, full renal compensation may be achieved is probably based on the observation of such cases as well as of patients suffering from complicating metabolic alkalosis.[5,6,10]

Evidence of the failure of the kidney to achieve full compensation in chronic respiratory acidosis is present in the data reported by Refsum[5] on 210 patients. Average blood hydrogen ion concentrations given for groups encompassing a 10-mm. pCO_2 interval reveals a linear relation with pCO_2. Robin's[6] study of 156 patients is more difficult to evaluate in view of the high frequency of complicating metabolic alkalosis. This is evidenced by a 12 per cent incidence of frank alkalosis in his group versus 4 per cent in the present series. Yet the pH-CO_2 diagram presented in his paper suggests that average pH tended to fall progressively as pCO_2 increased.

As shown in Figure 3, the pattern of man's acid-base response to chronic hypercapnia is virtually identical to that of dog.[14] It is of interest that in both, the relation between hydrogen ion concentration and pCO_2 is linear by inspection and by statistical analysis. This observation suggests that in man, just as in the dog, renal compensation is equally effective over a large range of pCO_2 and does not support the view that, at pCO_2's over 70 mm. of

*It has recently been shown in dogs that the pattern of adaptation to chronic hypercapnia is not affected by severe hypoxia.[13]

†These calculated values are in reasonable agreement with the incidence of normal hydrogen ion concentrations observed at different levels of hypercapnia in the present study (Table 2).

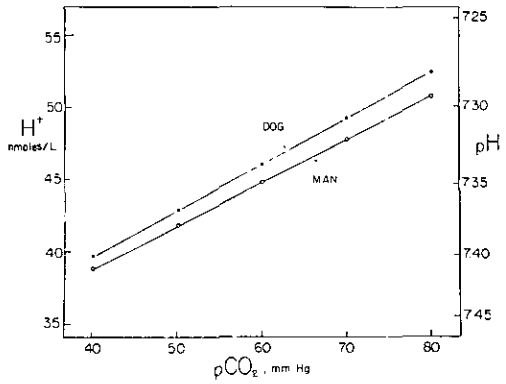

FIGURE 3. *Comparison between the Mean Hydrogen Ion (H^+) Response Line Observed in the Present Population and That Reported in Dogs during Chronic Hypercapnia of Increasing Severity.*[14]

mercury, adaptation depends solely on tissue-buffering processes.[5]

Because cases with superimposed acidosis and alkalosis are probably included in the present series, calculation of significance bands analogous to those of dogs would be meaningless. In acute hypercapnia, however, variance of hydrogen ion values at different pCO_2's is analogous in man and dog.[19,20] If it is assumed that in chronic hypercapnia also, variance of these values is the same in man as in dog, confidence limits not very different from the dog's can be derived for man (Fig. 4). It is fully recognized that final delineation of man's normal response to chronic hypercapnia will have to rest on carefully selected patients, free of complicating metabolic or acute respiratory acid-base disturbances.[14]

The usefulness of these bands in the appraisal of man's acid-base status is illustrated in Figure 4. After a control period of five to thirteen days, 6 hypercapneic patients, free of superimposed acid-base disturbances, were given for ten days 150 mg. of dichlorphenamide, a carbonic anhydrase inhibitor, per day.[28] Plasma bicarbonate concentrations before, during and five to seventeen days after treatment are plotted in relation to pCO_2 on a diagram figuring a significance band. It can readily be seen that, before dichlorphenamide therapy, all values for bicarbonate concentrations fell within the band. The acidifying effect of the drug is evidenced by a shift of the bicarbonate concentrations toward the acid side, all the values leaving the confidence limits. Discontinuation of the drug returned these values toward normal, 5 of them falling again within the significance band.

Summary and Conclusions

An attempt is made to delineate the "carbon dioxide response curve" for chronic hypercapnia in man, on the basis of a review of the acid-base status

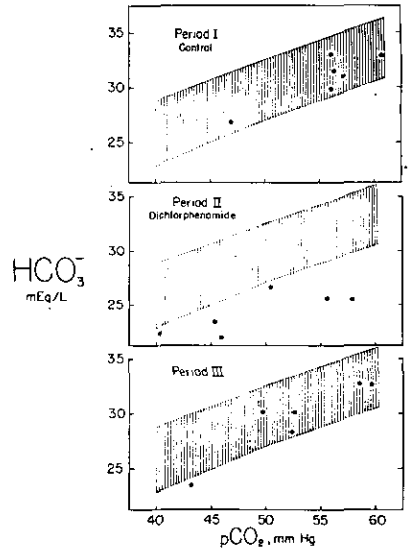

FIGURE 4. *Demonstration of the Usefulness of the "Significance Band" for the Plasma Bicarbonate Concentration (HCO_3^-) in Chronic Hypercapnia (in Uncomplicated Chronic Respiratory Acidosis, Values Are Expected to Fall within This Band with a Probability of 95 per Cent).*

Plasma bicarbonate concentrations of 6 patients with chronic hypercapnia are plotted before (Period I), during (Period II) and five to seventeen days after (Period III) a ten-day treatment with a carbonic anhydrase inhibitor, dichlorphenamide. (Note that before therapy all values fell within the "significance band.") The acidifying effect of dichlorphenamide is evidenced by a shift toward the acid side, the 6 values leaving the confidence limits. Discontinuation of the drug returned 5 of the 6 values within the band.

of 420 patients suffering from various degrees of chronic lung disease. The results of 781 arterial blood pH and total plasma carbon dioxide determinations are analyzed. Calculated plasma carbon dioxide tension (pCO_2) ranged from normal values to 77 mm. of mercury. The data show that, as pCO_2 increases, plasma bicarbonate rises in a curvilinear fashion, reaching an average value of 36.8 mEq. per liter at a pCO_2 of 70 mm. of mercury. In contrast, blood hydrogen ion concentration is linearly related to pCO_2 ($|H^+| = 0.30\ pCO_2 + 26.8$), reaching an average value of 47.1 nM per liter (pH = 7.33) at a pCO_2 of 70 mm. of mercury.

Since these data are derived from an unselected population, the incidence of superimposed acid-base disturbances is not known. From a consideration of the likely causes of complicating acid-base disturbances it seems that any systematic bias is more likely to shift the mean curves toward the alkaline rather than the acid side. Such a bias would exaggerate the degree of renal compensation. It is therefore concluded that in uncomplicated cases, acidosis is the natural companion of hypercapnia.

It is of interest that these relations between pCO_2 on the one hand and bicarbonate and hydrogen ion concentrations on the other are virtually identical to those reported in chronically hypercapneic dogs.

Significance bands for the bicarbonate response curve to chronic hypercapnia were derived for man, assuming that the confidence limits around the mean bicarbonate response curve were the same as those reported by Schwartz et al. in dogs made chronically hypercapneic. These bands are very close to those of dog. Their usefulness in the diagnosis of mixed acid-base disturbances encountered in chronic respiratory acidosis is illustrated.

We are indebted to Professor X. Aubert for assistance in the statistical analysis of the data.

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COLD WATER EXPOSURE AND THERMAL BALANCE

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3

COLD WATER EXPOSURE AND THERMAL BALANCE

PAUL WEBB

Most of the physiologic literature deals with cold water immersion of men without thermal protection. This collection starts with a paper by that pioneer in all things underwater, A. R. Behnke, co-authored by C. P. Yaglou, who contributed greatly to thermal physiology. Their immersions in cold water bordered on the heroic, and their temperature measurements in mouth, stomach, and rectum set a standard for thoroughness, as well as showing how fast the body core can cool.

A few years later, Pugh and Edholm (1955) answered the question of how certain people, in this case swimmers of the ever-cold English channel, can endure long periods of cold water exposure which would send most people into severe hypothermia. Those who endure are not only fat, they can generate a high level of heat from sustained muscular effort. Carlson, et al. (1958) agreed that body fat is an effective insulation, but that total insulation involves other elements, presumably circulatory; they calculated tissue conductances from metabolic heat produced and fall in body temperature during immersions in a cold tub.

Out in the real world, Korean and Japanese women, the ama, have been diving for pearls, summer and winter, for centuries; as S. K. Hong and colleagues have shown (Kang et al., 1965), these women stop diving when their internal temperatures reach 35°C. This is the temperature which marks the beginning of clinical hypothermia. There are many discussions of hypothermia, and a recent one by Golden (1972) is included here to describe how it occurs, its diagnosis, and its treatment.

The modern literature on survival, failure to survive, and accidental cold water immersion begins with Molnar's 1946 article, based on World War II experience with ship sinkings. A more recent analytical report (Hayward, Eckerson, and Collis, 1975) quantifies metabolic response and the fall in body temperature for men in life jackets in cold ocean water. (A complete and authoritative source is W. R. Keatinge's *Survival in Cold Water*. Oxford,Blackwell, 1969.)

Divers, of course, do not work in cold water without thermal protection. The modern classic on thermal protection in Beckman's 1967 article.

Finally, there are studies of thermal balance in hyperbaric gaseous environments. An early American report from a saturation dive is by Raymond, et al. (1968). A more recent French study by Varène, et al. (1976) defines heat exchange and thermal balance across a wide range of pressures. Heat loss from the respiratory tract increases remarkably in hyperbaric environments, as measured by my laboratory (Webb and Annis, 1966). The report is reproduced here because it is often cited but hard to find as a Navy contractor's report. An analytical treatment of the hyperbaric environment appears in the final paper (Webb, 1970).

COLD WATER EXPOSURE AND THERMAL BALANCE

PAUL WEBB

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Beckman E. L.: Thermal protective suits for underwater swimmers. *Mil Med* 1967; 132:195–209. Copyright 1967, Assn. of Military Surgeons of the U.S.

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IN: Mil. Med. 1967; 132:195–209.

Thermal Protective Suits for Underwater Swimmers

Capt. E. L. Beckman, MC, USN*

Abstract

An analysis of the problems of maintaining the thermal balance of underwater swimmers is presented. Current and planned developments to provide the necessary thermal protective equipment are described. A satisfactory garment for maintaining the thermal balance of underwater swimmers during a 4-hour work period in water at temperatures down to 29°F. must include both an insulative layer and a source of supplemental heating. The insulative layer must be as effective at depth as the popular ¼" unicellular, foam neoprene skin divers "wetsuit" in shallow water. A fabric in which the insulative value is independent of pressure change must be developed. In addition, a system of supplemental heating must be developed to supply the swimmer with approximately 350 to 500 thermal watts per hour. An electrical, resistance-wire heating system with a silver zinc battery for power was integrated with a "constant volume," pressure-compensated, insulative garment for use by SEALAB II aquanauts. This development is described in addition to the thermal protective garments planned for use by SEALAB III aquanauts which include a liquid heating system powered by an isotopic thermal generator.

Introduction

UNTIL VERY recently, the realm of Neptune was an inner sanctum, inaccessible to any but the most rigorous. The ability to withstand rigors was a prerequisite for admission to the fraternity of divers. However, marine scientists, engineers, and biologists who now find the need to penetrate inner space a part of their profession, have neither the desire nor the constitution to demonstrate their physical prowess as a prerequisite for their job. Just as the intrepid airmen of 40 years past begrudgingly admitted their need for protective, life-support equipment, so also divers of today are accepting the fact that their intrusion into the hostile environment of inner space can best be accomplished with the help of more adequate life support equipment.

Capt. Beckman received his B.S. and M.D. degrees from Northwestern Univ. and an M.S. degree from the Univ. of Southern Calif. Since he began his Navy career in 1941, Capt. Beckman has been Project Officer for various aviation medical installations. In 1961, he was appointed Project Officer, Naval Medical Research Institute, and successively appointed Head, Aviation Medicine Div.; Head, Environmental Stress Div.; and Director, Physiological Sciences Dept.

The need for such new equipment is being accelerated by the demands of the Navy's Deep Submergence Systems Program wherein divers are asked to carry out longer work assignments and to do tasks which require optimal psychomotor skills and maximal cerebration. Thus, the present trend in diving demands that better thermal protective clothing and breathing systems be provided.

The thermal environment in which the U. S. Navy underwater swimmer or diver must work is, in general, that of the continental shelf of North America. The pressure depth may reach 1,000 ft. and the sea water temperatures in certain areas may reach −2°C. (+28.4°F.) at shallow depths. On the deeper slopes of the continental shelf 5°C. (41°F.) is a more usual temperature. The length of the dive is at present limited by the thermal debt.

The present requirement for underwater life support systems requires the capability for free swimming as well as "hookah" diving with the air supplied through a hose. The capability to support a work period "outside" for 4 hours is also a design requirement. The activity level of work may vary from that of the relatively inactive scientific observer, to the rigorous work of the underwater construction diver. The life support system therefore must be designed to provide thermal support

* Presently assigned to NASA Manned Spacecraft Center, Houston, Tex.

Presented at the American Institute of Aeronautics and Astronautics meeting in Los Angeles, Calif., August 1966.

TABLE I

CONVERSION FACTORS

PHYSIOLOGISTS	ENGINEERS
Power	
1 Kilogram calorie/hr	=3.97 BTU/hr
1 Kilogram calorie/hr	=1.16 Watts
Work	
I Kilogram calorie	=3.97 BTU
I Kilogram calorie	=1.16 Watt Hr
Insulation	
1 CLO=0.18° C per kcal/ m^2/hr	=0.88° F per BTU/sq. ft./hr
1 CLO is that insulation which will transfer 5.56 kcal/m^2/hr/° C	=1.14 BTU/sq. ft./hr/° F

within these extremes of temperature, depth, and time.

Since the physical phenomena related to heat transfer are described differently by physiologists and engineers, Table I is given as a ready reference.

It is readily appreciated by anyone living in the temperate climate that the loss of body heat in local areas produces a loss of finger dexterity. Likewise, most people know from personal experience that general loss of body heat decreases cerebration and physical ability. The recent deep diving studies carried out by Hempleman[1] suggested that hypothermia adversely affects decompression and increases the incidence of "bends." Thus, there is a specific need to improve life support systems for the diver working in cold water.

Physical Factors Relating to Body Heat Loss

The loss of body heat from a diver to the enveloping cold water is governed by the same laws of thermodynamics that relate an ordinary physical body to its environment and the difference in temperature between the body and its surrounding water becomes the primary controlling factor.

The physical description of the human body in thermodynamic terms relates to the maximum temperature of the body, i.e., approximately 37°C. (98.6°F.) which physiologists call the "core" temperature. The skin temperatures of the body vary with the environment and in general are higher toward the central portion of the body and lower toward the extremities. The average human, by preference, maintains a mean skin temperature of 33°C. (91.4°F.) but accepts a minimal mean comfort temperature of 31°C. (87.8°F)[2]. When the skin temperature drops to approximately 13°C. (55.4°F.), the cold becomes painful and nerve damage ensues. The preferred temperature distribution and rates of heat loss by body areas for unacclimatized subjects as measured by Kerslake[2] are tabulated in Table II.

This table shows the temperature gradient from the torso and head to the hands and feet. The rates of heat loss from the various areas of the body for a resting subject are likewise shown and are seen to differ sharply from the rates of heat loss per unit area of these body compartments. The rates of heat loss per unit area of the hands and lower arms are surprisingly high when compared with the trunk and head surfaces. These data relate directly to the heat required per unit area for replacement therapy and correspond proportionally to the amounts of heat per unit area that must be replaced.

Another physical factor of importance in controlling the thermal balance is the heat content of the body. This relates, of course, to the specific heat. Although this dimension varies with different tissues, the mean specific

TABLE II

PROBABLE PREFERRED DISTRIBUTION OF SKIN TEMPERATURE AND HEAT LOSS FOR UNACCLIMATIZED SUBJECTS. (ABOUT 90% OF THE HEAT IS LOST AS SENSIBLE HEAT, THE REMAINDER BY EVAPORATION.)

Region	Area m^2	° F. Temperature	Heat Loss	
			kcal/hr	kcal/m^2/hr
Head	0.20	34.6	8	41
Trunk	0.70	34.6	29	41
Thighs	0.33	33.0	12	36
Calves	0.20	30.8	15	75
Feet	0.12	28.6	10	83
Arms	0.10	33.0	8	80
Forearms	0.08	30.8	9	113
Hands	0.07	28.6	8	114

TABLE III

PROPERTIES OF PURE GASES AND SELECTED MIXTURES OF GASES AT 27° C. (80° F. or 300° K), 1 ATMA*

Gases	Molecular Weight	Specific Heat—Cp		Density—ρ		ρCp	
		cal/gm° F	BTU/lb° F	gm/l	lb/ft³	cal/1° C	BTU/ft³ ° F
O_2	32.00	0.2198	0.2198	1.3026	0.0812	0.2863	0.0178
N_2	28.02	0.2486	0.2486	1.1438	0.0713	0.2843	0.0177
He	4.00	1.242	1.242	0.1684	0.0105	0.2092	0.0130
SF_6	146.07	0.159	0.159	6.0287	0.3758	0.9586	0.0598
Mixtures							
Air		0.2402	0.2402	1.1791	0.0735	0.2832	0.0177
20% O_2, 80% He		0.5608	0.5608	0.3986	0.0246	0.2235	0.0138
20% O_2, 80% SF_6		0.1621	0.1621	5.0838	0.3169	0.8241	0.0514
4% O_2, 96% He		0.9320	0.9320	0.2137	0.0133	0.1992	0.0124

* 1 ATMA = 1 atmosphere of pressure under absolute conditions, i.e., = 14.7 PSIA or 760 mm. Hg.

heat of the average human body is taken to be .83 kcal/kg/°C. Since the critical human hypothermic temperature for consciousness is 30°C. (86°F.), or a decrease of mean temperature of 7°C. (12.6°F.), then a loss of body heat of only 407 kcal (7°C. × 70 kg × .83 = 407 kcal) could cause a critical hypothermia.

The physiological factors which control the body temperature relate to the energy utilizing processes by which heat is generated in or lost from the body. There are three principle avenues of heat loss during immersion: (1) the process of respiration; (2) heat loss through the shell of the body by conduction-convection; and, (3) heat loss by urination and sweating.

Heat Loss Through Respiration During Immersion

The inspired air is heated in the lungs approximately to core temperature, is humidified approximately to saturation, and then expired with the resultant loss of the heat transferred from the lungs to the expired air volume. Physiologically, it has been demonstrated that the amount of this heat loss is proportional to the volume of air breathed per minute. This is based upon the observation that respiratory minute volume is proportional to the oxygen required to provide the energy for this work. Webb and Annis[3] have recently measured the respiratory heat losses which occur when gases of different specific heats and different densities are breathed. They studied various gas mixtures with different physical characteristics as shown in Table III.

They observed that the respiratory heat loss was a function of the specific heat of the gas times the density and they demonstrated that whereas divers breathing air at 1 ATMA pressure, lost approximately 10% of their metabolic heat through respiration, the same men breathing a more dense gas mixture increased their respiratory heat loss up to a maximum of 28% of their total metabolic heat production when breathing an HeO_2 mixture at 7 ATMA. This relationship is shown in Fig. 1. It can be predicted from this graph that if the function of ρCp is increased even more, which would occur when a diver breathes a mixture of He/O_2 at an ambient pressure of 650′ of water then the respiratory heat loss might approximate 50% of the thermal output of the body. This high respiratory heat loss must therefore be anticipated in the SEALAB III experiments.

Heat Loss Through The Skin During Immersion

The second mechanism of heat loss from the body is by conduction-convection transfer from the skin to the surrounding media. The amount of heat lost through this method is proportional to the temperature gradient between the skin and the surrounding environment, i.e., air or water. The rate of heat transfer is then controlled by the insulative value

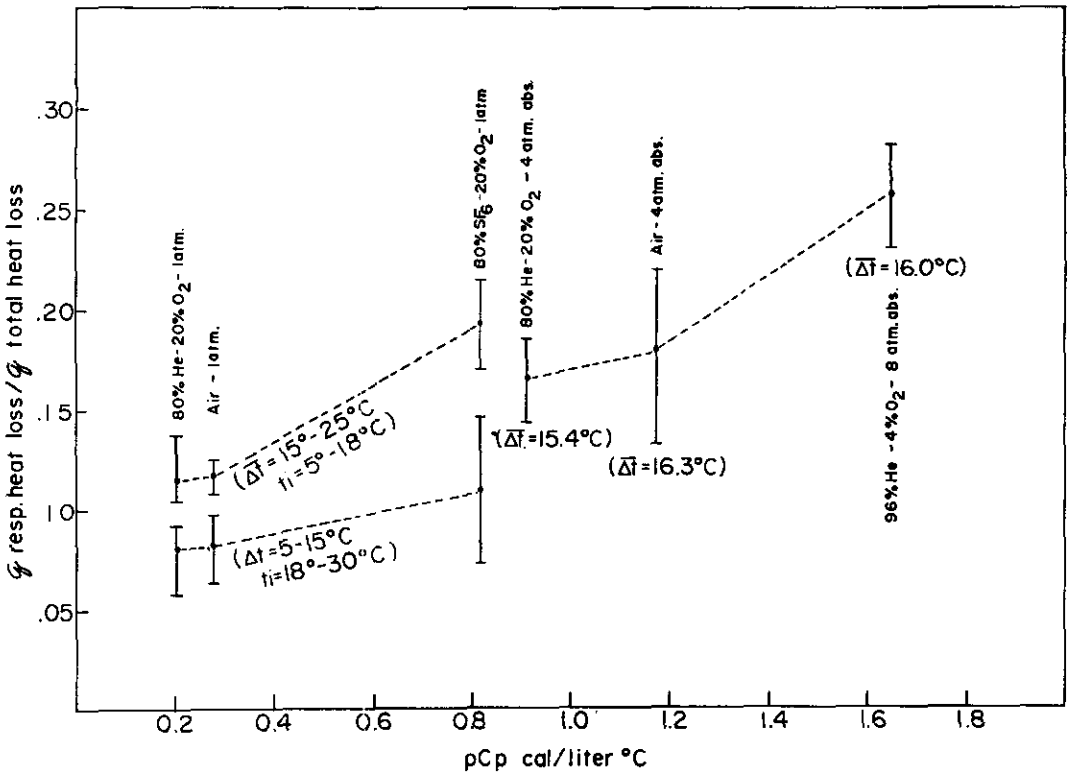


Fig. 1. The fraction of the respiratory heat loss to total heat loss is plotted as a function of PCp of the gas mixture. The greater the product of the specific heat and the density of the gas mixture, the greater the fraction of total heat loss is taken by respiratory heat loss.

of the body shell of skin and adipose tissue, the rate at which heat is conducted to the skin via the underlying vascular system, and the thermal capacity and conductivity of the environment. The rate of heat loss is limited by vasoconstriction of the blood vessels of the "shell" tissues of the body and by the thickness of the insulative skin and underlying adipose tissue. When skin temperature is decreased below a temperature of approximately 29°C. (84.2°F.) the peripheral blood vessels of skin and the adipose tissue begin to constrict and become maximally constricted with a further fall in skin temperature of a few degrees. The thermal conductivity of the skin varies with the degree of vasoconstriction and has been found during water immersion to vary with the temperature of the water from a value of 33.0 kcal/m²/hr/°C for an obese subject resting in 36°C. (96.8°F.) water down to 2.2 kcal/m²/hr/°C for the same subject resting in 10°C. (50°F.) water.[4] Thermal conductivity values of subjects tested in our laboratory fall midway between these extreme values. It is of interest that the thermal conductivity of fresh human adipose tissue and wet muscle when tested in vitro were 14.4 and 39.6 kcal/m²/hr/°C/cm respectively, (Henriques).[5] This can be compared with the thermal conductivity of water at 53 kcal/m²/hr (CUSP).[6]

The body likewise has a diuretic heat loss which is normally of small magnitude but may be significant under certain circumstances. There is a diuretic effect from immersion in water and in response to cold which increases the urine output. Experiments conducted by Beckman *et al.*[7] showed that the urinary volume may be increased to 1-3 liters in 3 hours due to immersion and chilling. The excretion of two liters of urine by a diver in 10°C. (50°F.) water would theoretically be a sufficient heat loss to decrease the mean body temperature by 1°C. (1.8°F.).

Heat Generation by the Body

The heat lost from the body is counteracted by the heat chemically generated within the body. The normal processes of life, i.e., digestion, conversion of carbohydrates to fats, the many chemical processes of the liver, the continual chemical processes which underlie cerebration of the brain, chemical functions of the kidneys, the rebuilding of muscle tissue, and the continuing action of the heart, i.e., the so-called basal metabolism of the body, generate approximately 40 kcal/m²/hr of heat when the 70 kgm subject is lying down and has not had any food for twelve hours. When the man is merely seated in a chair and resting comfortably, the increase in muscle tone required to maintain posture in the chair increases the metabolic thermal ouput to approximately 50 kcal/m²/hr. It has been established in normal physiological studies that the work done in basal metabolism and during the muscle contraction of exercises can be equated with the amount of O_2 consumed by the body. It has further been found that approximately 5 kcal of heat are generated by each liter of O_2 consumed. On the basis of these approximations, then the body heat generated can be approximated under various conditions of exercise by measuring oxygen consumption.[8]

The balance of the heat lost from the body and the heat gained from basal and muscle metabolism within the body determines the body temperature. Since the rates of heat loss and heat gain of the body may be of large magnitude (i.e., during strenuous work or immersion in cold water), the body temperature is, therefore, a delicate and sensitive indicator of the state of thermal balance.

Rates of Heat Loss From the Nude or Clothed Body During Immersion in Cold Water

Because of the high specific heat and the high thermal conductivity of water, the rate of heat loss may be very rapid when a human is immersed in cold water. The skin temperature under these circumstances rapidly approximates the temperature of water and for ordinary considerations may be assumed to equate

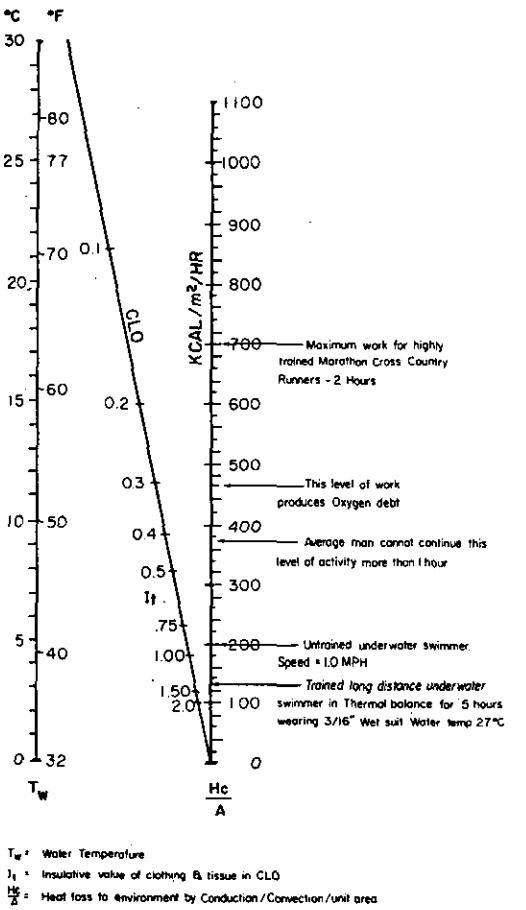


Fig. 2. Nomogram relating Water Temperature, Insulation of Clothing, and Rate of Body Heat loss during underwater swimming.

with water temperatures. This relationship is shown in Figure 2. In this nomogram, adapted from Smith and Hames,[9] the water temperature T_w is related to the heat loss per unit area from the skin by conduction-convection to the water environment and by inference to the insulation of the body surface described in CLO*[10] units. On the right bar of the nomogram, the heat loss is equated to the heat gen-

* CLO is a unit of insulation defined by Gagge, Burton and Bazett[10] as

$$\frac{0.18^\circ \text{ C.}}{\text{kcal/m}^2\text{/hr}} \quad \text{or} \quad \frac{0.88^\circ \text{ F.}}{\text{BTU/hr/sq. ft.}}$$

or that insulation which allows the heat transfer of 5.55 kcal/sq.m/hr at a temperature gradient of 1° C. (1.8° F.). In general, 1 CLO unit of thermal insulation will maintain a resting-sitting man, whose metabolism is 50 kcal/m²/hr indefinitely comfortable in an environment of 22° C. (70° F.) with relative humidity of less than 50 per cent and an air movement of 20 ft./min.

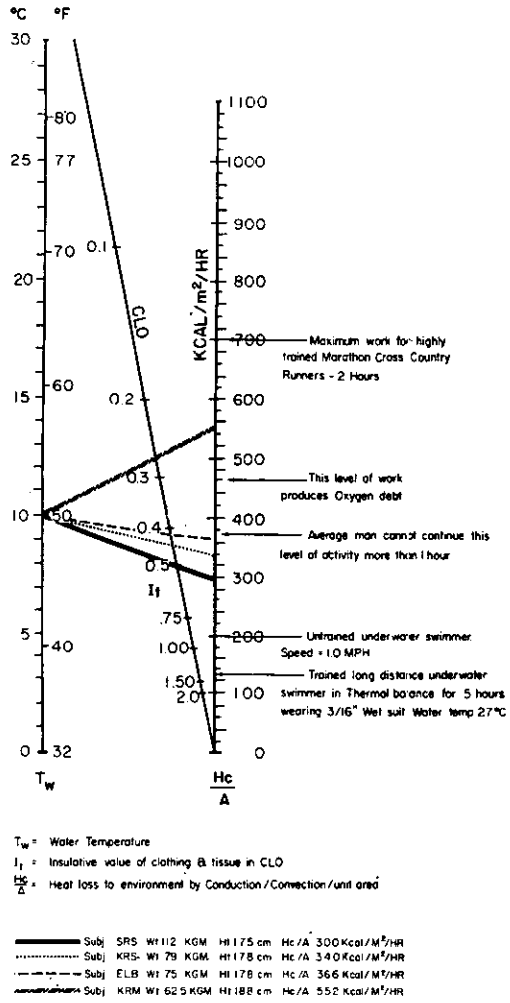


Fig. 3. Rates of Conductive-Convective Heat Transfer to Water at 10°C. from 4 Nude Subjects Immersed to Neck Level.

erated at various levels of work which the human can accomplish. It can be seen from this nomogram that the maximum human work level (i.e., that of a highly trained marathon, cross-country runner) is equal to 700 kcal/m²/hr at which work level these athletes can run for approximately two hours. The surface area of an average 70 kgm man is 1.8 square meters so that such a 70 kgm runner would generate approximately 1,260 kcal of heat per hour. Such runners are exceptionally well trained and even they must be sustained with water and glucose while running. The level of work which the average man can continue for one hour is less than 400 kcal/m². Underwater swimmers of the Underwater Demolition Teams are expected to swim at a speed of 1 Mi/hr at which level of activity they would generate approximately 200 kcal/m²/hr (Morehouse).[11]

The importance of this relationship becomes more meaningful in terms of the underwater swimmer in Figure 3 where the heat losses of four subjects immersed in 10°C. (50°F.) water are plotted on the basic nomogram. These subjects varied from a tall asthenic man who lost heat at a rate of approximately 550 kcal/m²/hr to a pyknic man who lost heat at a rate of only 300 kcal/m²/hr. It can be readily seen from this nomogram that none of these subjects could maintain their body heat by exercise or shivering so as to maintain sufficient heat to offset their heat loss. In addition, the effective insulation of the various subjects is seen to vary from a maximum of .5 CLO for the obese subject to .27 CLO for the thin subject. These differences in body skin and subcutaneous insulation represent the average ranges of insulation of the cold vasoconstricted skin. These subjects were also immersed in water at various graded temperatures and the heat loss measured and plotted on the heat loss nomogram as shown for one subject in Fig. 4. The heat loss decreased with increasing temperatures. However, for these water temperatures, the insulative values of the skin remain approximately constant for each subject.

The heat loss of one subject was determined while completely immersed and wearing heated garments under a wet suit. It was observed that this total heat loss varied only between 230 and 300 kcal/m²/hr regardless of whether his heat was generated by exercise or was supplied to the electrically heated or water heated suit. The effective insulation varied from only approximately .6 to .72 CLO (Fig. 5). The garments consisted of a 3/16" unicellular neoprene foamed (UNF) underwater swimmers wetsuit worn over an electrically heated or a water heated undergarment. The insulative value of the UNF 3/16" wetsuit measured on a copper manikin[12] (Table IV) was found to be approximately 0.6 CLO insulation (i.e., 0.78 minus .14 CLO). Since insulation is analogous to series resistances in an electrical circuit,

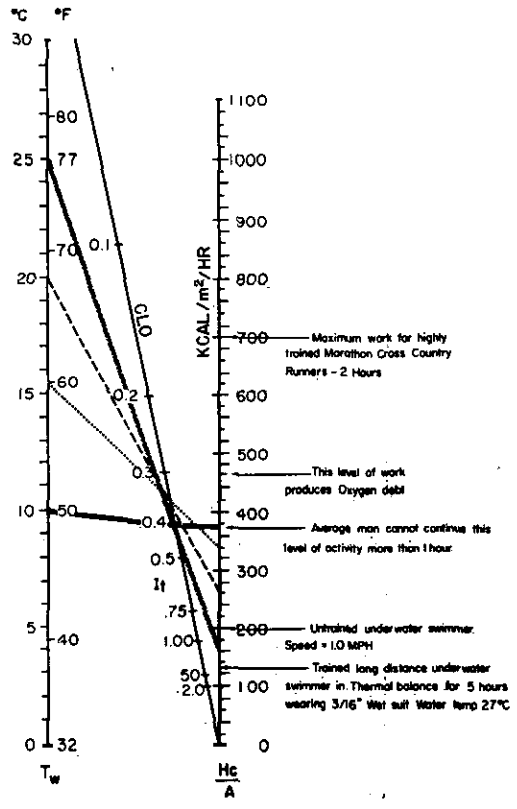


Fig. 4. Rates of Conductive-Convective Heat Transfer to Water at Various Temperatures of One Nude Subject Immersed to Neck Level.

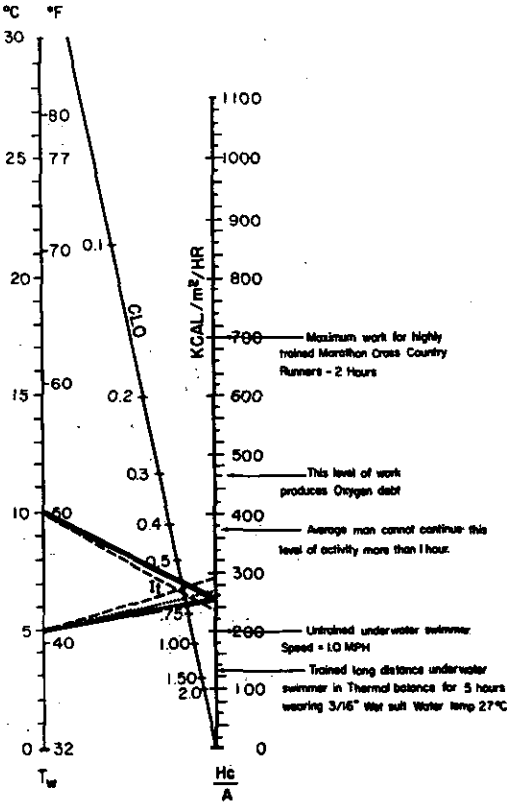


Fig. 5. Rates of Conductive-Convective Heat Transfer to Water at Various Temperatures from Submerged Subject Wearing Various Suit Assemblies.

TABLE IV

TOTAL INSULATING VALUES IN AIR AND WATER* (CLO UNITS)

Suit	Air	Still Water	Water Flowing 1 gpm	Rapidly Stirred Water
Nude Copper Manikin	0.62	0.14	—	0.11
Navy MK5a Dry Type Anti-exposure Suit	2.05	0.56	0.57	—
Underwater Swimmers Wetsuit (¼" Foamed Neoprene)	1.48	0.76	0.77	0.71
Underwater Swimmers Wetsuit ($\frac{3}{16}$" Foamed Neoprene)	1.32	—	0.78	—

* Tests conducted at the U. S. Army Research Institute of Environmental Medicine, Natick, Massachusetts, November, 1964.

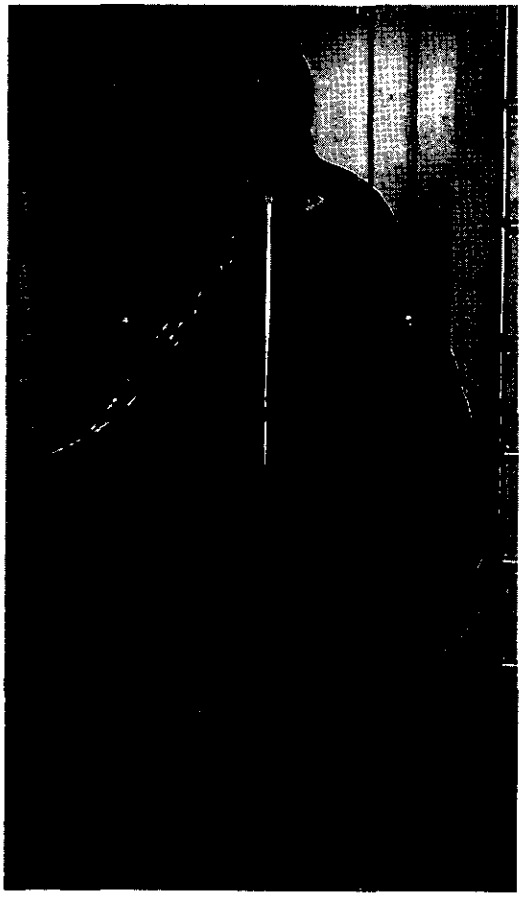


Fig. 6. Subject Wearing Four ¼" UNF Tailored Wetsuits for Tests of Optimal Underwear Insulation.

then the insulative value of unicellular underwater swimmers wetsuits and the heating garments would be additive to the insulation of the skin. However, it can be seen from Fig. 5 that the total insulation of the body plus the 3/16" wetsuit and undergarments was .6-.72 CLO whereas the insulation of the skin of the same subject immersed nude in cold water had an insulative value of approximately .4 CLO (as seen in Figs. 4 and 5). This difference is due to the fact that the skin was warmed by exercising or by the heating system to above the vasoconstrictive temperature of 30°C. (86°F.) so that the insulative value of the skin decreased. Thus, in designing a thermal protective garment for underwater swimmers, the effective CLO value of such a garment must be expected to be approximately the same value as shown in Figure 5. From these nomograms, it can likewise be seen that the rate of heat loss from the body immersed in water at temperatures below 10°C. (50°F.) will be greater than the amount of heat which can be generated by exercise for any prolonged period of time and much greater than the 50 kcal/m²/hr which is generated by the relatively inactive diver when doing skilled manual manipulations under water.

The Use of Insulative Garments to Limit Heat Loss

It is, therefore, apparent that some mechanism is needed to maintain the body temperature when the diver is working in cold water. There are two mechanisms which can be utilized: (1) to further limit the rate of heat loss by improved insulation, and (2) by supplying replacement heat. It has already been seen that varying the adiposity of the subject adds little effective insulation (Fig. 3—SRS 0.5 CLO). In an attempt to evaluate the feasibility of increasing the external insulation, a four-layer wetsuit was fashioned of ¼" UNF (Fig. 6). The subjects were immersed in 5°C. (41°F.) water, for a mean of five hours and were able to maintain body heat, but the hands and feet chilled to pain threshold. This suit provided a mean of 2.64 CLO of insulation to the five subjects, which was adequate thermal protection for the body. However, the suit was so bulky and ponderous as to effectively immobilize the subject, and had approximately 80 lbs of positive buoyancy.

The high rate of heat loss from hands and feet as shown in Table II cannot be effectively controlled by increased thickness of insulation on the basis of geometry. Figure 7 shows the relationship between thickness of insulation and effectiveness of insulation in CLO when applied to various geometric shapes and demonstrates that insulation of small diameter cylinders such as fingers cannot be efficiently increased above a ½" in diameter (van Dilla).[13] For this reason, provision of adequate insulation for fingers, hands, and feet becomes an insurmountable problem.

In addition to the geometrical limitations of insulation, the insulation effectiveness of a diver's wetsuit is adversely affected by the pressure of the water. The magnitude of this effect

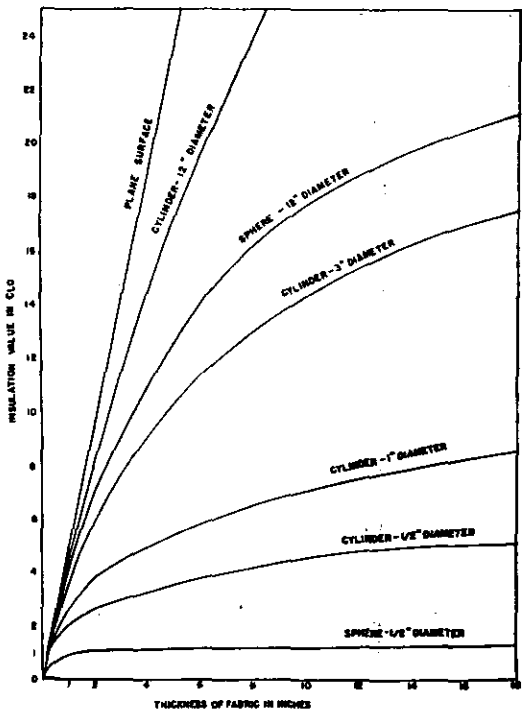


Fig. 7. Insulation of ideal fabric on a plane, cylinders, and spheres. From van Dilla, *et al.*[13]

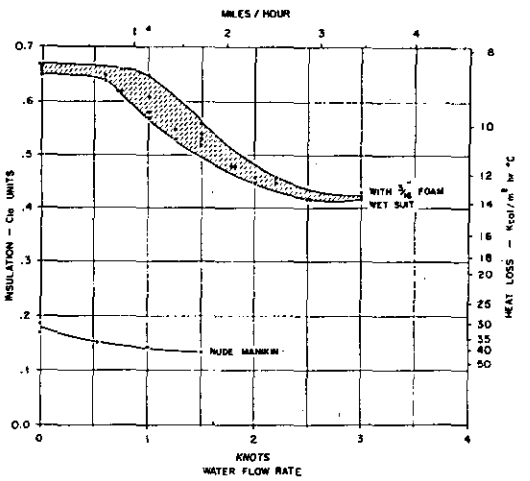


Fig. 8. Graph showing decrease in effective insulation of boundary layer of nude manikin and boundary layer plus wet suit on garmented manikin with respect to velocity of water flow.

is recorded in Table V by Betts[14] which shows that the insulation of a ¼" unicellular neoprene foamed wetsuit decreased in 50 per cent when the pressure was increased from the surface to a depth of 66'. Thus, the pressure effect upon insulation must be counteracted in order to provide an insulative garment effective at depth.

In addition, the effective insulation of a UNF wetsuit was found, by Goldman[15] (Fig. 8), to decrease as the velocity of water flowing over its surface was increased. The change in effective insulation was measured on a copper manikin immersed in water. Water was flowed past the manikin at controlled velocities. The combined insulation of the surface of the manikin and the 3/16" UNF wetsuit was found to decrease from approximately .65 CLO at a water velocity of 0 to ½ knot down to .42 CLO at 2.5 knots. This loss of effective insulation was due both to the compression of the insulative layer by ram pressure on the suit plus an increased rate of heat transfer as the velocity of flow past the manikin decreased the effective boundary layer. A similar effect of a smaller magnitude was noted when the copper manikin was studied without the suit which relates only to boundary layer phenomena.

When the water velocity, pressure, and geometrical limitations of air containing insulations are considered and added to the projected effects of the respiratory heat loss with added depths, it is apparent that an insulative

TABLE V

VARIATION IN INSULATION (IN CLO) OF UNICELLULAR NEOPRENE DIVER'S WETSUITS WITH DEPTH

Type of Suit Fabric	Surface	33 ft.	66 ft.	99 ft.	132 ft.	165 ft.
¼" double skin	.59	.38	.29	.22	.18	.14
¼" nylon lined	.59	.34	.27	.22	.18	.15
3/16" double skin	.45	.28	.21	.17	.14	.11
3/16" single skin	.46	.26	.20	.15	.12	.10

From Betts,[14] John, "Properties of Neoprene Suits" paper presented to British Sub-Aqua Club Scientific & Technical Group, August 1965.

TABLE VI

COMPARISON OF VARIOUS THERMAL SUPPORT-SYSTEMS FOR DIVERS

Thermal System	Reactants	Product	Power or Energy Density	Estimated Wt of 100 W/Hr Power Unit in Kg.	Duration of Power Cycle	Stage of Development	Estimate Cost of Power Unit in $ (Excluding Development Costs)
Wet Suit	¼" Unicellular Foamed Neoprene Divers Wetsuit	Insulation	.05 W/gm (Equivalent)	2.0		In Use	75.00
Secondary Battery	Silver-Zinc	Electricity	.1–.2 whr/gm	3.0	5 hrs	Evaluation	250.00†
	Silver-Cadmium	Electricity	.08–.16 whr/gm*	4.0	5 hrs	Evaluation	400.00†
Thermo-Chemical	$Mg+H_2O \xrightarrow{FE} MgO+H_2+[H]$	Heat	3.8 whr/gm*	2.0	5 hrs	Development	5.00‡
Fuel Cell	$NaAlH_4+2H_2O \rightarrow NaAlO_2+4H_2$ $2H_2+O_2 \rightarrow H_2O+[H]$	Heat	4.7 whr/gm*	35.0	300 hrs	Development	50,000.00‡
Radio Isotope	Plutonium—238	Heat	.55 W/gm**	8.0°	89 yrs	Development	250,000.00†
	Polonium—210	Heat	141.0 W/gm**	10.0°	0.4 yrs	Research	20,000.00†
	Thulium 170–171	Heat	.1–2.0 W/gm**	8.0°	.4–2.0 yrs	Research	50,000.00†

* Measured.
** Theoretical.
† Requires use of resistance heating suit Wt @ 2 Kg plus outer insulative garment @ 2 Kg = 4 Kg.
‡ Requires use of water conditioned suit Wt @ 3 Kg plus outer insulative garment @ 2 Kg = 5 Kg.
° Includes shielding.

layer, per se, will be inadequate to meet the requirement for maintaining thermal balance in underwater swimmers.

The Use of Replacement Heating Systems

Therefore, it is obviously necessary to replace the heat loss. Any system designed to replace heat must be considered in terms of: (1) the heat generation system; (2) the heat distribution system; and, (3) the heat transfer system. The present exploitation of "power conversion systems" for space application would immediately suggest that a power source for such replacement heating for divers would be a simple problem. This would be particularly true since divers must maintain neutral buoyancy while underwater so that the buoyant effect of their insulating garment must be counterbalanced by a weighting system, conventionally a lead-weighted belt. Thus, the substitution of a power source for the lead weights would be an obvious solution. The power densities of silver zinc and silver cadmium secondary batteries have been increased significantly so that such cells could be utilized for electrical resistance heating without a significant limitation from bulk or weight. Exothermic chemical processes would seem promising but have proven disappointing to date. Utilization of the Peltier effect for heat generation would likewise seem possible but such units are still too bulky and inefficient. Because of the high thermal energy release of radioisotopes, isotopic thermal generators offer the best compromise in terms of power supplied, weight and bulk. The relative merit of various power sources for thermal power supplied for divers is shown in Table VI.[7] The comparative values for different isotopes for thermal power generators are shown in Table VII.[16,17,18,19]

Methods of distributing heat to the body are limited by the maximum temperature and thermal flux that the skin (epidermis and dermis) will tolerate without producing pain or tissue damage. Stoll and Greene[20] measured the threshold for pain and tissue damage of human skin heated by thermal radiation. At low rates of heating, pain was perceived at a skin temperature of 43.7°C. (110.7°F.) after

TABLE VII

RADIOISOTOPES FOR USE AS ISOTOPIC THERMAL AND POWER GENERATOR FOR FREE DIVING

Radioisotope Fuel	Symbol	Half Life (Years)	Initial Power Density Watts/GM	Cost $ Per Watt		Major Radiations
				Present	Planned	
Plutonium	PU 238	89.0	0.55	1,000.00	53.00	Alpha, Neutron, Gamma
Thulium	TM 170	.4	2.0	20.00	5.00	Beta, Bremstrahlung
Thulium	TM 171	2.0	0.1	400–1,000.00	100.00	Beta, Bremstrahlung
Polonium	PO 210	0.38	141.0	780.00	10.00	Alpha
Promethium	PM 147	2.5	0.36	4,900.00	93.00	Beta, Bremstrahlung
Thallium	TL 204	4.0	.67	100.00		Beta, Bremstrahlung
Curium	CM 244	18.0	2.8		480.00	Alpha, Neutrons
Curium	CM 242	0.45	121.0		17.00	Alpha, Neutrons
Cesium	CS 137	30.0	0.2	21.00	21.00	Beta, X, (Gamma)
Cerium	CE 144	0.78	25.0		1.00	Beta, X, (Gamma)
Strontium	SR 90	28.0	0.93	20.00	1.00	Beta, X, (Gamma)

29 minutes at an irradiance of only 22 mcal/cm²/sec. (792 kcal/m²/hr or 921 watts). Although tissue damage was not studied at this level of irradiance, tissue damage at all other rates of heating was found to occur at irradiances only slightly greater than that required for onset of pain. These data are in close agreement with experiments on tissue damage of human skin by Moritz and Henriques[21] who used a conductive heating system (hot water) and observed that first degree burns without loss of epidermis were produced at a skin temperature of 44°C. (111.2°F.) maintained for 5 hours and second and third degree burns with complete epidermal necrosis occurred after 6 hours. This tissue damage occurred without producing the sensation of thermal pain under the conditions of their experiments. The onset of pain therefore cannot be relied upon as a threshold to warn against tissue damage under the conditions of long term heating which are required for heat replacement. Instead, the limits of a maximum local skin temperature of 43°C. (109.4°F.) and a termal flux of 750 kcal/m²/hr (872 watts) should not be exceeded in any continuous operating system of thermal replacement.

Electrical resistance-wire heating offers the greatest flexibility in heat distribution and provides the highest efficiency inasmuch as the heat is generated in the area where the heat is desired with a minimum of transmission loss. However, the high temperature of the wires requires a certain amount of insulation between the wires and the skin, which also serves to limit the possibility of electrical shorts and local burns. A second system for heat distribution has been developed primarily for use in cooling astronauts. This concept utilizes a "liquid heat transfer agent" to transport and distribute the heat to the various areas of the body. This system has certain advantages for the diver, inasmuch as there is less inherent danger of electrical shock and the amount of heat to be transferred can be varied by increasing the mass flow of hot water. Heating by this method may be accomplished by piping the hot water over the body through small plastic tubes or by merely flooding the inside of a wetsuit with hot water.

Transfer of heat into the body from the heating garments depends upon the types of garments to be used. The traditional "hard hat" diver uses an airfilled suit so that the heat is transferred through conduction-convection across a gas layer to the body. Unfortunately, such "dry suits" rarely remain dry for any length of time because of the effects of perspiration, small leaks in the system, and the compelling effects of cold and immersion diuresis. For these reasons and also because of the bulk and suit pinching of "dry" suits, the so-called diver's wetsuit, in which water is permitted to circulate between the surface of the body and the suit, has become popular. In this case, the heat transfer is accomplished by heating a thin layer of water which exists continually between the garment and the skin.

TABLE VIII

HEAT REQUIRED FOR MAINTAINING COMFORTABLE BODY TEMPERATURE OF DIVER WHEN WEARING 3/16" UNICELLULAR NEOPRENE FOAM (UNF) WETSUIT WITH MINIMAL ACTIVITY (TAKEN FROM FIG. 5)

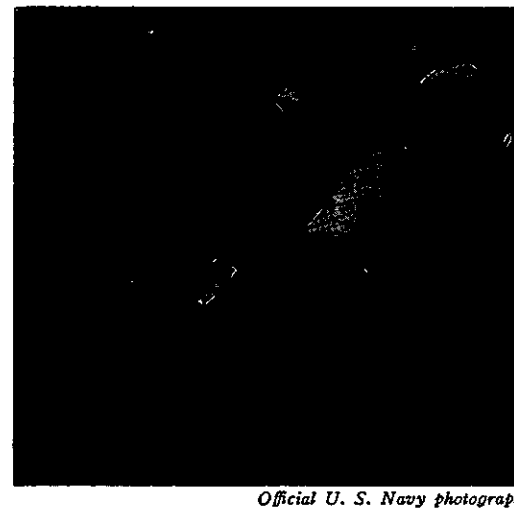
Water Temp. °C.	Rate of Body and Respiratory Heat Loss (kcal/m²/hr)	Total Heat Loss KCAL/Hr Body Surface =1.92m²	Heat to be Replaced* (KCAL/Hr)	Power Requirement of Suit if 60% Efficient	Power Requirement Thermal Watts
15	200	386	286	470	535
10	240	463	363	650	754
5	300	579	479	800	928
0	360	695	595	991	1,115

* Total Heat Loss Less Basal Metabolic Heat of 100 kcal/hr.

Obviously, heat transfer through water is far more efficient than through air. In the "wet" suit, fit is most important so that the amount of cold water which flows between the skin and the garment is limited. The quantity of heat that must be generated, distributed, and transferred to the body can be estimated from the heat debts shown in the nomograms of Figs. 3, 4, and 5 and from determinations of the efficiency of the generation and transfer system. This information has been compiled and tabulated as Table VIII. As can be seen from this table, a diver wearing a 3/16" unicellular neoprene foam (UNF) wetsuit while swimming in 0-5°C. (32-41° F.) water at a speed of less than ½ knot so that the heat loss due to water velocity is minimal and swimming at a depth less than 10' so that the insulative value of the UNF suit is not compromised by depth compression would require a thermal replacement system to supply approximately 1 kilowatt of power per hour if this swimmer were to be kept in thermal balance.

Evaluation of Diving Suits Which Insulate and Replace Heat

Various systems of improved insulation and replacement heating have been developed and are being tested and utilized in support of diving operations in cold water. A constant volume wetsuit, with resistance-wire heating was developed for SEALAB II aquanauts by the U. S. Rubber Company (Fig. 9). This suit is constructed with a matrix of connecting cell foam impregnated with rubber on both sides to form a waterproofed layer. This layer is then pressurized with an insulative gas to a pressure slightly greater than the ambient sea water pressure. The power supply for this suit was obtained either from eight silver zinc secondary cells which were pressure compensated for depth or by 12 volt AC power supplied through a cable from the SEALAB habitat. This suit was tested at the Army Research Institute of Environmental Medicine. (ARIEM), Natick, Massachusetts, to deter-



Official U. S. Navy photograph

Fig. 9. Aquanaut Wally Jenkins is shown on an excursion dive in the specially heated suits developed by the U. S. Rubber Company. Battery pack around the aquanaut provides current for warmth. Underwater photo by Dick Johnson, PH1.

mine the effects of gases of different thermal conductivity upon the insulative value of the suit and the thermal efficiency of the heating system, as shown in Table IX.

The suit was evaluated both on the sectional and the whole body copper manikins. The effective, mean insulative value of the suit when air filled and tested in air was 2.0 CLO. When purged with helium to simulate the SEALAB II conditions, the mean insulation of the suit was only 1.20 CLO. When purged with CO_2 the CLO value was increased to a mean of 2.38 when tested under the same conditions. The relative insulative effectiveness of the three different insulating gases when suffused through the same matrix material relate in the ratio of 5:3:6 for air, helium, and carbon dioxide. The thermal conductivities of the gases are in the ratio of 2:1:12, respectively. This suggests that the thermal conductivity of the included gas is not the controlling factor in determining the insulative effectiveness and implies that convective heat transfer may be more important than generally assumed. In addition, these data validate the concept proposed for use with this garment of purging with CO_2 to flush out the helium that diffuses into the garment when it is exposed to the 96% helium atmosphere of the SEALAB habitat.

Tests of this suit on the sectional copper manikin in a cold air environment were done to measure the thermal efficiency of the electric heating system. The mean thermal efficiency was found to be 74%. This high value is undoubtedly related to the fact that the heating wires are placed very close to the inner surface of the garment. Fig. 9 shows an aquanaut using this equipment.

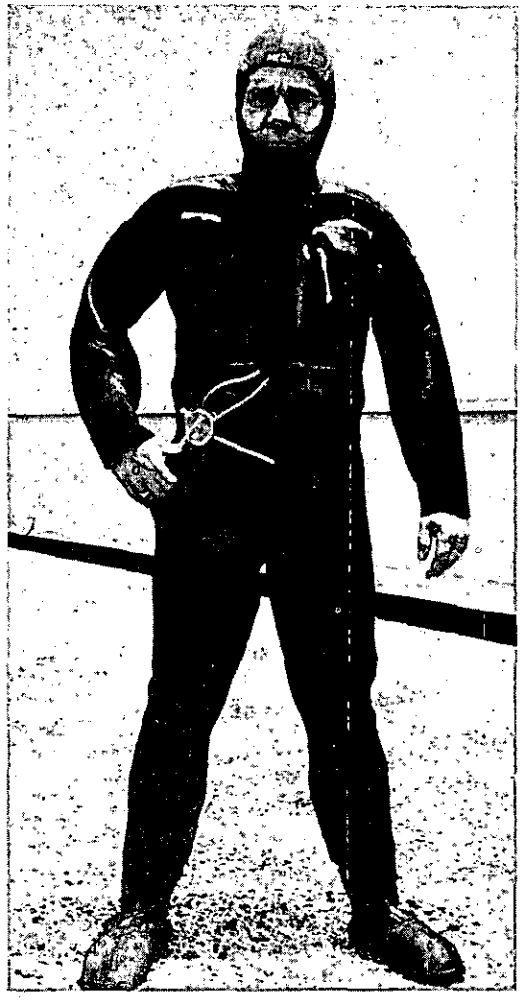


Fig. 10. "HYDRO THERM" divers suit provides thermal balance by free flooding with hot water.

A similar, electrical resistance-wire heated underwater swimmers wetsuit has been developed by the British* on contract for the U. S. Marine Corps Reconnaissance swimmers. This garment utilizes fine multistrand wire woven into a dacron matrix which is then sandwiched between two layers of thin unicellular, neoprene foam for waterproofing the wires. A silver zinc secondary battery supplies

TABLE IX

THERMAL CONDUCTIVITY OF GASES (K)
(cal/(sec-cm²)(° C. cm))
(APPROXIMATE VALUES AT ORDINARY TEMPERATURES AND 1 ATMA)

	$k \times 10^5$	(k_{gas}/k_{air})
Air 0° C.	5.68	1.
Carbon Dioxide (0° C.)	3.07	0.540
Helium (0° C.)	33.9	5.97
Hydrogen (0° C.)	32.7	5.76
Nitrogen (7° C.)	5.24	0.922
Oxygen (7°–8° C.)	5.63	0.990

* Vacuum Reflex, Ltd. Prestige House, Coombe Road, New Malden, Surrey, London, England.

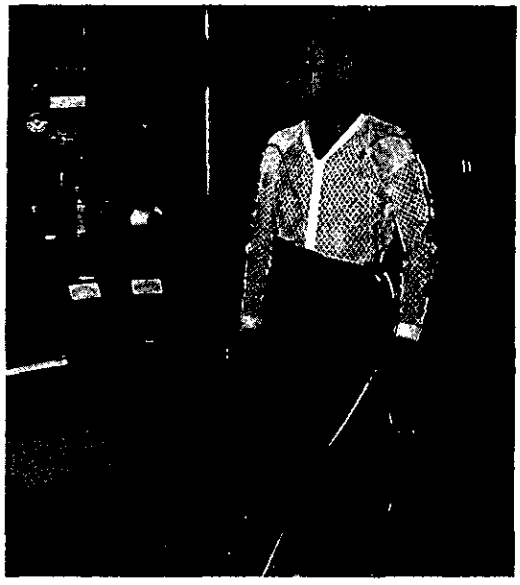


Fig. 11. Subject wearing "Liquid Filled Tubing" heating system under UNF underwater swimmers wetsuit.

24 volts and 750 watt hours for heating during free swimming. In this garment, there is no need to provide compensation for depth effects as the swimming is in shallow water. The electrical efficiency of this thermal replacement system was 55% when tested on the sectional copper manikin.

The use of water as the heating medium has certain advantages. One such garment is based upon the principle of enclosing the diver in an insulative garment and then flooding it continuously with hot water. This garment is very effective and has been in operational use by its originators* and had permitted divers to work 2-3 hours in water at temperatures of 4°-5°C. (39.2-41.0°F.) and at depths down to 200 ft.[22] This garment requires a hot water flow of up to six gallons a minute. Although relatively inefficient, this system provides a very effective working garment (Fig. 10).

The "liquid filled tubing garment" developed for NASA astronauts and used for cooling has proven to be effective when run backwards and supplied with hot water for heating aquanauts. Fig. 11 shows a subject wearing a liquid tubing garment under a standard UNF wetsuit. This type of garment was found to require a mass flow of water, i.e., approximately 1.0-1.2 liters/minute and the highest supply temperature tolerable, i.e., approximately 45°C. (113°F.) to provide adequate replacement heat for a subject wearing a $\frac{3}{16}$" outer garment in 5°C. (41°F.) water.

The liquid heating garment is ideally suited for use with a power cable supplied immersion heating system or with an isotopic thermal generator. A Plutonium 238 thermal generator is being developed by the Atomic Energy Commission for use by SEALAB III aquanauts and to be coupled with such a liquid heating garment. Thulium 170 and 171 would seem to offer advantages in heating and shielding exceeding those offered by Plutonium. These isotopes can be more readily obtained than Plutonium 238 and at a lower cost. Other isotopes have a more satisfactory power density but are less desirable in terms of half life, cost, and secondary radiation.

In summary, it can be said that the optimal thermal protective garment for underwater swimmers would be one which provides an adequate insulative layer which is unaffected by depth, is not significantly compromised by water flow, and which can be provided with an insulative gas layer which has an insulative value equivalent to that of air at 1 atmosphere. This insulative layer should ideally provide insulation equal to that provided by the 1" thick UNF but without limiting mobility. If this were attainable, then large amounts of supplemental heating would not be required. Such a utopia might possibly be approached by the concept of a rigid pressure suit as conceived for the lunar landing garment of astronauts* and proposed for adaptation to deep sea wear (Fig. 12). In this concept a rigid but maneuverable outer garment would permit man to stay dry and work in an atmosphere of air at 1 ATMA while diving in ambient pressures of many atmospheres. Supplemental heating needs would be minimal and if required, could be provided by an isotopic thermal and thermionic power system.

Just as in the aerospace field, the optimal

* Marine Contracting Inc., 3280 Post Road Southport, Connecticut.

* Litton Industries,[23] Space Sciences Labs, Beverly Hills, California.

Fig. 12. Artist's concept of the astronauts lunar landing rigid pressure suit modified and engineered for aquanauts.

life support system is the one that provides the operator with as near a normal "earth" type environment as possible. Until such an ideal garment can be achieved, considerable effort will be required to improve the insulative garment as well as the various systems of supplemental heating which are presently under development for thermal protection of the diver.

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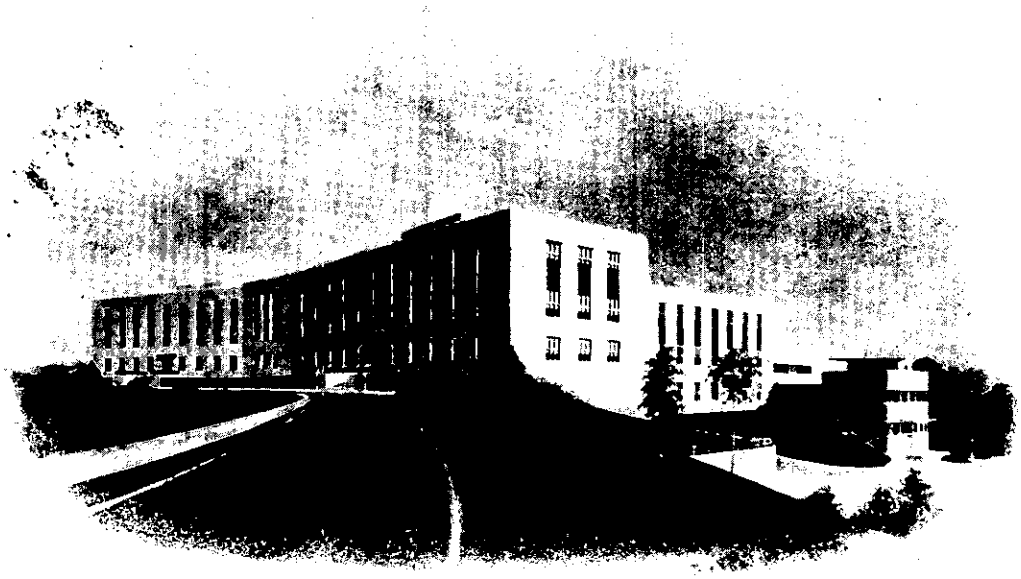

RESPONSES OF HUMAN SUBJECTS TO IMMERSION IN ICE WATER AND TO SLOW AND FAST REWARMING

Project X 189 Report No. 11

NAVAL MEDICAL RESEARCH INSTITUTE
NATIONAL NAVAL MEDICAL CENTER
BETHESDA, MARYLAND

23 March 1950

RESPONSES OF HUMAN SUBJECTS TO IMMERSION IN ICE WATER AND TO SLOW AND FAST REWARMING*

Project X-189 Report No. 11

By

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Captain, MC, USN

and

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*Reference may be made to this report noting authors, title, source, date, project and report numbers.

OBJECTIVE

The purpose of this study was to extend and amplify the excellent work done by Spealman (1) during the last war, under conditions somewhat simulating those of reviving men rescued from exposure in very cold water.

METHODS

Two nude subjects (A and B), 46 and 22 years of age, were immersed shoulder deep in ice water for about one hour, or until the toes became numb, then the exposure was terminated. The average water temperature varied from about 42°F. in the winter to as high as 50°F. in the summer, as the tank was not insulated. Following this drastic chilling, and after drying and dressing, the subjects were rewarmed by exposure to air at 73° to 100°F., or to water at 100° to 102°F., or first to warm air and then to hot water.

A third subject (C), dressed in customary outdoor winter clothing, was chilled in a cold chamber at -20°F. for about three hours, until his toes became numb. He was then rewarmed in air at 100°F. without changing clothes.

Before, during, and after chilling, observations were made of rectal, gastric, oral and skin temperatures using thermometers and thermocouples, and of pulse rate, blood pressure, lung ventilation rate, O_2 consumption and CO_2 production in the usual manner. Skin temperatures were measured on ten body areas in exposures to cold water, and on twenty-three areas in exposure to cold air. In all instances the big toe temperature was carefully observed. The blood morphology, hematocrit and serum proteins were studies only in one experiment.

Physical characteristics of subjects A,B, and C.

Subjects	Age	Height (CMS)	Weight (kilos.)		Specific gravity (whole body)	Total body water		Body fat content	
			Total	Lean Body mass		Liters	% Total weight	Wt. (kgs)	%
A - Medical officer	46	180	91.5	71.4	1.054	49.9	54.5	20.1	22
B - Diver	22	182	84.1	73.8	1.074	53.1	63.1	10.3	12.2
C - Technician	39	179	65.8	-	-	-	-	-	-

The specific gravity of the body was determined by the method of Behnke, Feen and Welham (2). The fat content based on this determination was computed from the formula of Rathbun, et al., (3). The water

content of the body was determined by the antipyrine method of Soberman et al. (4).

RESULTS

Chilling. When the nude subjects entered the water bath kept at 43°, they experienced excruciating pains all over the body during the short transitional period of intense vasoconstriction, when skin temperatures of immersed parts of the body were falling abruptly and deep tissue temperatures were rising. The peripheral heat loss during this transitional period was as high as 10,000 cal/hr. according to crude estimates by the Burton formula (5). The pain (except in the toes) subsided as soon as the skin temperatures began to level off reaching values only a few degrees above the water temperature (figs. 1 and 2). The deeper tissues then began to cool down rapidly, as indicated by a linear fall of rectal, gastric and oral temperatures. Goose flesh, cyanosis and shivering appeared early. Shivering progressed to a state of violent shaking which at times was paroxysmal in character. Real shivering, however, did not occur immediately upon immersion but only after deep body temperatures began to fall.

The time of exposure was limited in part by the occurence of numbness in the toes. In Subject B (fig. 2), an attempt was made to prolong the time of exposure by protecting the feet with woolen, diver's socks and rubber boots without much success. Although this helped in cushioning the fall of foot temperature, it did not prevent the eventual cooling of toes to the ambient water temperature.

The metabolic rate increased rather slowly, despite the drastic chilling and reached unusually high values that were five to six times greater than the resting rate. This however, was not enough to keep pace with heat loss (table 1). Although the metabolic rate of Subject A rose to a maximum of 560 cal/hr. at the height of shivering, the estimated heat loss (725 cal/hr.) exceeded heat production by 30 per cent. In Subject B, the heat debt also increased at an accelerated rate and the estimated total heat loss exceeded heat production by about 35 per cent near the end of exposure (table 1).

It should be pointed out that this was a new experience for Subject B and he was, therefore, quite apprehensive. His initial pulse rate, blood pressure, and metabolic rate were relatively high, and his hand and toe temperatures were below the ambient dry bulb temperature. On immersion he kept parts of his shoulders protruding outside the water to alleviate pain at the neckline. Subject A on the other hand, had been subjected to immersion in cold water on previous occasions; and except for painful toes, initial immersion shock, and the initial rewarming period, he was not too uncomfortable.

Subject C found chilling in air at 20° for three hours, was much less rigorous than chilling in wate at 42° to 50°F. Although the toe temperature was allowed to fall as low as 40° before terminating the exposure trunk temperatures did not drop below 80° The body cooled down slowly without shock or distress (fig. 4).

Rewarming. During the first stage of rewarming the shivering and distress were even more intense than during chilling. In all instances, skin temperatures rose rapidly, while the deeper temperatures continued falling steeply. The distress appeared to be associated with the "after-drop" of deep temperatures, when presumably the relatively warm blood rushed into the cold and dilated skin capillaries.

Distress disappeared when the skin became warm, when normal peripheral flow was reestablished, and deep temperatures began to rise. The more rapid the rewarming, the shorter the period of agony. To obtain relief from distress it was necessary to raise the bath temperature to values of 100° to 102°F At these temperatures shivering and cyanosis disappeared, giving way to a pleasant feeling of warmth, which persisted to the end of rewarming. In warm weather the subjects were removed from the hot bath before the rectal temperature returned to normal. Failure to do this resulted in overheating and discomfort for several hours during a warm summer day.

Rewarming of chilled subjects in air at 70° to 100°F consumed several hours and unnecessarily prolonged the agony from shaking chills (figs. 3 and 4). In a preliminary experiment in which no systematic rewarming was applied, the subject continued to shiver periodically all afternoon while performing his regular duties in a warm office.

Likewise, an attempt to establish peripheral circulation gradually by rewarming first in room air and then in warm water, resulted in prolonging the suffering. Prompt relief was obtained by immersion in warm water (fig. 3). No indication could be found that the hot baths were in any way injurious. Aside from general tiredness and sleepiness in the evening, there were no after effects.

Circulatory and blood changes. The pulse rate of Subject B decreased after immersion until shivering began, and then together with systolic and diastolic pressures increased considerably with chilling and returned to normal, or below, during the rewarming period. The pulse rate of Subject A showed less fluctuation. There were, however, considerable changes in blood pressure (table 2). The pulse rate was remarkably low in relation to the high oxygen consumption during shivering compared with the pulse rate associated with the corresponding oxygen utilization during normal exercise. This indicated either increased cardiac stroke volume or a marked reduction of oxyhemoglobin in the capillaries or a combination of these factors to a

degree far greater than that associated with normal exercise.

The changes in blood cell count (table 3), although slight, suggest another manifestation of the alarm reaction Selye (6) and the concomitant adrenocortical stimulation in response to the stress of abrupt body cooling.

The blood hematocrit and serum protein changes indicate some hemodilution during the rewarming and the subsequent period. There was no evidence of hemoconcentration during cooling at 31 minutes (table 4).

DISCUSSION

The phenomenon of temperature fall following immersion ("after-drop"). - The precipitous fall in deep body temperatures following the removal of the individual from cold water to a comparatively warm environment is of great interest and importance. It is accounted for at this time as indicative of the resumption of peripheral blood flow through the cold deeper layers of skin and the subcutaneous tissue. Return of the extremely cold blood to the central circulation thus may precipitate the observed fall of deep temperatures which in one experiment was greater during a period of 20 minutes with the individual in air (73°F.) than it was during the previous hour of immersion in cold water (50°F.) (fig. 3).

It is possible that this "after drop" in temperature in individuals rescued from cold water may bring about collapse and a state of shock, particularly if the deep tissue temperatures are on the borderline with reference to the maintenance of the function of the vital centers. Koenig's (7) similar conclusions are therefore reaffirmed.

The more marked "after drop" in temperature in Subject A, as compared with Subject B under similar conditions of rewarming (figs. 1,2), may in part be accounted for by the greater amount of subcutaneous fat and hence cold tissue in Subject A compared with Subject B. Presumably the temperature in muscles was not too far below the deep body temperature in view of the extreme shivering, and high rate of oxygen consumption.

Need for rapid rewarming of cold but uninjured tissues. - It follows from the previous paragraph that measures to promote the most rapid rewarming of cold, as distinguished from frozen, tissue or tissue injured by cold, are imperative. Although our rates of fall of rectal temperature differ considerably from those observed in ice immersion tests at the Dachau concentration camp (8,9), our conclusions relative to rapid rewarming are entirely in accord. Dramatic results were also obtained by Haterius, et al., (10) and

by Penrod (11) in rewarming anesthetized animals in baths at 40°-42°C., after chilling in ice water to a rectal temperature of 20°C. The anesthesia apparently prevented "cold shock" on immersion to ice water, while the unusually fast rewarming that is possible in small animals, by virtue of their small thermal capacity in proportion to their surface area apparently prevented heat shock on immersion in hot water.

Ames et al. (12) have found muscular exercise to be the best method of rewarming soldiers who had been moderately chilled by sitting quietly in a cold room while dressed in arctic clothing. Unfortunately this excellent method cannot be applied to exhausted shipwreck survivors after rescue from cold water. The use of warm air proved inadequate in Ames' work also. He did not try hot water, probably because it is not easily available on land in arctic regions.

In future work, an effort will be made to find ways and means of reducing or eliminating the period of distress during the first stage of rewarming. This is essential because, as previously indicated, it is during this critical period that many deaths occur in men rescued from exposure to intensely cold sea water. The "after drop" of deep temperatures will be reduced in future experiments by the use of two baths, side by side, so that the subject can be quickly plunged from cold into warm water.

The problem of elevating deep body temperatures in the presence of frozen or cold injured tissue. It is necessary to study the problem of restoring deep body temperature to normal by such means as diathermy and at the same time to treat the exposed parts, particularly the extremities, injured by immersion in cold water or freezing, in accord with approved measures. Additional study is necessary to determine whether or not the practice of gradual and careful rewarming, or rapid rewarming of injured parts plus pressure dressings is the best way to minimize tissue damage. There appears to be no contraindication to the use of diathermy or other measures to elevate deep tissue or body temperature. The experiments of Crismon, Fuhrman and Field (13) in which the lethal level of hypothermia was lowered in rats by the application of heat close to heart by means of a heating element placed in the esophagus, substantiate the rationale of this principle.

The current treatment however of extremities injured by cold is based upon the judicious and gradual rewarming of these parts. On the other hand, the extensive studies of Crismon and Fuhrman (14,15) demonstrated in rabbits the beneficial effects of rapid rewarming of quickly frozen tissues plus the application of pressure dressings. This work reopens the difficult problem as to the proper treatment of tissues injured by cold.

Based upon the fundamental studies of ice crystal formation at low temperatures, by Dr. H. T. Meryman of this Institute, it may be possible at this time to distinguish between the probable difference in injury produced by:

(a) rapid freezing of tissue (immersion in media at -55°C.) under conditions in which large ice crystals presumably do not form,

(b) slower freezing at relatively higher temperatures such that large ice crystals are formed,

(c) cold injury produced by immersion in water below 8°C. but without formation of ice crystals.

With large ice crystal formation in tissues, the damage may be irreversible and refractive to therapy. The best treatment of condition (c) on the other hand in which tissue is injured by cold without the formation of ice crystals may be in accord with the practice of gradual and careful rewarming of injured parts.

Absence of complications following immersion in cold water.- It is noteworthy that symptoms indicative of upper respiratory tract infection, allergy or other untoward effects did not occur following either late summer or winter immersion in cold water. There are individuals susceptible to cold who manifest urticarial wheals, collapse, and a shock-like state presumably from the excessive liberation of histamine or a histamine-like substance following relatively mild cold exposure.

These experiments present additional evidence of the innocuousness of this type of chilling particularly with respect to predisposing to respiratory infection. That an exposure in water (temperature 43°F.) for one hour approaches a limit with respect to the onset of tissue injury is suggested by periodic mild heat paresthesia in the toes which persisted for weeks in Subject A. This subject did not have similar sensations 15 months previously, following a similar exposure in water (temperature 50°F.).

Concluding note.- Hemingway (17) has employed diathermy to supply heat to dogs cooled in air and an extension of this work appears to be profitable. It should be possible, for example, to maintain normal deep temperature by means of diathermy, in mammals exposed to extremely cold air, to produce heat loss equivalent to that in cold water, and to determine heat loss under these conditions by measuremtnt of diathermy heat input and body heat production.

SUMMARY AND CONCLUSIONS

1. Two nude subjects were immersed shoulder deep in ice water for about one hour until the toes became numb, then the exposure was terminated. The average water temperature varied from about 42°F. in the winter to as high as 50°F. in the summer. Following this drastic chilling the subjects were rewarmed by exposure to air at 73° to 100°F. or to water at 100° to 102°F. A third subject dressed in outdoor winter clothing was chilled in a cold chamber at -20°F. for about three hours, until his toes became numb. He was then rewarmed in air at 100°F. without changing clothes.

2. Rectal, gastric and oral temperatures following initial rise fell linearly during the cold exposure period.

3. The conclusive finding in these tests was the abrupt fall of deep body temperatures in a comparatively warm environment (air temperature 73° to 100°F.) following immersion in the iced water or exposure to cold air.

4. In one experiment the fall of deep body temperature was greater during a period of 20 minutes with the individual in air (73°F.) than it was during the previous one-hour immersion in cold water (50°F.).

5. There were no untoward effects from the exposures to cold. The reduction or absence of pain after the initial immersion shock (except in the toes) and at the waterline skin areas protruding from the water) was noted. The feeling of intense cold occurred during the initial period of rewarming, despite a high surface temperature.

6. The onset and maintenance of shivering was associated not with the cooling of the skin, but with the fall in deep body temperature.

7. The need for rapid rewarming of the chilled body, to prevent the precipitous "after drop" of deep temperatures under the conditions of chilling in these experiments, is emphasized.

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Table 1. Metabolic rates and total heat loss of subjects chilled in water at 45 and rewarmed in water at 100° to 102°F.

Subject	Minute volume l.p.m. STP	O_2 Cons. l.p.m. STP	RQ	Total MR Cal/hr.	Instantaneous total heat loss Cal/hr. (approximate)	Instantaneou heat debt Cal/hr. (approximat
A (No breakfast)						
Before Chilling	8.5	0.304	0.75	86	86	±00
Before Chilling	8 1	0.284	0.80	82	82	±00
Chilling 2 min.	-	-	-	-	-	9050
Chilling 17 min.	20.6	0 692	0.93	206	226	20
Chilling 40 min.	35.9	1.850	1.08	560	725	165
Rewarming 2 min.	-	-	-	-	-	-2580*
Rewarming 19 min.	11.2	0.481	0.74	136	106	-30*
B (Had breakfast)						
Before chilling	9.2	0.343	0.85	100	100	±00
Before chilling	9.9	0.416	0.81	120	120	±00
Chilling 2 min	-	-	-	-	-	10400
Chilling 12 min.	35 9	1.39	0.86	405	405	00
Chilling 22 min.	38.2	1.31	0.95	392	507	115
Chilling 32 min.	40.4	1 63	0.94	486	591	105
Chilling 41 min.	41.4	1.54	0.97	463	598	135
Chilling 51 min.	43.7	1.54	1.05	467	637	170
Rewarming 2 min.	-	-	-	-	-	-7850*
Rewarming 18 min.	15.2	0.497	1.01	150	135	-15*

+ Computed from Burton's expression (5).

* Heat gain

Table 2. Pulse rates and blood pressures of subjects chilled one hour in water at 43° to 50°F. and rewarmed in water at 100° to 102°F.

Subject	Pulse rate	O_2 Consumption L/min.	Blood pressure (mm. Hg)	
			Systolic	Diastolic
A				
Dec 1949				
Before chilling	64	0.30	116	80
Chilling 17 min.	-	0.69	-	-
Chilling 26 min.	86	-	-	-
Chilling 40 min.	-	1.85	-	-
Chilling 49 min.	85	-	128	86
Rewarming 19 min.	85	0.48	-	-
Rewarming 28 min.	88	-	100	72
B				
Dec 1949				
Before chilling	87	0.34	133	80
Chilling 4 min.	82	-	-	-
Chilling 19 min.	80	-	132	84
Chilling 29 min.	100	-	130	80
Chilling 32 min.	-	1.63	-	-
Chilling 39 min.	104	-	160	100
Chilling 41 min.	-	1.54	-	-
Chilling 44 min.	120	-	165	100
Chilling 51 min.	126	-	155	100
Rewarming 8 min.	-	0.50	-	-
Rewarming 25 min.	86	-	110	75
A				
Sept 1948				
Water temp. 50°F.				
Before chilling	74	-	-	-
Chilling 20 min.	53	-	-	-
Chilling 38 min.	53	-	140	84
Chilling 56 min.	76	-	-	-
Chilling 65 min.	56	-	146	80
Rewarming 17 min.	86	-	-	-
Rewarming 20 min.	62	-	-	-
Rewarming 35 min.	65	-	90	60
Rewarming 52 min.	70	-	-	-
Rewarming 75 min.	86	-	110	70

Table 3. Blood counts in Subject B one hour in water at 43°F rewarmed in water at 100°F.

Time	W.B.C. No per cu. mm.	NEUTROPHILS			LYMPHOCYTES		MONOCYTES		EOSINOPHILS		BASOPHILS	
		BAND	Segmented									
		%	%	Total absolute per cu. mm.	%	Total absolute per cu. mm.	%	Total absolute per cu. mm.	%	Total absolute per cu. mm.	%	Total absolute per cu. mm.
Before chilling (1036)	6,600	2	49	3,366	39	2,574	4	264	4	264	2	132
Chilling 35 min.	7,950	6	66	5,724	16	1 272	10	795	2	159	0	0
2½ hours after rewarming	9,500	9	63	6,840	23	2,185	4	380	1	95	0	0
Following morning (0830)	7,450	2	41	3,203	46	3,427	7	522	4	298	0	0

Table 4.- Hematocrit and serum protein in subject B chilled one hour in water at 43°F. and rewarmed in water at 100°F.

Time	Hematocrit	Serum Protein (gr.%)
½ hour before chilling (1035)	52	5.898
Chilling 36 minutes	50	5.869
2½ hours after rewarming	47	5.320
Following morning (0830)	48	5.256

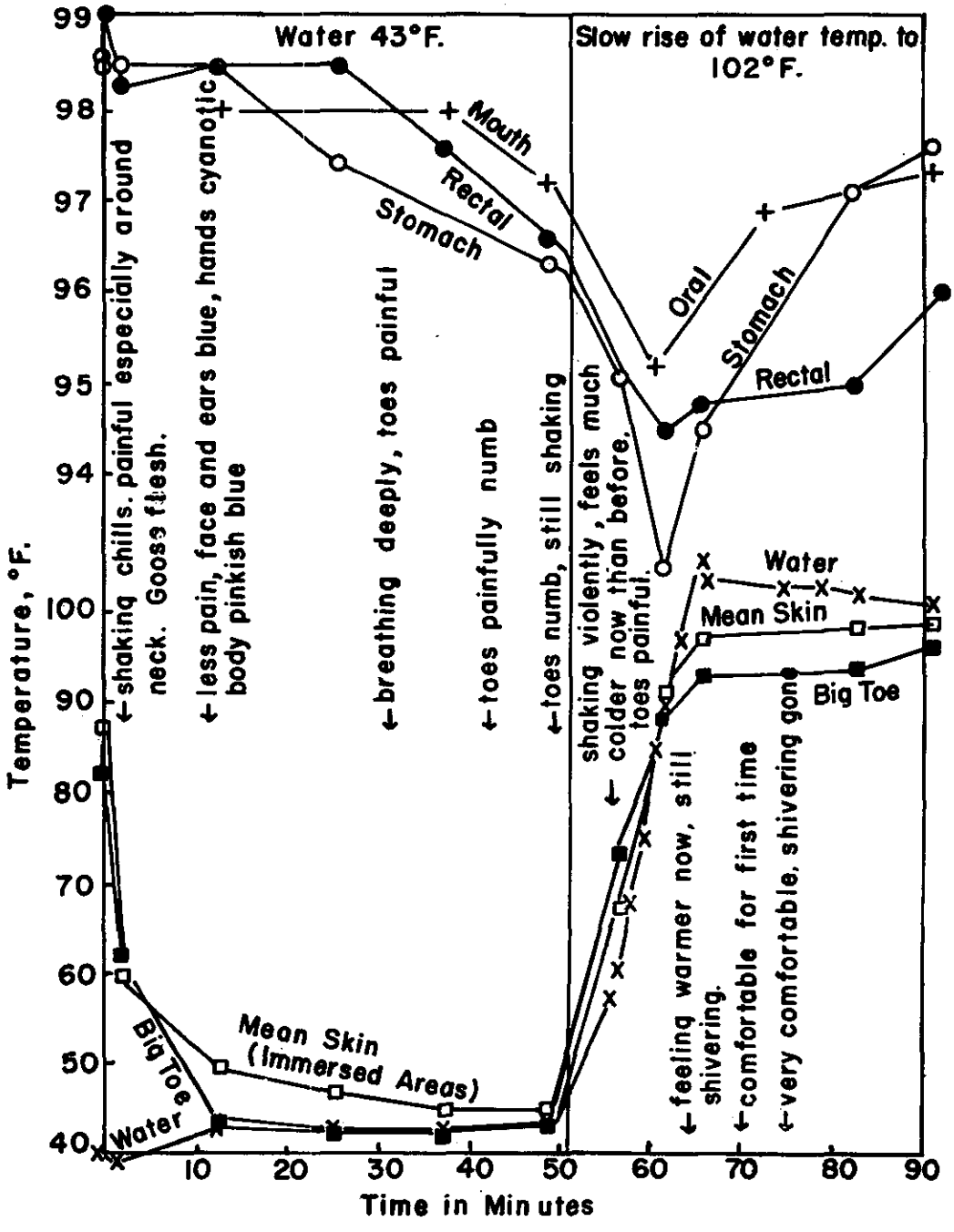

Figure 1.– Changes of deep and skin temperatures of subject A, chilled in water at 43° F. and rewarmed in water at 102° F.

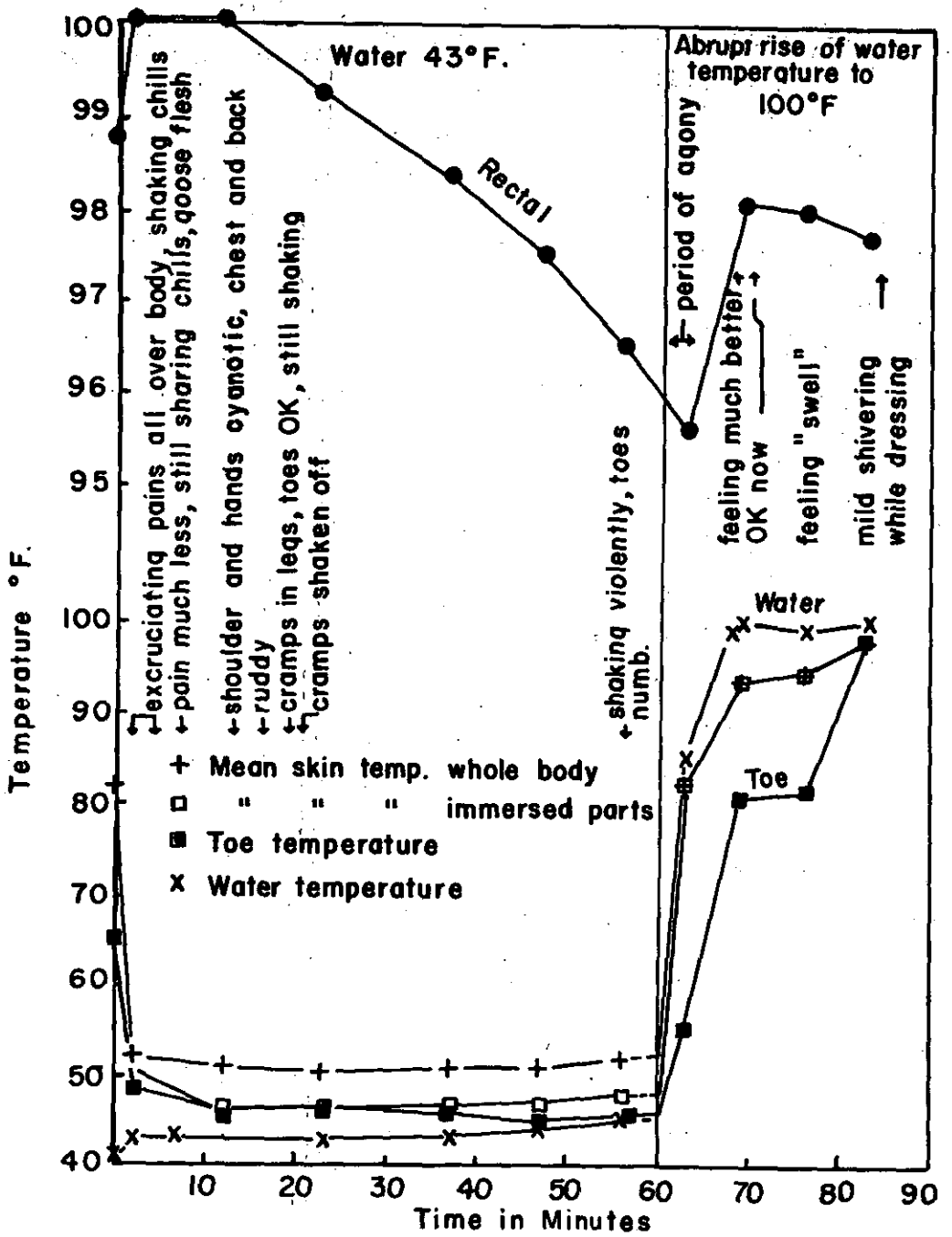

Figure 2.- Changes in rectal and skin temperatures of subject B, chilled in water at 43° F. and rewarmed in water at 100°F. Feet protected with woolen diver's socks and rubber boots.

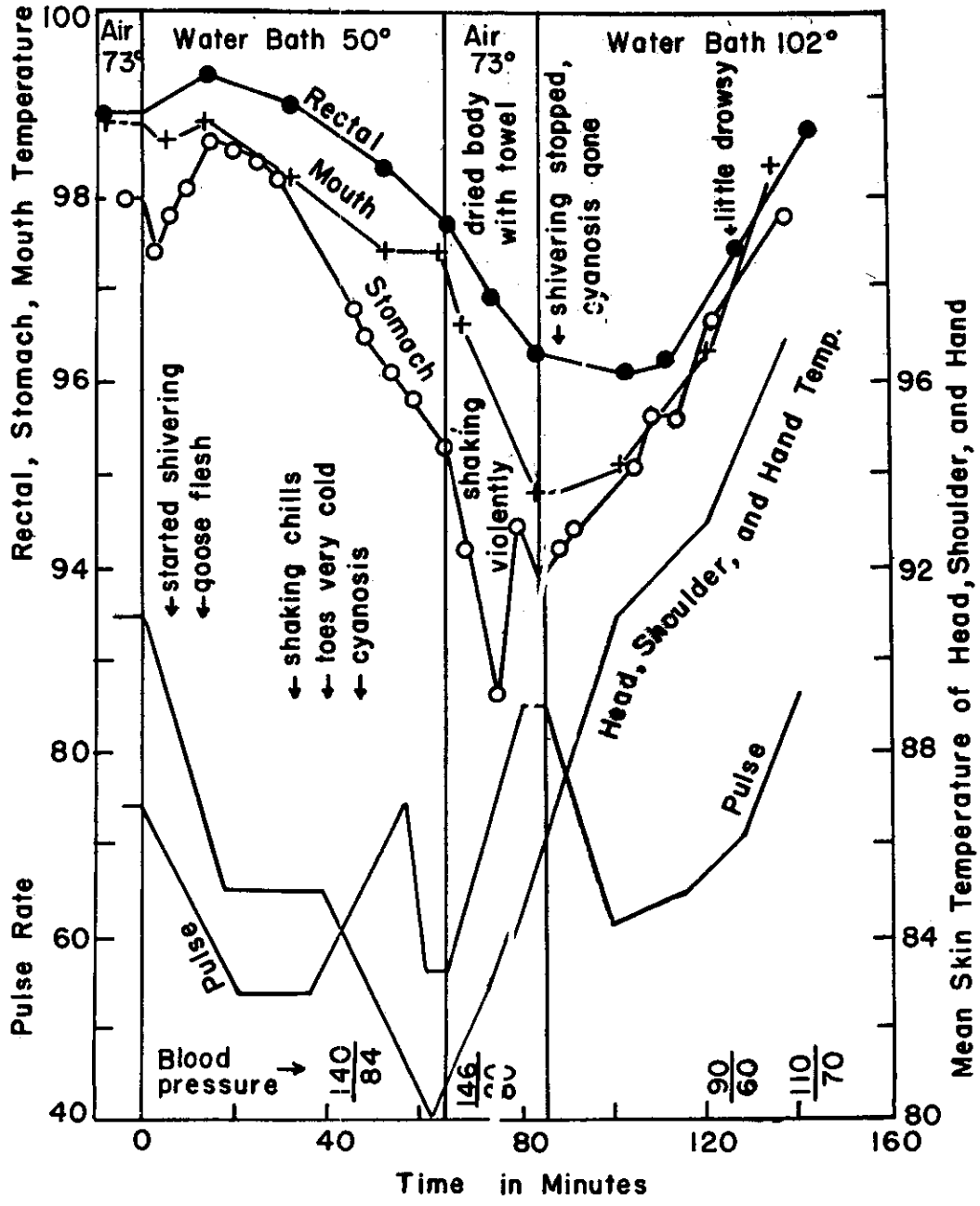

Figure 3.– Changes of deep and skin temperatures of subject A, chilled in water at 50°, and rewarmed first in air at 73° and then under water at 102° F.

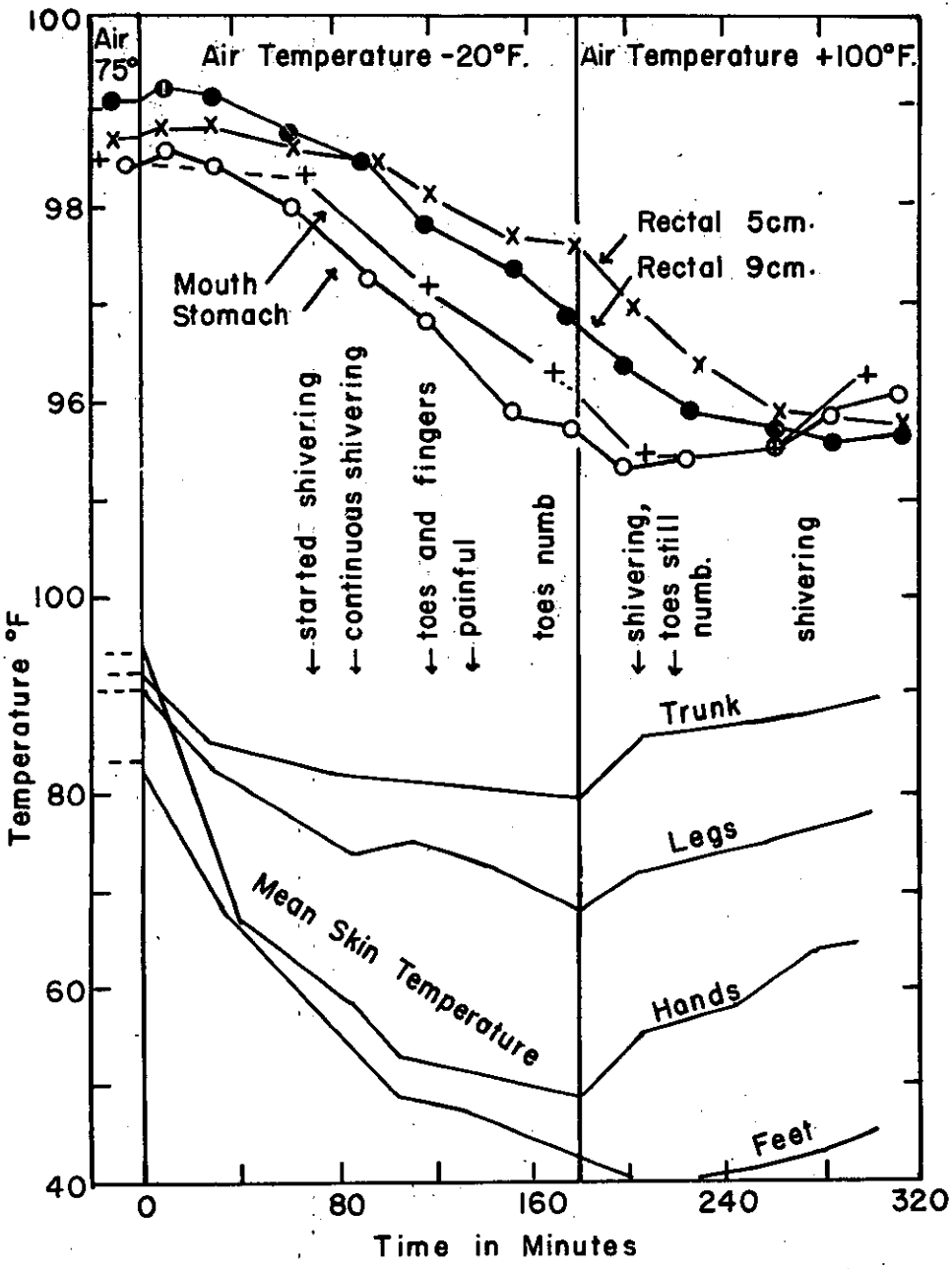

Figure 4.– Changes of deep and skin temperature of subject C, chilled in air at -20° and rewarmed in air at 100°F. without changing clothes.

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Immersion in Cold Water and Body Tissue Insulation

By Loren D. Carlson, Ph.D., Arnold C. L. Hsieh, M.D., Frank Fullington, B.S., and Robert W. Elsner, M.S.

GLASER[10] has called attention to the apparent contradiction between length of survival after accidental immersion in cold water and data from laboratory experiments performed in baths. Molnar[13] summarized survival reports, the Dachau experiments, and laboratory research by stating that exposure of one hour at 40° F. can be expected to be fatal to half of the men immersed, and that few if any would survive two hours. Yet marked exceptions can be cited. After experiments on a single subject, Glaser[10] explained this disparity by postulating that fit men can produce sufficient heat to avoid hypothermia. After studies of channel swimmers, Pugh and Edholm[14] emphasized the role of body insulation in survival in cold water. Body insulation, the reciprocal of conductance, can be calculated from the equation

$$I = \frac{T_r - T_s}{H}$$

in which:

I = insulation in °C./cal./m.²/hr.
T_r = rectal temperature, °C.
T_s = skin temperature, assumed to be bath temperature, °C.
H = heat loss, assumed to be 0.76 heat production calculated from oxygen consumption, the remainder being evaporative loss in respiration.

Pugh and Edholm[14] compared a channel swimmer to a non-swimmer, and found a two-fold difference in insulation while swimming or while in a water bath. These results were interpreted as refuting Glaser's explanation. Experiments reported herein were conducted to obtain further information about this disputed phenomenon.

METHODS

Nine men, suspended in a canvas seat, were immersed to the neck in a vigorously stirred bath. One subject was a trained marathon swimmer. The water was flowing constantly from a thermostatically controlled source. Cooling experiments were all preceded by an immersion for one hour at 33° C. The water temperature was then lowered gradually over a period of twenty minutes.

Rectal temperature was measured with a thermistor probe inserted eight inches. For determinations of the respiratory quotient, oxygen uptake was measured by a flowmeter and a paramagnetic oxygen analyzer, as well as by collections in a Douglas Bag with gas analysis by the Scholander[16] technique. Subjects reported in the basal condition, and each experiment

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was preceded by ingestion of 250 ml. of lemonade. In half of the experiments, 20 gm. of glycine was added to the lemonade because Gubner, De Palma and Moore[11] reported that the specific dynamic action of glycine is a mechanism for increasing peripheral blood flow, and Beavers and Covino[4] had observed the benefit of glycine in rewarming following hypothermia.

Skinfold thickness was measured with calipers of the type described by Best,[6] modified and calibrated by the methods which Brozek and his coworkers[7] suggested. Specific gravity was measured by weighing the subject in air and in water at 36° C. The weight in water was taken after a full expiration, and the residual air calculated from the equation: Residual air = 0.25 vital capacity (16 to 34 year age group), or residual air = 0.30 vital capacity (34 to 39 year age group). The percentage of fat was taken from the tables prepared by Rathbun and Pace,[15] Keys and Brozek,[12] and Allen and his coworkers.[1]

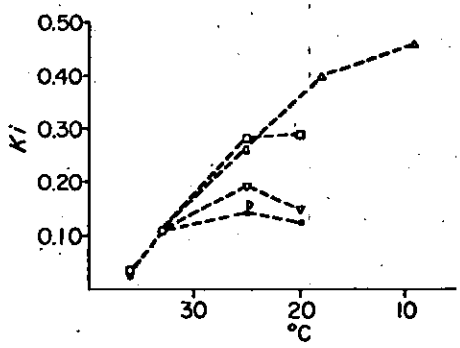

Fig. 1. Body insulation calculated at various water bath temperatures. Each symbol is a separate subject.

RESULTS

Body Insulation.—The body insulation, calculated from the equation given above, was determined at each bath temperature. The value was very low at 36° C., indicating marked vasodilation, but for all subjects increased to 0.11 °C./cal./m.²/hr. at 33° C. Below 33° C., the value of insulation was different in each subject, although the data for each subject were consistent (Fig. 1). The maximum value for insulation was related linearly to the individual's specific gravity (Fig. 2). Because the relative amount of fat was determined from the specific gravity, the correspondence was similar.

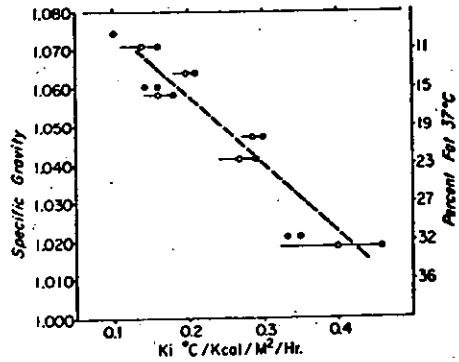

Fig. 2. Maximum values (solid circles) of body insulation found for various subjects in the water bath, average of several determinations (open circles). Lines denote the range between highest and lowest value.

Subcutaneous fat acts as an effective insulation during exposure to cold air.[2] If the body is assumed to be a cylinder of the height and volume of the individual, the relative proportion of the body participating as insulator may be calculated by assuming the insulation to be that of fat.[8] In such calculations the ratio of the "shell" to the "core" of the body varies from 0.35

TABLE I. SKIN FOLD MEASUREMENTS

Subject	Sp. Gr.	Thickness in Millimeters										
		Abdomen	Chest	Arm	Cheek	Back	Waist	Calf	Side	Knee	Chin	Thigh
BT	1.018	17.0	18.5	18.5								
NE	1.020	22.5	17.5	16.5	9.5	21.0	21.5	12.5	17.0	17.0	7.5	25
GG	1.041	13.0	7.0	10.0	6.0	10.0	14.0	8.0	7.0	9.0	4.0	
AH	1.047	9.0	6.5	4.0								
CG	1.058	7.0	4.0	4.0	4.0	5.0	5.0	4.0	4.0	6.0	3.0	
RE	1.060	7.0	6.0	8.0	4.0	6.0	5.0	8.0	5.0	4.0	4.0	
FF	1.064	8.0	4.0	6.0	5.0	6.0	7.0	7.0	4.0	7.0	4.0	
LC	1.064	6.5	5.0	4.5	5.5	5.5	4.0	4.5	4.0	5.5	2.5	5
DB	1.074	4.0	2.0	3.5	4.0	4.0	5.0	3.0	2.0	3.5	2.0	3.5

TABLE II. SPECIFIC GRAVITY AND PER CENT FAT

Subject	Sp. Gr.	Per Cent Fat (20°C.)	Per Cent Fat* (37°C.)	Per Cent Fat†	Per Cent Fat† (Skinfold)	Per Cent Fat* (14 Per Cent Normal Reference)
BT	1.018	41	32	31	—	33
NE	1.020	40	32	30	32	30
GG	1.041	29	23	21	22	23
AH	1.047	26	21	19	—	21
CG	1.058	20	15	14	14	17
RE	1.060	19	15	14	17	15
FF	1.064	17	13	12	17	14
LC	1.064	17	13	12	14	14
DB	1.074	12	8	8.1	9.9	10

*Based on Keys and Brozek's[12] method.
†Based on Allen et al.[1]. Adiposity multiplied by 0.62.[13]

to 0.74. When the value of 18 kcal./m.²/hr./°C. was used for tissue conductance, the apparent tissue thickness acting as insulation was 5 mm. at 36° C. bath temperature, 20 mm. at 33° C., and 73 mm. at the high value of insulation found. The skin and subcutaneous fat thicknesses, measured in some subjects, are given in Tables I and II. Table II shows the variety of expressions of the percentage of fat. In the subject with highest specific gravity, skin and subcutaneous fat measurements were: arm, 3.5 mm.; chest, 4.5 mm.; abdomen, 5 mm. In the subject with lowest specific gravity, the values were: arm, 18.5 mm.; chest, 18.5 mm.; and abdomen, 17 mm.

Oxygen Consumption.—The heat input at the low bath temperature, calculated from the oxygen consumption, varied inversely with the insulation

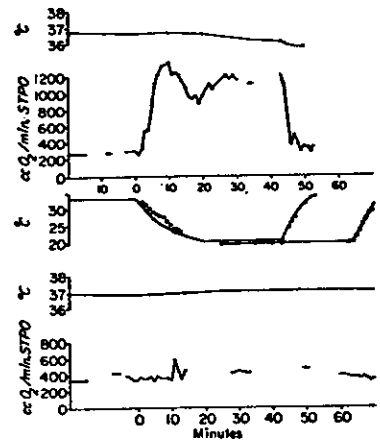

Fig. 3. Representative data from a poorly insulated (upper) and a well insulated subject (lower). Bath temperature with time is shown in solid circles for upper curve and open circles for lower curve. Rectal temperature in degrees C. Oxygen consumption is cc./min. Bars indicate data from Douglas bag compared to flowmeter data. See Table III for further details.

TABLE III. METABOLISM AND INSULATION VALUES AT DIFFERENT BATH TEMPERATURES

Subject*	Sp. Gr.	SA m²	33° C.				25° C.				20° C.				8°-16° C.			
			MV l/min	Cal m²/hr	RQ†	Ki‡	MV l/min	Cal m²/hr	RQ†	Ki‡	MV l/min	Cal m²/hr	RQ†	Ki‡	MV l/min	Cal m²/hr	RQ†	Ki‡
BT+	1.018	2.65	9.3	49	.91	0.08					10.8	58	.91	0.32				
−			6.8	—	.99	0.12					10.5	47	1.05	0.40	8.6	52	—	0.57
−			9.9	46	.96	0.13					10.1	54	.85	0.46	13.8	64	—	0.50
−															16.8	70	—	0.38
−			8.2	46	.86	0.11									10.6	63.5	.82	0.42
															17.3	88.8	.84	0.46
NE−	1.020	2.16	7.7	44	.97	0.11	9.8	45	.94	0.35								
−			7.4	42	.94	0.10	7.9	46	.89	0.33								
GG+	1.041	1.88	6.3	41	.90	0.13	9.7	65	.87	0.24								
−			6.1	44	.86	0.12	7.8	55	.85	0.29								
HH+	1.047	1.95	6.9	43	.97	0.09	8.6	43	.91	0.27								
−			7.3	42	.99	0.09	7.4	40	.83	0.30								
+			6.8								12.7	81	.93	0.29				
−			7.9	38	1.00	0.13					12.3	77	.96	0.29				
CG+	1.058	1.81	6.2	43	.89	0.11												
−			6.7	43	.91	0.12												
+			6.6	46	.98	0.10												
−			6.2	49	.89	0.12												
+			5.8	41	.87	0.13	15.8	111	.92	0.14								
−			6.9	46	.94	0.11	11.8	86	.91	0.18								
RE−	1.060	1.92					16.4	91	.86	0.16								
−			6.6	36	1.06	0.10	16.5											
FF+	1.064	2.04	7.2	43	.92	0.12												
−			8.5	46	1.01	0.10												
+			6.4	40	.88	0.10	11.6	57	1.00	0.21								
−			6.6	41	.89	0.10	14.7	67	.99	0.18								
+			7.3	44	.90	0.11					19.5	128	.94	0.13				
−			6.2	40	.88	0.13					19.0	127	.95	0.17				
§LC+	1.071	1.92	6.94	45	.92	0.11												
−			7.2	49	.86	0.09	25.2	126	1.00	0.11								
+			7.1	44	.92	0.12	20.4	86.5	1.02	0.13								
−			7.4	45	1.00	0.11	29.2	136	.99	0.16								
+			6.5	45	.92	0.10					30.4	175	.98	0.12				
−			6.2	42	.84	0.12					30.0	166	.95	0.13				
DB−	1.074	1.68	6.3	45	.92	0.10	28.3	163	1.10	0.09								

*Plus sign indicates ingestion of 20 gm. glycine before the experiment.
†RQ=respiratory quotient.
‡Ki in °C./cal./m.²/hr.
§Specific gravity differs from figure in Tables I and II owing to change in weight between measurements.

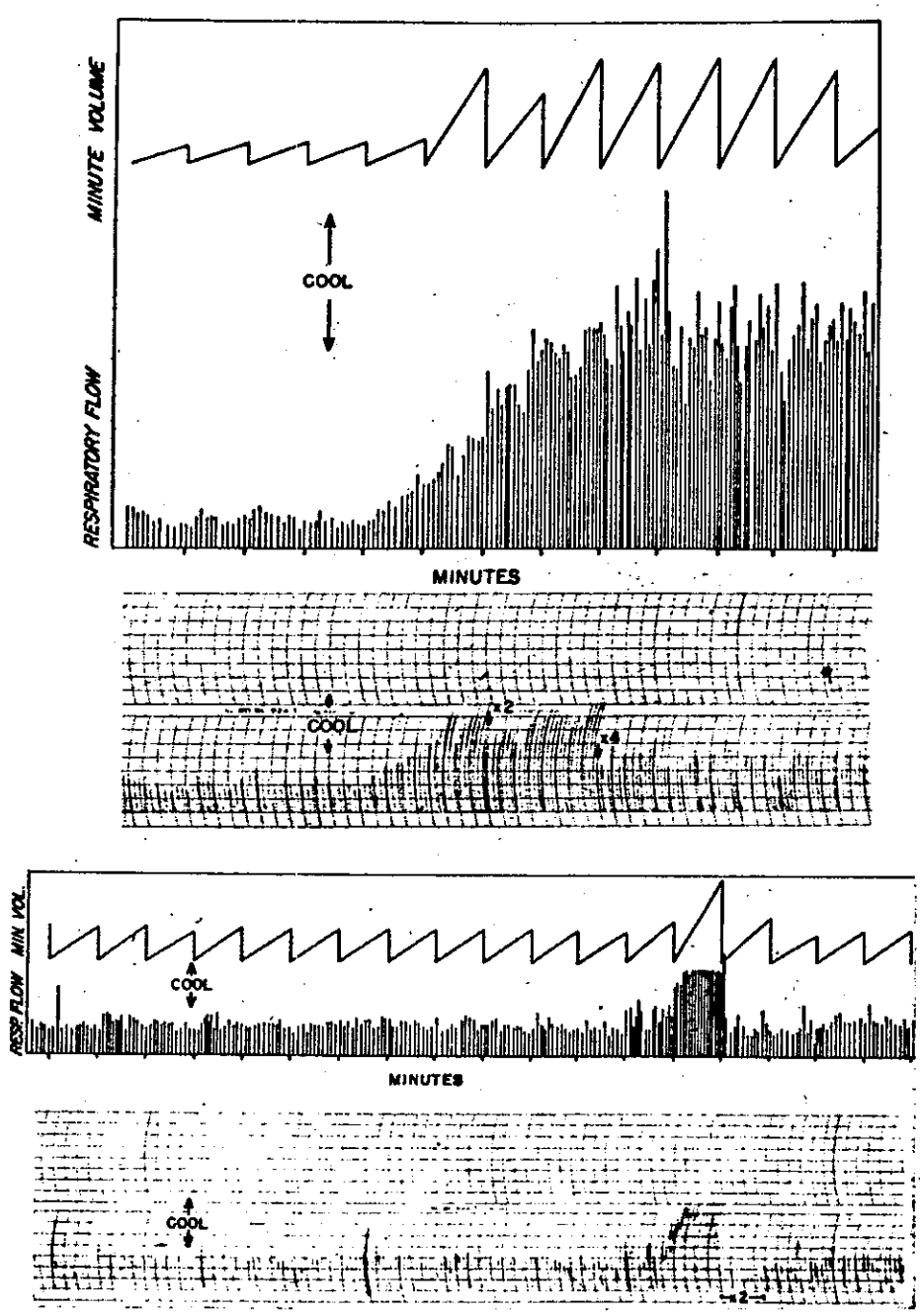

Fig. 4. Respiratory flow and minute volume from flowmeter in a poorly insulated (above) and a well insulated subject (below). Note burst of shivering shown by hyperventilation in lower record.

(Table III). Shivering was apparent in subjects with low insulation values. Representative data from a subject with low insulation and from one with high insulation are shown in Figure 3. In the poorly insulated subject (upper curve), oxygen consumption increased five-fold during shivering. In the well-insulated subject (lower curve), shivering was not apparent except during the bath cooling period, and his oxygen consumption increased very little. The latter subject was the marathon swimmer, who had spent as much as fourteen hours swimming in water between 4° C. and 8° C. His caloric output while swimming averaged 275 cal./m.²/hr.

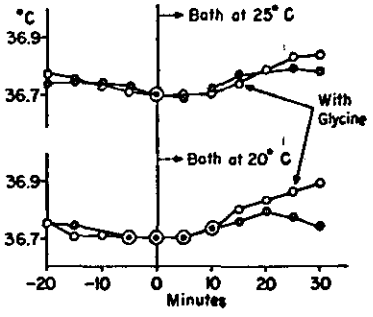

Fig. 5. Average data from all subjects comparing effect of ingestion of glycine at 25° C. and 20° C.

The time course of oxygen consumption with temperature drop indicates that the poorly insulated subject began shivering within four to five minutes after a bath temperature drop of 2° to 3° C. With rewarming, he stopped shivering within a few moments and at temperatures below those at which he had begun shivering. The respiratory flow and minute volume of these two subjects is shown in Figure 4. Here the rapid increase in ventilation in the poorly insulated subject is evident. In the professional swimmer, a short period of hyperventilation, accompanied by noticeable shivering, always occurred after eight to ten minutes. This period passed rapidly, and thereafter ventilation proceeded at a level slightly higher than normal.

Rectal Temperature.—Rectal temperature patterns were determined by the amount of body insulation (Fig. 3), varying from a steady drop to the often-reported rise followed by a drop. On rewarming, the rectal temperature dropped in every case. A slight benefit from the ingestion of 20 gm. of glycine was shown in the rectal temperature (Fig. 5). While there was no consistent change in any of the other parameters measured, glycine administration altered the rectal temperature.

DISCUSSION

The individual variations in insulation, related to specific gravity and to fat content, affect survival time in two ways. First, an increased insulation increased the survival time by reducing the amount of heat needed to maintain rectal temperature. With a fixed heat input, rectal temperature would drop more slowly. Secondly, the increased insulation is an increase in the storage factor, varying the amount of body tissue capable of cooling. Further, it is evident that, if the assumptions are correct, the portion of the body acting as insulation is greater than the portion which is fat. The plausibility of this condition has been

shown by Burton[6] in his calculation that more than 50 per cent of the body lies within 2.5 cm. of the surface. Because, as shown by Bazett,[3] all of the arms and legs may cool, the relative portion of the body weight involved in cooling may be even greater. Legs and feet are 37 per cent of the body mass; arms and hands, 13 per cent; and the trunk, 43 per cent, of which 15 per cent is within 2.5 cm. of the surface. Thus 71 per cent of the body could participate in cooling. In the heaviest subject, 84 kg. might have cooled from 35° C. to a mean temperature of 29° C., giving up $6 \times 0.7 \times 120 \times 0.83 = 403$ calories. The muscle mass must certainly participate in this event, and vigorous shivering may nullify this benefit. In the subject with the least insulation, the value would be $0.3 \times 70 \times 6 \times 0.83 = 105$ calories. These factors seriously affect short-term studies. In our studies, a steady state as such was not achieved, but the calculations were made at a time when the oxygen consumption was maintained and the rectal temperature was dropping at a steady rate.

Whether one calculates the energy input necessary to maintain rectal temperature or the time required to cool to a given rectal temperature, the values obtained bear a simple arithmetic relation to the insulation value, varying four-fold. The specific gravity of the majority of individuals lies between 1.040 and 1.090, which would give a range of values for insulation from 0.08 to 0.30 °C./cal./m.²/hr.

In these experiments, the ingestion of 20 gm. of glycine had little value. It is apparent that a knowledge of the body insulation is necessary to describe individual responses to cold environments.

SUMMARY

Subjects in whom fat constituted 8 to 32 per cent of the body weight were immersed at 33° C., 25° C., 20° C., and in some cases, at 9° C. One subject was a professional distance swimmer. All experiments began with a control period at 33° C. The water temperature was then lowered to the desired temperature. Body insulation, calculated by the Burton equation, varied directly with specific gravity, ranging from 0.10° C./cal./m.²/hr. to 0.40° C./cal./m.²/hr. However, the fraction of the body calculated to be involved as insulation was always greater than the estimated fat content. The professional swimmer increased his metabolism without visible shivering or loss of tissue insulation. Visible shivering always was accompanied by a reduction in body insulation. These results seem to explain the wide variation in survival times during cold water immersion.

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ACCIDENTAL HYPOTHERMIA

By F. St. C. Golden

ABSTRACT

Some of the environmental factors which adversely affect body temperature regulation are briefly outlined.

Advice on diagnosis and on both first aid and curative treatment of accidental hypothermia is proposed.

1. The Problem (Environmental Factors)

a. *On Land*

The threat to life in a cold wet environment is very great, death usually being either directly or indirectly a consequence of lowering of the deep body temperature, *ie*, hypothermia. Experts say it is much more difficult to survive in a cold/wet than in a cold/dry environment where the temperatures encountered are of much greater magnitude. The explanation for this apparent paradox lies in the 'wetness' which decreases the insulation of clothing and increases heat loss from the skin.

The insulation of clothing, including anoraks, is reduced 50 per cent by wetting alone (Pugh, 1966A). Add to this the decrement due to air movement in strong winds and the insulation provided by clothing will be very small, somewhere in the order of 0.3 clo, which is the insulation of air alone at lower wind velocities, for example 5 mph. The detrimental effect of the wind may best be seen in the Siple (1945) vind chill index shown in Fig 1.

In view of the recent criticisms of the Siple Index it is only fair to quote Siple's (1949) own view of his index expressed in Newburgh. 'Even though these values are not precisely applicable to the cooling rate of the body, they are of the approximate order of magnitude.'

From the Siple Index it may be seen that an individual without adequate insulation, in a moderate temperature and with a moderately high wind speed, will be required to make major compensatory physiological adjustments in order to survive.

b. *In Water*

A more serious threat to life from hypothermia is present when the body is immersed in water at 20°C or less (Molnar, 1946). The rate of loss of body heat in water is approximately 25 times that in air because of the difference in specific heat of water and air and the thermal conductivity of water (Beckman, 1963). Fig 2, showing the Barnett (1962) adaptation of the Molnar Graph (1946), gives some indication of survival times expected for a normally clothed (1 clo) 70 kilogram man immersed in water.

This graph should not be interpreted too literally and should only be used as an approximate guide.

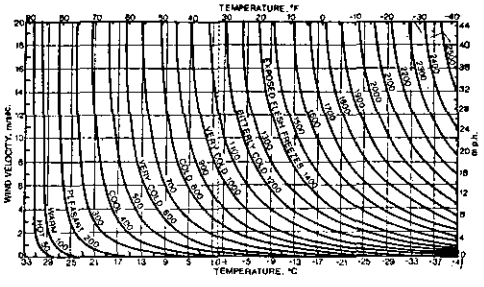

Fig 1. *Graph showing cooling effect of wind at various ambient temperatures (from Siple, 1945).*

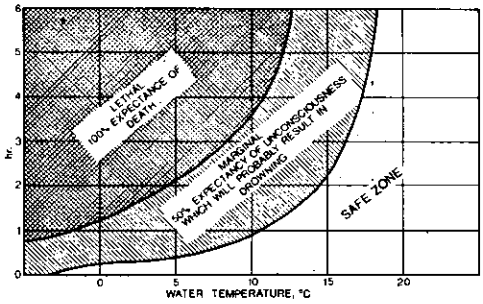

Fig 2. *Expectation of life for a normally clothed individual during cold water immersion (from Barnett,* 1962).

The many factors which influence man's survival time in cold water have been more than adequately covered in this symposium by Professors Hervey and Keatinge.

2. Aetiology

As this symposium was solely concerned with Cold/Wet Survival, the type of hypothermia under discussion must be of 'Accidental' nature, and thus accidental hypothermia can be defined as an unintentional lowering of the body temperature below 35°C in an otherwise healthy individual. The deep body temperature may be lowered by environmental conditions alone, or in combination with some individual body characteristic. The rate of lowering of body temperature will depend largely on the environmental conditions. The consequences to the body of a lowering of temperature will ultimately be the same, *viz,* hypothermia progressing to death, unless reversed; however, the rate of fall of body temperature is important from the treatment aspect. The degree of disturbance in the 'milieu intérieur' likely to be encountered appears to be inversely proportional to the rate of fall in body temperature. For a simple guide to optimum treatment it is therefore helpful to classify accidental hypothermia according to the duration of exposure.

Accidental Hypothermia
- (A) Acute (<6 hours)
- (B) Sub-acute (>6 - <24 hours)
- (C) Chronic (>24 hours)

A. *Acute Accidental Hypothermia*

In acute accidental hypothermia the body loses heat extremely rapidly and suffers from profound hypothermia in six hours or less. It is caused classically by accidental immersion in cold water of 15°C or less.

The physiological disturbances seen in the patient are brought about almost exclusively by a rapid fall in deep body temperature, without any major accompanying disturbance in the water and electrolyte balance.

Complications

The condition may be complicated by partial drowning or, if the water temperature was below 10°C, by cold injuries of the extremities. In shipwrecks there may have been some inhalation of fuel oil, or burns. Additional complications may arise during treatment, which will be discussed later.

B. *Sub-Acute Accidental Hypothermia*

This type of accidental hypothermia has a moderately long duration of onset, six hours plus. It is the type of hypothermia encountered classically in mountain climbers and 'fell walkers' as described by Pugh (1964, 1966B). In this instance not only has the body been struggling to maintain a normal body temperature in adverse environmental conditions for a period of hours, but also there is usually a considerable energy output entailed in the exercise being undertaken during this period. The temperature regulating mechanisms of the body are sacrificed in order to fulfil the muscular demands for energy. The high energy output gradually exhausts the body, and plays a major contributory

role in the eventual collapse and deepening hypothermia.

Into this category must also come the survivors who were immersed in water of 15°C plus for more than six hours, and are hypothermic on rescue. The intense shivering endured by these people over the period of immersion is likely to produce a state of exhaustion similar to that encountered in the 'fell walker', while the duration of onset permits time for compensatory adjustments to be made in the 'milieu intérieur'.

Complications

These may have been contributory to the development of hypothermia, such as head or spinal injury or some other form of immobilising injury. Complications such as cold injury or frostbite may develop concurrently with hypothermia, or fish bites in sub-tropical waters and, as in the acute form, additional complications may develop during treatment. (These will be discussed later.)

C. *Chronic Accidental Hypothermia*

Chronic accidental hypothermia may take 24 hours or more to develop. It is the type classically seen in geriatric practice.

In this type of hypothermia, as a consequence of the prolonged vascular reaction to cold, considerable compensatory adjustments have taken place in the water and salt balance of the body. The problems associated with this form of hypothermia are outside the scope of this symposium and the reader is referred elsewhere (Emslie Smith, 1958; Duguid, Simpson and Stowers, 1961; Hockaday, Cranston, Cooper and Mottram, 1962; McNicol and Smith, 1964; British Medical Association 1964; Royal College of Physicians, 1966; Hockaday, 1969).

3. Diagnosis

The diagnosis of hypothermia is easy if suspected. The problem arises when there is some accompanying traumatic or pathological condition which diverts the attention of the examining doctor.

The cardinal sign is coldness of the skin. This should immediately make one suspect concomitant hypothermia. Frequently hypothermia is suspected but dismissed when the oral temperature is recorded as being 35°C (or higher if the thermometer has not been adequately shaken) using a conventional clinical thermometer which has 35°C as its lowest calibration. Accurate temperature recordings are not absolutely necessary for the diagnosis of hypothermia, but, if temperatures are being recorded, a special low reading (24° to 41°C) thermometer should be used, preferably in the high rectum. As the thermometer does not record pH or electrolyte imbalance good clinical judgment is more important than arbitrary temperature recordings, especially in the management of the hypothermic patient. As an aid to clinical judgment a list of clinical signs and symptoms encountered at various body temperatures is shown in Fig 3.

4. Treatment

The best treatment of hypothermia is indisputably preventive. The requirement for a symposium such as this indicates however that, despite all the available knowledge on prevention, incidents of accidental hypothermia still occur. Accordingly some advice on optimum methods of treatment is summarised below.

At the onset it must be emphasised that every effort must be made to treat hypothermia victims, no matter how hopeless the condition appears. This should be done even with people apparently dead from hypothermia as full recovery has been reported even after one hour in profound hypothermia with complete cardiac arrest (Niazi and Lewis, 1958). The definition of death in hypothermia is 'failure to revive'. A speedy decision should be made

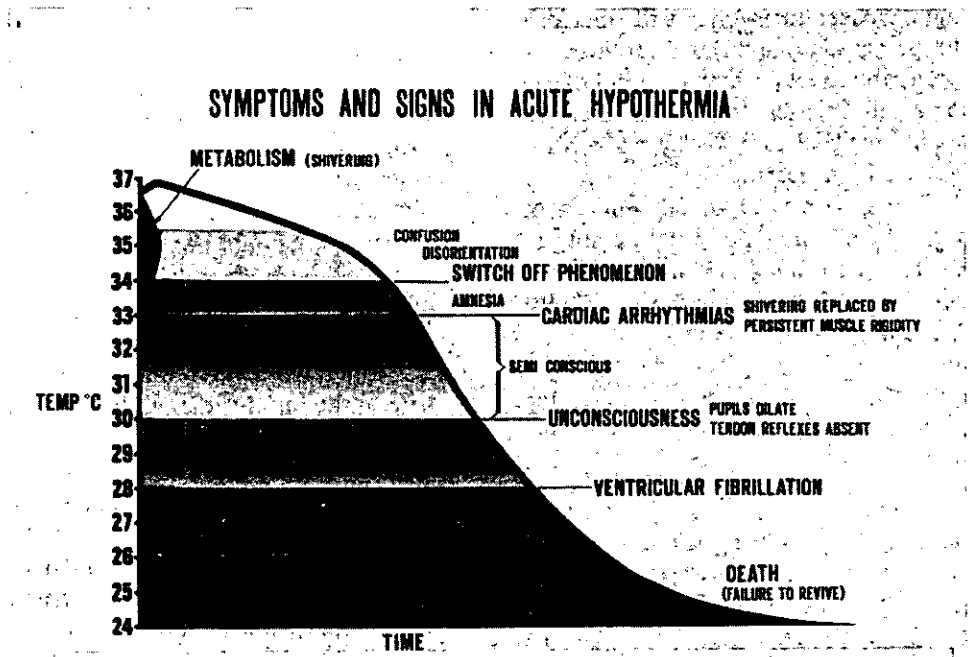

Fig 3. Curve representing behaviour of body temperature during cold water immersion with associated signs and symptoms encountered at the various body temperatures.

Fig 3.

in the method of treatment to be adopted and this must be rigidly adhered to. There is no time for cautious indecision.

The problem confronting every doctor in treating such cases is whether to replace the lost body heat rapidly or slowly and what, if any, supportive therapy should be given.

Basically the answer depends on whether one is dealing with a straight-forward thermal problem, perhaps with minor alterations in the pH and water/electrolyte balance, or with a thermal problem complicated by a major imbalance in pH and water/electrolyte content of the body. In the former a speedy reversal of the thermal problem is all that is required, leaving the body to readjust the remaining minor physiological imbalances itself. In the latter such a speedy reversal of temperature, creating a rapid return of cellular metabolic demands, could not be tolerated by the body and would in all probability prove rapidly fatal.

Therefore in summary:

		Treatment of choice
Accidental Hypothermia	A. Acute	Rapid Rewarming
	B., Sub-acute)	Slow Rewarming
	C. Chronic)	

A. ACUTE ACCIDENTAL HYPOTHERMIA

(i) First Aid Treatment

Remove the victim from the hypothermia producing environment. Reduce all manhandling of the victim to a minimum, do *NOT* massage or rub vigorously. If within 20 or 30 minutes of a hospital or expert medical care,

lightly cover the victim with blankets to prevent any further heat loss, or preferably enclose him in a polythene bag and transfer him immediately to expert medical care. If oxygen is available, administer it.

If not within 20 or 30 minutes of expert care then positive attempts at resuscitation must be made immediately as outlined below under curative treatment.

Complications which may possibly develop during first aid treatment or transportation are:

a. *Hypotension*: A shock-like state may develop as the peripheral tissues rewarm and the existing cold vasoconstriction is abolished; the 'bleeding' into the peripheral tissues will then produce severe hypotension. It is therefore advisable to transport the patient in a slightly head down attitude. Avoid using an excess of blankets or hot water bottles and definitely NO ALCOHOL.

b. *Unconsciousness*: This may be present on rescue, or, should the casualty be semi-conscious on rescue, it may develop 10 to 15 minutes later. In this instance the continued fall in deep body temperature after rescue, the so called 'after drop', may well lower the temperature sufficiently to cause unconsciousness. The hypotension mentioned above may in itself produce unconsciousness.

Whatever the cause of unconsciousness the usual procedures of maintaining a clear air way should be remembered.

c. *Cardiac Arrest*: Cardiac arrest due to either asystole or ventricular fibrillation is the terminal event in hypothermia. Fibrillation may arise during rescue, when the manipulative efforts of the rescue may trigger fibrillation in the cold sensitised myocardium, or it may develop shortly after rescue, when the returning chilled blood from the reviving peripheral circulation returns to the heart.

Should it occur, external cardiac massage should be commenced immediately, preferably at a slower rate than one would use on a normothermic patient.

But a word of caution is necessary about a hasty diagnosis of cardiac arrest in profound hypothermia when marked peripheral vasoconstriction, extreme bradycardia and dilated pupils are a feature of the condition. Attempts at cardiac massage at this stage will undoubtedly precipitate ventricular fibrillation.

d. *Respiratory Arrest*: The intense respiratory depression always found in deep hypothermia makes it difficult to tell sometimes whether respiratory arrest has occurred. Should it follow cardiac arrest, it should be treated by expired air resuscitation. This should not be carried out too vigorously as it may produce hypocapnia which would be detrimental to the body at this time (Keatinge, 1969).

(ii) Curative Treatment

In acute accidental hypothermia the body temperature has been lowered rapidly (< 6 hours). The body makes major vascular adjustments in an effort to conserve body heat, but there is insufficient time to make major alterations in its electrolyte composition. Therefore one is dealing predominantly with a thermal problem complicated by minor alterations in acid/base and water/electrolyte balance. The treatment of choice therefore is a rapid reversal of the hypothermic state (Alexander, 1945; Niazi

and Lewis, 1958; Behnke and Yaglou, 1950; Keatinge, 1969). This is best achieved by immersing the body in a bath of water heated to 40-41°C if naked, or at 44-46°C when clothed, remembering to keep the water stirred and adding hot water intermittently to maintain a reasonably constant bath temperature. The manhandling required in undressing the patient, who will have considerable muscle rigidity, may be so great as to precipitate ventricular fibrillation. Accordingly, if clothed on rescue, immerse him in the bath with his clothes on and cut these off, in the bath, when recovery is well established. If possible only the trunk should be immersed, keeping the limbs out of the bath (Keatinge, 1969). Oxygen should be given by an oro-nasal mask if available (95 per cent O_2 + 5 per cent CO_2). Leave the patient in the bath until he says he feels warm, then remove him and place him in a warmed bed.

In general, apart from the obvious active interference required for complications should they arise, all forms of interference should be avoided. Abnormalities of the intra and extracellular fluid will return to normal of their own accord when normal cell temperature is restored.

Complications which may develop during resuscitation:

a. *Hypotension*: Sudden collapse during rewarming may be due to hypotension. If so, remove the patient from the bath and tilt the head down until consciousness returns, then replace the patient in the hot bath keeping the limbs elevated. In severe cases however, 500 cc of warmed Plasma IV should prove helpful, particularly if the victim has been rescued from the sea where he may well have inhaled some sea water in his semi-conscious state before rescue.

b. *'After drop' in body temperature*: During rewarming, either rapid or slow, there will be a further fall in deep body temperature, demonstrated in Fig 13, page 169. This can be as much as 3°C (Alexander, 1945) and can therefore prove a major problem during resuscitation. Both human (Alexander, 1945; Behnke and Yaglou, 1950) and animal (Zingg, 1969) experiments have shown that the survival chances are greater with rapid than slow rewarming in acute accidental hypothermia.

c. *Cardiac Arrest*: Ventricular fibrillation is likely to occur at myocardial temperatures below 28°C (Ross, 1957; Cooper and Ross, 1960). This is especially likely during the rewarming phase (Fairley, Waddel and Bigalow, 1957) when the chilled acidotic blood from the peripheral circulation returns to the core circulation in large amounts. Added to this the blood is generally hypoxic and hypoglycaemic at this stage because of the demands of the reviving tissues for both oxygen and sugar. Fairley *et al* (1957) quote an example of a 35-year-old woman who had regained consciousness following a period of hypotherm'a for cardio-vascular surgery, who developed ventricular fibrillation at a deep body temperature of 36.6°C. Anti-arrhythmic drugs should not be given prophylactically as they can produce cardiac arrest or precipitate fibrillation in hypothermia (Drugs and Therapeutic Bulletin, 1971). Atrial fibrillation is common in hypothermia and does not require any specific treatment.

Should cardiac arrest develop during the rewarming phase cardiac mas-

sage must be commenced immediately and maintained until such time as DC defibrillation can restore sinus rhythm. Büky (1970) has shown that in cases of ventricular fibrillation after cardiopulmonary bypass surgery, magnesium sulphate, 0.1 g/kg body weight, administered IV during the rewarming phase, rapidly facilitates the restoration of sinus rhythm as the body temperature reaches 30°C. This occurred spontaneously in 66 per cent of cases, while in the remaining 33 per cent only one single application of the defibrillator was required to restore sinus rhythm. Linton and Ledingham (1966) say that defibrillation is likely to be maintained only when the myocardial temperature is at least 28°C. Below this temperature the adverse effect of temperature on oxygenation of the myocardium and the interference with conduction make defibrillation unlikely to succeed. Similarly in severe acidosis defibrillation is unlikely to succeed. The acidosis should therefore be treated with $NaHCO_3$, preferably warmed before transfusion. In really profound hypothermia, including those apparently dead, external cardiac massage and tracheostomy with positive pressure respiration is always worth trying. Under these circumstances partial rewarming of the torso with hot water (44°C) should be considered in an effort to speed up the rate of rise of myocardial temperature.

d. *Respiratory Depression*: As mentioned in A(i)(d), marked respiratory depression occurs in hypothermia but, nevertheless, sufficient ventilation is taking place to cope with the low metabolic demands of the body. Therefore slow shallow respiration is not in itself an indication for treatment.

During resuscitation there will be an increasing demand for O_2. It is hoped that revival of the respiratory centre will keep pace with this increasing metabolic requirement, in which case 95 per cent O_2 + 5 per cent CO_2 administered by oro-nasal mask should satisfy the need.

Unnecessary insertion of an air-way can precipitate ventricular fibrillation by causing reflex bradycardia (Drugs and Therapeutic Bulletin, 1971). Artificial ventilation can also cause ventricular fibrillation by producing an abrupt fall in the arterial pCO_2 (Brown and Miller, 1952). Should artificial ventilation be necessary great care should be exercised not to over-ventilate during the initial stages of rewarming, as the hypocapnia produced would have the most disastrous consequences on both the oxygen dissociation from the blood and the cerebral blood flow. However, if the patient has been partially drowned then intermittent positive pressure ventilation (IPPV), will aid the expansion of partially collapsed and oedematous alveoli. If IPPV is being used it should be used in conjunction with a heated humidifier (Ledingham and Mone, 1972).

e. *Intravenous Therapy*: Should intravenous therapy be necessary all intravenous fluids must be preheated to 38°C before transfusion (Freeman and Pugh, 1969) to prevent a further and possibly disastrous fall in core temperature.

B. SUB-ACUTE ACCIDENTAL HYPOTHERMIA

In sub-acute hypothermia the onset of hypothermia is a relatively slow process accompanied by excessive muscular exercise in the form of shivering or actual exercise or both. The lowered body temperature inhibits the aerobic metabolism of glucose. The resultant build-up of lactate

and the body's inability to deal with this lactate at lower temperatures, aids the production of a metabolic acidosis. Simultaneously many compensatory physiological adjustments are taking place in an effort to conserve heat.

There is a peripheral vasoconstriction with a resultant increase in central venous pressure, causing a suppression in the production of ADH and therefore a cold diuresis, while at the same time there is a shift of fluid from the vascular to the interstitial tissues. The net result is a reduced blood volume, haemoconcentration and an increasing blood viscosity. Added to this there is exhaustion of the body's glycogen stores and a fall in the blood pH (Neil, 1956). The net overall result is a considerable disturbance of the 'milieu intérieur'. However, the evidence (Pugh, 1966B) is that unconscious or nearly unconscious patients revive spontaneously once further cooling has been prevented.

(i) *First Aid Treatment*

On the hillside, basic first aid treatment is to remove the victim from the hypothermia producing environment. In this instance stop, shelter, remove all wet clothing, including underwear, and replace with dry clothing; if necessary have others contribute some item of clothing if no spare clothing is available. If possible place the victim in a sleeping bag. Enclose the sleeping bag in a large polythene bag and insulate from the ground by making a mattress of a thick layer of heather or gorse. If conscious give the victim some hot sweet drinks. NEVER give alcohol.

A decision must then be taken whether to divide the party and send for help, or to place some strategic distress/location beacons and await rescue. This decision will have to be made by the party leaders and will depend to a large extent on such facts as party size, individual fitness, time of day, weather conditions and local rescue facilities.

Complications which may develop during treatment or transportation are:

a. *Hypotension*: This occurs for similar reasons to those discussed in acute accidental hypothermia. However, the long time interval normally encountered between diagnosis and curative treatment, with intervening difficult transportation problems combined with the marked haemoconcentration, make this a potentially serious hazard in sub-acute hypothermia.

The development of hypotension, producing as it does a reduction in coronary perfusion, may be the triggering factor in producing ventricular fibrillation in many of these cases who are rescued alive but die during transportation down the mountain.

Having diagnosed hypothermia it is advisable to lay the patient with his head down the incline of the hill or transport him in the head-down position. He should never be allowed to walk even if he insists he has recovered sufficiently to do so.

Caution should be exercised in ensuring that the stretcher bearers themselves do not become exhausted and thus likely victims of hypothermia.

b. *Unconsciousness*: as in A(i)(b).

It should be remembered that an initial head injury may have played a significant role in the production of hypothermia in the patient under care and therefore a detailed neurological examination must be carried out to rule out possible intracranial trauma in all incoherent, semicomatose and unconscious patients.

c. *Cardiac Arrest*: as in A(i)(c).

d. *Respiratory Arrest*: as in A(i)(d).

e. *Hypoxaemia*: Is particularly likely to occur as the metabolic demands of the body increase, therefore administer oxygen if it is available.

(ii) Curative Treatment

A rapid reversal of the lowered body temperature in sub-acute accidental hypothermia would seriously embarrass the ability of the body to adequately oxygenate and perfuse the vital body tissues, as well as worsening the already disturbed water and electrolyte balance. Therefore the treatment of choice must remain slow rewarming at room temperature with full supportive therapy as indicated.

Perhaps it is worth sounding a word of caution at this stage about a too literal interpretation of serum electrolyte estimations while such a major disturbance of the distribution of body fluids exists. Likewise it is inadvisable to base any corrective action on results obtained from stagnated cold peripheral venous blood. Ideally an arterial catheter should be used for blood sampling and pressure monitoring. It is generally unnecessary and unwise to try and correct biochemical disturbances in hypothermia until rewarming is well established (Lancet, 1972).

Ninety five per cent Oxygen + 5 per cent CO_2 should be given in all cases. If indicated, IPPV should be used, not only as a means of counteracting the hypoxaemia but also in re-expanding collapsed and oedematous alveoli more rapidly than would occur spontaneously. IPPV is also an efficient central heating system when used in conjunction with a heated humidifier (Ledingham and Mone, 1972).

Although there is no evidence to prove that steroids have any dramatic effect in profound hypothermia they cannot be justifiably withheld. On this point it is worth noting that the lowest rectal temperature ever recorded, in a subsequent survivor of accidental hypothermia, was in a young negress in Chicago who was admitted to hospital with a rectal temperature of 18°C (Laufman, 1951). Her temperature increased rapidly to 20°C following an intramuscular (Rectus Abdominus) injection of 200mg of Cortisone. In view of the poor degree of absorption likely in such circumstances the exact significance of this sudden rise in temperature cannot be definitely ascertained; it could have been purely coincidental. In sub-acute hypothermia adrenal exhaustion from prolonged stress is likely and therefore there probably is a place for steroids in its treatment (Duguid *et al*, 1961).

Complications likely to be present during, or arising from, treatment:

a. *Cardiac Arrest*: treat as in A(ii)(c).

b. *Acidosis* — The metabolic acidosis usually increases as rewarming progresses (Fairley *et al*, 1957). This should be treated with $NaHCO_3$ 4.2 per cent warmed to 38°C before administration, as with all IV therapy.

c. *Hypoglycaemia* — This should be treated with 5 per cent glucose saline.

d. *Hypokalaemia* may also develop during rewarming, for which corrective action may be necessary.

e. Occasionally, acute gastric ulceration and/or acute pancreatitis may complicate sub-acute accidental hypothermia, although both are more usually encountered in the chronic variety (Mant, 1969).

f. A possible late complication of sub-acute hypothermia is acute nephrosis (Laufman, 1951; McKean, Dixon, Gwynn and Irvine, 1970).

Finally, it cannot be over-emphasised that the definition of death in hypothermia is failure to revive.

5. Conclusion

(i) Immersion in cold water produces rapid falls in deep body temperature accompanied by minor alterations in blood pH and electrolytes. The treatment consists of rapid reversal of the body temperature by immersion in a hot bath at 41°C.

Generally speaking it is unnecessary and unwise to try and correct the biochemical disturbances. If necessary, then it should not be undertaken until the rewarming is well established.

(ii) Accidental hypothermia produced in situations which involve high muscle energy expenditure over a period of time is usually accompanied by moderate to severe biochemical changes which may require correction, but again only when rewarming is well established. In this instance rewarming should be slow.

(iii) Attempts at resuscitation must be made even in those apparently dead.

Acknowledgment

The assistance of Surgeon Commander J. Rivers, RN, for his helpful suggestions in writing this paper is gratefully acknowledged.

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The Symposium was followed by a most interesting discussion. Unfortunately for reasons of space it has not been possible to include extracts in this issue, but it is hoped that an account may appear next year.

(Editor)

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Thermal Balance and Survival Time Prediction of Man in Cold Water

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Metabolic rates and rectal temperatures were continuously monitored for humans immersed in cold ocean water (4.6–18.2 °C) under simulated accident conditions. The subjects wore only light clothing and a kapok lifejacket while either holding-still or swimming. While holding-still, metabolic heat production (H_m, kcal · min^{-1}) was inversely related to water temperature (T_w, °C) according to the equation $H_m = 4.19 - 0.11T_w$. This thermogenic response pattern is shown to be similar to that for exposure to air of the same temperature when air velocity is just over 5 m.p.h. (2.24 m/s).

The thermogenic response was one-third efficient in balancing the calculated heat loss in cold water, resulting in hypothermia at a rectal temperature cooling rate (C, °C · min^{-1}) dependent on water temperature (T_w, °C) according to the relation $C = 0.0785 - 0.0034T_w$.

Although swimming increased heat production to 2.5 times that of holding-still at 10.5 °C water temperature, cooling rate was 35% greater while swimming.

A prediction equation for survival time (t_s, min) of persons accidentally immersed in cold water (T_w, °C) has the form $t_s = 15 + 7.2/(0.0785 - 0.0034T_w)$, based on the findings of this study, and it is compared to pre-existing models.

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La consommation d'oxygène et la température rectale ont été mesurées de façon continue chez des sujets immergés en eau océanique froide (4.6–18.2 °C) dans des conditions d'accident simulé. Les sujets, légèrement vêtus et porteurs d'une veste de sauvetage, nageaient ou étaient au repos. Au repos, la production métabolique de chaleur (H_m, kcal · min^{-1}) est inversement reliée à la température de l'eau (T_w, °C) suivant l'équation $H_m = 4.19 - 0.11T_w$. Ce type de réponse thermogénique est semblable à celui observé lors de l'exposition à l'air de même température et pour une vitesse de l'air de 5 m.p.h. (2.24 m/s).

La production de chaleur est insuffisante de 3/4 pour compenser la perte de chaleur calculée en eau froide, d'où une hypothermie caractérisée par une vitesse de diminution de la température rectale (C, °C · min^{-1}) dépendante de la température de l'eau suivant la relation $C = 0.0785 - 0.0034T_w$.

La nage augmente la production de chaleur de 2.5 fois à une T_w de 10.5 °C tandis que la paramètre C augmente de 35%.

L'équation prédisant le temps de survie (t_s, min) des personnes accidentellement immergées en eau froide (T_w, °C) est de la forme $t_s = 15 + 7.2/(0.0785 - 0.0034T_w)$ d'après les présents résultats. Cette équation a été comparée aux modèles préexistants.

[Traduit par le journal]

Introduction

It is well known that the high heat capacity of water presents a challenge to homeothermy of immersed man even when the temperature of that water is as high as 20–30 °C, and is a severe challenge at temperatures below this range. Whether man maintains heat balance or progresses into hypothermia during prolonged immersion is dependent on the magnitude of the thermogenic response and the efficiency of insulative mechanisms against heat loss. Factors which affect heat loss in cold water have received some attention (Witherspoon *et al.* 1971; Hayward *et al.* 1973*a*). This study is particularly concerned with evaluating the thermogenic response of man to cold water, as evidenced by increased metabolic heat production, and its relation to rate of progress into hypothermia.

Several studies have documented changes in the measures of thermal balance in man when immersed in water above 20 °C (Goff *et al.* 1956; Carlson *et al.* 1958; Craig and Dvorak

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1966; Lapp and Gee 1967). Much less information is available on the heat balance of man immersed at water temperatures below 20 °C, as has been pointed out in a review by Bullard and Rapp (1970). That which is available is mostly the work of Keatinge, who has extended the temperature range down to 15 °C, and with a few individuals to as low as 5 °C (Cannon and Keatinge 1960; Keatinge 1960; Keatinge 1961*a*). Also, some data are available based on one individual at 9 °C (Carlson *et al.* 1958) and two subjects at 6 °C (Behnke and Yaglou 1951). Data available on the thermal balance of channel swimmers (Pugh and Edholm 1955; Pugh *et al.* 1960) in water near 15 °C provides information that cannot be used to predict cold water responses of "average" subjects because the channel swimmers possess the unusual characteristic of combining large amounts of subcutaneous fat with capacity for high-level, endurance heat production while swimming. In the gruesome studies conducted on 50 subjects at Dachau Concentration Camp from 1942 to 1944 (Alexander 1946), many physiological changes associated with profound cooling (water temperatures of 2–12 °C) and rewarming of subjects were measured, but rate of oxygen consumption as a measure of thermogenic response to the cooling was not included.

In summary of the available information, there is inadequate data to provide a reliable, quantitative relationship between the magnitude of the thermogenic response of nonexercising man and water temperature below 20 °C, a range in which most deaths from accidental hypothermia occur. This study attempts to provide such a temperature–metabolism relationship.

Continuous measurements of oxygen consumption and rectal temperature were obtained on 12 subjects (six male, six female) who held still while immersed at three different water temperatures (4.6, 10.5, and 18.2 °C). For comparison with these nonexercising data, the effects of slow swimming at 10.5 °C were also measured.

In order that the results be most applicable to accidental situations, immersions were conducted in the sea, using persons of average build, who wore standardized, light clothing and a kapok lifejacket.

In addition to the emphasis on thermogenesis of man in cold water, the study also attempts to obtain enough data on cooling rates of subjects at different water temperatures to be able to derive prediction equations for extent of hypothermia and survival time of accidental immersees.

Methods

Immersions were conducted in the waters adjacent to Vancouver Island at locations and times of year to provide the range of water temperatures desired. Canadian government research ships were used as mobile laboratories.

Subjects

Table 1 provides a summary of subject characteristics for each immersion series. Activity in the water was described either as "still," when the subject was buoyed by a lifejacket (standard, kapok model) and made as little movement as possible during the immersion, or "swim," when the subject (wearing the lifejacket) was continuously engaged in moderate swimming activity. The swimming comprised a variety of strokes (side, breast, scull) at a frequency of about 30 per minute and was similar to the type of prolonged swimming to be expected if a person was attempting to reach shore.

In all cases, the subjects wore standardized clothing consisting of long-sleeved, cotton shirt; long, cotton pants; ankle socks; and running shoes. Undershorts were worn by the males and a two-piece bathing suit by the females. This clothing was chosen to simulate reasonably that of the majority of accidental immersions by recreational boaters.

Twelve subjects (6 male, 6 female) volunteered for the immersions. All participated in the four immersions except three individuals who had to be replaced for immersion series 1 and 4. One female subject could not be replaced for series 1. Since the immersion series were conducted at three periods (August, September, January) separated by at least 30 days, no opportunity for acclimatization of the subjects to the cold stress seems possible, and avoids this complication. Subjects were chosen to represent the "average" young adult human in terms of body size and fatness. Appropriately, females were approximately three-quarters the body size of males and had slightly greater amounts of subcutaneous fat, as indicated by skinfold thickness. Age of the males was greater, due to the participation of the three authors.

Those volunteers accepted for the study met necessary safety criteria stipulated by the University Committee for Research Involving Human Subjects. Age had to be between 19 and 29 (the authors were exceptions). Each underwent medical screening, which included recent examination and approval for participation by their personal physician, and ECG monitoring during an exercise stress test with the observations approved by a cardiologist familiar with our experimental procedures. Each volunteer signed a

consent form which described subject involvement in the study.

Oxygen Consumption and Body Temperature Measurements

Continuous measurements of oxygen consumption and rectal temperature were obtained during the following experimental regimen. A 5-min rest period with the subject sitting in the ship's laboratory (18–20 °C) preceded a 1-min interval necessary for movement to the ship's deck, down a ladder, and into the sea. Immersions lasted for periods of 25 min to 1 h depending on the water temperature. Each subject left the water when the rectal temperature had decreased to 35.0 °C or at a slightly earlier time if the subject was experiencing too much discomfort. At the warmest temperature (18.2 °C), the immersion was terminated after 1 h. Subjects were rewarmed in a whirlpool bath with water temperature beginning at 25 °C and raised to 42 °C over the first 10 min.

An index of shivering activity was also obtained continuously, using electrodes placed over the lateral muscles of the neck.

Sea conditions during immersions were selected to be as constant as possible with respect to waves and current. Typically, the current was about 0.1 $m \cdot s^{-1}$ and wave action was minimal (<10 cm height).

Oxygen consumption was measured using an open-system technique. The subject wore a full face mask through which air was drawn at rates of 50–80 $l \cdot min^{-1}$ depending on rate of oxygen consumption. The effluent air flowed through a flexible, plastic tube of 2.5 cm inside diameter and 30 m in length to a suction pump in the ship's laboratory. Air flow rate was measured with a gas meter (American Instrument Co.), and a continuous sample of the effluent air was routed to an oxygen analyzer (Beckman Instruments, model F3) and the oxygen concentration recorded potentiometrically. Ninety percent response time of the system was 40–50 s.

Rectal temperature was obtained using a thermistor inserted 15 cm beyond the anus. The lead wires for the thermistor and for the EMG electrodes entered through a seal into the tube carrying the effluent air from the subject's mask, and in that floating "umbilicus," returned to the ship's laboratory for monitoring on an oscillograph (Beckman Instruments, model 411).

This recording system facilitated continuous readings of the desired variables while the subject rested in the laboratory, entered the water, and was immersed, including swimming back and forth along the ship's side. Electrocardiograms were also monitored with this system, but will not be reported here.

Results

Time Course of Thermogenic and Cooling Responses

The time course of changes in oxygen consumption and rectal temperature under the four experimental conditions are shown in Fig. 1. Each line is the mean of 11 or 12 individuals of both sexes, as described in Table 1. Continuous, smooth lines were drawn by computer (using the cubic spline function) through the mean values of these variables, for 11 or 12 individuals, at 1-min intervals. Oxygen consumption while holding-still approximately doubled within the first 2 min of immersion due to the intense peripheral stimulation accompanying the rapid decrease in skin temperature. As skin temperature stabilized at the lower levels, and subjective discomfort of the immersees lessened, oxygen consumption decreased. Other recordings not included here have shown that skin-surface temperature over most of the body stabilized within 1 °C above the water temperature. By 10 min of immersion, oxygen consumption at each water temperature was established at a level that changed only very slowly upward over the remainder of the immersion. Qualitative inspection of the electromyographic recordings substantiated previous findings (Cannon and Keatinge 1960; Carlson *et al.* 1958) that shivering intensity is highly correlated with levels of oxygen consumption during cold exposure. In an apparent attempt at thermoregulation, oxygen consumption (equivalent to heat production or thermogenesis) was greater with colder water temperatures. Particular analysis of this relation is given in the next section. At this point, however, it can be seen that despite greater heat production with colder water temperature, hypothermia resulted in all instances while holding-still, with the rate of fall of rectal temperature increasing as the water temperature decreased. Particular analysis of this relation of cooling rate to water temperature and the efficiency of the thermogenic response are presented in later sections. Here, we can summarize that heat production while holding-still is responsive to water temperature, but is quantitatively inadequate to offset hypothermia.

This introduces the question of whether greater heat production with voluntary movement is more effective in the maintenance of thermal balance. Fig. 1 shows that the oxygen consumption of individuals swimming moderately in a lifejacket is approximately 2.5 times as great as that while holding-still at the same water temperature (10.5 °C). Despite this much greater heat production, the time course

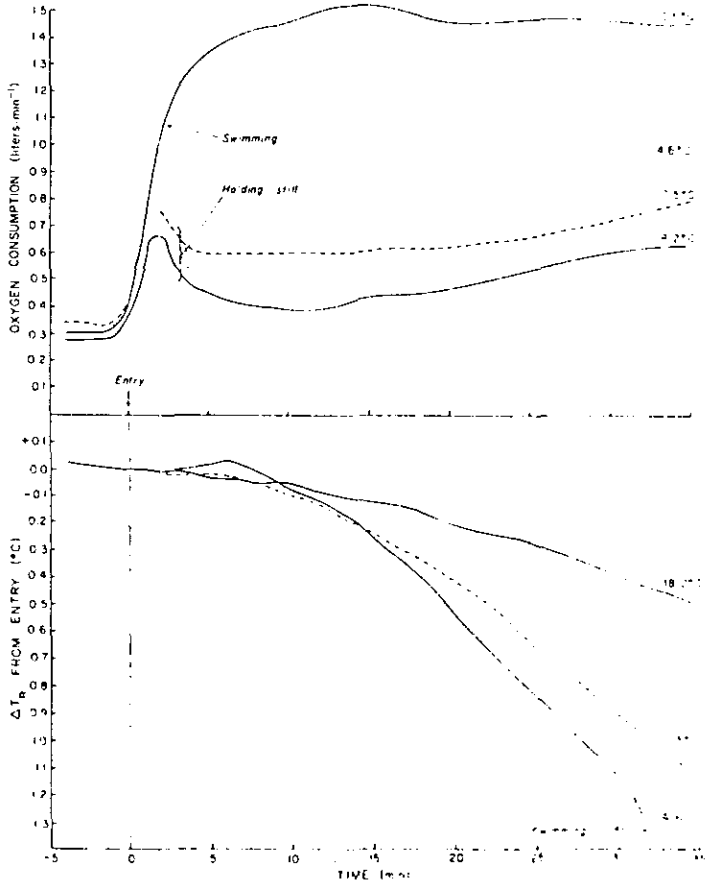

FIG. 1. Time course of changes in oxygen consumption and rectal temperature (ΔT_R) during immersion of humans in the ocean at three different water temperatures and with two activities. Each line is the mean for 11 or 12 individuals and joins values for 1-min intervals. Significant differences ($p < 0.05$) occurred in the oxygen consumption records between swimming and all the holding-still records from 2 min onward. Among the holding-still records, significant differences occurred between 4.6 °C and 18.2 °C from 8 min onward. Significant differences in the amount of fall of rectal temperatures were established by approximately 20 min in all comparisons except between swimming at 10.5 °C and holding-still at 4.6 °C. Before entry at time zero, subjects were sitting at rest under thermoneutral conditions. Mean rectal temperature at entry time was 37.44 °C with a standard deviation of 0.28 °C.

of change in rectal temperature shows an initial, slight rise followed by a decrease that by 15 min is established at a greater rate than that while holding-still at the same water temperature. If the cooling rates over the interval from 15 to 25 min are used as criteria, a significant ($p < 0.05$) difference in cooling rate is observed, with swimming being 1.35 times that of holding-still. Conversely, these subjects proceeded into hypothermia while holding-still at 0.74 times the rate while swimming. Since this finding substantiates previous information on the detrimental effect of activity (using underwater rowing apparatus) on heat balance of

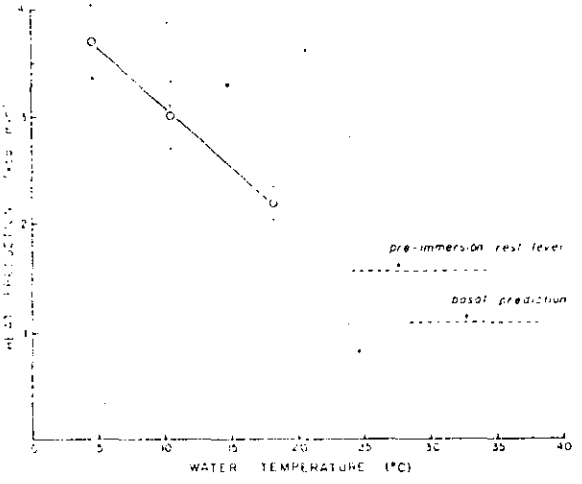

FIG. 2. Relationship between metabolic heat production and water temperature of subjects immersed in the ocean while holding-still and wearing light clothing and a lifejacket. Dotted line is a linear extrapolation for purposes of estimating critical temperatures and the regulated body temperature. Vertical lines denote standard errors of the means.

TABLE 1. Physical characteristics (means ± S.E.) of subjects participating in four series of immersions

Immersion series	Sea temperature (°C)	Activity[a]	Sex	*n*	Age (years)	Weight (kg)	Height (cm)	Skinfold thickness[b] (mm)
1	4.6	Still	M	6	30.0 ± 3.7	83.7 ± 1.4	183.3 ± 1.8	9.6 ± 0.9
			F	5	19.6 ± 0.4	54.0 ± 1.2	163.1 ± 2.6	10.6 ± 0.7
2	10.5	Still	M	6	31.5 ± 3.0	79.3 ± 1.9	179.1 ± 1.7	8.9 ± 1.0
			F	6	22.2 ± 1.2	56.6 ± 1.9	163.4 ± 2.1	15.5 ± 1.6
3	18.2	Still	M	6	31.5 ± 3.0	79.3 ± 1.9	179.1 ± 1.7	8.9 ± 1.0
			F	6	22.2 ± 1.2	56.6 ± 1.9	163.4 ± 2.1	15.5 ± 1.6
4	10.5	Swim	M	6	30.7 ± 3.5	81.9 ± 1.9	180.8 ± 2.2	9.0 ± 1.0
			F	6	22.5 ± 0.7	60.6 ± 3.2	168.9 ± 1.9	14.8 ± 1.6
Mean values for all series								
Males					30.9 ± 1.5	81.1 ± 0.9	180.5 ± 0.9	9.1 ± 0.5
Females					21.7 ± 0.5	57.3 ± 1.2	165.2 ± 1.1	14.3 ± 0.8
All subjects					26.7 ± 1.1	69.0 ± 2.3	173.0 ± 1.3	11.7 ± 0.6

[a]See text for detail.
[b]Based on triceps site on arm.

average subjects in cold water (Keatinge 1961*a*), further analysis of these responses will be confined to the holding-still situation.

Analysis of the Thermogenic Response to Cold Water

To examine the thermogenic response, some measure of the mean magnitude of this response and its variation was required. Fig. 1 shows that a steady-state response level does not occur in the subjects while holding-still. However, some segment of the response for each individual, which approximates a steady-state level and represents the early thermoregulatory heat production before significant hypothermia results, is required for this analysis. Accordingly,

the mean rate of oxygen consumption for each individual during the interval 10–25 min of immersion was utilized as the single measure of thermogenic response. The dependency of this response upon water temperature, skinfold thickness, body weight, and sex was determined by multiple regression analysis. Significant ($p < 0.01$) dependency upon water temperature was found, but the regression was not improved by inclusion of values for sex, weight, or the small range of skinfold thickness. Consequently, a simple linear relationship between water temperature and the thermogenic response of all individuals can be presented (Fig. 2). The relationship is described by the equation

$$[1] \qquad H_m = 4.19 - 0.117T_w$$

in which H_m is metabolic heat production in kilocalories per minute (using caloric equivalent of oxygen of 4.83 kcal·l^{-1} (1 kcal = 4.186 kJ)), and T_w is water temperature in degrees Celsius. The standard error of estimate is 0.93 kcal·min^{-1} and the standard error of the regression coefficient is 0.029 kcal·min^{-1}·°C^{-1}. Extrapolation of the regression to a hypothetical zero heat production occurs at a water temperature of 38.09 °C and is less than 1 °C greater than actual rectal temperature at this stage of immersion. Similarity of the extrapolated value to the body temperature is a theoretical expectation of metabolism–temperature curves of homeotherms (Barnett and Mount 1967; Hart 1971). The levels of heat production in this study compare favorably with those available from Keatinge (1961*a*), who observed a metabolic rate 7% lower than our prediction in men holding-still at 5 °C while wearing arctic clothing. At the same temperature, his unclothed subjects had a heat production 25% greater than our prediction, which may be a reasonable indication of the sparing effect of the clothing in our study.

In Fig. 2, the levels of heat production during pre-immersion rest and for a single, basal metabolism prediction for the subjects (Guyton 1971) are added to allow estimation of critical temperatures (ambient temperatures at which thermogenic response is initiated). Based on these values, critical temperatures for these subjects (wearing light clothing and a lifejacket while holding-still in the sea) would be 23.8 °C based on the pre-immersion rest level of heat production, and 28 °C based on predicted basal heat production.

Analysis of Cooling Rate Relative to Water Temperature

Fig. 1 showed that deep body cooling was not established at fairly uniform rates until approximately 15 min of immersion. Accordingly, measures of cooling rates for individuals should be based upon some time interval after 15 min. Since at the coldest water temperature (4.6 °C) some individuals exited the water before 30 min of immersion, the most valid interval for cooling rate assessment in this study is 15–25 min of immersion. In Fig. 3, the mean cooling rates of all subjects for the above period are related to water temperature. A significant ($p < 0.01$) regression occurs between these two variables described by the function

$$[2] \qquad C = 0.0785 - 0.0034T_w$$

in which C is cooling rate in degrees Celsius rectal temperature decrease per minute and T_w is water temperature in degrees Celsius. The standard error of estimate is 0.016 °C·min^{-1} and the standard error of the regression coefficient is 0.0005 °C·min^{-1}·°C^{-1}. Extrapolation of this regression to zero cooling rate occurs at 23.1 °C water temperature. This "critical temperature" for cooling under these conditions compares closely with the critical temperature prediction of 23.8 °C based upon the thermogenic response data.

Analysis of the cooling rates for their relation to skinfold thickness showed no significant correlation over the small range of skinfold thickness present in the subjects. In relation to the sex of the immersees, cooling rate was significantly ($p < 0.05$) correlated only in the case of the immersion at 10.5 °C in which the cooling rate of males was 0.60 times that of females. In this instance, the females had a significantly ($p < 0.01$) lower body weight than the males. Since it has been shown that smaller body size increases cooling rate (Keatinge and Sloan 1972), this is probably the attribute of the females that is associated with

their faster cooling. When all the immersions at three temperatures are considered, males cooled at 0.84 times that of females, but the difference was not significant. For this reason, the cooling rate analysis of Fig. 3 was based upon the data for both sexes.

Efficiency of the Thermogenic Response

Despite the apparent regulation of heat production according to water temperature, the fact that hypothermia ensued at the experimental water temperatures of this study indicates that the regulated heat production has low efficiency in meeting actual heat loss. To attempt quantification of this efficiency requires some estimate of heat loss in the water. In this study, the only means to predict heat loss is by body temperature decrease and an assumed caloric equivalent thereof. Body heat loss would be greater than indicated by deep body temperature decline during the first stage of immersion. However, by 15 min of immersion, peripheral temperature gradients should be well established such that deep body temperature decline thereafter should be a reasonable basis for assessing further heat loss. The rate of deep body temperature decline according to water temperature is predicted by Eq. 2. For the purpose of the efficiency estimate, a value of 0.9 kcal/kg of body weight per degree Celsius decline in rectal temperature will be used as the heat equivalent.[2] By multiplying this factor by cooling rates of the individuals and their body weights, an estimate of net heat loss is obtained. Actual, total heat loss is the sum of net heat loss and heat production (Eq. 1). If total heat loss by this approximation is regressed against water temperature (Fig. 4), a relationship is obtained

$$[3] \qquad H_L = 0.07 - 0.32T_w$$

in which H_L is total heat loss in kilocalories per minute and T_w is water temperature in degrees Celsius. The standard error of estimate is 1.69 kcal·min^{-1} and the standard error of the regression coefficient is 0.05 kcal·min^{-1}·°C^{-1}.

[2]The actual specific heat of the tissues may be slightly different from this value, which has been used by Stolwijk (1970) to estimate heat capacity of tissues other than fat and bone.

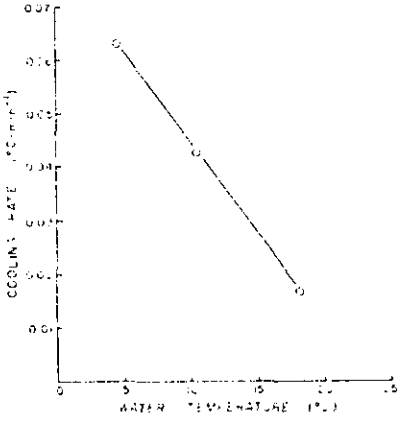

FIG. 3. The influence of water temperature on deep-body cooling rate (rectal temperature) of subjects immersed in the ocean. Dotted line extrapolates to predict the critical temperature for central hypothermia under the conditions of this study. Vertical lines denote standard errors of the means.

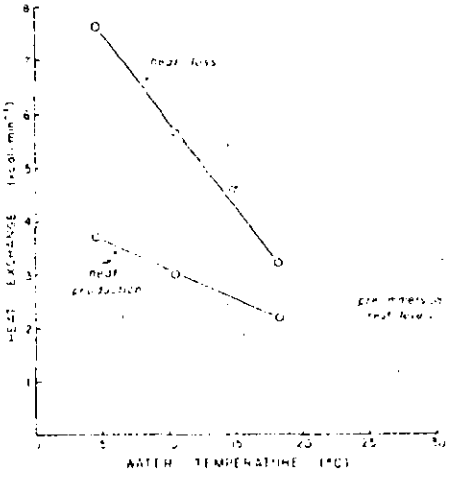

FIG. 4. Comparison of calculated heat loss (see text) at different water temperatures with the measured rates of heat production.

Also plotted in Fig. 3 is the heat production curve. The comparison of heat production with total heat loss yields the following estimate. Increased heat production above the resting level in response to water temperature below 23 °C is only 34% efficient in balancing increased heat loss under these conditions. This

low thermogenic efficiency accounts for the progressive hypothermia which ensues.

Prediction Equations for Degree of Hypothermia and Survival Time in Cold Water

The cooling rate data of the subjects in this study allow construction of equations that predict either the rectal temperature when water temperature and immersion time are known, or a hypothetical survival time when water temperature alone is known. Such predictions will be pertinent to experimental or accidental immersion conditions similar to those of this study, namely, persons of average build, holding-still, and wearing light clothing and a standard lifejacket. The validity of the predictions requires two *a priori* assumptions. Firstly, some deep body temperature must be arbitrarily chosen to represent the point at which hypothermic death will, on the average, occur. The only information on unanesthetized humans cooled to such an extent is that of the Dachau prisoner-of-war studies (Alexander 1946). Although deaths that occurred in these studies took place at 26–27 °C rectal temperature, unconsciousness and "incipient death" (in terms of risk of spontaneous cardiac fibrillation and chances of successful rewarming in rescue operations) were at a higher rectal temperature. Quoting from the report of these studies, "Death impends at rectal temperatures below 30 °C," (p. 62) provides the best evidence available for selecting a rectal temperature of 30 °C as the criterion of hypothermic "death." The second assumption required is that there is a continuation of the linear decline in rectal temperature in the range of 35 °C down to 30 °C while in cold water. Again, no data are available relevant to accidental hypothermia except the Dachau studies (Alexander 1946). These show that there is an essentially linear decrease over this range (see Figs. 15–20 of the Alexander report and Burton and Edholm (1955), p. 206), which warrants linear extrapolation down to 30 °C of our cooling rate data.

The following prediction equations are based on cooling rates after 15 min of immersion when the mean rectal temperature for the holding-still immersions was 37.2 °C (down an average of 0.2 °C from the start of immersion).

The equation to predict rectal temperature (T_R in degrees Celsius) as a function of immersion time (t in minutes) and water temperature (T_w in degrees Celsius) is

$$[4] \quad T_R = 37.2 - (t - 15)(0.0785 - 0.00347T_w)$$

when $t \geq 15$ min and $T_w \leq 23$ °C.

Survival time of persons such as our subjects under these simulated accidental immersion conditions would be

$$[5] \quad t_s = 15 + \frac{7.2}{0.0785 - 0.00347T_w}$$

in which t_s is survival time in minutes, T_w is water temperature in degrees Celsius (≤23 °C), and "incipient" death is assumed to occur at a rectal temperature of 30.0 °C. Confidence limits for this prediction can be calculated by substituting the confidence limits of the cooling rate expression ($0.0785 - 0.00347T_w$) determined by its standard error of estimate.

Discussion

The results of this study show that the early thermogenic response to water immersion at different cold temperatures is predictable. However, this response is inadequate to maintain thermal balance, since the rate of heat production is only about one-third the rate of heat loss. This finding suggests that the regulated heat production is appropriate for an environment in which the rate of heat loss is about one-third that of water. Interestingly, Molnar (1946) calculates that heat loss of man in air is about one-quarter to one-half that in water of the same temperature. Similarly, Hall (1972) estimates heat loss in air to be 25–44% that in water. On this basis, it appears that the regulated heat production of man resting in cold water is of a magnitude suitable for response to air of the same cold temperature. To confirm this generalization, comparison of our results for thermogenesis in water with those of other workers for thermogenesis in air is required. In comparison with results for men resting in still air over a range of cold, ambient temperatures (Spurr *et al.* 1957; Iampietro *et al.* 1960; Keatinge 1961*b*; Hurley *et al.* 1964; Raven *et al.* 1970), our heat production response of men in cold water is approximately

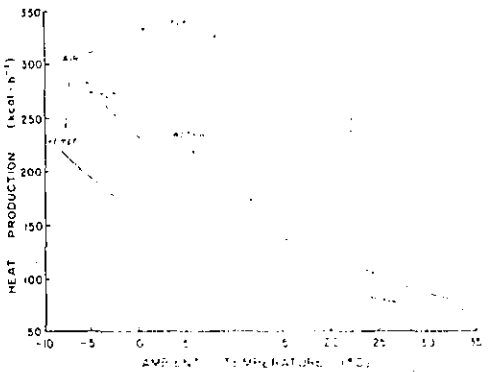

FIG. 5. Comparison of the heat production of our subjects in cold water (dashed line) with that of nearly nude men exposed to cold air at three wind velocities. Air curves are from Iampietro *et al.* (1960).

50% higher at any given temperature. However, in comparison with the response of nearly nude men to cold air when that air is moving at just over 5 m.p.h. (2.24 m/s) (Iampietro *et al.* 1960), our results are not significantly different. To emphasize this point, Fig. 5 compares our thermogenic response curve for men in cold water with the curves for men at different air temperatures and wind velocities, taken from the most thorough information available on this response (Iampietro *et al.* 1960). It can be concluded that there is a similar, peripheral, thermoregulatory stimulus from the skin for metabolic heat production in our subjects in cold water as there is in nearly nude men in cold air of the same temperature but moving at just over 5 m.p.h. Similar skin temperatures and consequent firing rates of cold receptors must apply for lightly clothed man in cold water and for man exposed to mild wind chill at the same ambient temperature. In longer durations of immersion in cold water, the onset of central hypothermia occurs more rapidly than in air and causes further increases in the magnitude of heat production. The interaction of peripheral and central inputs to thermoregulation in such long-duration immersions in cold water requires clarification, and is being studied in our laboratory.

This study has confirmed the findings of Keatinge (1961*a*) that activity in cold water (such as swimming) significantly increases the cooling rate of immersees. Previous results (Hayward *et al.* 1973) have shown thermographically the greater areas of surface heat loss caused by swimming. Keatinge's (1961*a*) unclothed subjects cooled at a 47% greater rate while performing rowing activity than while sitting still in 5 °C water. This compares favorably with our finding of a 35% greater cooling rate while swimming than while holding-still at 10.5 °C. The rate of heat production of our subjects while swimming at 10.5 °C was not significantly different from that of subjects performing a similar level of swimming activity at the warmer temperature of 24 °C (Andersen 1960), indicating that exercise thermogenesis is independent of water temperature.

It has been shown by Craig and Dvorak (1968) that at water temperatures above 24 °C, exercising is preferable to holding-still in preventing hypothermia. Also, Glaser (1950) advised that cold water immersees swim or struggle to keep warm, but his conclusions are open to question. He did not actually measure deep body temperature of his single subject who swam at 20 °C for an unknown duration. Therefore, Glaser's (1950) results do not permit extension down to 20 °C of Craig and Dvorak's advice to exercise for maintenance of body temperature. The conclusion is warranted on the basis of the results of Keatinge (1961*a*), this study, and those of Pugh and Edholm (1955) for some channel swimmers, that for accidental immersions in water temperatures of below 20 °C, while not wearing special survival suits, exercise thermogenesis such as swimming is accompanied by an increased rate of progress into hypothermia. The obvious corollary to the advice not to swim is that it applies only to the situation in which shore or other means of escape from the water is too far away to reach before the faster rate of cooling while swimming renders the person so hypothermic that swimming is no longer possible. What distance this may be at different water temperatures, for subjects wearing clothing and lifejackets, is at present unknown.

The survival time prediction equation derived in this study requires careful evaluation in comparison with previous knowledge. Predictions of survival time in cold water or the duration of "useful activity" are available from

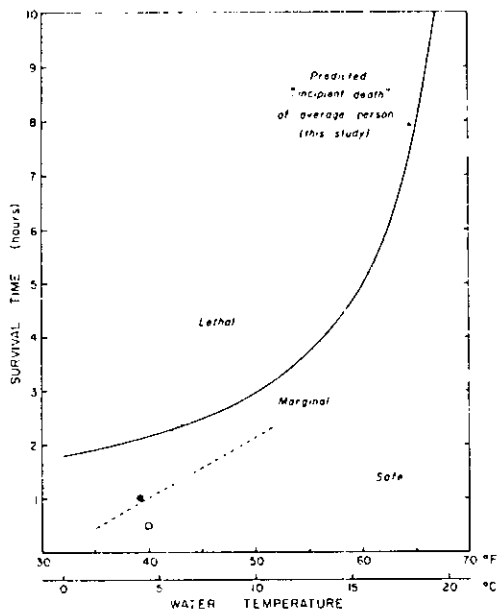

FIG. 6. Comparison of various predictions of survivorship or tolerance time of man in cold water. Solid line is based on Eq. 5 of this study and predicts 50% survival time based on "incipient death" at 30 °C rectal temperature. Dashed line is estimate of Molnar (1946) for 50% survivorship of Dachau prisoners. Dotted lines are from the widely used chart of the U.S. Navy (DeForest and Beckman 1962; Whittingham 1965), which is based on Molnar's report (1946) and which delineates a "marginal" zone (50% expectancy of unconsciousness which will probably result in drowning) from a "lethal" zone (100% expectance of death) and a "safe" zone. Closed circle is prediction from the theoretical nomogram of Smith and Hames (1962) for 50% survival at 31 °C body temperature. Open circle is predicted tolerance time (duration of useful activity; mean body temperature of 32.8 °C) for person with 0.8 clo of insulation (Hall 1972).

several reports. Molnar's (1946) prediction is a graph derived from review of the findings of the Dachau prisoner-of-war study (Alexander 1946). The predictions of Smith and Hames (1962) and of Hall (1972) are based upon theoretical expectations of heat production, heat loss, and insulation. Since the wartime studies reviewed by Molnar (1946), prediction of survival time based on new experimental data on actual cooling rates of humans has not been presented. The survival time prediction equation of this study presents such new data for comparison with existing models. Summarization of this comparison is best accomplished with a composite graph (Fig. 6) including our prediction and all or samples of the predictions of other authorities. The term "50% survival time" as used by others means essentially the same as our "incipient death." That is, the 50% who have not survived may not actually be clinically dead in terms of complete cardiac failure, but are at some point of incipient death (unlikely to be able to be successfully recovered to normothermia). Our line delineates when the average person (or 50th percentile) reaches such a point of irreversible hypothermia. The major difference between previous estimates and our model is that the earlier estimates predict too low a survival time at the lower water temperatures. Burton and Edholm (1955) have also noted this apparent underestimation of survival time based on the Dachau prisoners, and suggest this may reflect the condition that the prisoners were "unlikely to be well nourished." Similarly, Molnar (1946) mentions that "the influence of possible emaciation and weakness due to starvation is not adequately checked" relative to the survival time data of the prisoners. Certainly, the data of Behnke and Yaglou (1951) and of Keatinge (1961*a*) suggest longer survival time than that which Molnar (1946) predicts.

In summary, our prediction equation for survival time in cold water seems to be the most valid available for the accidental immersion situation. It predicts best for persons of average adult size and fatness, and average thermogenic response to cold water. Large body size extends survival in accidental immersions in cold water (Kreider 1967), and conversely, smaller body size, as that of children, would decrease survival time based on the data of Keatinge and Sloan (1972) and our own unpublished findings. Subcutaneous fatness is the best documented determinant of cooling rate in cold water (Carlson *et al.* 1958; Keatinge 1960; Pugh *et al.* 1960; Sloan and Keatinge 1973), with the greater such fatness, the longer the survival expected. However, in the majority of persons who could become accidental immersees in cold water, the variation of subcutaneous fat level is not large, such that other factors may play a greater role in determining survival. One factor is the type and amount of clothing worn and the insulative value, if any,

of the lifejacket. More study is required as to the effect of this variable. Also, the effects of the adoption of special, heat-retaining postures in the water or of huddling of several persons may have greater effect than fatness on survival, and are being studied in our laboratory. Our results showed that there is also considerable variability amongst individuals in their thermogenic response to cold water. Hall (1972) also mentions the "extreme individual variability in threshold, intensity and ability to maintain a high metabolic level" as a complicating factor in survival. This variability probably accounted for our inability to find a significant difference between males and females. We noted some individuals who would shiver intensely (and cooled more slowly), whereas others shivered very little under the same circumstances. Yet, this variability was unrelated to sex, size, or fatness. Similarly, Girling (1964) noted this phenomenon and categorized "shiverers" and "non-shiverers" in their metabolic response to cold air. This variability is apparently unpredictable, but could also help to account for differences in survival time in cold water. Other variables that would effect survival time are alcohol consumption and exhaustion. Haight and Keatinge (1973) have shown that both these variables reduce blood glucose and cause failure of the metabolic response and vasoconstriction of men in cold air. Drinking alcoholic beverages before immersion or prolonged physical exertion that led to exhaustion before or during immersion would markedly reduce survival time.

Finally, the experimental predictions of survival time in cold water, including our own, are based on the condition that the subject is not swimming or otherwise grossly active. It is doubtful that this condition could apply when very rough water conditions prevail. Survival time under such conditions may long evade experimental assessment.

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Energy metabolism and body temperature of the ama[1]

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KANG, D. H., P. K. KIM, B. S. KANG, S. H. SONG, AND S. K. HONG. *Energy metabolism and body temperature of the ama.* J. Appl. Physiol. 20(1): 46–50. 1965.—Rectal temperature and oxygen consumption were determined in the ama while diving during the summer and winter. In addition, a dietary survey and a physical-fitness test were conducted. The average rectal temperature fell to 35.3 C after 45 min of work in summer (water temp., 22–26 C) and to 34.8 C after, 30 min of work in winter (water temp., 10–13 C). The lowest rectal temperature was 33.2 C in summer and 34.3 C in winter. $\dot{V}O_2$ increased to nearly 1 liter/min in summer and to 1.4 liter/min in winter. One can calculate that the total extra energy expenditure for diving work is approximately 1,000 kcal/day in both winter and summer. The actual dietary survey showed that the total caloric intake of the ama is 3,000 kcal/day in both summer and winter, which exceeds the daily requirement for nondiving women of comparable age by 1,000 kcal. The protein intake was not different between summer and winter. Physical fitness, as judged by the score of Harvard step-up test, was significantly better in the ama than in the control in both summer and winter. Moreover, physical fitness was poorer in winter as compared to summer in the control, whereas it was excellent throughout a year in the ama.

cold stress physical fitness

DURING THE PAST FEW YEARS a series of studies has been conducted in our laboratories on the diving women of Korea (ama). These have described the mechanics of diving, the pattern of alveolar gas exchange, and various adaptative manifestations as seen in both the respiratory and the thermoregulatory systems (4, 5, 7, 13, 15). One of these studies showed that the oral temperature of the ama drops to 33 C in winter (10 C water) and to 35 C in summer (27 C water) (7). The extent of such a reduction in the oral temperature is quite impressive and it is important to know to what extent this reflects a decrease in deep body temperature as measured, for example, from deep in the rectum. It was also noted that the ama have an elevated basal metabolic rate (BMR) during the winter (7) and an increased maximal tissue insulation (4). The increase in BMR during winter was attributed to the severe cold-water stress to which these divers are exposed daily; however, the cold stress was not quantitatively defined. Moreover, additional information on the amount of protein intake was needed before the elevated BMR could be attributed solely to the cold stress. With these considerations in mind we have: 1) measured the rectal temperature as well as the oxygen consumption during the course of a diving shift in order that the magnitude of heat exchange could be computed quantitatively, and 2) surveyed the diet in order to estimate the caloric and protein intake. In addition, a physical fitness test was also performed to see if this score could be modified by the seasons.

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METHODS

Summer studies were conducted in July of 1961 and 1962 and winter studies during January of 1962 and 1963. All experiments were carried out in Young Do, Pusan, where nearly 300 ama are daily engaged in diving.

Measurement of Heat Exchange During Diving Work in Water

Five ama (see Table 1) were selected for this study. Experiments were carried out in the field where the ama dive to a depth of approximately 5 m. A boat was used so that all measurements could be taken in the normal diving location and with minimum interference with the usual diving pattern.

Measurement of rectal temperature. While each subject was preparing for her daily diving routine on board, a rectal probe approximately 10 cm in length was inserted into the rectum. The temperature during the rest period on board was recorded by a tele-thermometer (Yellow Spring Instrument Co.). The subject then entered the

TABLE 1. *Physical characteristics of subjects*

Subj.	Age, yr	Height, cm	Weight, kg	SFT, mm
A	33	166	67	29.5
B	38	153	55	20.0
C	33	149	50	7.0
D	37	151	52	26.5
E	45	157	57	29.0

SFT = total of ten skinfolds less 40 mm.

water with the probe in position and commenced diving. During the diving period the rectal temperature was recorded every 5 min by an observer on board.

Determination of mean skin temperature. When the subject was resting on the boat before diving, the skin temperature was measured with a thermistor placed on the forehead (H_f), the chest (H_c), a forearm (H_a), and a lower leg (H_l). The mean skin temperature (H_s) was then computed by using the following formula: $H_s = 0.05\ H_f + 0.45\ H_c + 0.14\ H_a + 0.36\ H_l$. During the period of diving the skin temperature of the forehead alone was measured at certain time intervals and the skin temperature of the rest of the body was assumed to be identical to the surface water temperature. The mean skin temperature was then computed as before.

Measurement of oxygen consumption ($\dot{V}_{O_2}$). During rest periods between dives expired gas was collected in a Douglas bag for 5-min periods. Its volume was measured immediately by passing it through a dry gas meter on the boat. Duplicate samples of expired gas were drawn into syringes rinsed with saturated LiCl. These were analyzed later in the laboratory by a Scholander microgas analyzer. Oxygen consumption (STPD) was computed by the following formula: $\dot{V}_{O_2} = \dot{V}_E\ (0.209 - F_{E_{O_2}})$, where $\dot{V}_E$ and $F_{E_{O_2}}$ refer to the minute volume and the fraction of oxygen in the expired gas, respectively.

The oxygen consumption was first determined while the subject was resting on the boat and then during the diving period. During the latter period, measurements were taken every 5–10 min. At the time of measurements, the subject was asked to stop diving and to come to the side of the boat. During this measurement, the subject was resting on a float at the surface of sea water.

Dietary Survey

The "precise weighing method" recommended by FAO (10) was used. This method requires accurate weighing of all food just prior to and immediately after meal times. In the present investigation the investigators visited the homes of eight ama at every meal time for four successive days. For the calculation of calories and of nutrients of the diet, various food composition tables were used (1, 2, 9, 16).

Physical Fitness Test

The "slow form" of the modified Harvard step-up test was employed (14). The test was modified to accommodate the short height of the Korean women so that instead of using a bench 20 in. high, we used a bench 12¾ in. high. Twenty subjects each were chosen from ama and nondiving women and the scores of the tests were compared. These subjects participated in our previous studies and their physical characteristics are given in an earlier publication (15).

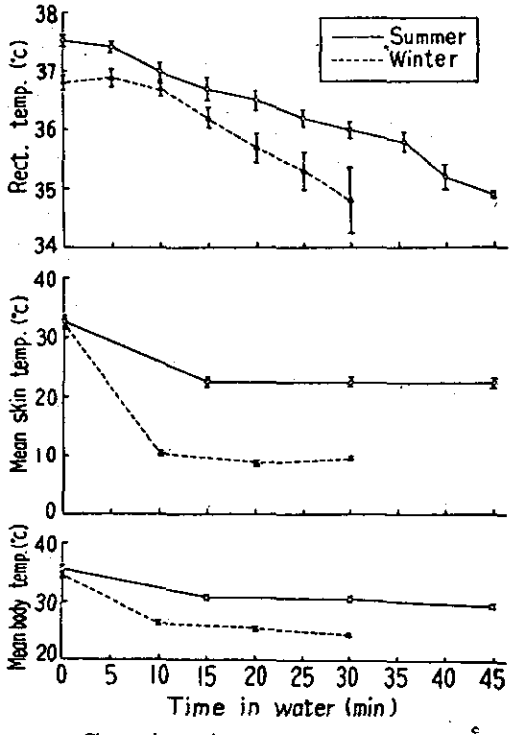

FIG. 1. Changes in rectal, mean skin, and mean body temperatures during a diving work shift. (Means ± SE.)

RESULTS

Changes in Body Temperature

The time course of the rectal temperature, mean skin temperature, and mean body temperature (0.6 × rectal temp. + 0.4 × mean skin temp.) while the ama are working in water is shown in Fig. 1. These values are the average of nine measurements on three subjects.

Although there were considerable individual variations, the rectal temperature remained unchanged during the first 5–10 min in water, after which it fell. By the end of a 45-min work period in the summer the average rectal temperature was lowered to 35.3 C. By the end of a 30-min work period in winter the average rectal temperature was 34.8 C. Although in the winter the duration of a shift was usually 30 min, in three trials it was 20 min. In one of the latter, the rectal temperature at the end

of 20 min was 34.7 C, at which point the subject gave a signal to come out of the water. However, she was asked to stay in water as long as she could tolerate it. Within the next 10 min the rectal temperature fell to 32.2 C and she had to be rescued from the water. The lowest rectal temperature which other subjects tolerated in winter on a voluntary basis was 34.3 C as compared to 33.2 C in summer.

The mean skin temperature between the summer and the winter varied with the difference in the water temperature. Therefore, the calculated mean body temperature at the end of a work shift was approximately 30 C in the summer as compared to 25 C in the winter.

Oxygen Consumption

Values obtained from individual experiments are summarized in Table 2. The oxygen consumption before the dive while the subject was resting on the boat averaged 454 and 388 ml/min in the summer and the winter, respectively. When the subject entered water, the oxygen consumption increased almost immediately in all cases, followed by a slight further increase during the rest of work period. However, the magnitude of increase in the oxygen consumption was much greater in the winter than in the summer. On the average, the oxygen consumption increased by 2-fold in the summer and by 3.5-fold in the winter in response to the cold water and the exercise. Although we were not able to estimate the energy cost of the diving per se, it probably does not change with the season. Thus, since the oxygen consumption was determined while the subject was resting on a float near the boat, the 75% higher oxygen consumption during winter is most likely due to shivering in response to the temperature of water.

Heat Exchange

In three subjects (*A*, *B*, and *C*), the rectal temperature and oxygen consumption were measured simultaneously during the work shift and their heat balance was computed quantitatively (see Table 3).

The rate of heat production [$\dot{V}_{O_2}$ (liters, STPD) × 4.83] was of the order of 2 kcal/min during the rest period on the boat in both summer and winter. As the changes in oxygen consumption indicate, heat production during the diving shift increased 2-fold in the summer and 3- to 3.5-fold in the winter. Despite the greater increase in winter heat production, the mean body temperature was lowered more in the winter than in the summer, indicating a greater rate of heat loss.

The extra heat production above resting values during the diving shift was 109 kcal in the winter. The reduction in body heat content during the diving shift was 293 and 466 kcal in the summer and the winter, respectively. Therefore, by the time the ama terminated one diving shift, they had lost an equivalent of 388 kcal in the summer and 557 kcal in the winter. The over-all heat loss was nearly 50% greater in winter compared to summer despite the fact that the duration of a shift was only half as long in winter as in summer.

TABLE 2. *Oxygen consumption during the period of diving work (ml/min, STPD)*

Subj.	Date	Before Dive	Minutes in Water					
			5	10	15	20	25	40
Summer (water temp. 22–26 C, air temp. 30 C)								
A	Aug. 1961	379			841			1,144
A	July 1962	386		819			1,045	1,062
A	July 1962	527		908			840	1,150
B	July 1962	479		634			776	830
B	July 1962	507		832			996	1,105
C	July 1962	469			1,039		1,120	1,122
C	July 1962	486		1,045			1,073	1,075
D	Aug. 1961	458			764			667
E	Aug. 1961	396			562			482
Mean		454		847	801		975	960
Winter (water temp. 10–13 C, air temp. 5–9 C)								
A	Jan. 1962	375		936		1,186		
A	Jan. 1963	274	1,110		1,351			
A	Jan. 1963	423	1,325		1,364		1,562	
A	Jan. 1963	468	1,171		1,455		1,679	
B	Jan. 1962	377		945		1,290		
B	Jan. 1963	301	1,016		1,213			
B	Jan. 1963	438	902		1,086		1,137	
B	Jan. 1963	537	1,109		1,098		1,328	
C	Jan. 1962	246				932		
C	Jan. 1963	423	699		1,177			
C	Jan. 1963	433	1,170		1,217		1,272	
C	Jan. 1963	360	1,312		1,186			
Mean		388	1,090	940	1,238	1,136	1,395	

Dietary Intake

The dietary composition is summarized in Table 4, along with mean values of caloric intake. The mean caloric intake was approximately 3,000 kcal/day in both summer and winter. Of this, nearly 80% was contributed by carbohydrates, primarily in the form of rice meal. Fat intake was very low, the daily consumption amounting to only 20 g. Protein intake was 80–90 g a day, of which 80–90% was from vegetable sources and thus low in biological value compared to animal protein.

Physical Fitness

The mean values of Harvard step-up test scores are shown in Table 5. In general, the score was significantly greater in both seasons in the ama as compared to the control, indicating better physical fitness in the former. In the control group, the score was significantly lower in the winter than in the summer. However, this was not true for the ama. In other words, the ama, unlike the control, maintained excellent physical fitness all year around.

DISCUSSION

In an earlier study conducted in our laboratories (7), the oral temperature of ama at the end of a voluntary work shift averaged 34.9 and 33.2 C in summer and

TABLE 3. *Heat exchange during diving*

	Subj.	Summer (July 1962)				Winter (January 1963)			
		Before dive	Minutes in water			Before dive	Minutes in water		
			10	25	40		5	15	25
Mean body temp., C	*A*	36.59	31.29	31.10	30.08	35.24	26.19	25.44	24.92
	B	36.15	31.48	30.83	30.51	34.64	26.10	25.80	25.14
	C	36.77	31.43	30.91	30.44	34.29	25.86	24.98	
Mean		36.43	31.40	30.94	30.34	34.72	26.05	25.37	25.02
Rate of heat prod., kcal/min	*A*	2.20	4.17	4.05	5.34	1.87	5.77	6.72	7.82
	B	2.38	3.54	4.04	4.67	1.98	5.00	5.47	5.95
	C	2.31	5.04	5.27	5.33	1.96	5.12	5.77	
Mean		2.29	4.25	4.45	5.11	1.94	5.30	5.99	6.88
Cumulative extra heat prod., kcal	*A*		19.7	47.3	94.5		19.5	68.0	127.5
	B		11.6	36.7	71.1		15.1	50.0	89.7
	C		27.3	71.8	117.1		15.8	53.9	
Mean			19.5	51.9	94.2		16.8	57.3	108.6
ΔHeat content, kcal	*A*				−362				−575
	B				−256				−435
	C				−263			−388	
Mean					−293			−466	
Total extra heat loss, kcal	*A*				457				703
	B				327				525
	C				380			442	
Mean					388			557	

Each value represents the average of two to three measurements on each subject. *Subject C* could not engage in diving work for more than 20 min in the winter.

TABLE 4. *Daily intake of various nutrients in the ama (g/day)*

Subj.	Summer (July 1962)				Winter (Jan. 1963)			
	Carbohydrate	Fat	Protein		Carbohydrate	Fat	Protein	
			Animal	Vegetable			Animal	Vegetable
1	632	28	28	71	436	23	7	68
2	577	14	14	65	536	32	16	69
3	570	13	8	62	360	11	0	34
4	697	15	13	81	736	16	3	87
5	671	18	42	62	752	37	10	116
6	613	15	13	68	649	34	7	104
7	714	17	36	76	686	28	15	89
8	627	16	21	69	527	22	11	84
Mean	637	17	22	69	585	25	9	81
Total cal. intake, kcal/day	3,065				2,925			

Each value represents the average of data obtained over a period of four successive days.

TABLE 5. *Harvard step-up test score*

Season	Ama	Control	*P*
Summer	111.7±5.3	97.6±3.7	<0.05
Winter	103.3±2.9	86.6±3.5	<0.025
P	>0.1	<0.05	

Values are means ± standard error. Average of 20 subjects in each group.

winter, respectively. Since the lower oral temperature in the winter was accompanied by a lower temperature of sea water, it was concluded that tolerance to cold was increased in the winter. However, at that time it could not be shown whether oral temperature really represented deep body temperature in cold water. Hence deep rectal temperature was measured in the present investigation. As shown in Fig. 1, rectal temperature at the end of a work shift was approximately 35 C in both summer and winter. This indicates that oral temperature did represent the deep body temperature in summer, but was lower than rectal temperature in the winter. Similar discrepancies between rectal and oral temperatures were noted in channel swimmers leaving water of 16–18 C (12). Although the reasons for this difference are not clear, we may speculate that either the colder water surrounding the body may have cooled the blood perfusing the head or a greater general vasoconstriction including the oral cavity may have occurred in the winter.

Although the final rectal temperature was not different between the two seasons, the water temperature and

hence the skin temperature was considerably lower in the winter. Therefore, mean body temperature at the end of a voluntary work period was much lower in winter compared to summer. This is consistent with the earlier conclusion that tolerance to cold is increased in winter. However, a word of caution should be given in respect to the computation of the mean body temperature. We have employed a conventional formula, 0.6 × rectal temp. + 0.4 × skin temp., in the present studies although the validity of this formula when a subject is exposed to cold water (10 C in the winter) is not proved.

The reduction of rectal temperature is impressive in summer or winter. By comparison, the average rectal temperature of channel swimmers on leaving water of 16–18 C was 36.0 C (12). Considering the heavy insulative fat of these swimmers and their high sustained metabolic rate, which was two to three times greater than that we measured in the ama, their higher body temperature is understandable. However, even a nude man asleep under an open sky rarely tolerates a rectal temperature below 35.0 C and a skin temperature below 27 C (3).

Iampietro et al. (6) exposed young men nude for 2 hr to cold wet environments and studied their heat exchange. A comparison of these data with ours indicated that the increase of heat production of the ama in summer was roughly equal to that of nude subjects exposed to an air environment of 50 F, 30–90% relative humidity, and a windspeed of 10 mph (6). However, the reduction in mean body temperature was greater in the ama compared to the subjects employed by Iampietro et al. Thus the daily cold stress of the ama even in summer is more severe than that of Iampietro's subjects. It is not difficult to imagine how severe the cold stress must be in winter, leading us again to conclude that the ama is subject to a more severe voluntary cold stress than any other group of human beings yet described.

The total extra heat loss during an entire work period was 388 kcal in the summer and 557 kcal in the winter. Since the duration of a work shift is shorter in winter the rate of heat loss is approximately twice as great when diving in the winter as in the summer. However, the ama work three shifts a day in the summer and only one or, rarely, two shifts in the winter. Therefore, the total extra heat loss for diving work is of the order of 1,000 kcal/day at all seasons. This represents the minimal amount of energy which ought to be supplied to the ama in order to compensate for heat lost to the water. The dietary survey indicated that the ama were satisfying this need rather well. Regardless of the season, they consumed 3,000 kcal/day whereas the observed caloric intake of nondiving women of comparable age was 2,000 kcal/day (8).

The protein intake was approximately 90 g/day in both seasons. Although this may be sufficient in quantity, the quality of protein is so poor that it is questionable whether or not it is satisfactory. Nevertheless, this finding substantiates the conclusion that the observed increase in BMR of the ama in the winter (7) is not related to higher protein intake. This means that the severe cold stress which the ama receive in the winter is likely to be responsible for this increase in BMR. One disturbing fact is that there was no difference between the two seasons in the total daily extra heat loss. This strongly suggests that the mechanism which triggers the development of cold adaptation is not necessarily related to the magnitude of total daily heat loss so much as to the degree of heat debt incurred during each diving period.

We are grateful to Drs. Hermann Rahn and D. W. Rennie for their keen interest and advice in the conduct of this investigation as well as for their kind comments and discussions in the preparation of this manuscript. It is also our pleasure to thank Chin Kyung Kim for her valuable assistance in the conduct of dietary survey.

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SURVIVAL OF HYPOTHERMIA BY MEN IMMERSED IN THE OCEAN

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The survival time of men immersed in cold water has not as yet been adequately determined, although it is a matter of practical importance when disasters occur at sea. The shortening of survival time in water is apparently related to the acceleration of body heat loss in water as compared with air, but the amount of hypothermia that can be tolerated and the reasons for greater heat loss in water have not been clearly defined. The usual explanation, that water conducts heat from the body twenty to twenty-five times more rapidly than air, is inadequate, as will be shown later.

The immersion experiments of Lefèvre [1] were, on the whole, of too short duration to establish tolerance limits. Refrigeration of patients (Fay,[2] Talbott,[3] Dill and Forbes [4]) showed that man's body temperature may be reduced by several degrees without endangering life, but the environments employed during induction were not ones that could be quantitatively characterized. Spealman [5] measured changes of rectal temperature in volunteers who were immersed in water as cold as 50 F. He did not, of course, continue his observations beyond an interval which he considered safe. Thus, the toler-

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Admiral H. W. Smith granted the author permission to examine the shipwreck reports in the Bureau of Medicine and Surgery. Lieut. Comdr. P. H. Futcher and Mrs. Groves of that office rendered assistance. Dr. E. F. Adolph gave invaluable encouragement and help.

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ance to cold water, i. e. the maximal duration of immersion in water at different temperatures with survival, has not yet been established for man.

SURVIVAL OF IMMERSION IN THE SEA

This definition of tolerance uses death as an end point, but in laboratories men cannot be exposed to the death point. There are, however, in the course of human events natural experiments which can be utilized with profit. Critchley [6] recorded that of 10 men from a torpedoed vessel only 1 survived half an hour of immersion in sea water of 29 F. (there was a large amount of field ice about). The staff surgeon of the *Takasago,* in the naval war between Japan and Russia during 1904-1905, died after one hundred and ten minutes of exposure in the sea at 47 F. In 1805 a volunteer, working for Currie, remained immersed outdoors for half an hour without clothing in water at 42 F. A corpulent man of 29, clad in indoor rig and overcoat, remained swimming for nine to fourteen hours in the sea at 30 F., while two companions died after two and one half hours of immersion. One may doubt this last case; it does not seem possible that a man, even a corpulent one, can swim for nine hours at 30 F.

To establish more precisely the relation between duration of immersion and sea water temperature of shipwreck survivors, Admiral H. W. Smith permitted examination of the reports on rescues at sea in the files of the Bureau of Medicine and Surgery, U. S. Navy, Washington, D. C. The reports originated from either the ships' doctors or the pharmacists' mates of the U. S. Navy on duty at the time of rescue. They concerned men picked up from ships of the U. S. Navy and Coast Guard, U. S. and foreign merchant ships, German and Japanese naval vessels and U. S. Navy and Army airplanes whose personnel ditched at sea.

Of the several hundred reports on file from April 1942 to April 9, 1945 only those were selected from which the following information could be gleaned: (*a*) Temperature of the sea water, or else both the date and location of either shipwreck or rescue. In the latter case, sea surface temperatures were obtained from the World Atlas of Sea Surface Temperatures, United

6. Critchley, M.: Shipwreck Survivors, London, J. & A. Churchill, Ltd., 1943.

States Navy, 1944.[7] (*b*) The exact duration of immersion in the ocean in which men were continuously covered by water up to the neck or shoulders. Clothing varied from shorts alone to full deck clothing appropriate to the latitude, including kapok jacket.

The data which fulfilled these requirements are plotted in chart 1. Each point represents at least 1 man who survived the given hours of immersion at the temperature indicated. In many cases more than 1

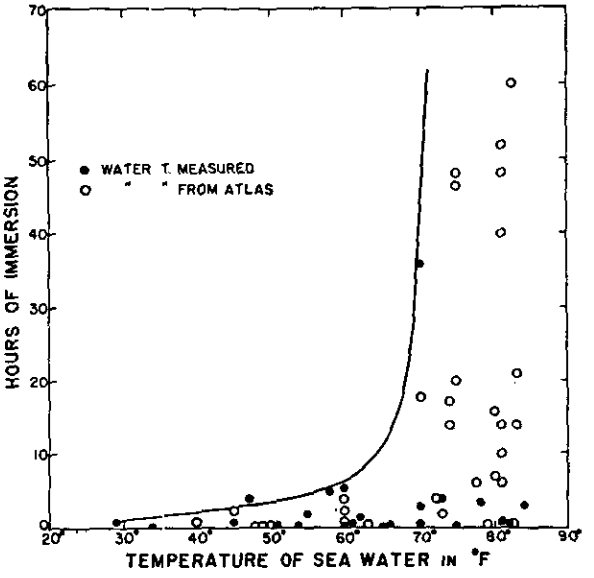

Chart 1.—Duration of immersion of shipwreck survivors in ocean waters of diverse temperatures. The data are from the files of the Bureau of Medicine and Surgery, U. S. Navy. Open circles, sea-water temperature was measured at time of rescue. Black dots, sea-water temperature was obtained from the World Atlas of Sea Surface Temperatures on the basis of date and location of shipwreck or rescue. Each point represents the survival of at least 1 man. The curve was drawn above all the reported survival times except for the one point at 47 F. which is excepted for reasons given in the text.

man survived. The continuous curve on the graph was drawn so that it lay above all the reported durations of immersion with survival, except for the one point at 47 F. for reasons to be discussed. It is possible that a few men could survive immersions for longer than the

7. World Atlas of Sea Surface Temperatures, Publication 225, U. S. Navy, Hydrographic Office, 1944.

Correction. Legend of Chart 1 should read: ..Black dots, sea-water temperature was measured at time of rescue. Open circles, sea-water temperature was obtained from the World Atlas...etc.

times indicated by this curve; on the other hand, many men died in shorter times.

Several factors contributed to the shortened survival time of men who died before rescue, and it is not possible to say to what extent hypothermia was the determining lethal factor. These factors included drowning due to high seas or fainting or exhaustion, drinking sea water, wounds, injuries, depth explosions and burns. Few men died after rescue, and these usually because of some assignable cause other than hypothermia — wounds, injuries, burns or shock induced by these factors. Treatment given the rescued, in addition to that necessary for wounds and shock, varied from slow to fast rewarming, with or without hot food, or drinks or brandy. It is worthy of note that the reports mentioned no cases of upper respiratory disease. One man immersed for forty hours in water of 80 to 83 F. appeared to have bronchopneumonia. Two men, who may have been among those on rafts and exposed for two to three days, developed pneumonia after rescue; another man died of bronchopneumonia after rescue; water temperature was about 76 F. Talbott [3] also found that respiratory infections did not appear in his hypothermic patients, and Critchley [6] similarly remarked about the dearth of respiratory disease among the survivor cases which he studied.

A brief description of a few rescues will illustrate the kind of information available in some of the reports:

CASE 1.—The disaster occurred on Nov. 1, 1943. Four men were rescued from a raft after four hours of exposure; they were in good condition. Nineteen men were immersed for one to one and one-half hours; 4 were unconscious, 5 irrational, and all were suffering at the time of rescue. One of the unconscious men had clamped his teeth on his tongue, which then bled, and he had aspirated blood and salt water into the upper respiratory passages. His breathing was stertorous for thirty minutes after rescue. Another of the unconscious men was very cyanotic, more so than the others; his breathing was gasping and irregular. He recovered consciousness about one hour after rescue, but the cyanosis continued for several more hours. This otherwise informative report could not be used for the purposes of chart 1, as neither the sea water temperature nor the location of the disaster was given. The water was probably very cold, as 4 men became unconscious after only one to one and one-half hours of immersion.

CASE 2.—A ship was rammed and it sank in three minutes. Thirty survivors were picked up from rafts after exposure of

one and one-half to four hours. There were 2 cases of bad burn and shock; 67 dead were identified and 48 were reported missing. Some "drowned and others died of exposure because the water was 39 F. with a high sea and a wind velocity of scale 7. Some of the survivors who held on to rope couldn't let go and rescuers had to cut frozen rope to release them. . . . It appears miraculous how the survivors could have endured such cold water. Most of them who were rescued were in an unconscious state and, when they became conscious, complained of numbness of extremities and hands. What is considered noteworthy is that there were no subsequent ill effects and they were physically fit for duty after forty-eight hours; while so many of the others in the same period of rescue were frozen to death [sic]." The rescued were placed under tepid showers and into warm beds; they were then fed hot soups and hot coffee. This interesting report could not be put into chart 1 because the extent of the immersion is not clear.

CASE 3.—On June 6, 1944, 220 men were picked up after immersion in water of 54 to 56 F. for periods up to two hours. Most suffered from the immersion; many showed effects of severe psychic trauma. There were 2 cases of drowning and several of burns. The rescued were undressed, dried, blanketed and given warm liquids and brandy. Other rescue operations have involved even more men and have required several hours for completion.

CASE 4.—A small ship, dumping defective ammunition, exploded and sank in thirty-five minutes. Fourteen men survived; 11 were in the water about half an hour, 3 more for about one hour; the water temperature was about 40 to 45 F. Only one had on a life jacket; he was badly burned and the captain had put the jacket on him; he died in the hospital. Sixteen men were reported missing. It is difficult to understand, for reasons which will become evident, how 3 men could be in water of 40 to 45 F. for one hour without life jackets and still be able to hold their heads out of the water.

CASE 5.—Twenty-three survivors were immersed in water of 47 F. for four hours. This is an unusual case, because calculations (to be made later) show that, after an exposure of four hours in water of 47 F., the rectal temperature would be below 75 F. It does not seem likely that as many as 23 men in one group could survive such a great reduction in rectal temperature. Certainly their condition at the time of rescue could have occasioned more remarks than were available in the report.

The curve in chart 1 appears to approximate a hyperbola, indicating that the product of deficiency in sea-water temperature and survival time is a constant.

From this relation one may suppose that death due to the hypothermia of immersion always occurs at approximately the same body temperature and that survival time is dependent on the rate of cooling imposed by the water temperatures. The curve changes its slope rapidly at sea-water temperatures between 60 and 70 F.; unfortunately there are not enough adequate data to establish precisely this part of the curve. Further, the rectal temperatures of the survivors were not measured at the times of rescue, and thus the foregoing supposition cannot be checked.

SURVIVAL OF EXPERIMENTAL IMMERSION

Immersion experiments done on prisoners at the Dachau concentration camp have been reported by Alexander.[8] Appendix 7 in his report contains photostats of three tables and several graphs from which conditions of survival can be obtained. These data are considered as objective and valid. Body weights and heights are given for only 5 subjects (51 to 82 Kg., 153 to 183 cm.); thus, the influence of possible emaciation and weakness due to starvation is not adequately checked. The subjects were usually clothed in aviator's garb, including headgear and rubber or kapok life-jacket. Rectal and skin temperatures were measured with thermocouples. The skin thermocouple was fastened over the fifth thoracic vertebral spine and was presumably under water during the test. Those experiments in which a foam suit was worn are not included here.

Data concerning immersion time are plotted in chart 2. Care was taken to avoid duplicate representation of any experiment; thus, averages are not included in chart 2. Of the thirty-six experiments shown, only 1 man was immersed for a period longer than that given by the curve in chart 1. This man was large (82 Kg., 183 cm.) and unclothed during the test; he survived one hundred and seventy-five minutes of immersion and received subsequent diathermy over the heart. Not one of the remaining 35 was exposed as long as the times shown by the curve in chart 1. Twelve of the men in chart 2 died, 2 before removal from the water, 10 in seven to fourteen minutes after removal; of

[8] Alexander, L.: The Treatment of Shock from Prolonged Exposure to Cold, Especially in Water, Report 250, U. S. Department of Commerce, 1945.

these, 3 were administered strophanthin and 2 were given artificial respiration. Five of the survivors were administered strophanthin and 4 were placed in cradles with sixteen light bulbs. There is no indication as to the postexposure treatment of the remaining subjects, and proof is not complete that any of the treatments significantly prolonged survival.

Also shown in chart 2 are the durations of exposure of Spealman's [5] subjects and a portion of the curve in chart 1. Evidently the upper line represents an outside

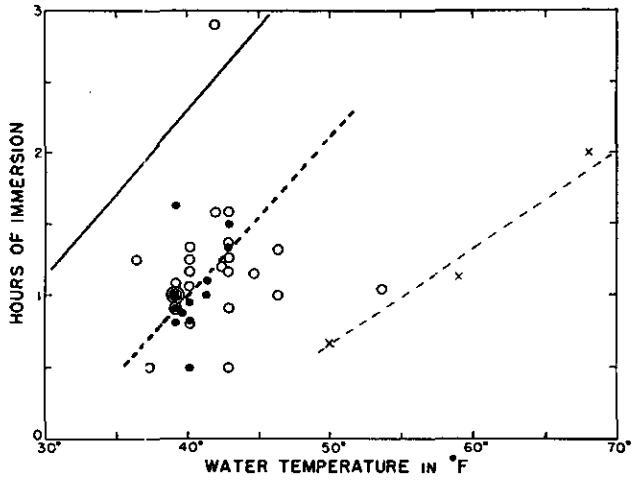

Chart 2.—Duration of immersion in experimental hypothermia. Circles, Dachau prisoners who survived; black dots, Dachau prisoners who died during or shortly after immersion (Alexander,[6] 1945); crosses, volunteers of Spealman [5] (1945). Light dashed line through Spealman's data, safe; continuous line from the curve in chart 1, few if any survivors; heavy dashed line, probable survival of 50 per cent of persons exposed.

limit of tolerance; few men will survive as long as indicated by it. The light dashed line in chart 2 through Spealman's data represents a safe duration of exposure, one which will not produce fatal hypothermia. Exposures for durations indicated by the heavy dashed line are fatal to many men. For example, an exposure of one hour in water at 40 F. can be expected to kill 50 per cent of the men immersed. These statements are made on the assumption that the head is always kept out of the water by the life-jacket, and that therefore drowning is not a factor to be considered.

Rectal temperatures at the time of death also are given for 8 of the 12 subjects in chart 2. Careful examination of appendix 7 disclosed that additional subjects survived cooling to equal rectal temperatures (table 1). The lowest rectal temperature which was survived was 77.5 F. The lowest at which death occurred was 78.3, the highest 86.5. A patient subjected to hypothermia died at 74 F. (Fay [2]) but another survived the same rectal temperature (Talbott[3]). Other patients or inebriates have survived 75, 75.2, 75.6 and 76.4 F. (Talbott,[3] Dill and Forbes.[4]) Of the 20 subjects in table 1 having a rectal temperature below 85 F., 35 per cent died; of the 7 below 80 F., 57 per cent died. Probably no man immersed in water can survive a rectal temperature below 75 F.

TABLE 1.—*Lowest Rectal Temperatures of Dachau Prisoners Immersed in Water at 40.1 to 53.6 F.*

Rectal T., Degrees F.	Died	Survived	Per Cent Surviving
75.0-79.9	4	3	43
80.0-84.9	3	10	77
85.0-90.0	1	11	92

Rate of fall of rectal temperature can be approximately ascertained. In four of eleven cooling curves (Alexander) the rectal temperature started to drop soon after immersion; in the remaining seven there was a delay of about a quarter of an hour before much diminution began. Spealman also found an initial delay. The reduction in rectal temperature then proceeded more or less linearly for about an hour, but in water of 68 F. or warmer the rectal temperature then leveled off (Spealman). In colder water the further course of the rectal temperature is given for only 1 subject (Alexander's figure 12 in appendix 7); after fifty minutes the rectal temperature leveled off more or less exponentially during the remaining two hours. Fall of rectal temperature during the first hour in water is plotted against water temperature in chart 3. The curve is not linear, though it may be below 60 F.

For water temperatures below 60 F. calculations made on the basis of chart 3 give reasonable times of survival. In table 2 are given calculated and observed

survival times for several water temperatures on the assumption that a drop in rectal temperature from 98.6 to 78.6 F. is the limit for survival. Where calculated and observed survival times agree, it may be concluded that the rates given in chart 3, based on the first hour of immersion, may be used linearly for succeeding hours. Where the observed survival time is less than the calculated, as in water at 40 F., death occurred at a rectal temperature higher than 78.6 F., as it actually did. Where the observed survival time exceeds the estimated, as in water at 47, 45 and 42 F.,

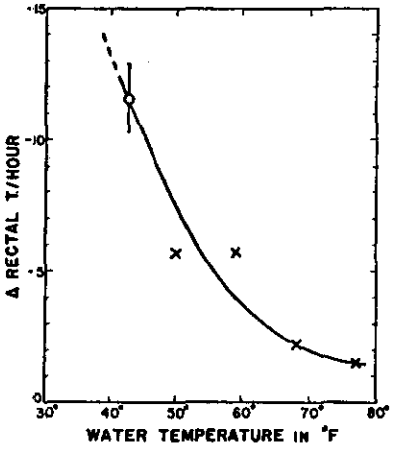

Chart 3.—Fall of rectal temperature in Fahrenheit degrees per hour during the first hour of immersion in water of diverse temperatures. Crosses, data from Spealman [5] (1945). Circle, mean of data from figures in appendix 7 of Alexander's report [8] (1945); the bar represents the standard error.

either 78.6 F. was not the limiting rectal temperature or cooling proceeded exponentially after the first hour, or both. In the case of the subject surviving immersion for 2.9 hours in water at 42 F., as described in the preceding paragraph, the rectal temperature did drop more or less exponentially after the first fifty minutes to reach about 75.2 F. at one hundred and seventy-five minutes. The cooling of the 23 men who survived four hours in water at 47 F. (case 5 just described) may have followed a similar course though it is hard to believe that 23 men in one group survived a rectal temperature of about 75 F.

Spealman's observation that the rectal temperature ceases to fall after about one hour in water warmer than 68 F. explains why the curve suddenly rises steeply in chart 1. Apparently in water warmer than 60 to 68 F. heat production keeps pace with heat loss at a somewhat reduced rectal temperature, and possibly fatigue is the limiting factor. In colder water, however, heat loss exceeds heat production, which, in fact, becomes reduced as the body cools.

The data of Dill and Forbes [4] concerning the heat production of schizophrenic patients subjected to hypothermia are plotted in chart 4. These patients were

TABLE 2.—*Estimated and Observed Survival Time of Men Immersed in Cold Water*

Water Temperature, Degrees F.	Computed Drop in Rectal T. (From Chart 3), Degrees F. per Hour	Computed Time for Drop in R. T. to 78.6 F., Hours	Observed Survival in Charts 1 and 2	
			Hours	Number of Men
60	3.8	5.5	2.8 to 5.5	59
58	4.3	4.7	2 to 5	59*
47	9.0	2.2	4.0	23
45	10.2	2.0	2.5	Some
42	12.0	1.7	1.6, 2.9	1, 1
40	13.0	1.5	1.4	1†

* Some men were on rafts.
† Three men are known to have died in less than one hour.

under light anesthesia during the induction of hypothermia, and so their heat productions may not have been as high as for men immersed in the sea. Spealman found that heat production rose to five to six times basal instead of about three times as observed on the schizophrenic patients. The curve in chart 4, however, suggests that heat production falls off from a peak at rectal temperature of 95 F. to basal or less at rectal temperature of about 80 to 85 F. At the lower rectal temperature the patients were no longer under the influence of the anesthetic.

COMPARISON OF BODY COOLING IN AIR AND IN WATER

The relation between body temperatures and environmental temperature for both men in water and nude

men sitting in air in shade (Adolph and Molnar [9]) is shown in chart 5. The data are taken at one hour of exposure. All surface temperatures are for the back alone and were measured with a thermocouple (uncovered for the air experiments). The back surface temperature of the man in the air was about the same as the mean of temperatures measured on ten different areas. It is somewhat surprising to find that the back surface temperature of the man (clothed though he be) can be 9 to 23 Fahrenheit degrees higher than the water temperature. Burton and Bazett [10] assumed that for

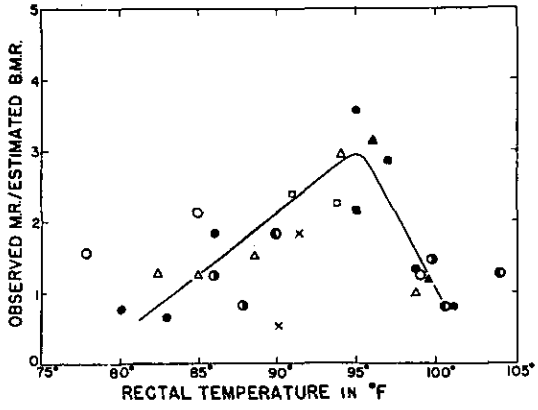

Chart 4.—Relation between the ratio of observed metabolic rate to estimated basal metabolism and the concurrent rectal temperature for refrigerated patients. Data from Dill and Forbes.[4] Each symbol represents a different narcotized patient; the narcosis had worn off at the lower temperatures.

the nude man the surface temperature was the same as water temperature in their warm bath experiments.

Chart 5 shows that in air at 40 F. the rectal temperature did not diminish within one hour and the internal temperature gradient was about 30 Fahrenheit degrees. In water at 40 F., however, the rectal temperature dropped about 11 to 12 Fahrenheit degrees within one hour and the internal gradient was either 25 Fahrenheit

9. Adolph, E. F., and Molnar, G. W.: Exchanges of Heat and Tolerances to Cold in Men Exposed to Outdoor Weather, Am. J. Physiol. **146**: 507, 1946.

10. Burton, A. C., and Bazett, H. C.: A Study of the Average Temperature of the Tissues, of the Exchanges of Heat and Vasomotor Responses in Man by Means of a Bath Calorimeter, Am. J. Physiol. **117**: 36, 1936.

degrees, using the observed surface temperature, or about 47 Fahrenheit degrees, if Burton and Bazett's assumption is correct.

The difference in thermal behavior of the body in air and in water is often accounted for by saying that water conducts heat twenty to twenty-five times more rapidly than air. This explanation, however, is inadequate, as Bazett and Spealman pointed out to me in a discussion and as a few simple calculations show

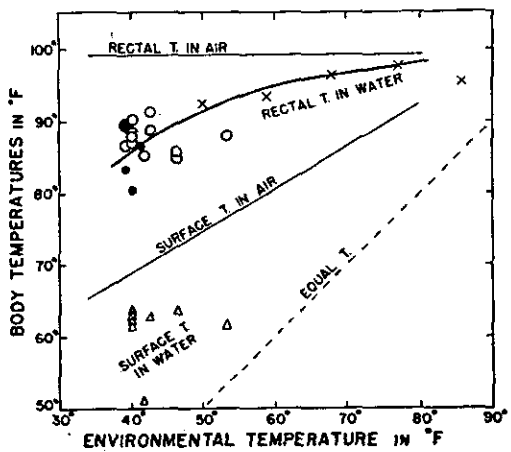

Chart 5.—Relation between body temperatures and environmental temperatures in water and in air (latter from Adolph and Molnar [9]) at the end of the first hour of exposure. Surface temperature was measured only on the back with a thermocouple (uncovered in the air experiments). Crosses, rectal temperatures from Spealman;[5] at 50 F. the rectal temperature was extrapolated to one hour from a forty minute exposure. Circles, rectal temperature of Dachau prisoners who survived. Black dots, rectal temperature of prisoners who died (Alexander [8]). Triangles, back surface temperature of these prisoners. In the air men sat nude in outdoor shade.

(table 3). Estimates indicate that heat loss from the body in the water is only about twice that in air, or only one-tenth the amount expected on the basis of the ratio of water/air conductivity. There are, of course, errors in the estimates of table 3, but they cannot be great enough to bring heat loss in water to more than three to four times that in air.

Table 3 also shows that in water even at 60 F. body cooling is far in excess of heat production. Hence the rectal temperature falls and survival time is limited.

In water at 70 F., however, body cooling is no longer excessive and tolerance is not limited.

Although heat loss in water is only about two times that in air, and not twenty to twenty-five times, yet this 100 per cent increase must be explained. Two reasons can be brought forth: 1. The effective surface area for heat loss in the air is only 75 per cent of the total area (Winslow, Herrington and Gagge [11]), because the medial surfaces of the legs exchange heat with

TABLE 3.—*Estimated Heat Loss from Body in Air and Water During First Hour of Exposure*

Environment	Heat Production, Calories per Hour	Storage, Calories per Hour	Total, Calories per Hour
Air, shade, 40 F.	250	400	650
Water, 40 F.			
If surface temperature = 62 F.	350	725	1,075
If surface temperature = 51 F.	350	990	1,340
Air, 60 F.	120	230	350
Water, 60 F.			
If surface temperature = 61 F.	350	535	885
Air, 70 F.	85	140	225
Water, 70 F.			
If surface temperature = 71 F.	140	200	340

Heat exchanges in air are taken from Adolph and Molnar.[9]

Heat production of men in water is assumed to average 5 × basal (5 × 70) during the first hour, except in water at 70 F., where it is assumed to be 2 × basal. Decrement in stored heat is estimated as the product of change in average body temperature (in centigrade degrees) times body weight (70 Kg.) times 0.83 (the specific heat of the body). Change in average body temperature is assumed to be the average of the changes in rectal temperature and surface temperature. Initial surface temperature is assumed to be 90.5 F.

each other, and the arms with the trunk; in water, heat is lost over the whole surface. 2. Because of the low specific heat of air, the layer of air immediately next to the skin is quickly warmed and is actually at a higher temperature than dry-bulb temperature (McGlone and Bazett [12]). Even a high wind does not remove all this warm air layer. On the other hand, because of the high specific heat of water the water adjacent to the surface is not warmed so much

11. Winslow, C.-E. A.; Herrington, L. P., and Gagge, A. P.: The Determination of Radiation and Convection Exchanges by Partitional Calorimetry, Am. J. Physiol. **116**: 669, 1936.

12. McGlone, B., and Bazett, H. C.: The Temperature of the Air in Contact with the Skin, Am. J. Physiol. **82**: 452, 1927.

and is easily displaced. The net result is that the surface temperature is reduced more in water than in air. Consequently there is a steeper initial internal temperature gradient in water. The amount of heat flowing from the deep tissues to the surface is determined by the temperature gradient between these two regions and by the conductivity of the intervening tissues (Burton[13]). As the conductivity cannot be reduced below a minimal amount, once vasoconstriction is complete this tissue conductivity would be the same in air and in water. But because of the greater internal temperature gradient when in water there would be more heat flowing through the outer shell of the body into the water.

Because heat production does not keep pace with heat loss, the rectal temperature falls; the internal gradient has reached its limit. In water warmer than 68 F. heat production of three to six times basal can keep the rectal temperature around 95 F. In colder water, body cooling exceeds heat loss and the rectal temperature continues to fall. As this diminution proceeds below 95 F., heat production also falls off until it is only about basal in value at a rectal temperature of 80 to 85 F. Respiratory and cardiac irregularities are reported then to supervene and, if allowed to continue, lead to the death of the individual.

It should be pointed out that useful data can be secured by any one on a rescue vessel who has a watch, a thermometer and a ready wit. Eventually diverse methods of rewarming can be adequately compared.

SUMMARY

The recorded times of immersion of shipwreck survivors, on file in the Bureau of Medicine and Surgery, U. S. Navy, were plotted against the sea-water temperatures (chart 1). A curve was drawn above the highest recorded times of immersion; the curve rises steeply for water temperatures above 60 F. Analysis of data on body cooling led to the conclusion that this curve represents a limit of tolerance which probably few men can exceed and many cannot approach.

13. Burton, A. C.: The Application of the Theory of Heat Flow to the Study of Energy Metabolism, J. Nutrition 7: 497, 1934.

Tolerance to water at temperatures below about 68 F. is limited by the loss of body heat at a rate which exceeds heat production. The internal temperature gradient cannot be maintained, and the rectal temperature falls at a rate which becomes increasingly greater, the lower the water temperature. Once the rectal temperature falls below about 95 F., heat production decreases. Respiratory and circulatory irregularities appear, and death ensues.

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Special Articles

THE PHYSIOLOGY OF CHANNEL SWIMMERS

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THIS paper presents the results of three years' study of some of the factors concerned in the ability to endure immersion in cold water. People showing unusual tolerance of cold have been compared with people showing unusual intolerance.

In 1951 there was a swimming-race across the English Channel in which eighteen of twenty competitors swam from France to England in times ranging from 12 to 20 hours in water at 15.5° C (60° F). This is of great interest because records of shipwreck survivors show that persons immersed in the sea at 60° F usually live only about 5 hours, and seldom more than 6 hours, death being due to hypothermia (Molnar 1946).

The swimmers in the 1951 race all conformed to a certain *physical type, very different from that of athletes* who cover long distances on land by running, cycling, skiing, or mountain climbing. Some of the swimmers were frankly obese; others were of stocky build and had well-rounded contours concealing the muscular pattern (fig. 1).

Investigations

The swimmers in 1951 could not be followed in the race across the Channel, but one of them, a Greek (J. Z.), generously allowed *observations to be made on him* during an attempt on the record for swimming Lake Windermere (10½ miles).

At Windermere the water-temperature was 15·8° C (60·4° F), similar to that in the Channel. The swimmer's rectal and deep-muscle temperatures were measured before and after practice swims and after the attempt on the record, which lasted 6 hr. 50 min. Observations were also made on a subject (G. P.) with poor tolerance of cold, who was *a mountaineer and former long-distance* runner and skier, but only enjoyed swimming in warm waters. Other measurements included those of body form, distribution of fat, and consumption of oxygen during swimming. The effect of immersion in a cold bath without swimming was studied to assess the importance of the high metabolism of swimming in the maintenance of body-temperature. Three other subjects were also studied, of whom two were fat and one was thin. In 1954, when another Channel race was held, measurements made on all sixteen competitors included skin-fold thickness; and rectal temperatures were measured on four swimmers at the finish of the race.

The investigations were made to try and answer the following questions:

How do long-distance swimmers maintain their heat balance?

Do they keep up a high level of energy expenditure exhausting to the average person?

Do they lose heat less rapidly because of their body form and thickness of subcutaneous fat?

Can they continue to swim in spite of moderate hypothermia?

The physical characteristics of the subjects of the experiments are shown in table I, and those of the 1954 Channel swimmers in table II.

J. Z., aged 42, had swum the Channel three times, once staying in the water for 20 hours. He claimed that his resistance to cold had increased over the years owing to his practice of wearing a minimum of clothing and of swimming in very cold water.

TABLE I—DETAILS OF SUBJECTS OF EXPERIMENTS

Subject	Age (yr.)	Height		Weight		Surface area (sq. m.)	
		(cm.)	(ins.)	(kg.)	(lb.)	DuBois's formula	Measured
J. Z.	42	164	64·7	95·9	211	2·04	2·02
G. P.	41	183	72·0	75·5	166	1·98	1·86
O. G. E.	42	183	72·0	71·1	158	1·92	..
K. H.	23	178	70·0	67·0	148	1·82	..
W. M.	21	170	67·0	68·2	150	1·78	..

G. P., aged 41, was a healthy subject with very little *subcutaneous fat.*

O. G. E. was an apparently slim man aged 42.

The two other subjects J. M. and K. H. were young Naval ratings of average physique.

Methods and Results

Body-temperature

The body-temperatures of J. Z. and G. P. were measured, before and after swimming at Windermere, in a boat-house 10 yards from the lake, with an ambient *temperature of 16°C (60·8°F). Rectal temperature* was measured with a copper 'Constantan' thermocouple protected by a plastic catheter and inserted to a depth of 5 inches. Needle thermocouples were used to measure muscle temperature.

Before his attempt on the record J. Z. greased his body with 3 or 4 lb. of anhydrous lanolin which formed an uneven layer averaging 1 mm. thick. In swimming he used the crawl throughout, his stroke-rate being 52 a minute for the first 3 hours and decreasing then to 50 strokes a minute. J. Z.

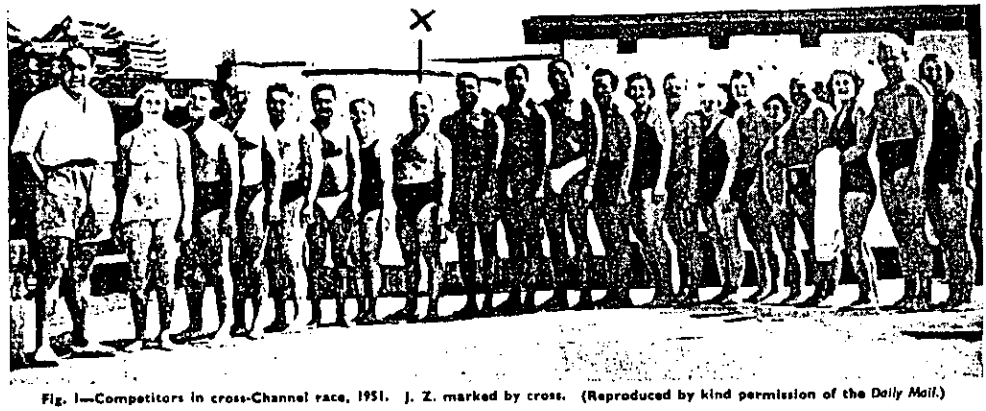

Fig. 1—Competitors in cross-Channel race, 1951. J. Z. marked by cross. (Reproduced by kind permission of the *Daily Mail.*)

TABLE II—MEAN MEASUREMENTS OF 1954 CHANNEL SWIMMERS COMPARED WITH BRITISH FACTORY WORKERS AND YOUNG GIRLS

	Channel swimmers 1954 (males)		Factory workers 1952 (males)		Channel swimmers 1954 (females)		Schoolgirls	
	Mean	Range	Mean	Range	Mean	Range	Mean	Range
No. of subjects	12		228		4		39	
Weight (lb.)	188·6	168–229	147·5	108–230	158·0	147–175	135·0	104–171
Height (cm.)	169·6	157–181	170·9	154–182	162·3	156–168	168·3	158–179
Biacromial breadth (cm.)	40·9	39–43	38·5	33–42	38·7	36–41	36·7	32–41
Bitrochanteric breadth (cm.)	34·8	32–36	32·8	29–35	35·2	33–39	31·0	30–37
Mid-thigh girth (cm.)	57·6	54–62	50·9	40–63	60·9	55–67	..	..
Superficial tissue thickness (mm.):								
Biceps	5·8	4–9	2·7	2–6	9·5	6–12	5·5	3–13
Triceps	11·8	9–20	5·7	3–13	15·0	12–17	10·2	4–21
Subscapular	16·0	11–35	7·8	3–21	13·6	10–16	9·4	4–18
Subcostal	14·1	7–23	7·7	3–21	12·9	8–17	7·1	3–16
Supra-iliac	13·8	9–22	..	..	15·5	11–21	9·1	4–17
Abdomen	18·4	14–26	8·9	4–23	23·4	18–30	12·1	7–26
Age (yr.)	34	23–58	35	17–58	27·5	21–35	16–17	..

rested for less than a minute every 2 hours to take food; he consumed 70 g. of glucose and approximately 6 oz. of hot milk and coffee. At the end of the attempt, which lasted 6 hr. 40 min., he was in good condition and ran up the beach. The layer of grease was still present over his trunk, thigh, and arms. His forearms and legs were intensely pale; his brachial pulse was only felt with difficulty, and his radial pulse was impalpable until 50 minutes later. His blood-pressure was 130/90–95 mm. Hg 53 minutes after the swim, compared with 120/75 mm. Hg before, and his body-weight had decreased from 211 to 209 lb. The temperature measurements occupied 30 minutes, during which he stood nude; he did not shiver or complain of cold. Eosinophil-counts were 357 per c.mm. before the swim, 22 per c.mm. 3 hours after the swim, and 435 per c.mm. the next morning.

TABLE III—RECTAL TEMPERATURE OF J. Z. SHOWING EFFECT OF SWIMMING

Windermere swim no.	Before entering water	Time after leaving water	Water-temperature	Duration of swim (min.)
1	37·8°C (100°F)	9 min. 37·8°C (100 F) 11 ,, 37·8°C (100°F) 28 ,, 38·2°C (100·8°F)	13·8–15·8°C (56·3–60·4°F)	62
2	37·6°C (99·7°F)	3 min. 37·9°C (100·2°F) 5 ,, 37·7°C (99·9°F) 10 ,, 37·6°C (99·7°F) 16 ,, 37·5°C (99·5°F)	13·8–15·8°C (56·3–60·4°F)	73
3	..	3 min. 37·4°C (99·3°F) 18 ,, 37·2°C (99·0°F)	15·8°C (60·4°F)	409

Observations were also made before and after practice swims lasting 73 and 63 minutes. In these J. Z. swam across the lake to a river, where the water-temperature was 13·8°C (56·8°F). The crossing took 15 minutes each way; so J. Z. was swimming in the river for 33 and 43 minutes respectively.

His rectal temperature was virtually unchanged after the practice swims and only slightly reduced after swimming for 6 hr. 50 min. (table III). His stroke-rate during practice was 51–58 a minute, which was higher than in the long-distance swim; so heat production was presumably correspondingly increased. The eosinophil-counts were unchanged after the practice swims.

Tissue temperatures are shown in fig. 2. The deep-muscle temperature in the thigh was above the rectal temperature, and the deep temperature in the forearm was only 2°C below the rectal temperature. The deep-muscle temperature (4·8 cm. depth) fell rapidly when muscular activity ceased; during swimming the muscle temperature was probably higher than those plotted in fig. 2.

These results, taken together, show that, in spite of considerable cooling of the superficial tissues, the temperature of the central body mass remained normal. J. Z. must have reached a stable state in which the effective thermal insulation of the outer tissues was such that heat production balanced heat loss.

The second subject, G. P., intended to swim for an hour in Lake Windermere. He had an initial sensation of intense cold, which gradually diminished, and after 10 minutes he felt no discomfort. When he had been swimming for 20 minutes, shivering started in his jaw muscles, and his swimming movements began to be restricted because of weakness, which steadily increased until at 30 minutes he was forced to give up. On getting out of the water G. P. could not stand; he crawled on to the jetty, and had to be assisted to the boat-house. Violent generalised shivering lasted 20 minutes. His rectal temperature (fig. 3), which was 34·5°C (94·1°F) 4 minutes after leaving the water, compared with 37°C (98·6°F) before entering it, reached 33·7 C (92·7°F) 10 minutes later, after which it began to rise.

Swimming in water at 20·5 C (68·9 F) G. P. developed suddenly muscular weakness after 41 minutes; his rectal temperature, measured 3 minutes later, had fallen to the same level as that reached after 30 minutes in Lake

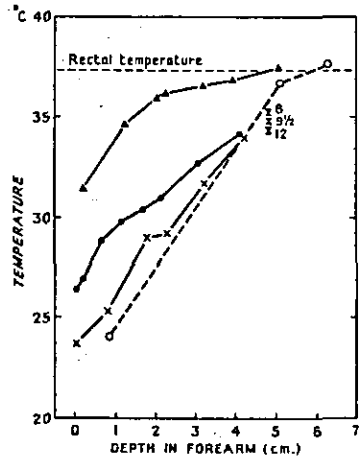

Fig. 2—Temperature gradients:

×—× in J. Z.'s forearm after long-distance swim of 409 min.

o--o ditto in thigh.

•—• in J. Z.'s forearm after 60 min. immersion without swimming in water at 16°C.

▲—▲ in G. P.'s forearm under normal conditions.

x deep forearm temperature at 8, 9½, and 12 min. after leaving the water after 63-min. swim.

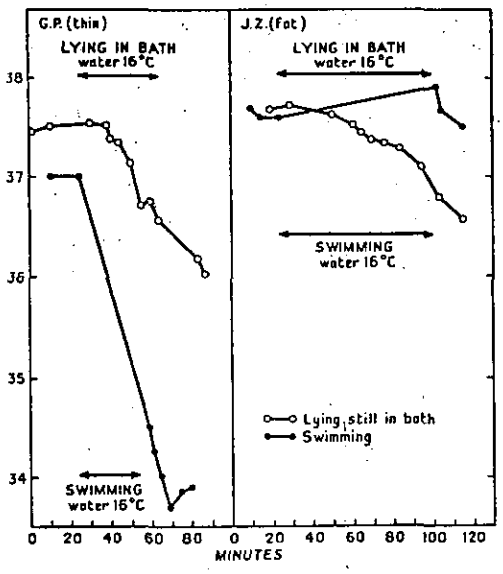

Fig. 3—Rectal temperatures after swimming and during immersion without swimming in water at 16 C in G. P. (thin) and J. Z. (fat).

Windermere. In slightly warmer water, 21·8°C (71·2°F) G. P. swam for an hour before complaining of weakness. At higher temperatures still he continued for an hour without any weakness, but even in water as warm as 25·3°C (77·5°F) his rectal temperature fell slightly (fig. 4).

Expenditure of Energy in Swimming

Expired air was collected in a Douglas bag, connected to a mouth-piece by tubing, 1 inch in internal diameter,

TABLE IV—OXYGEN CONSUMPTION (LITRES/MIN.) AND ENERGY EXPENDITURE (CAL./MIN.)

Subject	Lying		Sitting		In bath 16°C (60·8°F)		Swimming		
	Cal.	O_2	Cal.	O_2	Cal.	O_2	Cal.	O_2	
J. Z.	1·55	0·31	1·75	0·35	3·80	0·74	10·85	2·17	Slow crawl
	..	..	..	..	4·95	0·99	13·5	2·70	Crawl 56 strokes/min.
	..	..	..	..	4·75	0·95	12·0	2·40	Crawl 56 strokes/min.
	..	..	..	..	..	..	14·8	2·96	Crawl 58 strokes/min.
G. P.	1·45	0·29	1·70	0·34	8·30	1·66	10·3	2·06	Breast stroke moderate
	..	..	..	..	..	..	10·4	2·07	Breast stroke moderate
	..	..	..	..	..	..	10·8	2·16	Breast stroke moderate
O. G. E.	1·30	0·26	2·3	0·46	3·5*	0·70	10·5	2·10	Breast stroke moderate

* Bath temperature 21·8°C (71·2°F).

In swimming, speed through the water is a deceptive index of work-rate since it is affected by so many variable factors—e.g., waves, wind, and currents. J. Z.'s speed in Windermere varied from 1·7 to 1·3 m.p.h. He started at 1·7 m.p.h. A head wind soon sprang up, and the water became choppy; his speed fell to 1·3 m.p.h. In the last hour the water was calm, but by this time he was tiring and could not make more than 1·3 m.p.h. His stroke-rate, on the other hand, was remarkably constant at 50–52 strokes a minute. In swimming-baths speed is affected by the turns at the end of the bath. Both in open water and in baths the apparatus *for collecting expired air may cause drag.*

Expert swimmers using the crawl are probably much more efficient than average swimmers using breast stroke. Thus O. G. E. and G. P. swimming at the pace they normally use, when asked to swim for, say, half an hour, only swam at about 1·1 m.p.h., whereas J. Z. even after 6 hours was still doing 1·3 m.p.h.

In view of these considerations it seems unwise to do more than use the three categories slow, moderate, and fast as an index of effort in swimming.

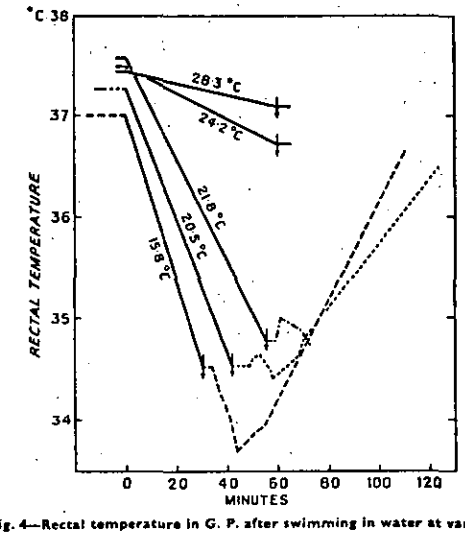

Fig. 4—Rectal temperature in G. P. after swimming in water at various temperatures.

Time 0 = time entering water.
↓ = time leaving water.

The water temperatures are shown above the corresponding rectal temperatures.

which passed underneath the subject as he swam and up between his legs. The bag was supported by a pole until it was partially full, when it was allowed to float behind the subject. The inlet valve was fitted to a plastic tube curving over the subject's head, so that he could use the crawl stroke. The results are presented in table IV.

Using the crawl, at a stroke-rate of 56–58 a minute, J. Z.'s oxygen consumption was 2·40–2·97 litres a minute. During the long-distance swim of 10½ miles his stroke-rate was 50–52 a minute; so probably his oxygen consumption was 2·1–2·6 litres a minute. G. P., using the breast stroke, had an oxygen consumption of 2·1–2·2 litres a minute, which is comparable with J. Z.'s long-distance energy expenditure.

On a surface-area basis the heat production was about the same: J. Z. 4·70–5·90; G. P. 5·30–5·55 calories per square metre a minute. In spite of the identity of heat production, G. P. became hypothermic in 30 minutes swimming in water at 15·8°C (60·4°F), in which J. Z. could maintain thermal equilibrium for many hours.

TABLE V—CONDITIONS BEFORE BATH EXPERIMENTS ON J. Z.

Room-temperature	Time in cold bath (min.)
1 hour at 19°C (66·2°F)	73
3½ hours at 15·8°C (60·4°F)	63
2 hours at 26°C (78·8°F)	48

Effect of Immersion in Water without Swimming

J. Z.'s rectal temperature was measured on three occasions while he lay in a vigorously stirred bath kept at 16°C (60·8°F). His skin-temperature remained not more than 0·5°C (0·9°F) above that of the water, unless stirring was discontinued, whereupon the skin-temperature rose rapidly.

Before immersion, J. Z., dressed in his usual clothes—i.e., light worsted trousers and short-sleeved shirt open at the neck—spent 1–3 hours sitting still at various room-temperatures (see table V). The changes in his rectal temperature are shown in fig. 5 (one experiment is omitted because the thermocouple was defective). Heat production was increased by

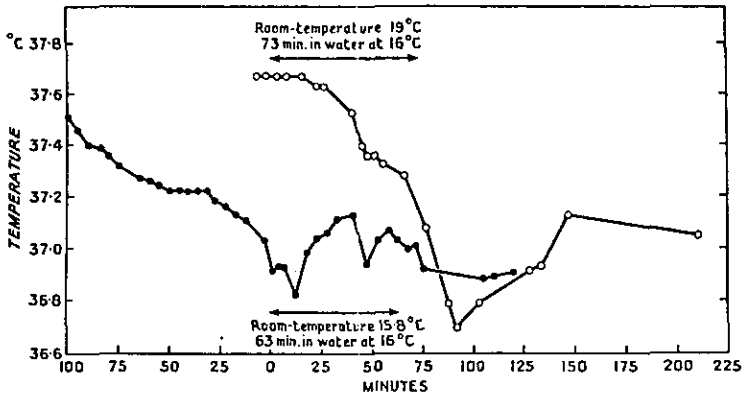

Fig. 5—Rectal temperature in J. Z. during immersion in a cold bath (16°C).

●——● Two hours sitting in room at 15·8°C before entering bath. Oxygen consumption 990 and 950 c.cm. a minute during immersion.

o——o 1 hour in room at 19°C. Oxygen consumption 740 c.cm. a minute during immersion.

shivering (see table IV) but was inadequate in one experiment to prevent a slight fall in body-temperature.

He did not complain of discomfort other than boredom, and once he read a newspaper while lying in the bath. Shivering was never prominent and consisted of a fine tremor. He maintained his body-temperature rather better when swimming than when lying still in water at 16°C (60·8°F).

Similar experiments were planned with G. P. as subject. The results of the first experiment are shown in fig. 3 and table IV.

Before immersion G. P., dressed in his ordinary clothes, was engaged in sedentary work at a room-temperature of 18°C (64·4°F).

Violent shivering began within 2 minutes of his entering the bath, and continued throughout the experiment. Discomfort was intense for the first 5 minutes in the bath and gradually passed off, giving way to a sensation of great cold. After 33 minutes he asked to be taken out, and had to be lifted from the bath because muscular rigidity made him incapable of voluntary movement. The experience was so unpleasant that he was unwilling to repeat the experiment.

Comparison of this experiment with the effect of swimming in water at a similar temperature shows that, in the case of G. P., although there was a considerable fall in rectal temperature in the bath it was much less steep than when he was swimming, which is in contrast to the results obtained with J. Z. This is in spite of the fact that G. P.'s oxygen consumption was less in the bath than when he was swimming in Lake Windermere (table IV).

Mean Skin-temperature in Air and Thermal Sensation

The mean skin-temperature of J. Z. showed an unusual relationship with sensations of comfort. The level of mean skin-temperature associated with thermal comfort in most people is 33·5–34·0°C (92·3–93·2°F) (Hardy and Soderstrom 1938, Gagge et al. 1938, Yaglou and Messer 1941). J. Z., on the other hand, was comfortable with a mean skin-temperature of 30–31°C (86·0–87·8°F). He wore few clothes and habitually slept naked at night at a room-temperature of 15–16°C (59·0–60·8°F) with only a sheet to cover him. In the experiment described above, when J. Z. sat in a room at 26°C (78·8°F), his mean skin-temperature rose to 32·5°C (90·5°F) and he complained of feeling too hot.

Other subjects usually first complained of cold when their skin-temperature fell to 32·5°C (90·5°F), and of severe discomfort when it fell to 30°C (86°F). These results (table VI) are consistent with the findings of Gagge et al. (1938) and Hardy and Soderstrom (1938).

No studies appear to have been made on subjects showing exceptional tolerance of cold. J.Z.'s resting metabolism is well within normal limits (table IV); so his tolerance of cold differs from that of patients with thyrotoxicosis, who have a high skin-temperature and increased heat production.

Studies on Other Subjects

Experiments similar to those described above were made with three other subjects. The results are shown in fig. 6. Again there was an association between the amount of subcutaneous fat and the effect of immersion on body-temperature.

G. P. and O. G. E. swam together for 60 minutes in water at 21·8°C (71·2°F). O. G. E.'s rectal temperature rose by 0·25°C (0·45°F), whereas G. P.'s fell by 2·8°C (5°F). J. M. and K. H. also swam together in water at 19°C (66·2°F) for 35 minutes; by then J. M.'s rectal temperature had risen 5·0°C (0·9°F) and K. H.'s had fallen 1·3°C (2·3°F). O. G. E. and J. M. were fat, and G. P. and K. H. were thin (table I). Neither O. G. E. nor J. M. was obese in the ordinary sense, and O. G. E. would usually be described as of slender build. Until measurements were made, it was not suspected that these two subjects had such a considerable subcutaneous layer of fat.

K. H. and O. G. E. were also the subjects of experiments in baths, the results of which are shown in fig. 4. K. H. cooled less rapidly in the bath than when he was swimming, resembling in this respect the other thin subject, G. P.

In O. G. E., on the other hand, the rectal temperature fell while he lay in a bath at 21·8°C (71·2°F), whereas when he was swimming in water at that temperature his rectal temperature rose. O. G. E. therefore resembled J. Z. O. G. E.'s metabolism, due to shivering, rose to about the same level as J. Z.'s, both being considerably less than G. P.'s shivering metabolism (table IV).

Anatomical Measurements

The regional thickness of the skin and subcutaneous tissue was estimated in all five subjects from the thickness

TABLE VI—SKIN-TEMPERATURE AND THERMAL SENSATION IN AIR

Mean skin-temperature		Thermal sensation of subject			
°C	°F	J. Z.	G. P.	R. B. P.*	H. D. L.*
35·0	95·0	..	..	..	..
34·5	94·5	..	Too hot	..	..
34·0	93·2	..	..	..	..
33·5	92·3	..	Comfortable	Comfortable	Comfortable
33·0	91·4	..	..	..	..
32·5	90·5	Too hot	..	..	Slightly cold
32·0	89·6	..	Cold	..	..
31·5	88·7	..	..	..	..
31·0	87·8	Comfortable	..	..	..
30·5	86·9	..	..	Very cold	..
30·0	86·0	Comfortable	Very cold	..	..
29·5	85·1	..	..	..	..
29·0	84·2	Comfortable	..	..	..
28·5	83·3	..	..	..	..
28·0	82·4	Comfortable	..	..	..
27·5	81·5	..	..	..	..
27·0	80·6	Slightly cold	..	..	..

* Observations on Arctic crews.

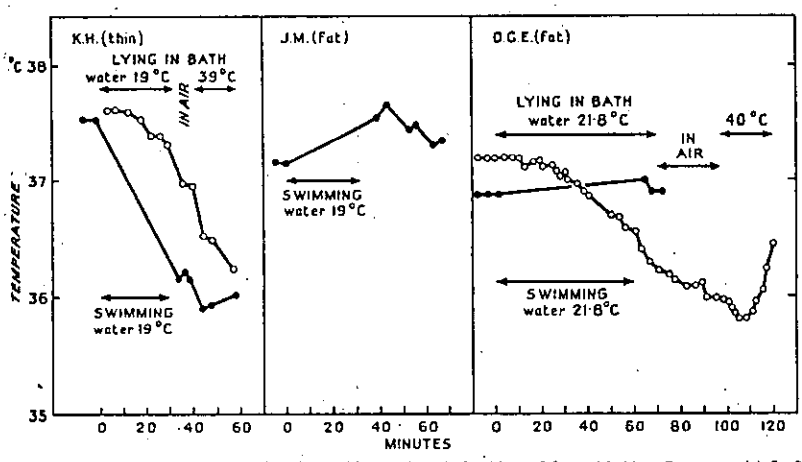

Fig. 6—Rectal temperature during swimming and in cold bath in 3 subjects, 2 fat and 1 thin. Compare with fig. 3. ●—● Swimming. O—O Lying in bath.

of the skin folds. These were measured with spring-loaded callipers exerting a pressure of 1 kg. and with jaws measuring 3 sq. cm. The skin-fold thickness so measured corresponded approximately to double the thickness of the subcutaneous layer of fat determined radiographically. The results are shown in fig. 7, where the subjects are divided into two groups, fat and thin. The difference between the thickness of subcutaneous fat in these two groups is striking and corresponds to their tolerance of cold water. Diagrammatic silhouettes of J. Z. and G. P. are shown in fig. 8.

Conductance and Insulation

These findings suggest that tolerance of cold water is related to the thickness of the subcutaneous fat. The thermal conductivity of human fat and muscle has been redetermined by Hatfield and Pugh (1951) and Hatfield (1952) who found fat to be about three times as good an insulator as muscle and almost twice as good as skin. These figures are for tissue removed from the body, without a blood-supply. Fat is avascular, compared with skin and muscle; so the difference in thermal conductivity in vivo would be even greater, depending on the volume of blood-flow to the different tissues.

The over-all thermal conductance of the body (effective thermal conductance) can be calculated from the skin and rectal temperatures and the heat production (Hardy and Soderstrom 1938). The effective thermal conductance K, in calories per square metre an hour per degree centigrade, is given in the equation:

$$K = \frac{H}{Tr - Ts}$$

where Tr = rectal temperature in °C
Ts = mean skin-temperature in °C
H = heat production in calories per square metre an hour minus 12%, representing heat loss from the lungs.

Effective thermal conductance has two components. It is a measure of the passage of heat through the tissues by direct conduction and of the convective heat flow due to the circulation of the blood. Calorimetric studies have shown that, below a certain environmental temperature, effective thermal conductance becomes minimal and constant, and under those conditions cutaneous blood-flow is too small to play a significant part in heat loss.

The effective thermal insulation of the tissues is the reciprocal of the effective thermal conductance and can be converted into Clo units by multiplying by 5·56 (Gagge et al. 1941).

The effective thermal conductance in the vasoconstricted state is 9·3 in men and 7·0 in women, the Clo value being 0·6 and 0·8 (Hardy and DuBois 1940).

Approximate values for effective thermal conductance and insulation have been calculated for J. Z. and G. P. swimming and lying still in water (table VII). Such calculations, when based on stable conditions, may be regarded as reasonably reliable, and this condition is fulfilled in the case of J. Z. In the case of G. P., who did not reach a stable state, allowance has to be made for loss of stored heat associated with continued body cooling, and the estimation of this factor is difficult (Burton and Edholm 1955). As an approximation, stored heat loss has been calculated as follows:

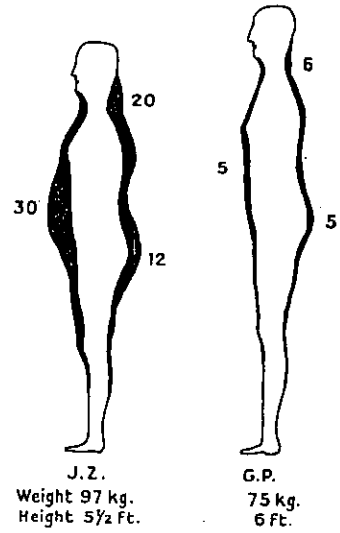

Fig. 8—Silhouettes of J. Z. and G. P. Numerals indicate thickness of subcutaneous fat (mm.) at the corresponding points. Height of figures is to scale but not thickness of fat.

Stored heat loss = rate of fall in rectal temperature near end of experiment × specific heat of tissues × body-weight × 2/3. / surface area

The value for the bath experiment was:

$$1{\cdot}4 \times 0{\cdot}83 \times \frac{75{\cdot}5}{1{\cdot}9} \times 2/3 = 30{\cdot}7 \text{ calories per square metre an hour.}$$

G. P., swimming in water at 25·3°C (77·5°F) showed only a small fall in rectal temperature (0·8°C) (1·4°F) after an hour. It has been assumed that under these conditions stored heat can be ignored.

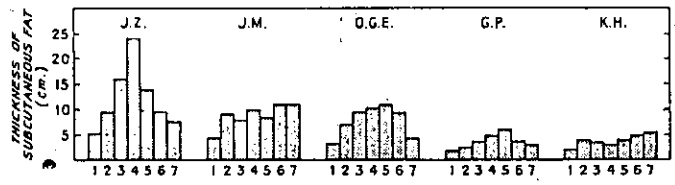

Fig. 7—Thickness of subcutaneous fat in 5 subjects: 3 fat (J. Z., J. M., and O. G. E.) and 2 thin (G. P. and K. H.) at 7 sites: 1, forearm; 2, arm; 3, chest; 4, abdomen); 5, back; 6, thigh; and 7, leg.

TABLE VII—EFFECTIVE THERMAL CONDUCTANCE AND INSULATION

—	Metabolism (kg. cal./m.²/hr.)	Heat dissipated through tissues (kg. cal./m.²/hr.)	Temperature °C (°F) Skin	Rectal	Difference	Conductance (kg. cal./°C/m.²/hr.)	Insulation (Clo)
Subject J. Z. (2·0 sq. m.)							
Swimming ..	660	290·5	16·0 (60·8)	37·4 (99·3)	21·1 (39·5)	13·4	4·2
Bath	270	118·8	17·0 (62·6)	37·1 (98·8)	20·1 (36·2)	5·9	9·4
Subject G. P. (1·5 sq. m.)							
Swimming ..	630	291·6	25·3 (77·5)	37·1 (98·8)	11·8 (21·3)	24·7	2·3
Bath	498 + 30·8*	261·3	16·0 (60·8)	36·6 (97·9)	20·6 (37·1)	12·7	4·4

* Stored heat loss.

Table VII shows that conductance was much greater in both men while swimming than in the bath. This is attributable to the peripheral localisation of the extra heat production of muscular work.

In G. P. conductance was so great that even the metabolism of swimming was insufficient to prevent hypothermia from developing in water at 21·8°C (71·2°F), and water warmer than 25°C (77·0°F) was necessary for a stable thermal state. In J. Z., on the other hand, although conductance was twice as high when he was swimming as it was when he was motionless in water, the metabolic production of heat was enough to prevent his body from cooling.

Channel Swimming-race, 1954

The cross-Channel race in August, 1954, provided an opportunity to collect more information on long-distance swimmers.

Methods

The rectal and oral temperatures of four of the seven successful competitors were recorded immediately after completion of the crossing. The rectal thermometer was introduced to a depth of 3½ inches and left in place at least 3 minutes. The measurement was repeated in doubtful cases. Other observations included sea-temperature, weight and distribution of grease used by the swimmers, food intake during the swim, and stroke-rate.

All 16 competitors were examined before the race, and measurements made of skin-fold thickness in collaboration with Dr. W. H. Hammond, to whom we are greatly indebted. The method used (Edwards et al. 1955) was to measure over six standard sites with spring-loaded callipers. Superficial tissue-thickness measurements were obtained from a chart relating fat-thickness measured by X rays and calliper readings. This method has been used for surveys on children and industrial workers (Hammond 1955); so there is a basis for comparing swimmers with other groups.

Results

The measurements are set out in table II, and the swimmers are compared with a group of British factory workers. The subcutaneous fat of the swimmers in all areas measured averaged twice the thickness found in the factory workers. All the measurements recorded on the swimmers fell at the extreme range of the frequency distribution for the factory workers.

The summarised figures given in table II, together with the heights and weights, provide further evidence that long-distance swimmers belong to a certain physical type, characterised by a large body-weight in relation to height. It is clear that none of the swimmers was thin.

Other observations made on the Channel swimmers are set out in table VIII. Two of the swimmers had rectal temperatures of 34·7°C (94·5°F) and 34·8°C (94·6°F) at the end of the race. This is similar to the rectal temperature of G. P. when he was forced to give up. The winner had a rectal temperature of 35·6°C (95·8°F), and the second woman to finish had a normal mouth temperature of 36·7°C (98·6°F).* These last two swimmers were fat, even by Channel swimming standards.

The grease used by the swimmers was anhydrous lanolin, and the amount used varied from nil up to 8 lb. When used, it was applied all over the body; the thickness differed greatly because the grease was smeared on with the fingers. The lanolin soon became hydrated, and much of it washed off, especially over areas exposed to rapid water flow, such as the hands, the feet, and the medial aspects of the arms. By the end of the race the average thickness in two subjects examined was judged to be less than 1 mm. There appears to be some loss of confidence among Channel swimmers in the effectiveness of grease, and one of them, when asked before the race why she used no grease, said she could keep warm without it and saw no point in carrying extra weight across the Channel. (The increased buoyancy was apparently not appreciated.)

In all the swimmers examined after the race the peripheral pulse was absent and the limbs were cold—to touch them was like handling fish. Measurement of blood-pressure was difficult owing to the small pulse volume at the elbow.

Procedure on a Cross-Channel Swimming-race

The swimmers leave Folkestone in their respective pilot boats about 7 P.M. and assemble on the beach at Cap Gris Nez about 11 P.M. The pilot boats wait offshore and

* We are indebted to Dr. Sabri, the Egyptian medical officer, for this figure.

TABLE VIII—1954 CHANNEL-RACE OBSERVATIONS

Order of finishing	Name	Sex	Country	Age (yr.)	Time in water hr.	min.	Body-temperature	Notes
1st	B. Pereira ..	M	Portugal	33	12	25	35·5°C (96°F rectal)	..
2nd	H. Hamad ..	M	Egypt	37	12	49	34·7°C (94·5°F rectal)	..
3rd	B. Fisher ..	F	Britain	27	14	25	..	Grease on face and neck only
4th	J. Zirganos ..	M	Greece	41	16	23	..	Grease on trunk only
5th	M. Feather ..	F	Britain	21	16	23	36·7°C (98·6°F mouth)	No grease
6th	A. Abertondo ..	M	Argentine	35	16	53	..	No grease
7th	El Sousi ..	M	Syria	27	17	55	34·8°C (94·6°F rectal) 34·1°C (94·0°F mouth)	5 lb. grease 1–2 mm. thick
Competitors who did not finish:							*Cause of failure:*	
	N. Barnie ..	M	Scotland	57	17	5	Fatigue	1½ lb. grease.
	J. Kaunwersgaard	F	Denmark	35	14	50	Fatigue	..
	B. Tomlie ..	M	Lebanon	23	16	approx.	Fatigue	..
	J. McClelland ..	M	Britain	..	15	..	Unspecified	..
	A. Rizzo ..	M	Malta	28	11	..	Fatigue	..
	B. Puysour ..	M	U.S.A.	26	14½	..	Cold	..
	K. Wray ..	M	Britain	28	3	..	Pulled shoulder muscle	8 lb. grease
	D. Beltrum ..	M	Mexico	36	5	..	Cramp	..

are marshalled by two control boats equipped with radio. About midnight the swimmers grease themselves and get ready. They all start together at about 12.30 A.M., 4 hours before high water at Dover. Each swimmer is accompanied by a motor pilot boat and a rowing-boat. The first competitor usually finishes about midday and commonly lands near St. Margaret's Bay. The last swimmer may not finish until after dark and may land anywhere between Folkestone and St. Margaret's Bay. On landing, the swimmer has to wade out of the water: he then returns to his pilot boat and is taken back to Folkestone. The times are checked by the swim marshal in one of the control boats. The other control boat maintains communication with the swim marshal and with the shore.

Other Swimming-races

During our time spent with the Channel swimmers, we heard descriptions of other long-distance swims, some of greater duration and others in colder water than the Channel. These are reported briefly here because they do not appear to have been published.

On Dec. 31, 1953, a 42-km. race took place in the Nile, near Cairo, two and a half times round an island. The water-temperature, measured by Dr. Sabri, was 11°C (51·8°F), and only two out of thirty-two competitors finished the race. They were in the water for 14½ and 17 hours. About half the competitors gave up in less than 7 hours because of cold.

In 1953 J. Z. swam in the Bosphorus in water at 8°C (46·4°F) for 4 hours. He was then removed semi-conscious and remained in this condition for 3 hours. (He and his trainer were convinced that he had been poisoned.)

Among very long swims there are two outstanding ones, both in warm waters. One was of continuous swimming for 70 hours in the Mississippi, travelling 300 km. down stream; and in the other, in the River Plate, 200 km. was covered in 75 hours. In both cases the water-temperature was said to be about 21°C (70°F).

Disturbance of Consciousness

There are several instances of disturbance of consciousness in long-distance swimmers, presumably due to cold. In 1946 Hamad, the Egyptian swimmer, had to be taken out of the Channel after 7 hours. He was in a confused state—e.g., he asked for cotton-wool to wipe his eyes and then attempted to eat the wool. In 1951, when Hamad was 35 lb. heavier and much fatter, he won the Channel race. In 1945 another Egyptian swimmer, who was considered to be too thin by his trainer, was also removed after 7 hours; he was unconscious for 3 hours.

The winner of the Ladies Race in 1951 became hallucinated after wading ashore and complained that she saw animals in the water. Similar hallucinations were experienced by a swimmer in the 1954 race, who was removed from the water after 7 hours, because of cold.

Discussion

Partial answers can now be given to the questions asked in the introduction.

Do Channel swimmers tolerate hypothermia better than others? The answer appears to be yes, because the level of rectal temperature measured in two of the cross-Channel swimmers was as low as in G. P. when he was forced to give up swimming in Lake Windermere. It seems unlikely that this tolerance of hypothermia is an important part of the ability to withstand cold. J. Z. could maintain his body-temperature for very long periods when G. P. could not, and it can be suggested that the rectal temperature falls only when the swimmer is becoming fatigued and his expenditure of energy decreases.

The muscular weakness experienced by G. P. when his rectal temperature fell to 34·5°C (94·1°F) was quite distinct from cramp or fatigue; this phenomenon needs further study.

Is the heat production of Channel swimmers exceptionally high, enabling them to maintain heat balance even in cold water? J. Z., in short practice swims, had an energy expenditure of 350–400 calories per square metre an hour. On longer swims, when the stroke-rate fell, the energy expenditure was possibly about 310–350 calories per square metre an hour. The energy expenditure of other Channel swimmers has not so far been measured, but the values obtained with J. Z. are comparable with those of G. P. and O. G. E. Glaser (1950) reports a value of 365 calories per square metre an hour for "moderately hard swimming" (expired air was collected in a Douglas bag during swimming).

Karpovich and Millman (1944) studied in many subjects the energy expenditure during sprint swimming. They collected the expired air after the subject had swum a distance of 60–120 ft. holding his breath. Very high calorie values were obtained, up to 80 calories a minute. The manner of measuring and the nature of the sprints make it difficult to compare the results with those obtained in the present study, where the swimmers were in a stable state. However, swimming the breast stroke at 1·7 m.p.h. cost 18 calories a minute, which is a little more than the calorie expenditure of J. Z. swimming slightly faster. It is clear that J. Z.'s energy expenditure during swimming is not exceptionally high. If, in this respect, J. Z. is typical of Channel swimmers, the answer *to the second question is* in the negative. What is remarkable, however, is the total energy expenditure of a Channel swimmer. The time spent in crossing the Channel is 12–20 hours, and the rate of stroke is maintained approximately constant throughout. In the case of J. Z. this means an energy expenditure probably averaging 750 calories an hour—i.e., a total expenditure of 9000–15,000 calories. This makes Channel swimming possibly the greatest feat of endurance in the world of sport.

An important aspect of heat production during swimming concerns the advice to be given to those in danger of shipwreck. Glaser (1950) wrote:

> "Fit men, who are in danger of immersion in cold water, might be advised to swim or struggle as hard as they can for as long as they can. If they try to preserve their strength by clinging to wreckage or floating on their lifebelts, they will die from cold. Perhaps more lives would have been saved in the past if this had been understood."

The present results do not support this statement. In the case of J. Z. the rate of body-cooling was very low when he lay motionless in a cold bath, and virtually nil while he was swimming. He would probably do equally well motionless or swimming. G. P., on the other hand, cooled more rapidly while swimming than while lying still, and he would almost certainly survive longer if he refrained from swimming or struggling.

This finding was confirmed in the other thin subject studied. O. G. E. had a slight fall of rectal temperature in the bath but not when swimming. The water-temperature was relatively high (21·8°C, 71·2°F), and the increase in heat production due to shivering in the water was small compared with the heat production of swimming. The traditional naval advice to cling to wreckage and not to waste energy by swimming is probably correct.

Do Channel swimmers lose heat less rapidly because of their physique? The spreading of grease over the body is common among long-distance swimmers and is relevant to this question. J. Z. used about 2 kg. of lanolin before the Lake Windermere swim. If it is assumed that all the lanolin was spread evenly over the whole body, the thickness of the layer can be calculated as follows:

Surface area of J. Z. = 2·04 sq. m.—i.e., 20,400 sq. cm.
Lanolin = 2000 g. of sp. gr. 0·97.
Vol. of lanolin = $\frac{2000}{0{\cdot}97}$ = 2060 ml.
Therefore on each sq. cm. there will be $\frac{2060}{20{,}400}$ of lanolin, about 0·1 ml., giving a thickness of 1 mm.

Larger quantities than 2 kg. (4·4 lb.) were used by some, up to 8 lb. (i.e., about 4000 ml.); so the average thickness in that case could have been up to 2 mm. Even then the increased insulation due to applied grease would be small, but it might have other useful effects, such as *reduction of friction*.

Perhaps the most important and certainly the clearest answer was obtained to the question of whether the heat loss in Channel swimmers was diminished owing to their body build. All the Channel swimmers were fat and many of them grossly fat. The increased insulation and the decreased rate of heat loss appear to be the chief factors enabling Channel swimmers to maintain body-temperature in cold water for a long time. Other factors, such as the length and volume of the limbs in relation to the trunk, were also considered. A man with short limbs and a large trunk *would cool less quickly than a* man of the same surface area but with long slender limbs and a small trunk. Calculations based on measurements on J. Z. and G. P. suggested, however, that only a minor part of J. Z.'s advantage could be explained by this difference. The important factor seemed to be tissue insulation.

This conclusion is similar to that of Scholander et al. (1950), who found no evidence of any difference in the body-temperature of Arctic animals compared with those in temperate or tropical zones, nor any difference in the resting metabolic rate. *There was, however, a very large* difference in the insulation, due to fur in land animals and to blubber in the water mammals—e.g., seals.

These findings regarding Channel swimmers were admirably summarised by Dr. Sabri when he said: "To be fat is good."

We are grateful to the Channel swimmers for their friendly coöperation, and particularly to Major Jason Zirganos, whose enthusiastic help provided the initial stimulus for this investigation. This work could not have been done without the assistance of Mr. S. Rockett, who was the swim marshal on *both cross-Channel races*. We are also indebted to Messrs. Butlins, the organisers of the race in 1954, for their coöperation.

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TECHNIQUE OF ADMINISTRATION

FROM A CORRESPONDENT

"Amongst old official men the point of practice most valued is conformity to standing rules and regulations. They are accustomed, with too much regard to their own convenience and too little to the specialties of cases, to insist upon adherence to system or precedent, called by euphemismus adherence to principle."—HENRY TAYLOR, *The Statesman*, 1836.

Sir Henry Taylor was writing about the Civil Service as it existed more than a century ago, long before the Welfare State had appeared upon the scene. But there is surely a parallel between the criticisms then current regarding the machinery of a system in Whitehall now long obsolete and those so often launched today at the administrators of the local authorities, the hospitals, and the other social services. It is tempting to speculate whether we have not reached a point where a more vital conception of the function of *administration is one of* our most pressing needs.

It all comes back, Taylor thought, to persons, capacity, and training. Part of his solution is to be found in what his book said about education. When the student is *four-and-twenty, the sooner* he is in authority the better:

"An early exercise of authority is, in the case of most men, necessary to give a capacity for taking decisions. Prudence is much more easily learnt than decisiveness; the former may be taught at any age, the latter only to the young."

What is the chief ingredient in administrative capacity? The most important qualification, Sir Henry declares, is "fitness for acting through others; since the importance of his operations vicariously effected ought, if he knows how to make use of his power, to predominate greatly over the importance which can attach to any man's direct and individual activity." How often is this simple "fitness for acting through others" still ignored in favour of the acquisition of "experience" or paper qualifications of one kind or another! A man must act through others; they must be carefully chosen (a topic upon which he has much to say); and "discipline" is a matter requiring the greatest care:

"The closeness or looseness of the discipline to be exercised must of course vary, not only with the nature of the man, but also and more distinctly with the nature of the work; and where the work is such that its effective depends much upon its conscientious performance, authority should be so used as in no degree to supplant the conscience, but on the contrary to support it; and the support should be given by an influential coöperation in which authority is rather felt than recognised. In such cases civil should be farthest from military and nearest to ecclesiastical discipline."

This is a penetrating passage widely applicable to the problems which so often flow from the attempt to discharge large-scale duties which depend upon conscientious performance. One has only to think of the large school or college—or perhaps par-*excellence the hospitals*—to sense how acute is the thought that runs through this passage.

He knew too that the use of "instruments" must not be carried too far. Consider such a passage as that in which he discusses précis-writing and insists on the importance of the personal handling of papers:

"He who has to act upon a long series of documents will hardly be able to master their contents without making an abridgement of them for himself. It is only a smatterer in business who will think it of much more than a preliminary assistance to him to have *such an abridgement made for him* by another."

Comparing past with present, where does Taylor's advice fail—most noticeably—now? Perhaps in its lack of the sense of scale and of the relationship between *human capacity and large-scale administration*. There is nothing in his book to correspond with the modern conception of "span of control." No superior, as such experts as Colonel L. Urwick would claim, can supervise directly the work of more than five, or at the most six subordinates whose work interlocks.

Much of the success achieved by the modern business consultant can be attributed to an intelligent application of this principle. Detail accumulates round the man at the top, and the temptation to add more and more subordinate staff directly responsible to himself is often found to be the cause both of *frustration in the business* and of personal breakdown in the individual thus overburdened. The solution is found in a regrouping of duties and responsibilities. Not more than five or six subordinates is the clue; and it has even been suggested by Mr. Graicunas[1] that there is a mathematical prin-

1. Relationship in Organisation. By V. A. Graicunas in Papers in the Science of Administration, quoted by L. Urwick in *The Elements of Administration*. London.

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Body temperature and metabolism in hyperbaric helium atmospheres[1]

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RAYMOND, L. W., W. H. BELL II, K. R. BONDI, AND C. R. LINDBERG. *Body temperature and metabolism in hyperbaric helium atmospheres.* J. Appl. Physiol. 24(5): 678–684. 1968.—Five male deep-sea divers were observed during pressure chamber dives and decompression over a pressure range of 4.3–14.6 atmospheres absolute (Ata). Observation periods were begun 12 or more hours after reaching maximum depth and continued during decompression. The chamber atmosphere was helium with small amounts of oxygen and nitrogen, and was quiescent and warm. Metabolic rate (seated, resting) increased only slightly above control, as large increases in convective heat transfer were accompanied by reductions in body heat transfer by radiation and evaporation. Mean skin temperature was reduced from its control value, and the high convective conductance (h_c) of hyperbaric helium narrowed the temperature gradient from skin to atmosphere to 1.6 C at 14.6 Ata. Rectal temperature was not reduced and shivering did not occur. Arterial blood pressure, respiratory rate, and expired minute volume showed no systematic change under pressure, but relative bradycardia was noted. No adventitious neuromuscular activity was observed. The divers' h_c values match those generated by a mathematical model for a cylinder undergoing natural convection.

diving; convective heat transfer; temperature regulation; metabolism; skin temperature; bradycardia

ALTHOUGH HELIUM has been employed in respirable atmospheres for many years (1, 14), its effects on man and other biological systems are still relatively unexplored. From the few preparations in which helium and the noble gases have been studied, a perplexing variety of inferences have been drawn. These include the observations that helium stimulates metabolism (12, 18, 37), that it depresses metabolic processes (10, 11, 27), and that it does not affect them (5, 17, 21, 28). The view has been advanced that helium may be a harmful atmospheric constituent (24), and altered neuromuscular function in hyperbaric helium has been reported (3, 4, 6).

Some workers have attributed the changes they observed to inherent pharmacologic properties of helium. Others have shown that by varying such factors as environmental temperature (16, 25, 33) they could magnify or minimize the helium-related phenomenon. Noting the nonspecific influences which helium-group gases may exert by changing the physical properties of atmospheres, Schreiner (34) has emphasized the existence of true pharmacologic effects as well. The partial pressures of inert gases at which such effects occur in man are not yet known.

We have recently observed some of the physiological functions of resting man during 5- to 8-day exposures in a helium-rich gas atmosphere at pressures of 4.3–14.6 atmospheres absolute (Ata) (3,270–11,100 mm Hg) and ambient temperatures averaging 28.4–29.3 C. Our results disclose little deviation from normal, except in the effects on skin temperature of an ambiance whose convective heat transfer coefficient greatly exceeds that of air at normal pressure.

METHODS

Five male deep-sea divers served as subjects. They are described in Table 1. All are participants in the US Navy Deep Submergence Systems Project's saturation diving program. Data were taken during pressure-chamber dives, prior to which each subject and observer were given several hours of instruction in the instrumental techniques. Control data in air at normal pressure were obtained inside the pressure chambers at the US Navy Experimental Diving Unit or at the Naval Medical Research Institute. Observations in hyperbaric helium (chamber P_{O_2} = 230, P_{N_2} = 850 mm Hg) at the Experimental Diving Unit employed the same subjects and instruments, and were begun 12 or more hours after

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TABLE 1. *Predive characteristics of subjects*

Occupation	Age, yr	Height, cm	Weight, kg	Heart Rate, beats/min	Blood Pressure, mm Hg	Resp Rate, breaths/min	$\dot{V}_E$, liters/min, ATPS
Physician	31	183	72.18	76	118/82	16	7.85
Damage control repairman	25	177	75.23	84	120/90	17	6.12
Human factors specialist	31	181	83.09	85	132/85	12	5.61
Marine biologist	31	176	82.59	73	132/80	9	5.66
Oceanographer	26	188	87.41	75	126/84	8	5.34
Mean	29	181	80.10	79	120/85	12	6.12

reaching the desired "depth" of 7.1 or 14.6 Ata (5,400 or 11,100 mm Hg). Measurements were continued insofar as permitted by other scheduling considerations during the decompression. Several decompression techniques were employed (R. D. Workman and R. C. Bornmann, personal communication) ranging from 50 hr for the shallower dives to 166 hr for the deeper dives which involved continuous ascent plus staged decompression.

Thirty minutes after meals the subject voided and began a balance period of 2–5 hr during which he sat quietly and had no intake or output of liquids or solids. Clothing was limited to swim trunks and a light cotton tee shirt which was removed at least 5 min before skin temperature was measured. The subject was weighed every 30–60 min on a platform balance with a sensitivity of 5 g (model TDXHH, Douglas Homs Co., Burlingame, Calif.) and determinations were made of body temperature, respiratory gas exchange, and environmental conditions. Core temperature was estimated by a rectal thermistor probe (T_r) inserted 10 cm within the anal verge. Mean skin temperature ($\bar{T}_s$) was calculated as suggested by Teichner (35) and using an infrared bolometer (model MT-3), Barnes Engineering Co., Stamford, Conn.). The low-voltage signal from the sensing head of this instrument was delivered to its readout console outside of the pressure chamber by means of an electrical hermetic connector (TBF model 5623-37PP, Deutsch Electronic Components Div., Banning, Calif.). The bolometer was calibrated against a black body whose temperature was measured by a thermistor (model 8412-6, Yellow Springs Instrument Co., Yellow Springs, Ohio) and a YSI-telethermometer (model 8410). The calibration of the telethermometer was not affected by exposure to helium and increased pressure, but the infrared bolometer read higher than actual by an amount which increased with increasing chamber pressure. The observed $\bar{T}_s$ was corrected accordingly. An attempt to use the bolometer to estimate core temperature from tympanic membrane readings was abandoned because the corrected values were 1.5–2.0 C below the simultaneous rectal temperatures.

Thermistor probes (YSI 8412-2) were used to measure the ambient (T_a) and "mean radiant" wall temperature (T_w), the latter by suspending the probe in the center of a hollow copper sphere 6 inches in diameter, painted with flat black enamel. Thermistor probes were selected on the basis of agreement within 0.1 C when compared to two thermometers certified by the National Bureau of Standards in the range of interest. Atmospheric humidity was measured using a lithium-chloride-polyvinyl alcohol-gold element (model Y477A, Honeywell, Inc., Minneapolis). Although it was not possible to calibrate this device systematically in hyperbaric helium, the instrument consistently read 98–99% relative humidity at those times when atmospheric saturation produced condensation on the chamber's interior, and it generally agreed within 2% relative humidity with an adjacent Dura-Therm Hygrometer (catolog no. 516/43, Chemical Rubber Co., Cleveland). Atmospheric movement at the subject was measured with a vane anemometer (type 3002 without jet, Alnor Instrument Co., Chicago) and the indicated velocity was corrected for atmospheric density to ambient meters per minute.

The expired minute volume ($\dot{V}_E$) was determined at ambient temperature and pressure, saturated (ATPS) by exhaling through a low-resistance mouthpiece (catalog no. 6421, Arthur H. Thomas Co., Philadelphia) and a dry-gas meter (types CD1 and CD4, Parkinson Cowan Ltd., London S.W. 1). Expired gas was collected in a Douglas bag and immediately led out of the chamber through a pressure-reducing valve. The expired oxygen and carbon dioxide fractions ($F_{E_{O_2}}$ and $F_{E_{CO_2}}$) were then determined at normal pressure, using a model F3M3 oxygen analyzer and a model IR215 carbon dioxide analyzer (Beckman Instruments, Fullerton, Calif.). Both instruments were calibrated before each analysis with certified gas mixtures (Matheson Gas Co., Rutherford, N. J.) whose oxygen and carbon dioxide content were determined in parts per million by a mass spectrometer. The chamber atmosphere was monitored at 15-min intervals so that inspired fractions of oxygen and carbon dioxide ($F_{I_{O_2}}$ and $F_{I_{CO_2}}$) were constantly available. $\dot{V}_E$ was converted to standard temperature and pressure, dry, and oxygen consumption ($\dot{V}_{O_2}$) was calculated using *equation 1*. $F_{E_{CO_2}}$ was sometimes unavailable, in which case a value of 0.82 was assumed for the respiratory quotient (RQ):

$$\dot{V}_{O_2} = \dot{V}_E \frac{F_{I_{O_2}} - F_{E_{O_2}}}{1 - F_{I_{O_2}}(1 - RQ)} \qquad (1)$$

Values of $\dot{V}_{O_2}$ were converted to metabolic rates (MR, kcal/m² per hr) using a caloric equivalent appropriate to the value of RQ. MR was adjusted for a small amount of heat "storage" which often took place in the form of a difference in $\bar{T}_s$ or T_r between the start and finish of a balance period. The adjusted value (MR′) of the seated resting subject was equated to the sum of heat losses by evaporation, radiation, and convection as in *equation 2*. Values of E were calculated from the sequential weigh-

TABLE 2. *Effects of hyperbaric helium environment*

Subj	Environmental Factors						Physiological Responses						
	P_T, Ata	D/Dc	T_a, °C	T_w, °C	V, m/min	P_w, mm Hg	$M_R' = E + R + C$ kcal/m² per hr	T_s, °C	T_r, °C	Pb, mm Hg	Heart Rate, beats/min	Resp Rate, breaths/min	$\dot{V}_E$, liters/min ATPS
2	14.6	3.27	29.5	29.7	2.8	18.9	48.9 = 14.0 + 4.0 + 30.9	30.6	36.5	132/85	60	14	6.4
3			28.0	28.1	0.9	21.2	64.0 = 6.8 + 7.0 + 50.2	29.8	37.0	129/73	75	12	5.6
5			29.3	29.4	1.1	24.4	41.8 = 8.0 + 6.6 + 27.2	31.0	36.0	128/86	60	15	7.4
Mean	14.6	3.27	28.9	29.1	1.6	21.5	51.6 = 9.6 + 5.9 + 36.1	30.5	36.5	130/81	65	14	6.5
1	11.9	2.89	28.6	28.8	0	27.6	58.0 = 12.1 + 11.1 + 34.8	31.4	36.2	117/87	60	12	11.9
2			30.8	30.6	0	20.4	48.6 = 7.3 + 6.6 + 34.7	32.2	36.7	131/81	58	14	7.6
5			28.5	29.5	1.10	20.8	45.0 = 10.8 + 7.4 + 26.8	30.3	36.2	130/80	69	16	7.8
Mean	11.9	2.89	29.3	29.3	0.4	22.9	50.5 = 10.1 + 8.4 + 32.0	31.3	36.4	126/83	62	14	9.1
1	9.1	2.51	28.7	28.5	0	25.4	42.2 = 8.6 + 10.0 + 23.6	31.9	36.5	118/85	68	14	9.6
2			30.4	30.2	0	19.3	50.1 = 10.4 + 7.8 + 31.9	32.1	36.6	128/93	59	14	5.4
3			29.7	29.7	2.4	20.0	63.8 = 10.6 + 8.9 + 44.3	31.8	37.2	141/77	80	12	6.3
5			28.4	28.4	1.4	21.7	36.7 = 7.7 + 8.5 + 20.5	30.5	36.0	125/83	64	11	7.1
Mean	9.1	2.51	29.3	29.2	1.0	21.6	48.2 = 9.3 + 8.8 + 30.1	31.6	36.6	128/84	68	13	7.1
1	7.2	2.24	28.5	29.0	0	28.3	53.8 = 8.6 + 13.3 + 31.9	32.2	36.6	120/86	65	13	9.2
2			29.3	29.2	0	22.9	57.3 = 9.2 + 12.2 + 35.9	31.2	36.7	131/89	59	14	4.6
4			28.6	28.7	2.0	18.7	49.2 = 13.8 + 10.4 + 25.0	31.3	36.2	134/89	69	10	5.6
5			29.4	29.3	1.0	22.7	40.8 = 11.4 + 7.0 + 22.4	31.0	36.1	128/82	63	13	7.7
Mean	7.2	2.24	29.0	29.0	0.8	23.2	50.2 = 10.8 + 10.7 + 28.7	31.2	36.4	128/87	64	13	7.0
1	5.7	2.03	28.4	29.1	0	25.4	45.4 = 4.7 + 13.7 + 27.0	32.3	36.8	114/85	72	12	8.2
4			28.5	28.7	1.8	21.3	48.1 = 7.8 + 10.0 + 30.3	31.2	36.4	136/92	72	10	5.8
Mean	5.7	2.03	28.4	28.9	0.9	23.4	46.8 = 6.2 + 11.9 + 28.7	31.8	36.6	125/88	72	11	7.0
1	4.3	1.84	28.2	28.7	0	22.2	43.1 = 13.9 + 15.9 + 13.3	32.4	37.4	120/84	79	15	12.2
2			28.9	28.7	0	23.6	46.2 = 10.2 + 11.1 + 24.9	31.3	36.5	132/85	55	13	5.1
3			29.5	29.5	0	21.6	54.1 = 21.6 + 11.1 + 21.4	32.3	37.2	145/74	82	11	5.9
5			28.6	28.5	0	21.4	44.9 = 8.2 + 11.4 + 25.3	31.3	36.1	130/80	67	11	7.6
Mean	4.3	1.84	28.8	28.8	0	22.2	47.1 = 13.5 + 12.4 + 21.2	31.8	36.8	132/81	71	12	7.7
1	1.0 (air)		29.6	29.8	7.6	16.9	55.8 = 24.4 + 21.0 + 10.4	34.8	37.1	118/82	76	16	7.8
2	1.0		26.7	25.7	0	11.4	52.2 = 17.2 + 26.2 + 8.8	32.1	37.5	120/90	84	17	6.1
3	1.0		26.2	26.8	6.1	11.7	52.9 = 14.2 + 18.4 + 20.3	31.3	37.1	132/85	85	12	5.6
4	1.0		28.3	28.4	0	22.0	44.2 = 13.7 + 17.3 + 13.2	32.6	36.5	132/80	73	9	5.7
5	1.0		28.3	28.4	0	21.9	33.8 = 12.9 + 8.7 + 12.2	32.8	36.1	126/84	75	8	5.3
Mean	1.0 (air)	1.00	27.8	27.8	2.7	16.8	47.8 = 16.5 + 18.3 + 13.0	32.7	36.9	126/85	79	12	7.4

ings, and R was calculated from T_a *and* T_w *using the* (corrected) relationships presented by Epperson et al. (13). Convection (C) was obtained by difference using *equation 2.*

$$M_R' = E + R + C \qquad (2)$$

Blood pressure was obtained by auscultation of the brachial artery using a vented aneroid sphygmomanometer, and heart rate from the radial pulse. No attempt was made to quantitate sensations of thermal comfort or discomfort, nor was any effort made to control or record caloric intake except for requiring abstinence during the balance periods.

RESULTS

The environmental conditions and corresponding physiological observations at the available total pressures (P_T) are compiled in Table 2. It was not possible to obtain data on all subjects at all depths because of the fortuitous relation of the dive and decompression schedule to the time of day, and to high-priority activities including sleep, meals, and experimentation (communications, microbiological, behavioral) by others. This circumstance limits the drawing of rigorous conclusions from our observations, but several over-all features are evident.

One such feature is the relative warmth, quiescence,

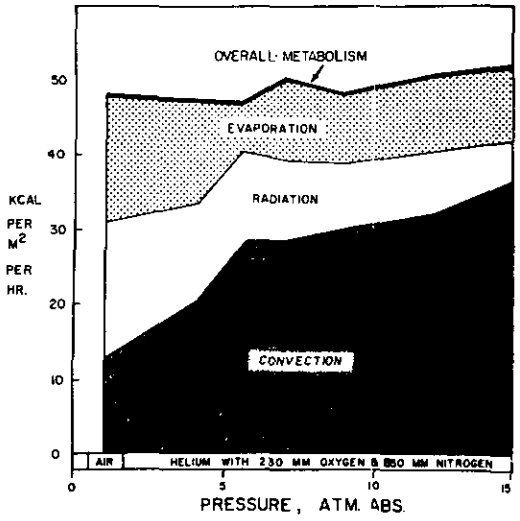

FIG. 1. Metabolic balance in He-O_2 under pressure. The over-all metabolic rate of divers seated in a hyperbaric, helium-rich atmosphere is not strikingly higher than normal. Changes in the relative amounts of heat transfer by evaporation and radiation offset the large increase in convective surface cooling.

and constancy of the chamber atmosphere during the periods of observation. Ambient (T_a) and "mean radiant" ($\bar{T}_w$) temperatures ranged between 28.0–30.8 and 28.1–30.6 C, respectively, and were generally in close agreement with one another. Velocity (V) over the body surface ranged from 0 to 1.6 m/min, but only at the highest pressure did it exceed an average of 1 m/min. Since several dehumidification schemes were employed during the present series of chamber dives, ambient water vapor pressure ranged between somewhat wider limits (P_W = 18.7–28.3 mm Hg, with relative humidity 46–99%). The density of the chamber atmosphere, relative to air at 1.0 Ata (760 mm Hg), was calculated from the observed composition, and expressed by the ratio D/Da. The value of D/Da during hyperbaric observations ranged from 1.84 to 3.27 since the initial descent to 1.42 Ata was made using compressed air to provide slight hyperoxia (F_{IO_2} = 230 and F_{IN_2} = 850 mm Hg). Table 2 also presents control data in air at 1.0 Ata, reflecting the cooler and drier chamber conditions of a comfortable normal atmosphere.

Physiological responses to these environmental conditions are presented in Table 2 and Fig. 1. In the figure, the ordinate represents the mean value of over-all metabolism and of each heat transfer mechanism in from two to five subjects at various depths (abscissa plots pressure in Ata). Several trends were evident. Over-all metabolism remained close to the control value. Shivering was not observed in any subject during any measurement period. Although shivering did interfere with sleep in several instances, environmental and physiologic data were not recorded during these periods. Figure 1 also makes clear the progressive increase in the convective mode of body heat transfer, with increasing pressure in helium. The value of C at 14.6 Ata is nearly three times its control value in air.

The increased convection was concomitant with a reduction in $\bar{T}_s$ in hyperbaric helium, even though the environmental temperature was warmer during the chamber dives than in control measurements. As shown in Fig. 2, the skin to gas thermal gradient was reduced from 4.9 (control) to 1.5 C at the highest pressure. The lower $\bar{T}_s$ tended to minimize heat transfer by radiation to the relatively warm chamber walls, contributing to the reduction in R evident in Fig. 1. Skin cooling also minimized evaporative heat transfer (7). Core temperature (T_r) was not greatly reduced at any pressure, despite the lower values of $\bar{T}_s$. The maintenance of normal over-all metabolism and core temperature are probably attributable to peripheral vasoconstriction. Although we did not attempt to measure this function, a rough index of skin conductance is provided by M_R' and the core to skin temperature gradient. This approach indicates that skin conductance was reduced by one-fourth at the highest pressure. However, since the values of T_r and $\bar{T}_s$ were measured at somewhat uncontrolled periods with regard to time of day and postprandial interval, we are reluctant to attribute a particular numerical significance to the changes in mean values available at present.

Results of blood pressure, heart rate, respiratory rate, and $\dot{V}_E$ measurements are also shown in Table 2. The mean values do not appear to differ substantially from

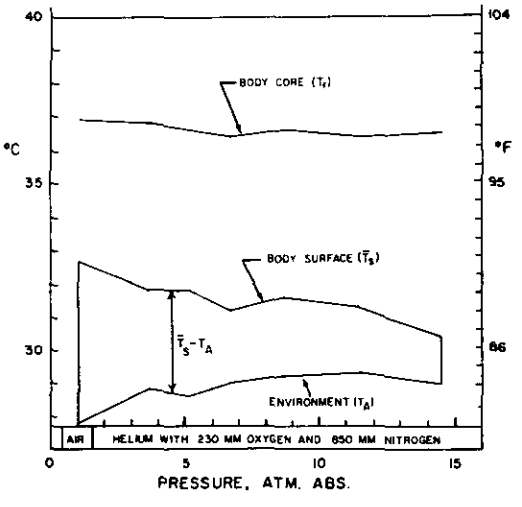

FIG. 2. The temperature differential between skin and ambient gas is narrowed in the helium atmosphere of the diving chamber, especially at increasing pressures. Rectal temperature averages slightly less than control in helium, but increasing pressures do not appear to have much effect on this value. Skin approaches environmental temperature in He-O_2 under pressure, but core stays warm.

controls except for a relative bradycardia. No myoclonus, fasciculations, or gross behavioral changes were evident in any subject.

DISCUSSION

The major finding of this study, increased convective heat transfer, is a natural consequence of the physical properties of hyperbaric helium atmospheres. To express the phenomenon algebraically, *equation 3* may be written, in which C, T_s, and T_a are as defined above, A represents the body surface area, and h_c is the convective heat transfer coefficient or convective conductance, in consistent units. The value of h_c depends upon the physical properties of the convecting surface and the enveloping fluid.

$$C = h_c A(T_s - T_a) \qquad (3)$$

From the data in Table 2, it is possible to derive h_c for the pressure range available in the present study, through the use of *equation 3*. Values of h_c so derived are presented in Fig. 3. Since h_c can also be predicted from mathematical (29, 31) or physical models (D. McK. Kerslake, personal communication), corresponding values are included in Fig. 3 for a sphere of 15.2 cm (6 inch) diameter and an erect cylinder of 30.5 cm diameter, 183 cm high (1 ft x 6 ft, (32)). The h_c data of the present study are in closest agreement with those generated by a mathematical model for natural convection from the cylinder. In view of the low velocity measurements obtained, natural rather than "forced" convection relationships might be expected to apply to our data. The application of such relationships to this problem have been discussed elsewhere (31). Qualitatively, high values of h_c are favored by the high thermal conductivity of such gases as helium, by the increased density of hyperbaric atmospheres, and by atmospheric movement. It is quite possible that a combination of such factors could increase the h_c of He to such an extent that it would approach the h_c of water, which is some 25 times that of air under normal conditions.

Whether physiological changes are caused by exposure to environments of high h_c depends mainly on ambient temperature and exposure duration. It is clear that in such environments T_s tends to approach T_a closely, but this need not compromise normal function. By merely providing a warm ambient, several groups have shown that normal metabolism can proceed undisturbed under these circumstances (13, 15, 25). Our data likewise give no clear evidence of hypermetabolism, despite the increased atmospheric pressure. The effect of increased h_c on metabolism in our study was limited by three factors. First, a high T_a (average, 28.4–29.3 C) was able to be provided, as desired for comfort. T_w was also high, minimizing radiant cooling. Furthermore, the quiescent atmosphere and relative inactivity of subjects kept h_c in the lower, "natural" convection range. As a result of these factors, the T_s values of the present study

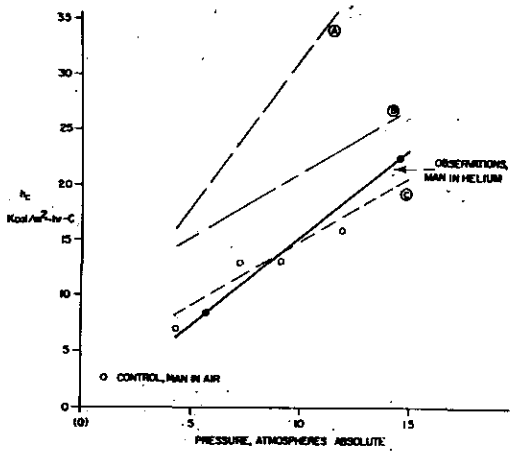

FIG. 3. The increase in convective conductance (h_c) with pressure in helium atmospheres differs with the method of analysis. Values of h_c observed from divers (—o—) are compared with data from physical (A) and mathematical (B) analyses for small spherical shapes and with mathematical model for large cylinder (C). The latter analysis, assuming natural convection, yields closest agreement with observations in man.

were only slightly cooler than normal, even at the greatest pressure. T_r was well maintained in the hyperbaric helium atmosphere, and no increase in resting metabolism occurred. No shivering occurred during measurement periods, and no other forms of adventitious muscle activity were detected. Although no systematic records of comfort were kept, the subjects generally felt "cool but not uncomfortable" during measurements. Complaints of excessive humidity were frequently offered, especially when relative humidity exceeded 90%. To what degree the low values of E during dives were due to high relative humidity is uncertain. The report of Buettner (8) suggests that humidity, as well as the reduced T_a, may have exerted a limiting effect (7). The lower values of R in hyperbaric helium are due to both the reduced T_a and the fact that T_w was higher during the dive than during the control period.

Since measurements of this nature may be difficult to obtain under operational circumstances, one might wish to draw inferences from these data which might be applicable to open-sea saturation diving chambers. In the latter circumstance, colder ambient and radiant temperatures may be combined with significant atmospheric velocities. For atmospheres colder than 30 C (9, 22) a hypermetabolic response should be anticipated, depending on the type of clothing provided. In cases of prolonged power failure, the potential thermal stress would be very severe. While the increase in caloric needs, respiratory gas exchange, and shivering are of the most compelling concern, an additional effect may be of equal importance. Vasoconstriction in skin and subcutaneous tissues due to lower temperature (2, 23) may interfere with the elimination of gas deposited in these sites during

activity, while they were relatively warm and vasodilated. The role of such temperature-dependent effects on decompression requirements does not yet appear to have been adequately studied. It may be speculated that peripheral cooling and consequent vasoconstriction contributed to the bradycardia seen in our subjects. However, the relative character of this observation suggests that predive anxiety may have influenced the control value of heart rate. More substantive studies of cardiovascular physiology under these conditions are needed to clarify such issues.

The techniques employed in the present work do not reveal any action of helium to stimulate or depress overall metabolic activity in man over the ranges of temperature and pressure available for study. It is possible that such actions may exist, even under the conditions studied, but that the observations we made were too gross or lacking in specificity to disclose subtle changes. Alternatively, complementary changes at different sites could escape notice. For example, an increase in oxygen consumption due to the respiration of abnormally dense gas media (19, 26), especially at reduced temperatures (P. Webb, personal communication), could be masked by simultaneous interference with cellular metabolism in hepatic or cerebral tissues (11). The observations we now report, therefore, neither support nor contradict the view that helium is potentially harmful to man. It is noteworthy, nevertheless, that we failed to detect signs of neuromuscular dysfunction which have been reported by others in hyperbaric helium atmospheres (3, 4, 6).

The practical implications of this work seem quite straightforward. The hyperbaric helium atmosphere of a permanent deep ocean habitat will require a high ambient temperature, especially if atmospheric velocity is significant and walls are cold, since the high convective conductance of pressurized helium will not permit the normal skin to gas thermal gradient which affords man a liberal "comfort zone" in the conventional atmosphere. Since exposures to hyperbaric helium are likely to be days or weeks in duration, however, the possible effects of high ambient temperatures, especially upon testicular metabolism (20, 36), diurnal variations in endocrine function, and the behavior of microorganisms may require much further study. Habitat temperature may also be an important determinant of acclimatization, cold-water behavior, and effective postdive performance.

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ENERGY BALANCE OF MAN IN SIMULATED DIVE FROM 1.5 TO 31 ATA

P. Varène, J. Timbal, H. Vieillefond, H. Guenard and J. L'Huillier

Experimental determinations of animal or human metabolism in He–O_2 atmospheres are numerous in the literature. After the early work of Cook et al. (6) an increase in oxygen consumption ($\dot{V}O_2$), if any, is usually related to an increase in skin heat losses (2, 7, 8, 12, 18, 19, 25), rather than to a cellular effect, although He might alter metabolic pathways in some biological systems (20).

Theoretical considerations show that skin convective heat losses must increase in the He–O_2 atmosphere at depth (9, 16, 23). However, few studies have been carried on in man to ascertain this point experimentally (17); the same remark holds true for the respiratory convective heat losses for which only predictive assumptions are available (22, 24).

This paper describes an attempt to make an experimental determination of the different parameters in the body heat balance equation at several levels of ambient pressure and He–O_2 atmosphere. For a resting subject this equation may be written as:

$$M \pm R \pm C_S \pm C_{Res} - E = \pm S \qquad \text{(watts/m}^2\text{)}$$

Where:

M = metabolic heat production
R = radiant heat exchange
E = evaporative heat loss
C_S = skin convective heat exchange
C_{Res} = respiratory convective heat exchange
S = heat body storage

In this equation where M, C_S and C_{Res} are the first points of interest, M, R, C_{Res}, E and S are directly estimated and C_S computed.

Experimental Procedure

Measurements were made in four subjects lying nude at rest in a He–O_2 atmosphere (P_{IO_2} = 300 mb), at six levels of pressure between sea level down to 300 meters depth (1.49;

2.28; 4.38; 8.36; 16.09; 30.79 ata). Control values were obtained at 1.5 ata in air. Ambient temperatures were always set for the thermal comfort of the subjects.

Metabolism was calculated from oxygen consumption measured by an open-circuit method, during three periods of 10 minutes at each pressure level for each subject. Gas analyses were duplicated using a fuel cell for O_2, infrared absorption for CO_2, and gas chromatography for both.

Heat exchanges by radiation *(R)* were computed from the mean skin temperature $(\bar{T}_s)$ and the mean wall temperature $(\bar{T}_w)$ according to the Stefan-Boltzmann law. Body heat storage *(S)* was computed from variations of the mean body temperature $(\bar{T}_b)$ with $\bar{T}_b = 0.66\ \bar{T}_{re} + 0.34\ \bar{T}_s$. Rectal $(\bar{T}_{re})$, skin and ambient temperatures were recorded using thermocouples, and averaged according to Colin and Houdas (5). Skin and respiratory evaporative heat losses were calculated from a weight loss recording. Respiratory convective heat losses (C_{Res}) were computed from respiratory flow $(\dot{V}_E)$, inspired (T_I) and expired (T_E) gas temperatures picked up with microthermocouples (13).

From these data, skin convective heat losses (C_s) were deduced according to the general equation of the body heat exchange balance:

$$Cs = M - (R + C_{Res} + E + S) \text{ watt} \cdot \text{m}^{-2}$$

A coefficient for skin convective heat exchanges *hc* was established from:

$$hc = \frac{C_s}{\bar{T}_s - T_a}$$

At each pressure level, a supplementary run was made during which each subject was investigated while breathing a precooled He–O_2 mixture for 20 minutes. The first measurements began after a resting period of 1 hour.

Results

The values of metabolism do not show any systematic variation with pressure: $\dot{V}_{O_2}$ does not change in three cases but decreases in one (FS, $P < 0.05$), $\dot{V}_{CO_2}$ increases significantly in two individual cases (BA, BB) and for the subjects, altogether ($P < 0.06$). Consequently R increases significantly with pressure for subjects altogether ($P < 0.01$) (see Fig. 1). Inhalation of cooled gases for 20 minutes does not modify the $\dot{V}_{O_2}$ values of the subjects, in spite of an important increase in respiratory heat loss at the deeper levels (see below). A decrease of 0.2–0.25 °C in rectal temperature (T_{re}) is observed at 30 ata at the end of the cooled gas inhalation period; this appears too small to induce a measurable increase in thermogenesis.

The ventilation ($\dot{V}_E$) does not vary significantly with pressure in three subjects but increases in one (BA, $P < 0.05$) (Fig. 2). No systematic variation of breathing frequency (f) or tidal volume (V_T) is observed.

$\dot{V}_A$ and $P_{A_{CO_2}}$ have been computed with $\dot{V}_E$ and $\dot{V}_{CO_2}$ assuming that dead space does not vary with pressure (21) but is only a function of V_T and f according to the formula given by Bargeton et al. (1). $\dot{V}_A$ does not show any variation with pressure, while $P_{A_{CO_2}}$ increases slightly. Cooled-gases inhalation does not modify systematically $\dot{V}_E$, V_T or f.

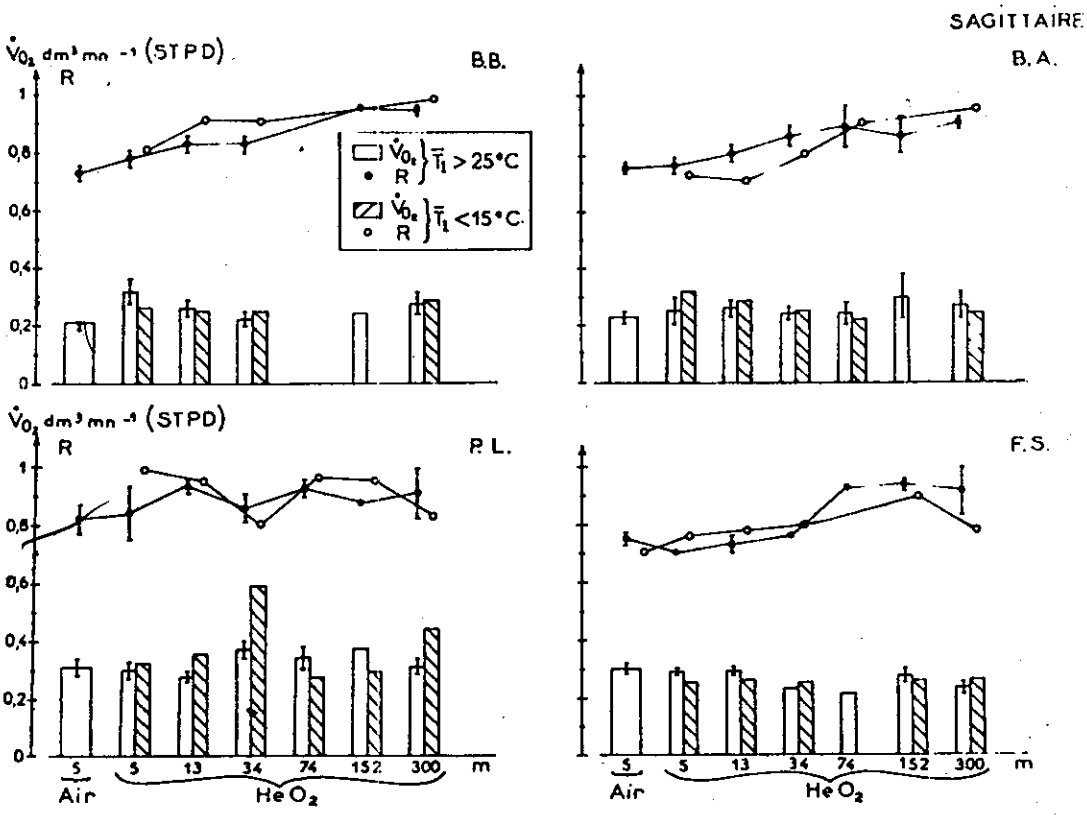

FIG. 1. Oxygen consumption ($\dot{V}_{O_2}$) and respiratory exchange ratio (R) measured for each subject as function of depth (meters of sea water) for two temperatures of inspired gases.

Heat loss by respiratory convection increases as inspired gas temperature *(T_I)* decreases and as depth increases according to predictions. The values obtained on each subject are shown in Fig. 3. Expressed as percentage of metabolism, the mean values computed for four subjects vary from 1 (T_I = 30°C and P_B = 1.5 ata) to 60 (T_I = 10°C and P_B = 31 ata) (Table II).

The values of ambient temperatures set in order to maintain the subjects in thermal comfort increase with depth. They are listed in Table I. Mean skin temperature *($\bar{T}_S$)* increases too as depth increases but less than dry bulb ambient temperature *(T_a)* or wall temperature *(T_w)*. Consequently the difference between T_S and T_w decreases and radiant heat loss decreases.

As a function of pressure, rectal temperature *(T_{re})* slightly increases from day to day. However, heat body storage computed on the 2 hours of each daily experiment from T_{re} and $\bar{T}_S$ shows no systematic variation with depth. Its value averaging 7 or 8 watts/m² is always found negative showing a slight body cooling during each experimental period.

In agreement with predictions, weight loss, from which evaporative heat loss is computed, does not change with pressure. It corresponds only to insensible perspiration.

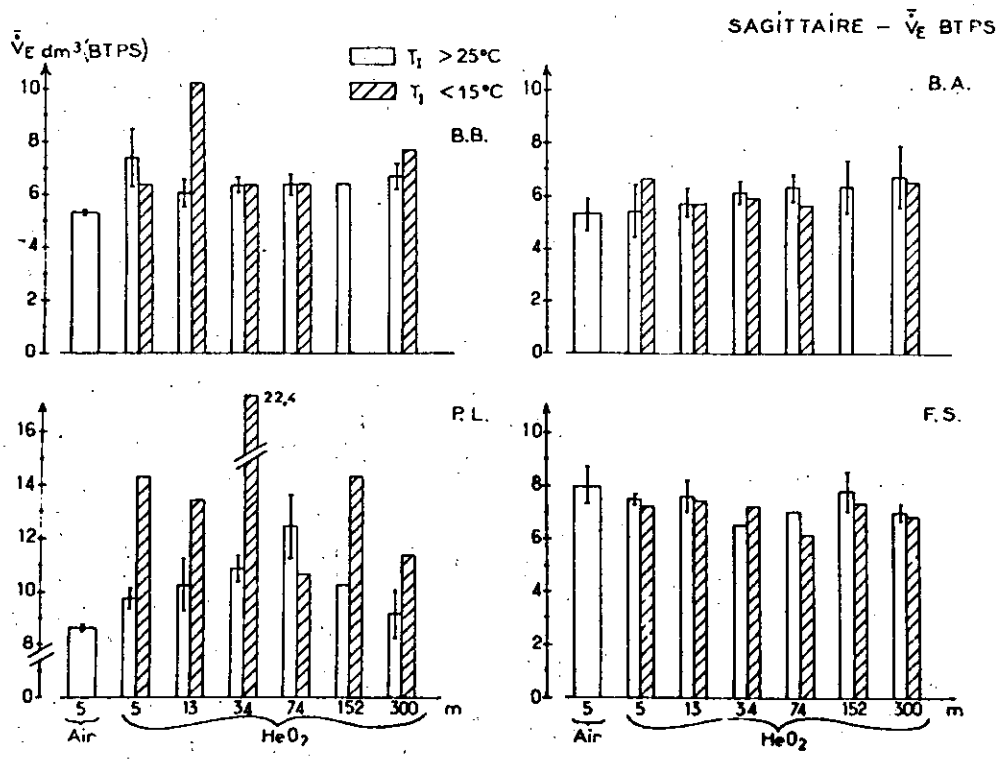

FIG. 2. Ventilation ($\bar{V}_E$) measured for each subject as function of depth (meters of sea water) for two temperatures of inspired gases.

Heat losses by skin convection, C_S, computed from data of M, R, C_{Res}, E and S are widely increasing for each subject with pressure. The mean values found for C_S rise from 14 watts/m² at 1.5 ata to 33 watts/m² at 31 ata in He–O_2 atmosphere. The control experiment at 1.5 ata in air gives a mean value of 8 watts/m². The association of an increase of C_S with a decrease of skin to ambient temperature difference leads to the computation of an exchange coefficient hc:

$$hc = \frac{C_S}{T_s - T_a}$$

which is ten times larger at 31 ata than at 1.5 ata (Fig. 4). The variation of hc with pressure (or other parameters like "convective constant" of Webb [23]) may be represented either by a first degree algebraic equation or by a power function.

Discussion

From a general point of view these results show that energy sources do not vary with pressure or He–O_2 mixture but that the avenues of the energy expenditure are widely modified.

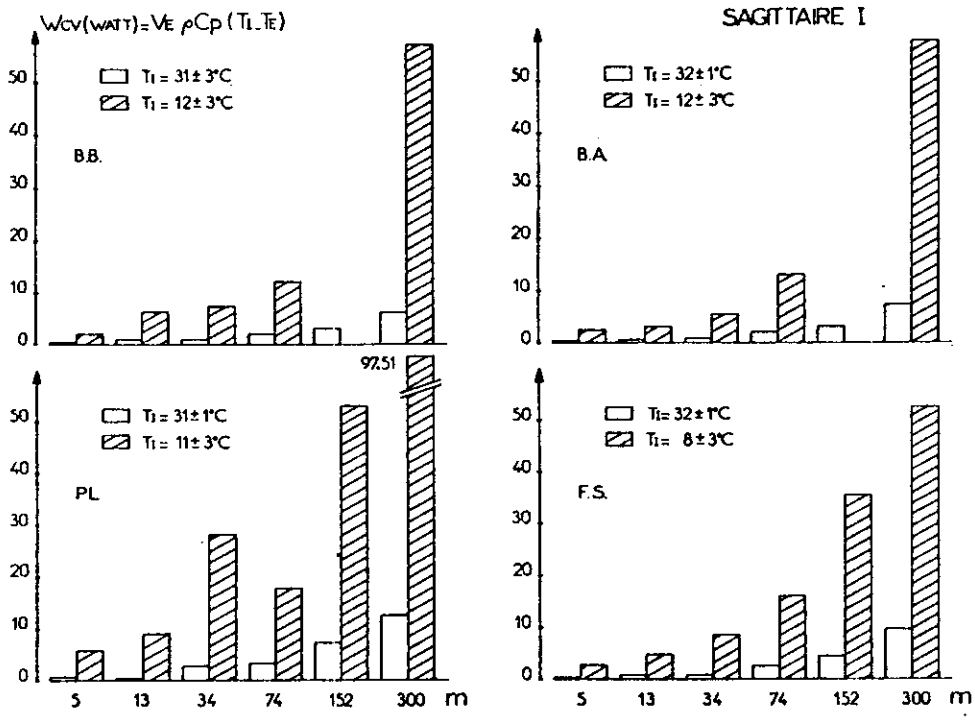

FIG. 3. Total respiratory convective heat losses ($\dot{W}_{CV} = C_{Res} \times A_D$, where A_D is the body area) measured on each subject as function of depth for two ranges in temperature of inspired gases.

The sharp increase in *hc* with the pressure rise agrees with the physical laws for convective heat exchange and implies that, as the pressure increases: 1) for the same temperature difference $(\bar{T}_s - T_a)$, absolute convective heat exchange increases; 2) the diver thermal balance becomes more and more unstable since for the same $\bar{T}_s$, a small variation in T_a induces a larger variation of convective heat exchanges.

These results are in agreement with those previously published up to 14 ata by Raymond et al. (17). Higher values for *hc* found by these authors may probably be related to the con-

TABLE I

MEAN VALUES OF DRY BULB TEMPERATURES (T_a) AND WALL TEMPERATURES (T_w) MAINTAINED IN THE PRESSURE CHAMBER, IN ORDER TO OBTAIN THE THERMAL COMFORT OF THE SUBJECTS

Temperature	Air	$He-O_2$					
	1.5 ata	1.5 ata	2.3 ata	4.4 ata	8.4 ata	16.1 ata	30.8 ata
T_a	26.5	28.7	29.6	30.0	30.7	31.8	32.4
T_w	24.8	26.4	27.0	28.2	28.3	30.1	31.2

TABLE II

RESPIRATORY CONVECTIVE HEAT LOSS (C_{Res}) EXPRESSED AS FRACTION OF HEAT PRODUCTION (M) IN FOUR SUBJECTS AT 30.8 ATA, FOR TWO TEMPERATURES OF INSPIRED GASES

	High T_I		Low T_I	
Subjects	T_I (°C)	C_{Res}/M	T_I (°C)	C_{Res}/M
BB	33.9	0.06	13.6	0.55
BA	33.4	0.08	9.4	0.69
PL	30.6	0.12	8.6	0.66
FS	31.0	0.12	7.5	0.63

vective respiratory heat exchanges which were not taken into account. The value for *hc* that was found at 1.5 ata in air (1.52 watts/m²/°C) agrees with the result of Hardy et al. (0.9 to 1.6 watts/m²/°C) in quiet atmosphere (10). These results are also in agreement with the opinion of authors who think that in He-O_2 atmosphere, no $\dot{V}_{O_2}$ variations occur as long as thermal comfort is maintained (12). The instability of the thermal balance at depth probably accounts for modifications of $\dot{V}_{O_2}$ or even $\dot{V}_E$ often found.

Another noticeable result of this study is the increase of the measured convective respiratory heat losses. The present values are in agreement with previous data obtained in air (11, 22) from which predictions had been made for deeper dives in He-O_2 (Fig. 5). The computation was based on:

1) the experimental fact that T_E may be represented by a simple function of T_I ($T_E = a + b\,T_I$) (see Fig. 5);
2) the assumption that the ratio $\dot{V}_{O_2}$ (STPD)/$\dot{V}_E$(BTPS) is constant with pressure and subjects.

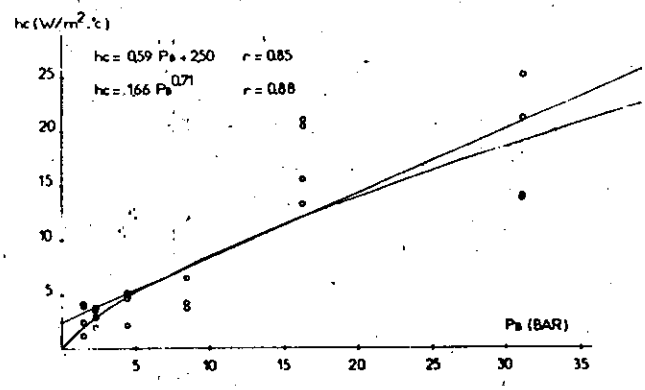

FIG. 4. Evolution of the exchange coefficient of skin convection *(hc)* as function of pressure. The equations give the linear and power functions which can fit the experimental data computed on four subjects.

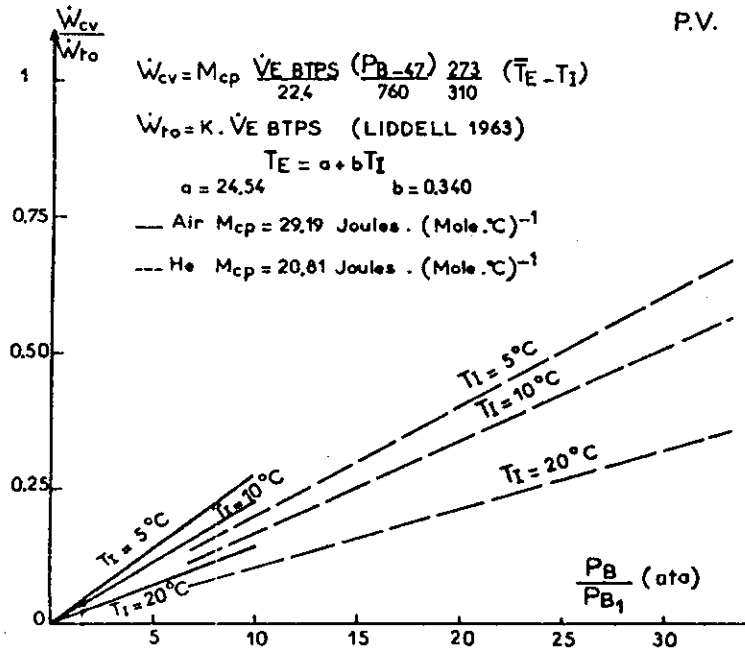

FIG. 5. Fraction of total heat production ($\dot{W}_{to}$) dissipated through respiratory convective heat loss ($\dot{W}_{cv}$) as function of pressure in ata (11).

In this representation

$$\frac{\dot{W}_{cv}}{\dot{W}_{to}} = \frac{C_{Res} \times A_D}{M \times A_D} = \frac{C_{Res}}{M}$$

The computation is made from molar ventilation $\dot{V}_{STPD/22.4}$, molar specific heat M_{cp} and values of a and b previously found in air (see text).

From 1), convective respiratory heat exchanges may be expressed as a function of T_I, $\dot{V}_E$ BTPS, specific heat (Cp.), and either volumic mass (P) or pressure (P_B).

From 2), the ratio of convective respiratory heat exchanges over the total energy sources C_{Res}/M may be expressed as a function of the same parameters without $\dot{V}_E$.

In the present experiment we have found values for coefficients a and b slightly different from those found in air. Coefficient a is higher (26.5 to 28.5°C against 24.0 to 24.5°C in air); coefficient b is lower (0.20 to 0.25°C against 0.32 to 0.34°C in air). This difference may probably be related to the fact that previous results were obtained in inspired dry air as opposed to wet air in the present work (15). Nevertheless, the values obtained at the deepest level of the present experiment and given in Table II show that they agree with predictions in Fig. 5.

The last main point brought out by this experiment is the increase of R. It may be noticed that such an increase was sometimes found in other work (3, 4, 21) without being discussed. If one admits that alveolar ventilation $\dot{V}_A$ is constant and that $P_{A_{CO_2}}$ is increased, $\dot{V}_{CO_2}$ must increase. Consequently R will increase if $\dot{V}_{O_2}$ remains constant. Such a remark however does

not give an answer to the question: why does R increase? An analysis error consequent to the large decrease of respiratory gas fractions with pressure may probably be excluded: firstly, because the gas analyses were made with two very different technics, and secondly because R always remained in normal range. Actually no physiological explanation may be given on this point with certainty and the true reason of the increase in R remains obscure. Nevertheless, whatever the explanation is, these conclusions on $\dot{V}_{O_2}$ will not be modified since the increase of R is consecutive to an increase of $\dot{V}_{CO_2}$.

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Webb Associates

RESPIRATORY HEAT LOSS WITH HIGH DENSITY GAS MIXTURES

by
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May 31, 1966

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RESPIRATORY HEAT LOSS WITH HIGH DENSITY GAS MIXTURES

Paul Webb and James F. Annis
Webb Associates
Yellow Springs, Ohio

INTRODUCTION

This study was done to provide empirical data for the respiratory fraction of body heat loss which may be sizeable when diving with open-circuit breathing gear, even though under ordinary circumstances it is small (approximately 5-10%). The quantity of heat lost from the respiratory tract for any gas mixture can be approximated from the physical properties of the gas mixture and the known or assumed respiratory ventilation rate. Such a calculation should be made with estimates of expired air temperature and water content based upon existing research, not with the assumption that expired air is at 37° C and saturated. That assumption has been repeatedly shown to be incorrect (Berg, 1933; Brebbia et al, 1957; Cole, 1953 and 1954; Fugitt and Riley, 1946; Goodale, 1896; Lasage, 1903; Liljestrand and Sahlstedt, 1925; Loewy and Gerhartz, 1914; Marshall and Specht, 1949; McCutchan and Taylor, 1951; Osborne, 1913; Perwitzschky, 1928; Seeley, 1940; Webb, 1951; Wortz et al, 1964).

Expired air temperature is always less than 37° C unless inspired air temperature is above 75° C and dry or above 55° C with a vapor pressure of 45 mm Hg or greater, as demonstrated by McCutchan and Taylor (1951). For the purposes of this report, we are concerned with air at much lower temperature and with much less water vapor, so that expired air temperature and water content will always be less than 37° C and 47 mm Hg. Previous work, cited in the preceding paragraph, has demonstrated that the temperature and the vapor pressure of expired air are functions of temperatures and vapor pressures of inspired air because of a heat exchange in the upper respiratory tract. This process has been quantified over a wide range of inspired air temperatures and vapor pressures. The process is one of heat conservation since respiration is reciprocal. Dry inspired air cools

and dries the lining of the upper respiratory tract, so that warm, moist expired air coming out gives up heat and condenses water vapor before it escapes from the nasal or oral portal. This process has been measured specifically by Seeley (1940), Webb (1951 and 1955), and Cole (1953 and 1954), who measured air temperature at various depths in the respiratory tract to discover where the heat exchange takes place. These experiments have established that most of the warming and moistening of inspired air is complete in the first 10 cm of the upper tract. Experiments on dogs by Moritz and Weisiger (1945) and by Moritz et al (1945) where the dogs breathed extremely cold or extremely hot air from -55° C to over 500° C confirm that the respiratory tract makes an excellent heat exchanger and that cooling or warming of inspired air takes place in a very short distance in the respiratory passages.

The heat conservation process has been termed variously the action of a "passive heat exchanger" (Webb, 1951), the "recovery of water vapor during expiration" (Seeley, 1940), and the action of "heat and moisture exchange apparatus" (Cole, 1953). Hardy (1961), and Jackson and Schmidt-Nielsen (1964) described the process as the action of a "countercurrent heat exchanger". By whatever name, it is a real process, the magnitude of which is best established empirically when new respiratory situations arise.

In diving, the high water pressure at depths is matched with high gas pressure in the breathing apparatus, and the density of the gas increases. Since sensible heat exchange is a direct function of specific heat and density of the gas mixture, the increasing density of the gas respired at depth increases respiratory heat loss. Further, since most of the ocean is cold, with water temperatures between 5° C and 15° C, and since the breathing equipment is cooled to water temperature, respiratory heat loss may be a significant avenue of heat loss for divers. We have found no specific estimates or measurements of respiratory heat loss in totally immersed subjects in the literature. Carlson et al (1958) assumed that for men lying still in a water bath 24% of their total heat loss was due to evaporation of water from the respiratory tract. Our purpose here is to provide empirically based methods for finding respiratory tract heat loss in underwater activities.

The United States Navy is engaged in ocean research with several major projects concerning man in the sea. The research reported here should be useful in defining respiratory heat loss for at least one common type of activity, namely free swimming with open-circuit breathing equipment (SCUBA). Further, from a judicious application of the empirical results reported here, fairly good estimates can be made for respiratory heat loss in other situations in diving and with other types of breathing gear.

METHODS

The methodology given in this section was devised to measure the major variables in the equation for calculating respiratory heat loss (see subsection entitled "Calculations"). Also presented are descriptions of subjects, facilities used, and other details of the experimental procedure.

Breathing assembly

The breathing assembly used throughout these experiments was the familiar open type of SCUBA demand regulator system used in underwater swimming. The apparatus was rigged to function as a demand delivery system in either air or water. The gas supply cylinder was not carried by subjects.

A bead thermistor was located in the SCUBA mouthpiece to measure the inspiration-expiration temperature. The flexible corrugated neoprene hose just outside the expiration valve was penetrated for the hygrometer sensor line. Near this connection the mouthpiece and hose were warmed to a controlled temperature to minimize condensation of water vapor in the apparatus.

In one group of experiments an ice-water-cooled copper heat exchanger was close-coupled to the subject with a short length (1 ft.) of the flexible hose to permit cooling and control of inspired gas temperature. The demand regulator was located upstream from the heat exchanger. To avoid the warming of the inhaled gas toward room temperatures (average 27-30° C) in the short length of rubber hose between the heat exchanger and the subject, a portion of the icewater flow was diverted through an insulated coil of 3/8" I. D. Tygon tubing wound around the hose. The heating and cooling of opposite ends of the mouthpiece assembly created a special situation in regard to the inspiration-expiration temperatures which must be taken into account when considering the data.

In all of the Yellow Springs laboratory experiments the expiration hose was attached to a Douglas bag collection system with which timed collection of respiratory volumes could be made and subsequently measured in a Tissot gasometer. Considering all of the in-line paraphernalia, breathing resistances were quite low as reported by either experienced or novice subjects.

It was possible to keep the SCUBA mouthpiece dry during the Yellow Springs experiments with subjects in the laboratory room. The hyperbaric experiments conducted at the Navy Experimental Diving Unit (EDU), however, were much wetter. The subjects were in water, they breathed longer on the mouthpiece, and they were in a prone swimming position -- all of which contributed to a collection of condensate and foamy saliva in the mouthpiece. In all cases the breathing gas mixtures came in dry. In the Yellow Springs experiments on the treadmill, where rapid interchange of subjects on the single breathing assembly was necessary, a practice was made of cleansing the orally inserted protion of the mouthpiece with a bacteriocidal agent followed by a distilled water rinse and drying between subjects. A similar procedure could not be arranged between the two diver-subjects in the EDU tank.

Temperature measurement

The inspired and expired gas mixture temperatures were measured by a delicate glass bead thermistor which was located just inside the neck of the rubber SCUBA mouthpiece and was positioned approximately between the lips when in use. The thermistor bead* was .023 inches in diameter and had a time constant of less than one second in still air. It was suspended by its four leads (two of them inactive electrically) at the center of a plastic ring which just fitted the rubber neck. The amplified output of a bridge containing the thermistor was continuously recorded on one channel of a two channel direct-writing oscillograph. Since the range in temperatures measured is relatively small and the lag time of the total system was less than 0.1 second in the rapidly-moving respired gas, it is thought that the true peak temperatures were obtained. To prevent shorting from moisture (saliva) the leads (but not the bead itself) were coated with an insulating varnish and the entry of the coaxial line at the wall of the mouthpiece was sealed against leaks with silicone rubber and neoprene cement.

* VECO type 37A3, Victory Engineering Corp., Union, New Jersey.

The thermistor was calibrated in both air and water against mercury thermometers with certified accuracy. In addition the system was calibrated in situ electrically, after an accurate temperature versus resistance curve was obtained, through the use of a decade resistance box. The absolute accuracy of the temperatures obtained was thought to be better than $\pm$ 0.5° C. The relative accuracy during a given experiment was estimated to be better than 0.1° C.

During experiments a continuous inspiration-expiration temperature curve was obtained. The respiration rate and breathing characteristics were easily seen on the record, which permitted detection of hyperventilation in novice subjects.

The inspiration temperatures (t_i) and the expiration temperatures (t_e) as recorded in the data are the results of the average of the peak deflections (on either side of the balance position) during the last minute of each experimental period. The last minute was considered the data point even though very often little change was noted in either temperature once a subject had reached respiratory equilibrium for a given work level. Depending upon work load this point usually was reached in two to three minutes.

Expired gas water content

To measure the water vapor content of the expired air a thermoelectric dew-point hygrometer* was used. This instrument gives direct readings of the dew-point temperature of the gas sample, from which the amount of water present by weight can be obtained from existing tables.

In the Yellow Springs experiments expired gas samples were drawn through the hygrometer sensing system located adjacent to the exhalation valve of the mouthpiece. To control condensation in the mouthpiece, hence to minimize the amount of water vapor not measured, the end of the mouthpiece near the expiration valve and the entire sensor assembly were heated to a controlled, pre-selected temperature (35° C or 39° C) and insulated in a fitted blanket of Dacron wool.

* Vapor Mate II control unit and Model 137-S-1-TH remote sensing head, Cambridge Systems, Inc., Newton, Massachusetts.

To avoid exposure of the hygrometer sensor to the hyperbaric pressures in the EDU chamber experiments a line was run from a needle valve placed near the exhalation valve of the mouthpiece to the hygrometer outside of the tank. The expired gas expanded across the needle valve to sea level pressure, and came through the chamber wall to the hygrometer at this pressure. Since the temperatures and pressures were known both inside and outside of the tank a computation using pressure ratios was made to give the water vapor content of the expired gas. Also, since expansion to 1 atmosphere pressure occurred at the needle valve on the mouthpiece, the gas sample in the line coming through the chamber had a vapor pressure well below saturation and condensation was avoided. Because liquid water and saliva were usually present in the mouthpiece and they readily leaked into the needle valve, we only had usable vapor pressure date from a few of the experiments.

In the EDU experiments in which unsatisfactory or no dew-point temperatures were obtained the calculation of expired water is based on the use of a value equal to 64% of the amount which would be present if the gas was saturated at the measured gas temperatures (t_e). The use of this value is based on the average hygrometer readings obtained during all of the experiments conducted in the Yellow Springs laboratory. These calculated values were consistent with the few measured values.

Respiratory volume

Another of the variables that must be known to fulfill the terms of the respiratory heat loss equation is the respiratory minute volume ($\dot{V}_e$). Throughout the experimental program the same basic measurement system was used. The system was composed of a low resistance parallel-plate flowmeter*, a sensitive electronic manometer** and a Sanborn integrating preamplifier and oscillograph. A differential pressure proportional to flow was converted to the electrical analog by the manometer, the signal was integrated to give the integral of flow -- volume.

* Vol-O-Flow Respiratory element, National Instrument Laboratory, Washington, D. C

** Model MM/M-3, Mercury Electronics, Glasgow, Scotland.

Because there were different densities and viscosities in the different gas mixtures, and because we were working at widely different pressures, it was found that a calibration curve was needed for each gas mixture and pressure. Even though the flowmeter calibration had been checked many times with air and the calculation of curves for the gas mixtures used could be made it was decided that "in-line" calibration during performance of the experiments would furnish believable empirical data. Therefore, during all of the 1 atmosphere experiments and synchronous with the data point a 1 minute Douglas bag collection of expired gas was obtained and immediately measured in a Tissot spirometer. The measured collections were correlated with the continuous volumetric records on the oscillograph. At the start of the EDU experiments a Parkinson Cowan dry gasometer was used to derive calibration curves for the gas mixtures and pressures to be used in the hyperbaric tests. Unfortunately, however, during the experimental dives the accumulation of water and saliva in the flowmeter altered the flow/resistance characteristics of the flowmeter. When we returned to Yellow Springs, a laboratory duplication of the wetted condition was made to derive a correction factor for the volume data obtained at the EDU. Due to the fact that the precise amount and distribution of saliva and water collected in the parallel plates of the flowmeter during the experiments could not be duplicated exactly, the correction factor derived and applied to the $\dot{V}_e$ data from the EDU tests is not entirely reliable. However, the influence of $\dot{V}_e$ on the expired air temperature and water content is very slight.

The volumes ($\dot{V}_e$) reported are for the conditions of measured expired gas temperature and pressure saturated (ETPS).

Yellow Springs laboratory arrangement

The general arrangement of equipment in the Yellow Springs laboratory is shown in the photograph of Figure 1. A block diagram of the breathing apparatus and instrumentation is shown in Figure 2.

Figure 1 - General arrangement of equipment in Yellow Springs laboratory.

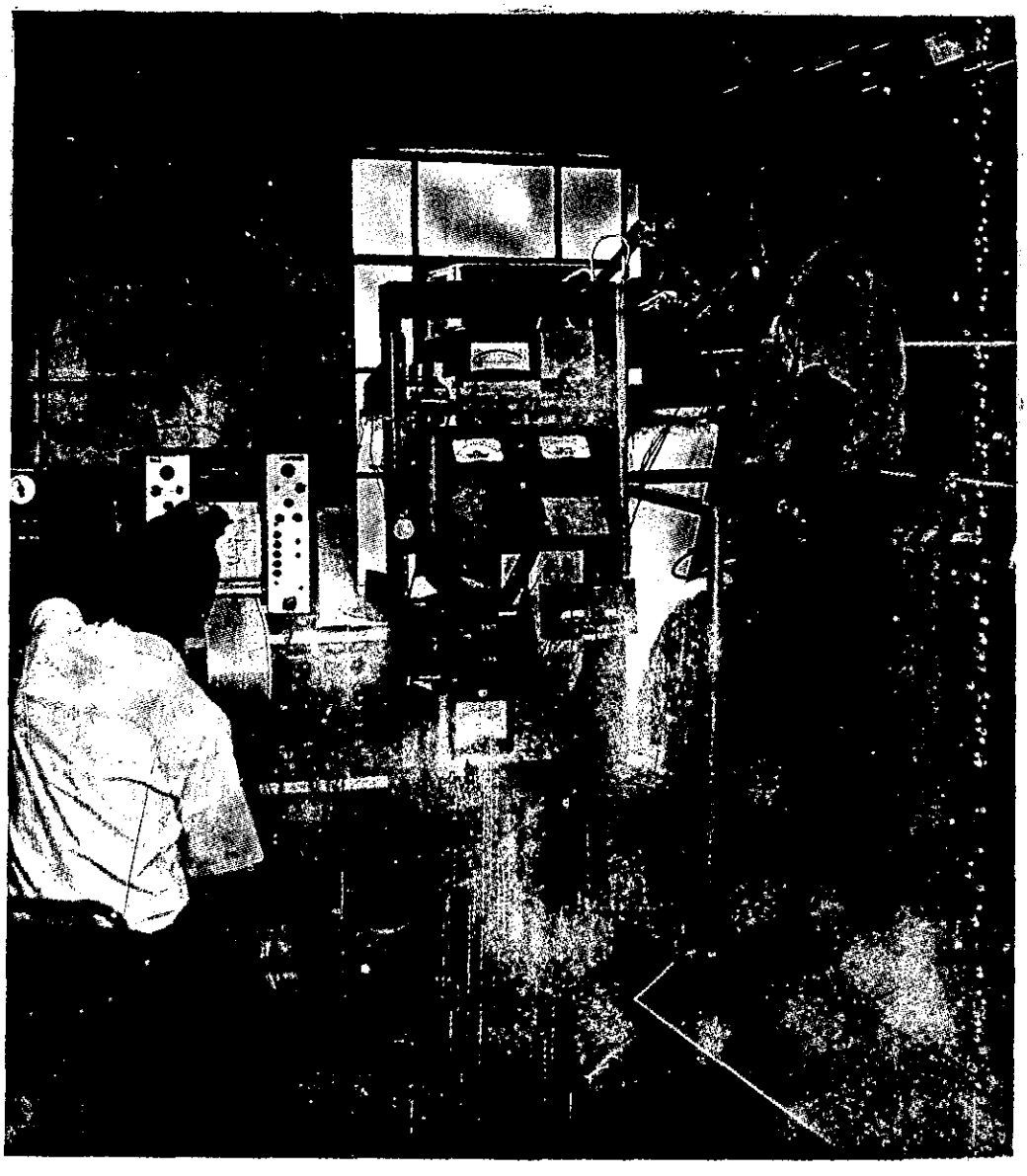
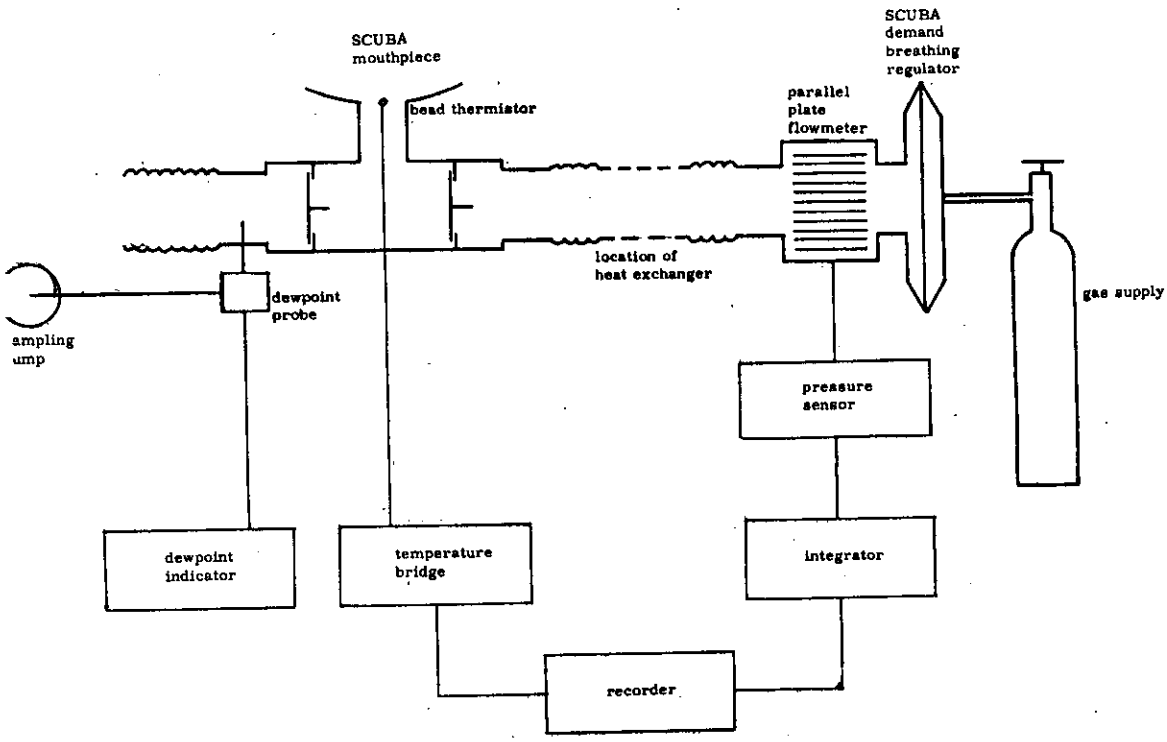


Figure 2 - Breathing apparatus and instrumentation for measuring respiratory tract heat loss.



Hyperbaric chamber -- EDU

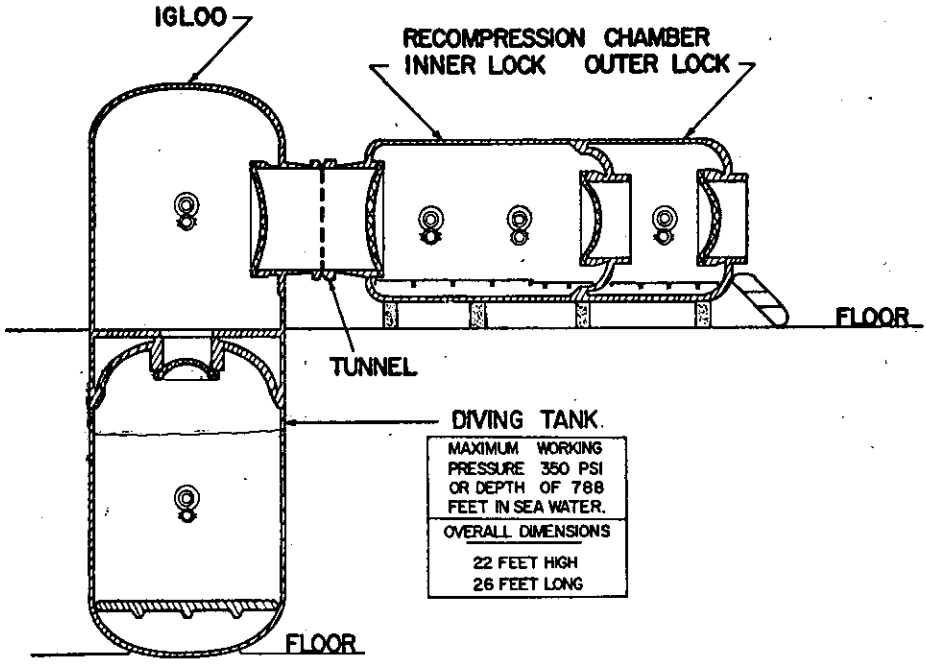
Following completion of the 1 atmosphere series in Yellow Springs hyperbaric experiments were performed in the facilities of the U. S. Navy Experimental Diving Unit located at the Washington Navy Yard, Washington, D. C. This facility for simulating diving conditions is a two-story, multi-compartment pressure chamber (see Figure 3). The upper level consists of a horizontal two-compartment diver recompression (or decompression) tank (13' X 16'). This compartment is connected via a tunnel-lock system to the upper dome (igloo) portion of the vertical diving chamber (22' X 8') which extends to the floor below. The lower section may be filled with water. It is in this section that the divers swim and are subjected to temperatures, pressures, and gas mixtures encountered in diving.

The entire chamber system may be pressurized to more than 24 atmospheres absolute (352 psia) and each of the four main compartments may be individually controlled for both pressures and gas mixtures to meet experimental demands and decompression schedules. Air was used in our experiments to achieve desired chamber pressures. The divers breathed gas mixtures through the same demand regulator and mouthpiece used in the Yellow Springs experiments. The breathing gas mixtures were supplied from a manifolded bank of cylinders. All gas mixtures were compounded and analyzed at EDU.

The chamber was operated by naval technician-divers under the supervision of the Unit medical officer. Two-way communications were maintained with the divers during the experiments and the dive supervisor checked on the welfare of the subjects through observation ports in the chamber wall.

Figure 4 is a photograph of two divers in dry suits about to descend from the igloo into the water in the lower section of the vertical chamber. The diver descending through the hatch is using the instrumented mouthpiece which holds the bead thermistor, and from which leads the needle valve and sample line to the dewpoint hygrometer. Figure 5 is a rear view of the same instrumented breathing apparatus on a diver entering the hatch. A standard SCUBA regulator fed from a "hookah" supply line is seen on the packboard, and to its left is the

Figure 3.



DIVING FACILITIES
AT
U.S. NAVY EXPERIMENTAL DIVING UNIT

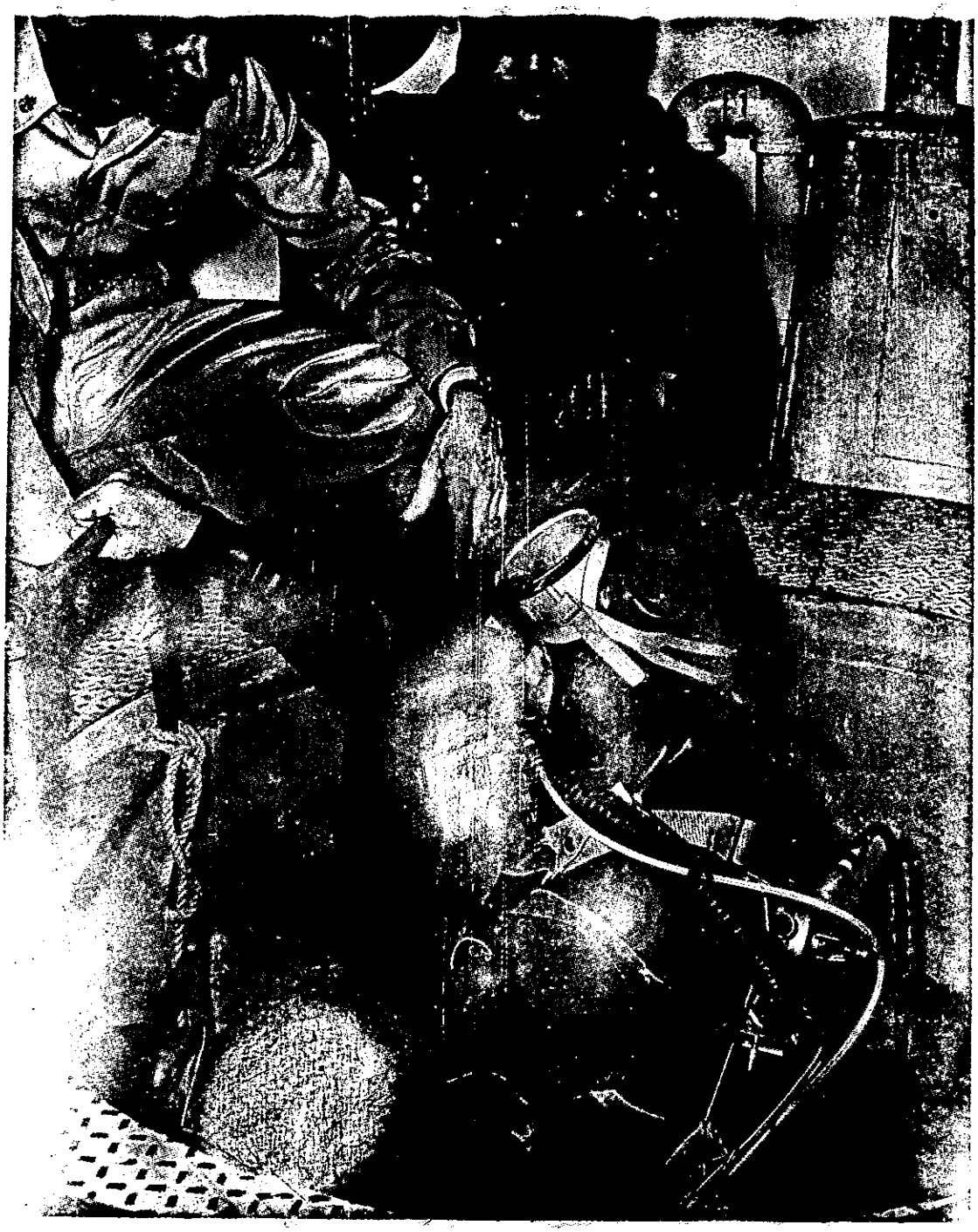
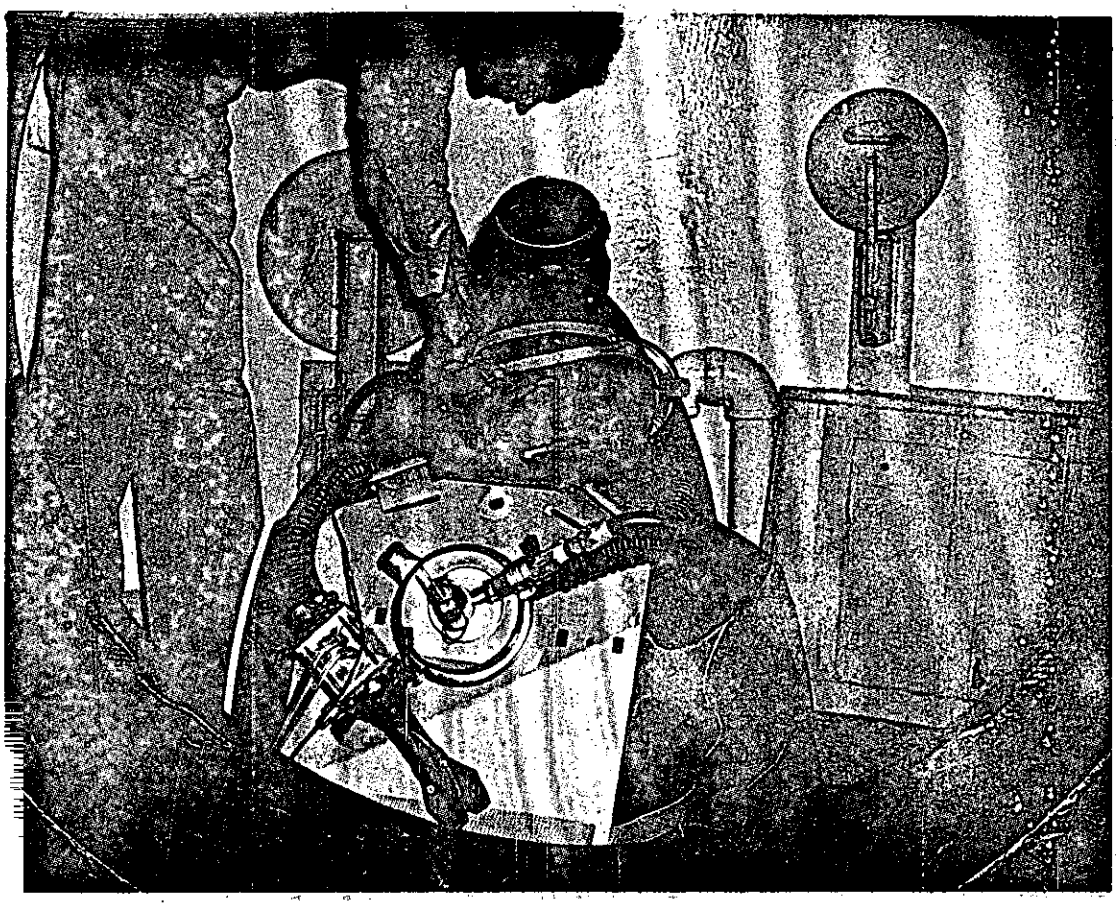


Figure 4 - Divers in dry suits descending from igloo into wet chamber.

Figure 5 - Breathing apparatus on diver entering hatch.



parallel plate flowmeter for determining $\dot{V}_e$. Figure 6 is a photograph of the measuring and recording apparatus located on the lower floor next to the water filled lower section of the vertical chamber.

Gas mixtures

The gas mixtures used were as follows:

Mixtures	Contents
Air	79% N_2, 21% O_2
He - O_2	80% He, 20% O_2
He - O_2	96% He, 4% O_2
SF_6	80% SF_6, 20% O_2

All gas mixtures were dry (2 ppm H_2O), delivered to subjects from high pressure gas cylinders and the demand regulator, and were pre-analyzed for content to an accuracy of $\pm$ 0.2%.

The kinetic gas properties which influence sensible heat loss from the respiratory tract and other pertinent properties are given for the pure gases and breathing mixtures in Table I. The values for the pure gases O_2, N_2 and He were taken at a common state (300°K, 1 atmosphere) directly from Drake and Eckert, (1959). The values for SF_6 were converted from manufacturer's data to the same conditions.

Figure 6 - Measuring and recording apparatus next to wet chamber.

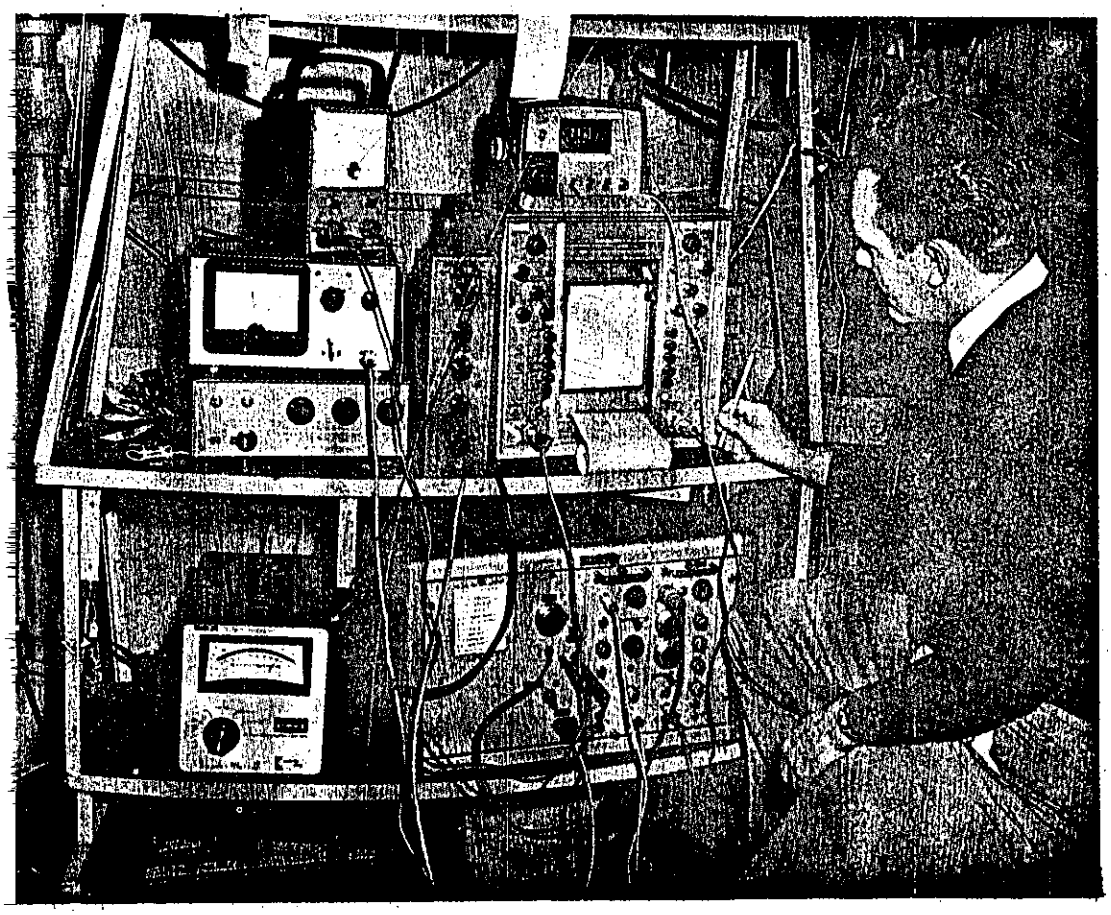


TABLE I

Properties of Pure Gases and Selected Mixtures of Gases at 27° C (80° F or 300° K), 1 Atm

Gases	Molecular Weight	Specific Heat - C_p		Density - ρ		ρC_p	
		cal/gm° C	Btu/lb° F	gm/l	lb/ft^3	cal/l° C	Btu/ft^3°
O_2	32.00	0.2198	0.2198	1.3026	0.0812	0.2863	0.0178
N_2	28.02	0.2486	0.2486	1.1438	0.0713	0.2843	0.0177
He	4.00	1.242	1.242	0.1684	0.0105	0.2092	0.0130
SF_6	146.07	0.159	0.159	6.0287	0.3758	0.9586	0.0598
Mixtures							
Air		0.2402	0.2402	1.1791	0.0735	0.2832	0.0177
20% O_2, 80% He		0.5608	0.5608	0.3986	0.0246	0.2235	0.0138
20% O_2, 80% SF_6		0.1621	0.1621	5.0838	0.3169	0.8241	0.0514
4% O_2, 96% He		0.9320	0.9320	0.2137	0.0133	0.1992	0.0124

Values for mixtures were computed from values for the pure constituent gases on the basis of mole fractions. The perfect gas approximation was found to be accurate for computing the density of SF_6 at temperatures above 0° C. Heat capacity per unit mass of mixture was calculated first, using the molecular weight and heat capacity per unit mass to compute the molar heat capacity of each constituent gas; second, weighting these values by the mole fraction (partial pressure); third, computing the average molecular weight of the mixture, and finally dividing the sum of the molar heat capacities of the fractions by the average molecular weight to obtain the heat capacities per unit mass of mixture. Once the values for a given mixture at a given condition is computed variations resulting from changes in temperature and pressure can be figured using the following rules:

-- heat capacity is constant in the range of conditions used
-- density is directly proportional to pressure and inversely to absolute temperature
-- viscosity and thermal conductivity are pressure independent, and their temperature dependence can be approximated as proportional to absolute temperature with an accuracy of $\pm$ 3% over the range of temperature from 0° C to 40° C.

The selection of helium gas mixtures was based primarily on their likely use in diving situations; the SF_6 - O_2 mixture was chosen because of its high density (6.139 gms/liter) at laboratory conditions. It was hoped that the use of gases with different physical properties would allow laboratory simulation of conditions of respiration and respiratory heat loss experienced at depth. Sulfur hexaflouride was the most dense, inert, and non-toxic gas available for breathing in concentrations up to 80%. Varying degrees of anesthesia were experienced by a number of subjects however, necessitating stopping the experiment after a few minutes. The effects ranged from mild emphoria to frank numbing of distal portions of limbs. Except for slight headaches no after effects were noted after breathing the 80% SF_6 - O_2 mixture for up to 15 minutes continuously and with ventilation rates as high as 70 liters/minute.

Calculations

The basic equation used in the calculation of respiratory heat loss (RHL) is the following:

$$Q_{RHL} = \dot{V}_e \rho C_p (t_e - t_i) + \dot{V}_e 0.058 (W_e - W_i)$$

where: Q_{RHL} = the quantity of respiratory heat loss in kcal/min

$\dot{V}_e$ = the respiratory minute volume in liters/min at standard temperature and pressure, dry

ρ = the density of the gas mixture in gm/liter

C_p = the specific heat of the gas mixture in kcal/gm° C

t_e = the expired gas temperature in ° C

t_i = the inspired gas temperature in ° C

0.58 = the latent heat of vaporization in kcal/gm

W_e = the expired gas water content in gm/liter

W_i = the inspired gas water content in gm/liter

The group of terms in the equation to the left of the + sign includes those quantities needed for calculation of sensible heat loss. Density, ρ, and specific heat, C_p, must be known for each gas mixture breathed. The standard values listed in Table I are taken from Drake and Eckert's Heat and Mass Transfer; for SF_6 the values are from data supplied by the manufacturer (Allied Chemical). Values for

the individual gases were converted to the required units and final values for the gas mixtures were computed using mol fractions. A sample calculation of the specific heat of a gas mixture is as follows:

Air at 27° C (300° K), 1 atm.

	Mole Fraction	C_p	Molecular Weight(MW)
1.	$X_{O_2} = 0.2092$	0.2198	32.00
2.	$X_{N_2} = 0.781$	0.2486	28.016
3.	$X_{argon} = 0.01$	0.1253	39.94

$$C_p = \frac{X_1 (C_{p_1})\ MW_1 + X_2 (C_{p_2})\ MW_2 + X_3 (C_{p_3})\ MW_3}{X_1\ MW_1 + X_2 MW_2 + X_3\ MW_3}$$

$$C_p = \frac{0.2092\ (0.2198)\ 32.00 + 0.781\ (0.2486)\ 28.02 + 0.01\ (0.125)\ 39.94}{0.2092\ (32) + 0.781\ (\ 28.02) + 0.01\ (39.94)}$$

$$\text{Calculated value for air } C_p = \frac{6.9616}{28..977} = 0.240245$$

$$\text{Handbook value for air } C_p = 0.02402$$

We computed a combined ρC_p for each gas mixture at one condition (ambient pressure 760 mm Hg, 293° K) which could be corrected for use at different conditions in the experiments. The ρC_p of a mixture is the sum of the ρC_p's of each fraction. The following method of calculation was used:

80% He - 20% O_2 at 20° C (293° K), 1 atm.

$$\rho C_p \text{ for helium} = \frac{PC_p}{nRT}$$

$$= \frac{(0.794\ \text{atm})^{**}(1.242\ \text{cal/gm° C})\ (4.00\ \text{gm/mol})}{(0.0820\ \text{liter atm/mol° K})^{*}\ 293° K}$$

$$= 0.165\ \text{cal/liter° C}$$

$$\rho C_p \text{ for } O_2 = \frac{PC_p}{nRT}$$

$$= \frac{(0.206 \text{ atm})^{**}(0.2178 \text{ cal/gm}^\circ\text{C})(32.00 \text{ gm/mol})}{(0.0820 \text{ liter atm/mol}^\circ\text{K})^{*}\ 293^\circ\text{K}}$$

$$= 0.0596 \text{ cal/liter}^\circ\text{C}$$

(therefore)

ρC_p for the He-O_2 mixture = 0.165 + 0.0596 = 0.2246 cal/liter° C at 1 atm, 293° K

* = the universal gas constant

** = the actual average analysis values for %O_2 and %He for this gas mixture

To convert the ρC_p value to new conditions of temperature and pressure the following correction was applied:

$$\rho C_p = 0.2246 \frac{P}{760} \frac{293}{T}$$

Corrected ρC_p's at temperatures from 0° - 30° C and at several pressures are shown in Table IV.

The ideal gas laws were considered valid for the experimental conditions.

To convert minute volumes from those obtained at the ambient conditions to minute volumes at expiration temperature and pressure saturated (ETPS), which were the values used in calculation of the respiratory heat loss, the following correction was applied:

$$\dot{V}e_{ETPS} = \dot{V}e_{ATP}\left(\frac{273 + t_e}{273 + t_a}\right)\left(\frac{B.P._{amb} - P_{H_2O_e}}{B.P._{amb} - 47}\right)$$

where: ATP is ambient temperature and pressure

t_a is ambient temperature in ° C

$B.P._{amb}$ is barometric pressure in mm Hg

$P_{H_2O_e}$ is vapor pressure of air saturated at expiration temperature

47 is vapor pressure of air saturated at 37° C

TABLE IV

Differences in ρC_p factors with temperature and pressure for gas mixtures used

TEMP. °C	PRESSURE											
	740 mm Hg			750 mm Hg			760 mm Hg (1 atm.)			3040 mm Hg (4 atm.)		6080 mm (8 atm
	Air	80% He 20% O_2	80% SF_6 20% O_2	Air	80% He 20% O_2	80% SF_6 20% O_2	Air	80% He 20% O_2	80% SF_6 20% O_2	Air	80% He 20% O_2	96% He 4% O_2
0	.3026	.2339	.8723	.3067	.2372	.8840	.3108	.2402	.8959	1.243	.9609	1.7498
1	.3015	.2330	.8691	.3055	.2362	.8809	.3096	.2393	.8926	1.238	.9573	1.7446
2	.3003	.2322	.8658	.3044	.2353	.8776	.3084	.2384	.8893	1.233	.9537	1.7385
3	.2995	.2315	.8634	.3032	.2344	.8743	.3073	.2375	.8859	1.229	.9501	1.7321
4	.2984	.2306	.8602	.3024	.2338	.8718	.3064	.2369	.8834	1.225	.9474	1.7259
5	.2972	.2298	.8569	.3012	.2329	.8685	.3052	.2360	.8801	1.221	.9439	1.7197
6	.2961	.2289	.8537	.3001	.2320	.8652	.3041	.2351	.8768	1.216	.9403	1.7134
7	.2950	.2280	.8504	.2990	.2311	.8619	.3029	.2342	.8734	1.211	.9367	1.7074
8	.2941	.2271	.8480	.2981	.2304	.8594	.3021	.2335	.8709	1.208	.9340	1.7013
9	.2930	.2265	.8447	.2970	.2296	.8561	.3009	.2326	.8676	1.203	.9304	1.6953
10	.2919	.2256	.8415	.2958	.2287	.8528	.2997	.2317	.8642	1.199	.9268	1.6888
11	.2910	.2250	.8390	.2950	.2280	.8504	.2989	.2310	.8617	1.195	.9242	1.6832
12	.2899	.2241	.8358	.2938	.2271	.8471	.2977	.2302	.8584	1.191	.9206	1.6776
13	.2888	.2232	.8325	.2927	.2262	.8438	.2966	.2293	.8550	1.186	.9170	1.6720
14	.2879	.2224	.8301	.2918	.2256	.8413	.2957	.2286	.8525	1.182	.9143	1.6656
15	.2868	.2217	.8268	.2907	.2247	.8380	.2945	.2277	.8492	1.178	.9107	1.6600
16	.2859	.2211	.8244	.2898	.2240	.8355	.2937	.2270	.8465	1.174	.9080	1.6544
17	.2848	.2202	.8211	.2887	.2231	.8322	.2925	.2261	.8434	1.170	.9045	1.6488
18	.2840	.2195	.8187	.2878	.2225	.8298	.2916	.2254	.8408	1.166	.9018	1.6432
19	.2828	.2187	.8154	.2867	.2216	.8265	.2905	.2246	.8375	1.161	.8982	1.6376
20	.2820	.2180	.8133	.2858	.2209	.8243	.2896	.2239	.8353	1.158	.8956	1.6320
21	.2812	.2173	.8106	.2848	.2207	.8211	.2886	.2231	.8321	1.154	.8924	1.6261
22	.2800	.2165	.8073	.2839	.2194	.8184	.2876	.2226	.8293	1.150	.8894	1.6205
23	.2791	.2158	.8057	.2829	.2187	.8159	.2866	.2216	.8265	1.146	.8864	1.6151
24	.2783	.2152	.8024	.2820	.2180	.8129	.2857	.2209	.8237	1.142	.8834	1.6097
25	.2772	.2143	.7992	.2810	.2172	.8102	.2847	.2201	.8210	1.138	.8805	1.6043
26	.2763	.2137	.7968	.2801	.2165	.8077	.2838	.2194	.8185	1.135	.8776	1.5989
27	.2752	.2128	.7935	.2791	.2157	.8050	.2828	.2187	.8158	1.131	.8746	1.5936
28	.2744	.2121	.7911	.2782	.2150	.8024	.2819	.2179	.8131	1.127	.8718	1.5882
29	.2732	.2113	.7878	.2773	.2143	.7997	.2809	.2172	.8103	1.123	.8688	1.5829
30	.2720	.2106	.7857	.2763	.2097	.7970	.2800	.2165	.8077	1.120	.8660	1.5777

Subjects

A total of 18 individuals served as subjects during the project. Twelve of these were involved in the Yellow Springs experiments, and the remaining six were U. S. Navy divers stationed at the Experimental Diving Unit. Three of the Yellow Springs subjects had had SCUBA training and experience and all with the exceptions of subjects SC and RC had previous treadmill experience. Many had been engaged in experiments where a variety of types of breathing devices were used. For those with less experience trial runs were made to familiarize the person with the system and characteristics of the breathing gas mixtures. Most subjects found the voice changes and slight anesthesia incurred with SF_6 to be an encouragement to participate rather than a detriment. The two young and inexperienced subjects were allowed to take part to see if their ages and smaller respiratory minute volumes would show some influence on the resultant respiratory heat loss. (It did not.)

Due to the rather mild nature of the physical exertion required by the experimental protocol for the Yellow Springs experiments persons of varying levels of physical fitness were permitted to participate. All subjects were given medical examinations previous to the experiments, and no subject showed any evidence of impaired respiratory or circulatory function. The Navy divers, in some cases, had more than ten years of diving experience and were considered to be in top physical condition. As can be seen in Table II, a considerable range existed in both subject age and body size.

TABLE II

Subject Characteristics

SUBJECT		AGE	WEIGHT		HEIGHT		SURFACE AREA
Code	Initials	Years	Lbs.	Kg.	In.	Cm.	M^2
Y.S. expt's							
A	JA	33	155	70.4	72.00	182.8	1.91
B	DB	28	171	77.7	68.75	174.6	1.93
C	BC	37	159	72.3	68.50	173.9	1.86
D	RC	13	103	46.8	61.25	155.6	1.43
E	SC	11	88	40.0	57.75	146.7	1.28
F	JE	28	156	70.9	67.75	172.1	1.83
G	GF	44	195	88.6	72.50	184.2	2.14
H	AH	28	189	85.9	68.50	173.9	2.00
I	RM	25	154	70.0	70.50	179.1	1.87
J	RT	27	171	77.7	73.50	186.7	2.04
K	PW	43	175	79.5	68.00	172.7	1.93
L	SW	16	135	61.4	69.00	175.3	1.74
EDU expt's							
M	BIG	35	220	100.0	74.00	187.9	2.29
N	BRO	38	195	88.6	71.00	180.3	2.10
O	BUC	36	212	96.4	69.00	175.3	2.13
P	MEE	34	200	90.9	75.00	190.5	2.21
Q	MES	28	165	75.0	68.00	172.7	1.88
R	ZUB	29	174	79.1	70.00	177.8	1.98
Range		11-44	88-220	40-100	57.75-75.00	146.7-186.7	1.28-2.29
Mean		29.6	167.6	76.18	69.17	175.69	1.92

TESTING PROGRAM

1 atmosphere experiments

This group of experiments was conducted in the Webb Associates laboratory in Yellow Springs, Ohio, and are referred to as the "Yellow Springs", or "1 atmosphere" experiments. The individual experiment protocol called for the subject to breathe the gas mixture being tested for a period of at least five minutes while standing at rest. This was followed immediately by a five minute or longer period of treadmill work designed to produce a given increase in minute volume ($\dot{V}_e$). The objective was to obtain data for $\dot{V}_e$'s ranging from 20-60 lpm for the various gas mixtures. The treadmill settings ranged from 3.0 to 3.75 mph and slopes of from 10-15% were used. During each session inspired-expired temperatures, minute volumes, and expired gas water vapor content were monitored continuously for changes with time. Equilibria in all three parameters were reached before a 1 minute "data point" period was started. Almost without exception this point was reached in the alloted five minutes period, but if not, the session was lengthened. It was from this "data point" that the final values of the inspired-expired temperatures, $\dot{V}_e$'s and hygrometer readings were taken.

The inspired gas temperatures were held constant for each experiment. In one group of experiments the incoming gas was cooled in a heat exchanger to obtain inspired gas temperature (t_i) between 0° and 10° C. By varying the breathing gas mixtures, minute volumes and inspired gas temperatures the three principal variables which influence respiratory heat loss were manipulated.

All of these experiments were performed in the general laboratory floor area where ambient temperatures were kept between 23° and 27° C, with vapor pressures between 10 and 15 mm Hg.

The number, type, and participation of subjects for the three gas mixtures used in the 1 atmosphere experiments is summarized as follows:

	Gas Mixture		
	Air	80% He, 20% O_2	80%SF_6, 20% O_2
No. of subjects	11	11	10
No. of work experiments	18	20	17
No. of rest experiments	17	20	19
Total No. of experiments	35	40	36

Hyperbaric experiments

The hyperbaric or EDU experiments were conducted in the Experimental Diving Unit facility described earlier in the report. Excluding a preliminary calibration and equipment check-out dive, a total of five dives were made over a three day period involving six Navy diver subjects. Using two divers at a time, three experiments were completed with the diving tank pressure equivalent to a depth in water of 100 feet (4 atm. abs.); the breathing gas mixture was air in one case and 80% He -20% O_2 in the other two. The two remaining dives were made to 230 feet (8 atm. abs.) with all four subjects breathing a 96% He - 4% O_2 gas mixture. No diving pair was subjected to more than one pressure level and breathing mixture per day. Two teams did, however, participate in dives to both depths on alternate days. The chamber operation including preparation of the breathing gas supply was performed by Navy diver-technicians under supervision of the master diver and the unit medical officers.

The experimental protocol consisted of subjecting the two-man team of divers to the depths (pressure) and breathing gas mixtures for a period of time sufficient for us to gather data for at least five minutes of rest and five minutes of work on each man while the pressure was held constant. The subjects were considered resting when only exerting enough effort to remain afloat in six feet of water. Immediately following the rest period the diver started to swim at a self chosen comfortable pace, and he maintained this for five minutes. Upon completion of the two test periods on one diver the breathing assembly was switched to the second member of the team and the cycle repeated. The data obtained was the same as that collected in the 1 atmosphere experiments, although some difficulty

was had with the respiratory volume measurement and the expired gas water content measurement, as explained in the Methods section. The last minute of each period was again considered the "data point".

The appropriate pre-analyzed gas mixtures were supplied to the subject through a high-pressure system from a bank of gas cylinders outside the chamber. No control of inspired gas temperatures was attempted. The tank water temperature was 10-11° C and quite constant for all three days of experiments. Transient changes in tank air temperature in the range 10° to 20° C were observed, and were related to the speed of compression and amount of pressure change. There was no associated change in temperature of the water. The divers were protected from the cold water by full body dry suits.

The experiments were so designed that all of the required data could be obtained within 30 minutes of the beginning of compression. This allowed the use of available decompression schedules. For the 100 foot dives lasting 30 minutes or less, the decompression schedule lasted 13 to 15 minutes, with short stops at 20 and 10 feet. One hundred per cent oxygen was breathed starting during the 20 foot hold. The decompression from the 230 foot dives required approximately three hours with the first stop at 120 feet and every 10 feet thereafter. The divers moved from the wet tank to the igloo and from there to the horizontal chamber to complete the long period of decompression in relative comfort. Air and 100% O_2 were used intermittently during decompression. Chamber compression rates were from 50 to 65 fpm at maximum. No decompression sickness (bends) was encountered.

RESULTS

The data from both the 1 atmosphere (Yellow Springs) and the hyperbaric (EDU) experiments is presented in Table III. A total of 132 experiments are listed. The data are grouped according to gas mixtures and experimental conditions and are arranged within each group in the order of increasing inspired gas temperatures (t_i). The experiments are not separated based on work or rest since the minute volumes served as an index of this difference. The first six columns of figures represent the data needed to calculate the respiratory heat loss (RHL). The calculated respiratory heat loss is given in the third column from the right, and the final column shows the percentage of total heat loss represented by the respiratory loss. The computed means of the various columns are placed separately at the bottom of the table. Figure 13 represents the curve from which the estimations of total heat loss were derived. This curve is the result of many metabolism measurements performed on many subjects over a wide range of treadmill work levels and rest in the Webb Associates laboratory, and it allows us to predict with reasonable accuracy the total energy production when only the minute volume is known.

Examination of the data shows that there is a fairly consistent relationship between the percentage of the total heat loss represented by the respiratory loss and the increasing ρC_p factor, but let us examine the inter-relationship of the other variables first. There are three intra-gas mixture variables which influence the respiratory heat loss -- Δt, WV expired, and $\dot{V}_e$. When considering inter-gas mixture relationships the ρC_p factor must be added to the list. The slight variations in ρC_p values are due to corrections for temperature and barometric pressure at the time of each particular experiment.

The intra-gas mixture variation in Δt is seen to be a function only of the inspired temperature; therefore any inter-gas mixture variations are due to the difference in the physical properties of the gas mixtures involved. To shed some light on this phenomenon a statistical analysis was performed on the inspired versus expired gas temperatures of the gas mixtures used in the 1 atmosphere tests.

Table III MEASURED DATA FOR COMPUTATION OF RESPIRATORY HEAT LOSS (RHL) AND TOTAL HEAT LOSS (H. L.)

Subject	t_i °C	t_e °C	Δt °C	ρC_p cal/l	W. V. exp. mgm/l	V_E l/min (ETPS)	RHL Kcal/min	Total H. L. Kcal/min	RHL % of total
Air - 1 atm.					**AIR**				
K	8.8	32.4	23.6	.2932	25.1	77.1	1.65	13.2	12.5
A	9.0	32.7	23.7	.2930	24.9	56.2	1.20	10.3	11.6
L	9.1	32.5	23.4	.2929	25.5	40.1	0.87	7.5	11.6
B	9.5	33.2	23.7	.2925	24.5	75.1	1.62	13.1	12.4
B	10.1	33.6	23.5	.2918	25.5	23.6	0.51	4.4	11.5
K	13.6	32.8	19.2	.2884	24.0	16.2	0.31	2.6	12.3
L	14.1	34.4	20.3	.2981	24.5	15.9	0.32	2.5	12.9
K	16.5	35.0	18.5	.2892	27.5	79.6	1.69	13.7	12.3
L	17.0	34.6	17.6	.2887	27.2	34.1	0.71	6.4	11.1
B	17.0	35.5	16.5	.2887	24.7	24.8	0.47	4.6	10.2
A	17.3	35.8	18.5	.2873	23.7	22.0	0.42	4.1	10.2
A	17.5	35.4	17.9	.2883	26.1	61.3	1.17	11.1	10.5
B	17.5	34.6	17.1	.2887	25.5	66.7	1.24	12.0	10.4
L	19.0	36.0	17.0	.2867	24.0	14.9	0.28	2.3	12.1
K	19.1	35.0	15.9	.2866	25.3	17.8	0.34	2.9	11.7
A	13.2	33.8	20.6	.2866	24.5	21.0	0.42	3.8	11.2
K	21.5	34.3	12.8	.2806	15.4	57.9	0.12	10.6	6.8
A	22.0	32.9	10.9	.2800	19.2	36.1	0.50	6.9	7.4
A	24.0	34.2	10.2	.2783	18.9	13.0	0.18	1.9	4.3
E	24.2	33.0	8.8			4.6		.85	
E	24.5	34.2	9.7			14.8		2.1	
D	24.8	33.7	8.9	.2776	21.3	26.2	0.39	4.9	7.8
G	25.4	33.7	8.3	.2769	25.6	12.3	0.21	1.8	11.8
G	25.7	34.7	9.0	.2768	25.0	49.1	0.83	9.1	9.2
D	25.7	34.2	8.5	.2765	21.0	8.9	0.13	1.5	8.7
K	27.2	33.1	5.9	.2750	18.3	43.7	0.53	8.1	6.6
J	27.5	36.5	9.0	.2748	21.5	9.5	0.14	1.8	9.0
J	27.8	37.0	9.2	.2746	21.8	35.0	0.53	6.6	8.1
C	28.1	35.0	6.9	.2728	14.7	25.4	0.26	4.7	5.6
K	28.5	34.5	6.0	.2738	17.3	8.7	0.10	1.5	7.0
B	28.5	34.0	5.5	.2738	25.7	25.9	0.43	4.8	8.8
I	28.7	34.3	5.6	.2738	14.4	15.1	0.15	2.3	6.4
I	28.7	34.3	5.6	.2738	14.0	28.4	0.27	5.2	5.3
C	29.0	35.3	6.3	.2732	14.3	8.9	0.09	1.5	6.1
B	30.0	33.8	3.3	.2720	25.7	6.0	0.25	2.3	11.1
Air - 4 atm. abs.									
M	14.2	32.1	17.9	1.161	21.6	63.8	2.15	11.2	19.2
M	15.0	32.7	17.6	1.178	21.7	14.1	0.47	2.0	23.5
N	17.8	33.6	15.8	1.167	36.8	7.6	0.12	1.1	11.1
N	21.1	34.9	13.8	1.153	24.6	27.8	0.84	4.9	17.1
					80%SF_6 - 20%O_2				
SF_6 - 1 atm.									
B	1.5	29.0	27.5	.868	24.5	58.5	2.22	9.7	23.0
A	5.0	29.7	24.7	.857	23.0	43.9	1.52	8.2	18.5
A	5.5	30.2	24.7	.855	24.3	16.8	.59	2.7	21.9
L	7.0	32.0	25.0	.850	24.2	42.7	1.51	7.9	18.9
L	10.0	32.9	22.9	.842	26.5	15.0	.52	2.3	22.2
B	10.0	33.4	23.4	.842	25.1	21.6	.74	3.9	18.9
L	10.9	34.1	23.2	.852	25.5	35.9	1.24	6.8	18.3
K	12.8	33.3	20.5	.846	23.5	74.2	2.30	13.0	17.7
K	14.5	34.0	19.5						
L	16.0	35.6	19.6	.838	21.3	17.4	.50	2.8	17.8
A	17.8	33.8	16.0	.830	25.5	42.7	1.20	7.9	15.2
K	19.2	33.7	14.5	.826	27.0	42.7	1.18	7.9	18.1
K	20.6	34.1	13.5	.822	25.5	17.7	.47	2.9	16.4
K	21.0	32.2	11.2	.811	19.0	42.9	.86	8.0	10.8
B	21.2	34.5	13.3	.819	25.1	19.6	.50	3.4	14.8
B	21.4	34.3	12.9	.820	27.5	47.6	1.26	8.8	14.4
A	22.5	34.8	12.3	.876	25.5	26.6	.68	4.9	13.8
H	22.8	33.4	10.7	.806	17.3	29.8	.55	5.5	10.1
K	23.3	35.0	11.7	.807	15.9	54.6	1.02	10.0	10.1
D	23.6	33.8	10.2	.876	17.5	26.6	.68	4.9	13.8
J	23.7	33.3	9.6	.803	15.9	21.4	.36	3.9	9.4
J	23.7	36.0	12.3	.803	16.5	38.4	.75	7.2	10.4
B	24.0	36.3	12.3	.802	16.9	34.0	.67	6.4	10.5
K	24.0	34.6	10.6	.802	14.3	61.3	1.03	11.1	9.3
B	24.3	33.3	8.6	.801	16.8	23.6	.40	4.4	9.1
E	24.7	33.8	9.1	.799	15.0	18.1	.29	3.0	9.6
D	24.8	33.8	9.0	.800	17.3	14.3	.25	2.2	11.2
H	24.9	34.9	10.0	.799	14.3	8.3	.13	1.2	9.1
A	24.9	34.1	9.2	.799	16.6	11.8	.24	1.7	14.6
E	25.2	34.3	9.1	.799	13.7	6.8	.10	1.3	7.8
C	26.0	35.0	9.0	.797	23.6	24.9	.52	4.6	11.2
K	27.6	35.4	7.8	.792	10.4	16.3	.20	2.6	7.6
K	28.0	34.3	6.3	.791	17.2	18.8	.28	3.2	8.9
C	28.5	35.2	6.7	.789	24.4	8.9	.17	1.2	14.0
F	29.2	35.3	6.1	.787	16.8	10.2	.15	2.6	5.9
A	29.3	36.3	7.0	.787	16.2	12.7	.19	1.8	10.8
I	29.3	35.7	6.0	.787	17.0	11.0	.16	1.6	10.5

Table III cont'd. MEASURED DATA FOR COMPUTATION OF RESPIRATORY HEAT LOSS (RHL) AND TOTAL HEAT LOSS (H. L.)

Subject	t_i °C	t_e °C	Δt °C	ρC_p cal/l	W. V. exp. mgm/l	$\dot{V}_E$ l/min (ETPS)	RHL Kcal/min	Total H. L. Kcal/min	RHL % of total
					HELIUM - OXYGEN				
80% He, 20% O_2 - 1 atm.									
A	11.2	32.8	21.6	.225	24.3	60.5	1.14	11.0	13.8
B	12.3	31.4	19.1	.224	22.4	30.2	.51	5.6	9.3
K	13.8	34.0	20.2	.226	24.7	76.7	1.45	13.3	15.7
L	14.8	34.3	20.1	.225	26.2	33.6	.66	6.3	10.5
B	14.8	33.2	18.4	.222	24.5	61.2	1.12	11.1	10.7
A	16.1	33.6	17.5	.221	22.3	19.0	.33	3.2	10.1
L	16.7	35.3	18.6	.225	27.8	15.1	.35	2.3	15.0
K	16.9	32.5	15.6	.223	25.5	85.9	1.57	14.6	10.7
L	18.5	34.5	16.0	.222	25.3	29.1	.53	5.3	9.9
K	19.0	33.7	14.7	.222	22.1	18.8	.30	3.2	9.5
B	19.2	34.8	15.6	.222	27.1	73.7	1.41	12.9	11.0
B	21.4	34.0	12.6	.220	26.2	32.3	.58	6.3	9.3
K	21.7	34.1	12.4	.220	23.4	14.6	.24	2.3	10.7
H	22.8	32.6	9.8	.216	14.6	25.7	.27	4.9	6.1
A	23.0	34.2	11.2	.216	28.6	55.7	1.06	10.2	10.4
L	23.6	36.3	12.7	.218	24.5	12.3	.21	1.8	11.8
B	23.6	32.3	8.7	.215	22.3	41.0	.61	7.6	8.0
H	23.8	32.6	8.8	.216	14.6	25.7	.27	4.8	5.7
A	23.9	32.3	8.4	.215	20.6	35.9	.48	6.8	7.1
A	24.3	33.8	9.5	.215	18.9	12.3	.16	2.2	13.1
A	24.5	34.6	10.1	.215	26.1	27.8	.48	5.1	9.4
E	24.5	33.5	9.0	.215	14.5	17.3	.18	2.4	7.3
J	24.5	33.8	9.3	.215	24.8	35.5	.58	6.7	8.7
D	24.8	33.8	9.0	.215	19.4	12.4	.16	1.8	8.8
B	24.9	32.3	7.4	.214	13.2	20.8	.19	3.7	5.2
E	25.0	34.5	9.5	.214	12.5	6.4	.06	.9	6.9
K	25.3	32.3	7.0	.214	12.8	62.0	.55	11.2	4.9
D	25.3	33.2	7.9	.214	21.0	19.0	.28	3.5	8.0
J	25.8	35.1	9.3	.214	24.5	14.3	.23	2.2	10.6
G	26.0	34.7	8.7	.214	24.5	44.8	.72	8.2	8.8
L	26.1	35.1	9.0	.214	10.4	13.2	.11	2.0	5.4
G	26.3	34.0	7.7	.214	23.6	17.1	.26	2.8	9.3
A	26.5	34.0	7.5	.213	14.4	29.4	.29	5.4	5.4
K	26.8	32.5	5.7	.213	17.2	42.0	.47	7.8	6.0
K	27.2	32.8	5.6	.213	14.4	12.7	.12	1.9	6.5
A	27.6	34.8	7.2	.212	13.4	14.8	.13	2.2	9.3
C	27.7	33.7	6.0	.212		25.4		4.7	
C	28.3	33.7	5.4	.212	25.4	10.6	.17	1.5	11.3
I	28.8	33.7	4.9	.212	18.5	26.6	.31	4.9	6.3
I	29.7	33.8	4.1	.211	14.5	14.2	.13	2.2	6.0
80% He, 20% O_2 - 4 atm. abs.									
R	11.3	30.2	18.9	.922	19.7	13.5	.39	1.9	20.2
P	12.8	30.0	17.2	.917	19.4	20.7	.56	3.5	16.1
O	13.2	29.8	16.6	.916	19.2	21.5	.57	3.7	15.3
Q	14.4	29.4	15.0	.912	18.8	16.4	.40	2.5	16.1
Q	15.7	28.3	12.6	.909	17.8	16.9	.41	3.1	13.5
O	17.5	32.6	15.1	.903	22.3	14.6	.39	2.2	18.0
R	18.2	32.1	13.9	.900	21.6	29.3	.73	5.2	14.1
R	19.0	33.0	14.0	.898	22.8	15.2	.39	2.3	17.3
96% He, 4% O_2 - 8 atm. abs.									
Q	10.5	29.5	19.0	1.686	18.9	20.3	.87	3.4	25.5
R	16.3	31.3	15.0	1.653	20.7	19.2	.71	3.1	22.5
Q	16.3	33.3	17.0	1.653	23.3	13.4	.56	1.9	28.9
R	16.5	32.5	16.0	1.652	22.2	13.9	.55	2.0	27.0
P	17.4	32.1	14.7	1.647	21.6	23.2	.85	4.2	20.5
P	18.0	33.6	15.6	1.643	23.5	64.5	2.53	11.3	22.4
O	18.3	34.2	15.9	1.641	24.3	16.4	.66	2.5	26.1
O	18.6	33.4	14.8	1.640	23.5	11.7	.44	1.6	27.5
No. of Expts.					MEAN VALUES FOR ABOVE GROUPS OF DATA				
Air - 1 atm.					AIR				
35	20.9	34.3	13.4	.283	22.3	30.7	0.56	5.5	9.5
Air - 4 atm. abs.									
4	17.0	33.3	16.3	1.170	26.2	28.3	.90	4.8	17.7
SF_6 - 1 atm.					80% SF_6 - 20% O_2				
37	20.2	33.9	13.7	.819	20.2	28.9	.71	5.0	13.5
80% He - 20% O_2 - 1 atm.					HELIUM - OXYGEN				
40	22.7	33.7	11.1	.217	20.9	30.7	.48	5.4	9.0
80% He - 20% O_2 - 4 atm. abs.									
8	15.3	30.8	15.4	.910	20.2	18.8	.48	3.1	16.3
96% He - 4% O_2 - 8 atm. abs.									
8	16.5	32.5	16.0	1.652	22.3	22.8	.90	3.8	25.1

The resultant curves and regression equations are given in Figure 7. There is no obvious explanation for the relatively shallow slope for air when compared to data from other studies. Comparisons are drawn in the Discussion section.

The relationship between t_i and t_e for all gas mixtures used in the hyperbaric experiments is given as a scatter plot in Figure 8. The limited number of data points do not warrant statistical treatment.

The water vapor content of the expired gas (WV_{exp}) tended to be somewhat higher when the cooler gases were breathed, but analysis of inter-gas mixture relationship of water content show no notable differences. In addition, the minute volume changes had little or no effect on WV expired.

The relationship between respiratory heat loss and $\dot{V}_e$ proved to be direct and linear. For this reason in Figures 9, 10, and 11 the respiratory heat loss is plotted as a function of the minute volume. One can see the steady increase in slope as the more dense gases are considered. In addition, intra-gas mixture variations due to Δt size and amount of expired WV can easily be seen. In Figure 9, for example, the four lower lines demonstrate the similarity of air and 80% He - 20% O_2 (1 atm.) when grouped into two classes of Δt (5° - 15° C Δt and 15° - 25° C Δt) using the measured WV expired. When the expired gas is considered saturated at the expired gas temperature the upper four curves result. As can be seen from this we were not able to demonstrate saturation of any of the gas mixtures at the expired gas temperature but rather an average of 64% of saturation. This is thought to be due to measurements being taken at different places in the mouthpiece. Curves for the 80% He - 20% O_2 mixture and air (both 4 atmospheres absolute) on Figures 10 and 11 are not shown for saturation at the t_e since the two lines would be nearly superimposed.

As previously mentioned we measured an average of 64% of the amount of WV expected if the gas were saturated at the expiration temperature. When grams expired per hour were calculated for both the measured and the saturated condition the curves in Figure 12 were obtained. Since the WV expired (or H_2O_e) were estimated for the EDU experiments, this data is not included in the curve.

Figure 7 - Regression curves for expired gas temperature (t_e) as a function of inspired gas temperature (t_i) for gas mixtures used in 1 atmosphere experiments.

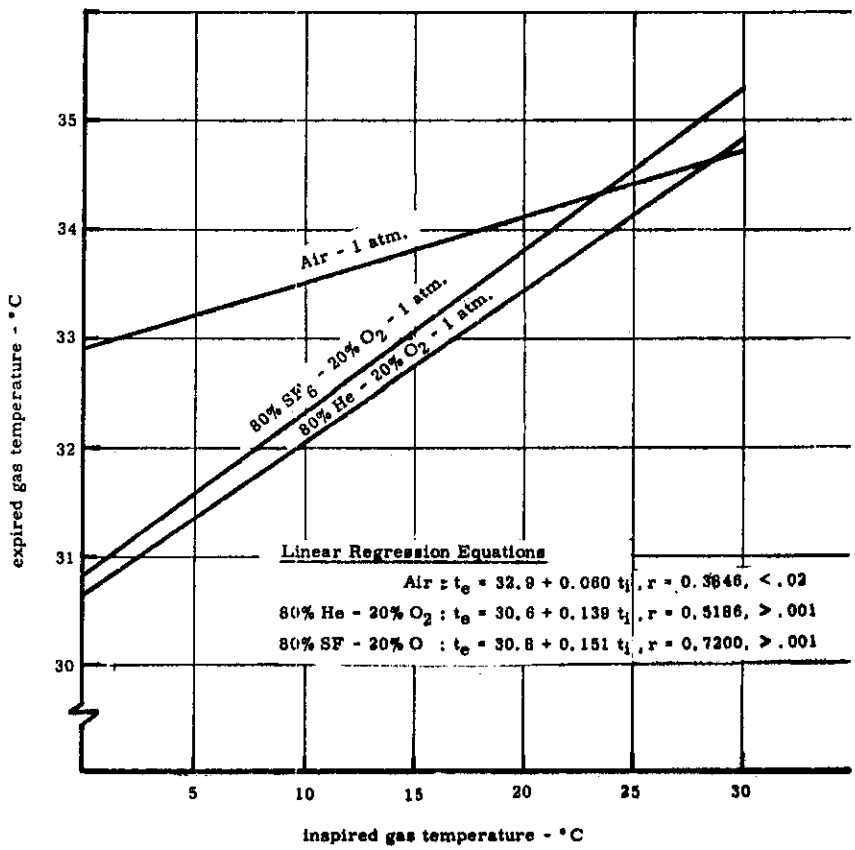


Figure 8 - Scatter plot of expired gas temperature (t_e) as a function of inspired gas temperature (t_i) for gas mixtures used in hyperbaric experiments.

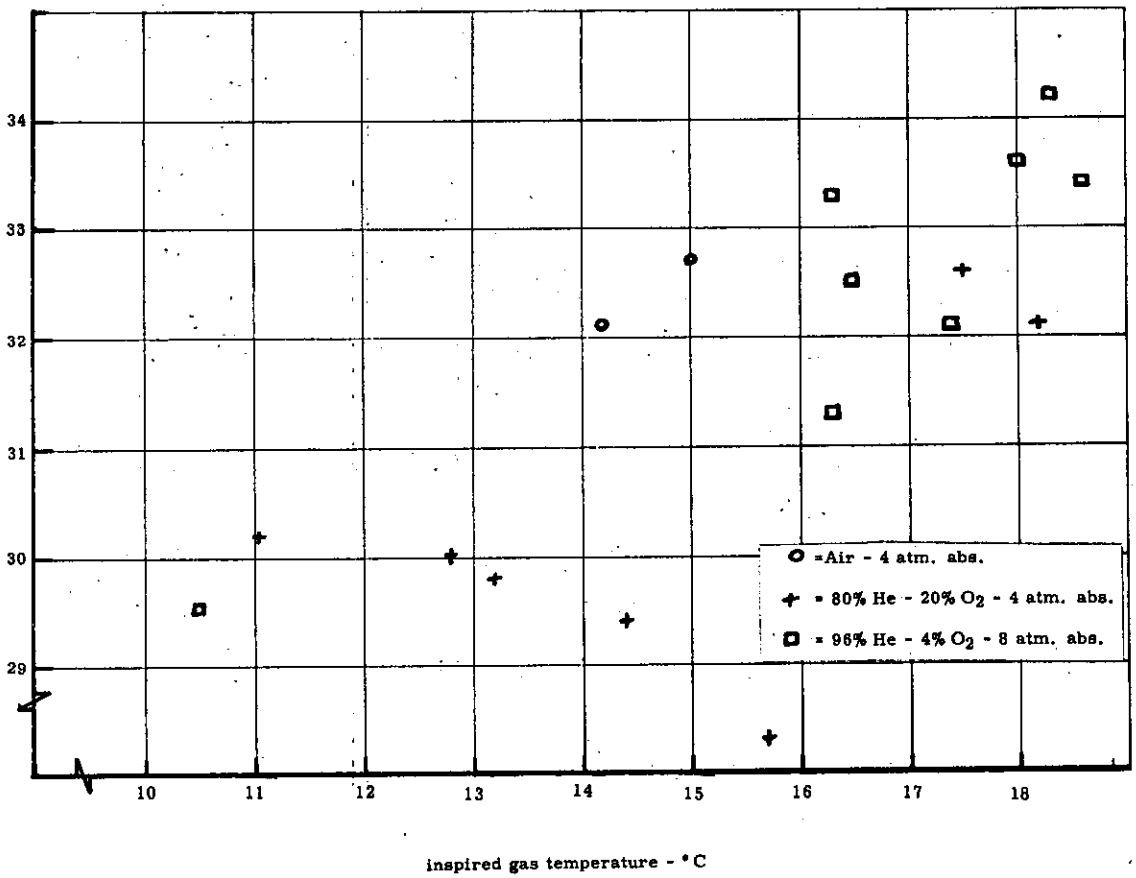


Figure 9 - Respiratory heat loss as a function of minute volume ($\dot{V}_e$) for gas mixtures with similar ρC_p's at 1 atmosphere showing influence of the inspiration-expiration temperature difference (Δt) and the expired gas water content (H_2O_e).

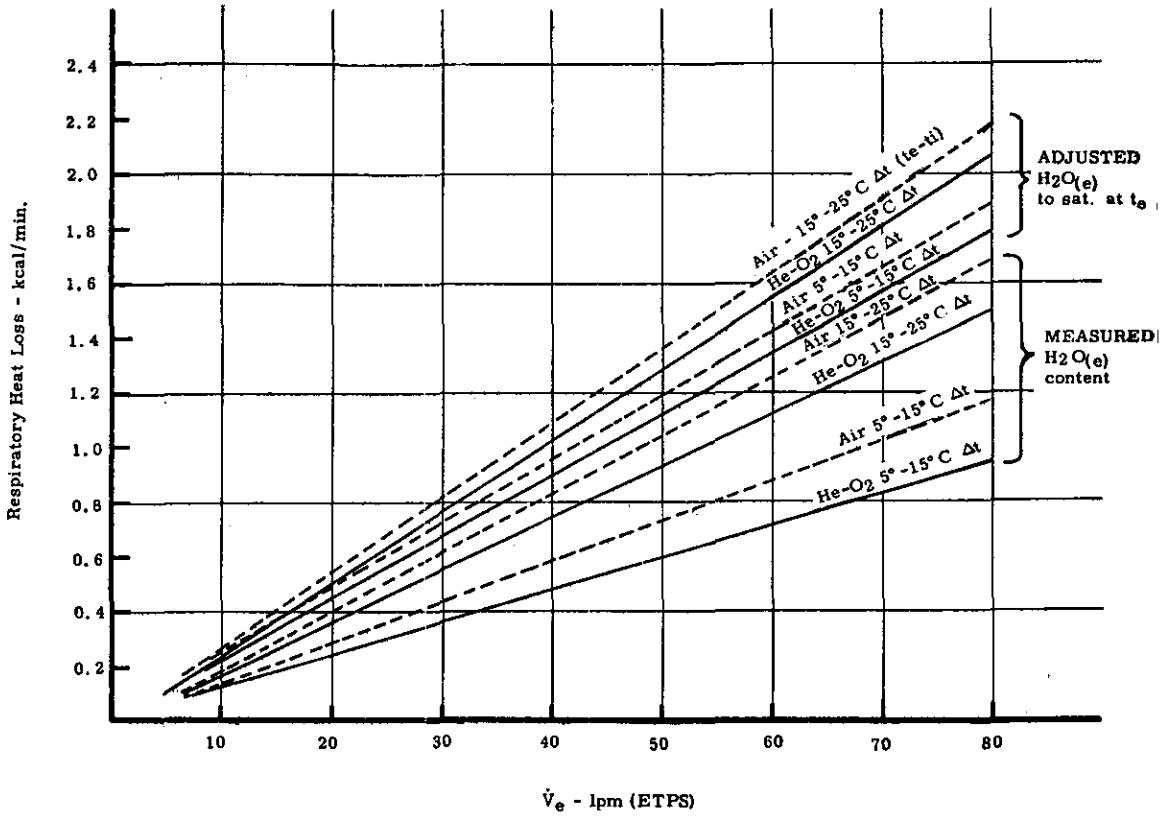


Figure 10 - Respiratory heat loss as a function of minute volume ($\dot{V}_e$) for gas mixtures with similar ρC_p's showing influence of inspiration-expiration temperature difference (Δt) and expired gas water content (H_2O_e).

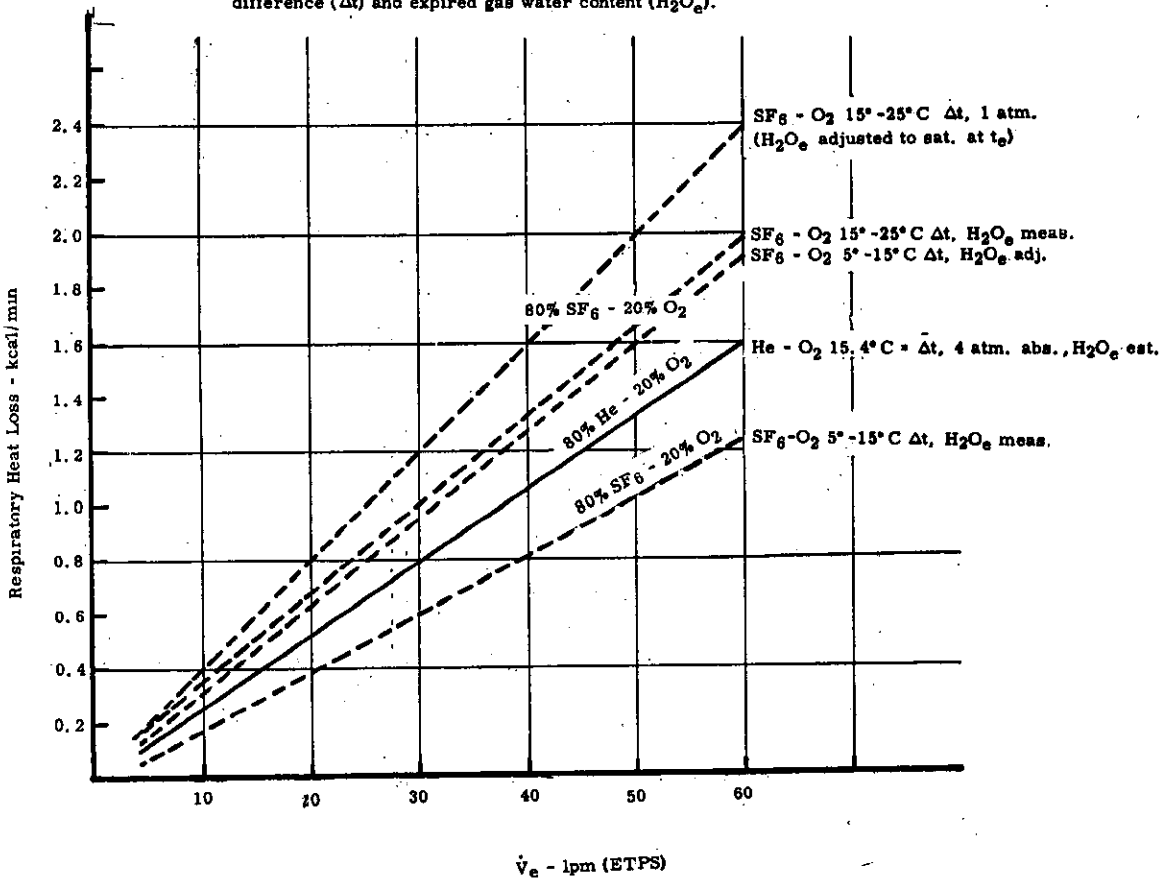


Figure 11 - Respiratory heat loss as a function of minute volume ($\dot{V}_e$) for 96% He - 4% O_2 at 8 atmospheres absolute and air at 4 atmospheres absolute showing influence of expired gas water content (H_2O_e) for the helium mixture.

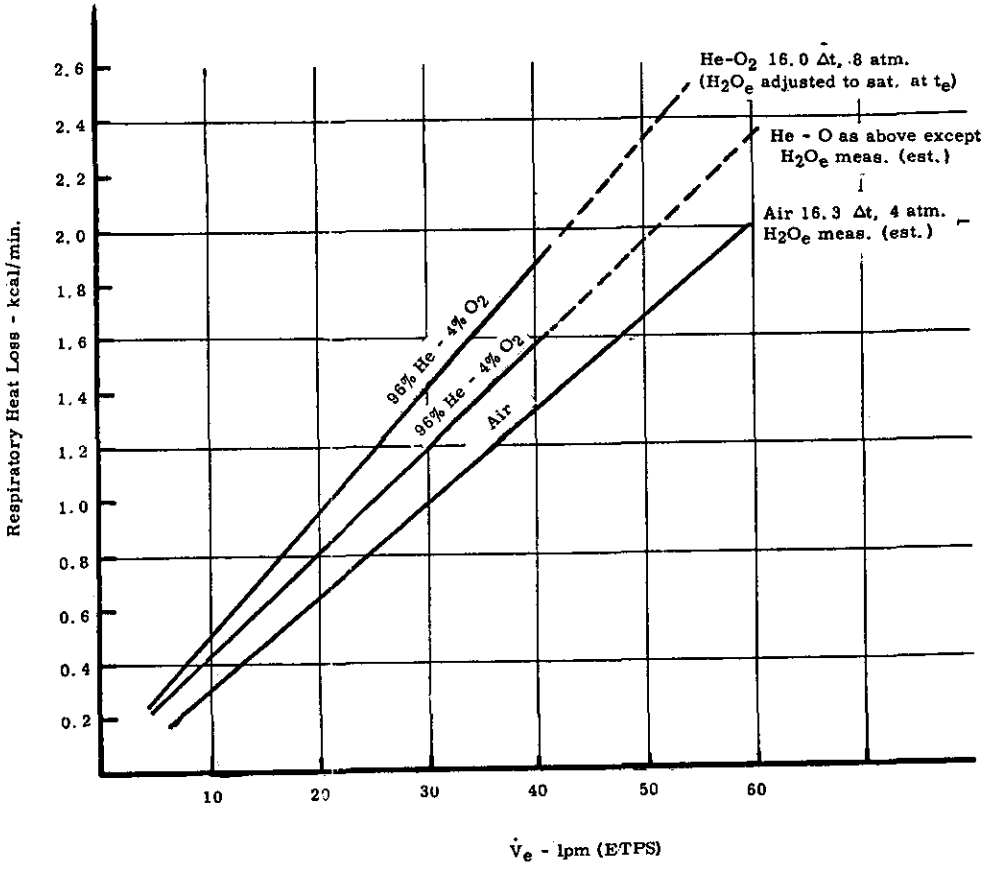
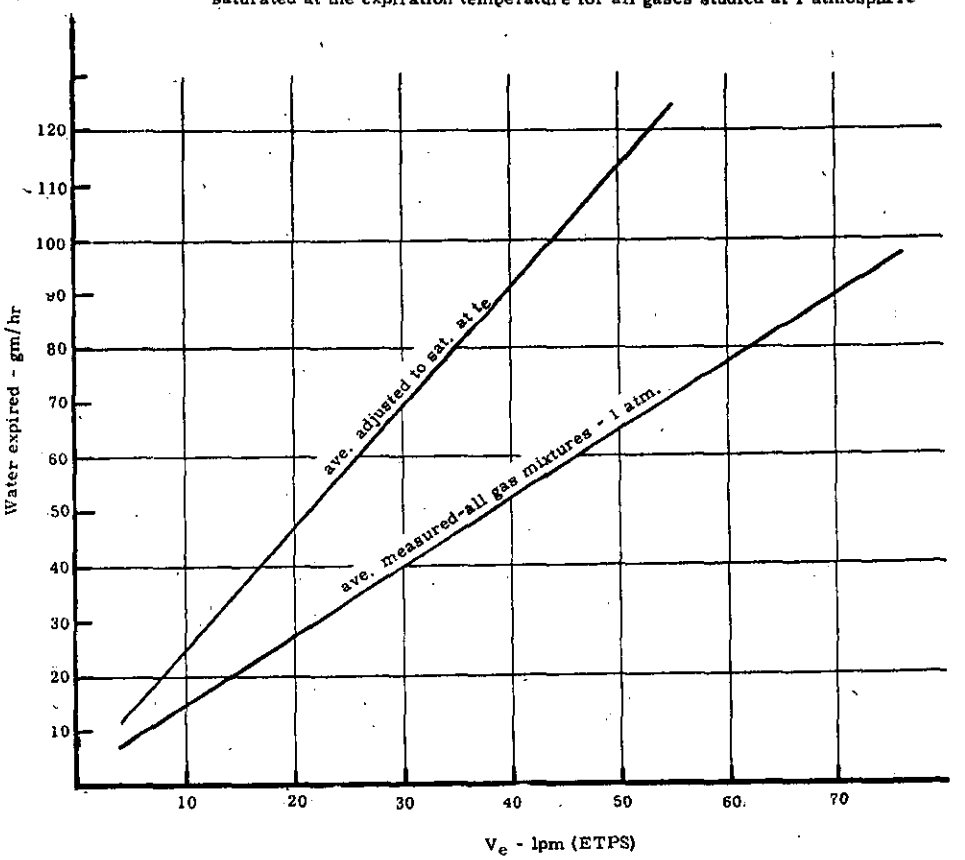


Figure 12 - Mass of water expired per unit time (H_2O_e gm/hr) as a function of minute volume ($\dot{V}_{e_{ETPS}}$) showing average measured value and amount if gas is saturated at the expiration temperature for all gases studied at 1 atmosphere



The results of the experiments are perhaps best summarized in Figure 14 in which respiratory heat loss per unit volume of air respired is shown as a function of ρC_p. The greater the density times specific heat, the greater the respiratory heat loss.

In Figure 15 the fraction of total heat loss represented by the respiratory heat loss is plotted as the dependent variable against the independent variable ρC_p. The points plotted are the mean values obtained for each gas mixture and condition while the bar represent the $\pm$ 1 Standard Deviation from the mean. The 1 atmosphere experiments are again separated into lower and higher Δt groups to give an indication of the effect of breathing cooler gas mixtures. The fraction ranges from a combined average of 0.09 with the gas mixture possessing the lowest ρC_p value (0.217 for 80% He - 20% O_2, 1 atm.) to 0.25 for the highest tested (1.65 for 96% He - 4% O_2, 8 atms. abs.). The relationship is a direct and reasonably linear one. Extrapolation of these data indicates that a point could be reached at which the loss of heat through the respiratory tract would equal (or exceed) the total quantity being generated. Assuming ideal gas laws to hold, rough calculations show that the depths at which this might occur are between 1500 and 2000 feet, which is far below depths now being explored by free-swimming divers equipped with open breathing equipment.

There are certain shortcomings in the data which should be taken into account in drawing conclusions such as the one above. First, the number of hyperbaric experiments is small, and the necessity of estimating the correct $\dot{V}_e$ and WV expired in these experiments makes extrapolations tenuous. Also subjects were not pre-saturated with the test gas, allowing for some dilution by nitrogen from tissues if He - O_2 was being breathed.

Figure 13 - Treadmill energy expenditure based on minute volume.
(unpublished Webb Associates data)

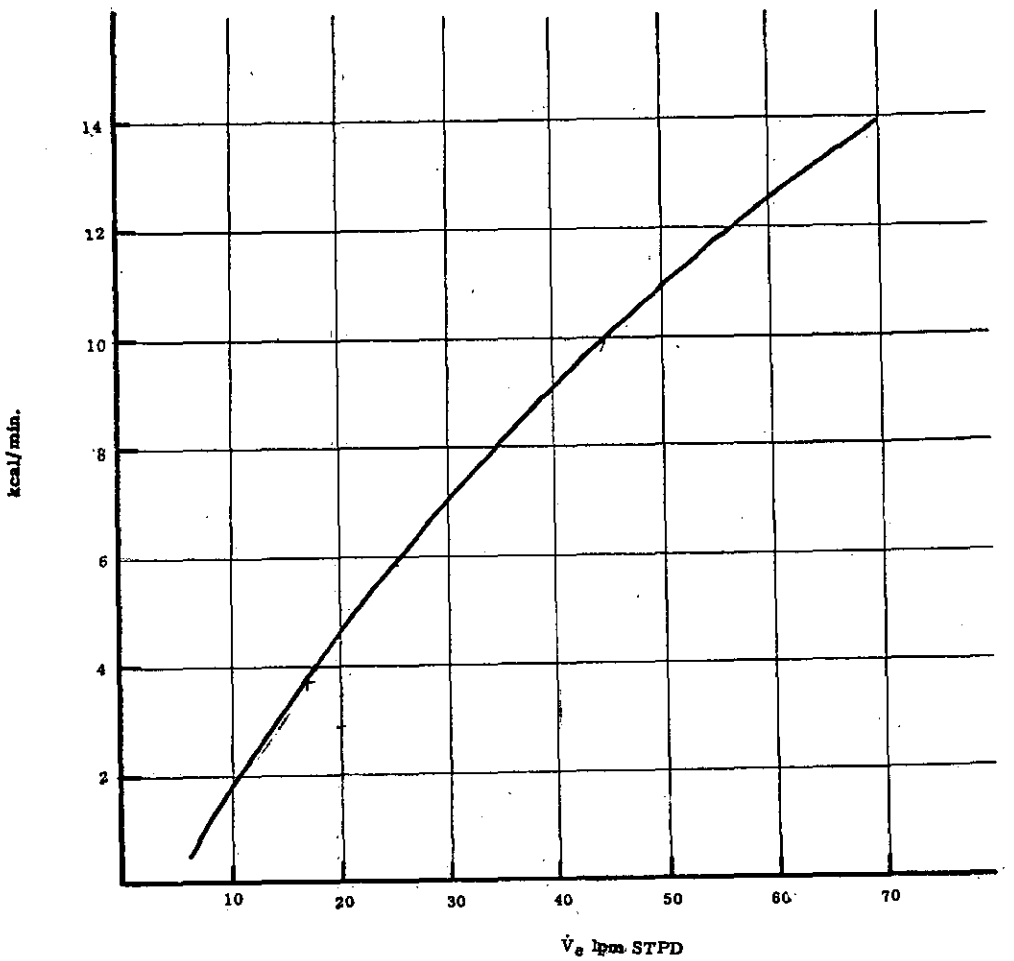


Figure 14 - Respiratory heat loss per unit volume gas for gas mixtures with different ρC_p products

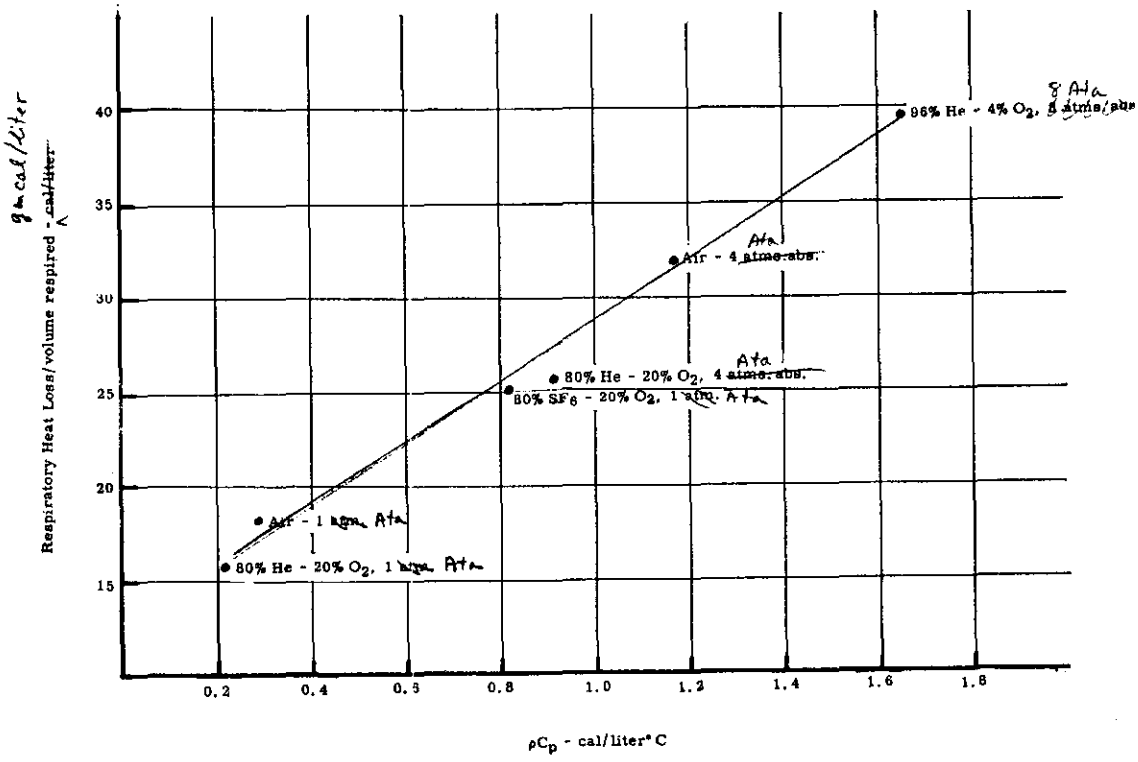
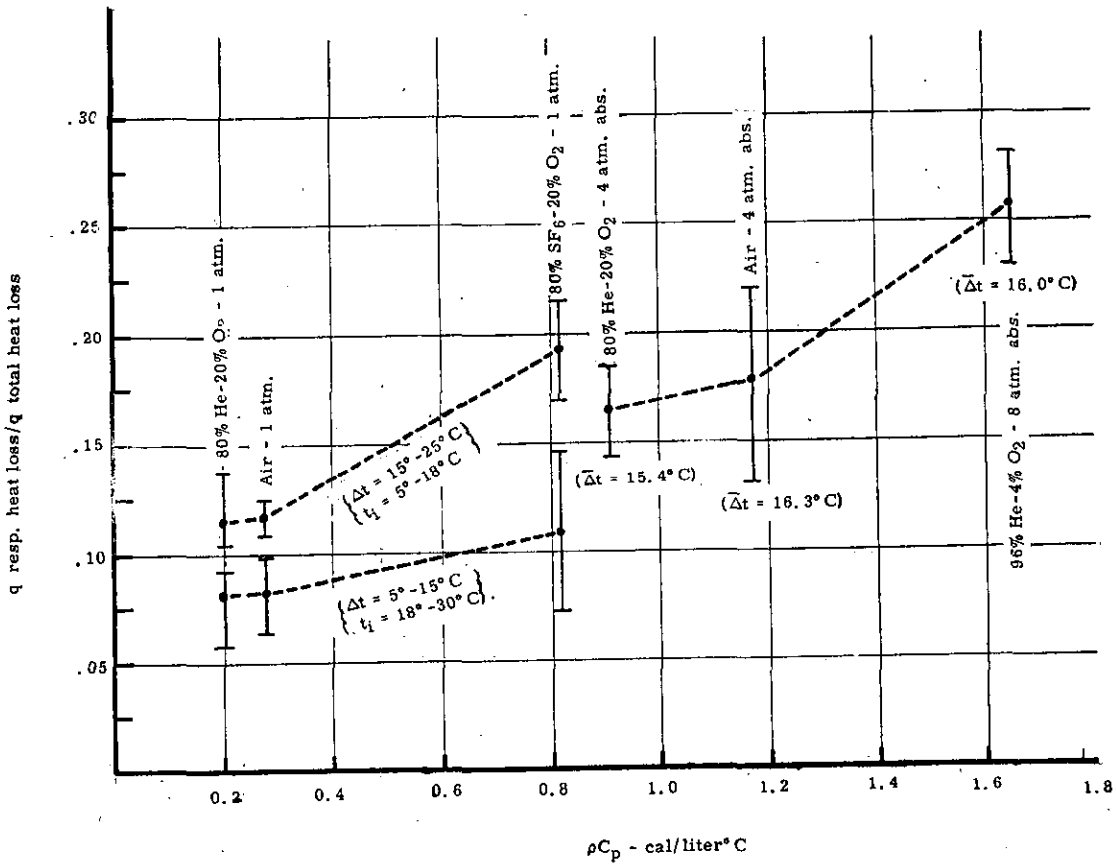


Figure 15 - Fraction of total heat loss represented by average respiratory heat loss (± 1 SD) for gas mixtures of various ρC_p's. For the mixtures studied at 1 atmosphere the data are divided into two groups of Δt.



DISCUSSION

In order to interpret the measurements reported here it is essential to understand the effect of the mouthpiece on heat loss from the respiratory tract. The mouthpiece extends the airway beyond the portal of the nose or mouth, and it is fully engaged in the passive heat exchange process of the upper respiratory tract.

It is worth repeating that the respiratory gas moving first in then out of the airway (upper respiratory tract plus any attached external apparatus) first cools the airway on inspiration, then warms the airway on expiration. Expired air then is giving off heat and losing water vapor as it travels outward. The lowest expired air temperatures and the lowest expired water vapor are found at the shallowest point in the airway; in deeper portions of the airway expired air is warmer and moister (Seeley 1940, Webb 1951).

In the experiments reported here where a mouthpiece was used as in diving, the mouthpiece and valve body with it were very much involved in passive heat exchange. Our bead thermistor was located about 7 cm deeper than the inlet or outlet of the airway. Our dewpoint sample, however, was taken at a point 2 cm past the exit of the airway. This was necessary since the dewpoint apparatus cannot follow rapid changes in water vapor and we had to sample expired air unmixed with dry inspired air -- hence the location beyond the exhalation check valve.

From this necessary arrangement of the breathing apparatus and sampling points it is reasonable to suppose that our maximum and minimum peaks of temperature were less than they would have been if there had been no mouthpiece or if we had measured at the inlet and outlet of the mouthpiece. Therefore, inspired air temperature was higher, and expired air temperature was higher at the point measured than it would have been at the inhalation and exhalation check valve, and it is reasonable to assume that the difference between inspired and expired temperature was less at the point measured than if the mouthpiece were not there.

Expired air beyond the exhalation check valve was considerably cooler than where measured by the bead thermistor. As the expired air cooled, it gave up water vapor by condensing, a supposition amply confirmed by the amount of condensate present in the mouthpiece in all of our experiments.

We believe, therefore, that our measurements of inspired and expired air temperatures were correct for the estimation of heat loss from the man, but incorrect in terms of heat exchange in the entire airway if the mouthpiece is included. We further believe that the low water vapor readings for expired air, which averaged 64% of saturation at the measured expired temperature, were incorrect in terms of the man's heat loss. The actual latent heat loss in the water content of expired air is better represented by using a figure for saturation at the measured expired temperature. For this reason we show both *measured water loss* and *"adjusted water loss" in Figure 9 through 12, believing* that the adjusted values are correct.

The difference in respiratory heat loss values using the measured and adjusted values for expired water are further demonstrated in Figure 16, where we have chosen two values for respiratory ventilation rate and two values for Δt, and plotted respiratory heat loss as a function of ρC_p of the gas mixture.

In comparing the present results with previous work done without a mouthpiece, it is again evident that the mouthpiece influences the temperature measurement strongly. Figure 17 shows the present measurement of expired air temperature while breathing air through a mouthpiece at 1 atmosphere with inspired temperatures from 0° C - 30° C and also earlier data from Webb (1955) over the same temperature range and breathing air at 1 atmosphere, the second curve being taken from measurements made in the nasal portal without external apparatus. The shallower slope of t_e versus t_i and the higher level of t_e for the mouthpiece data are consistent with the argument that the mouthpiece acts as an extension of the upper respiratory tract, and as such it conserves body heat, i.e. it reduces respiratory heat loss from the man.

Figure 16 - Respiratory heat loss as a function of ρC_p showing effect of minute volume ($\dot{V}_e$), inspired-expired temperature difference (Δt), and water content of expired gas (H_2O_e).

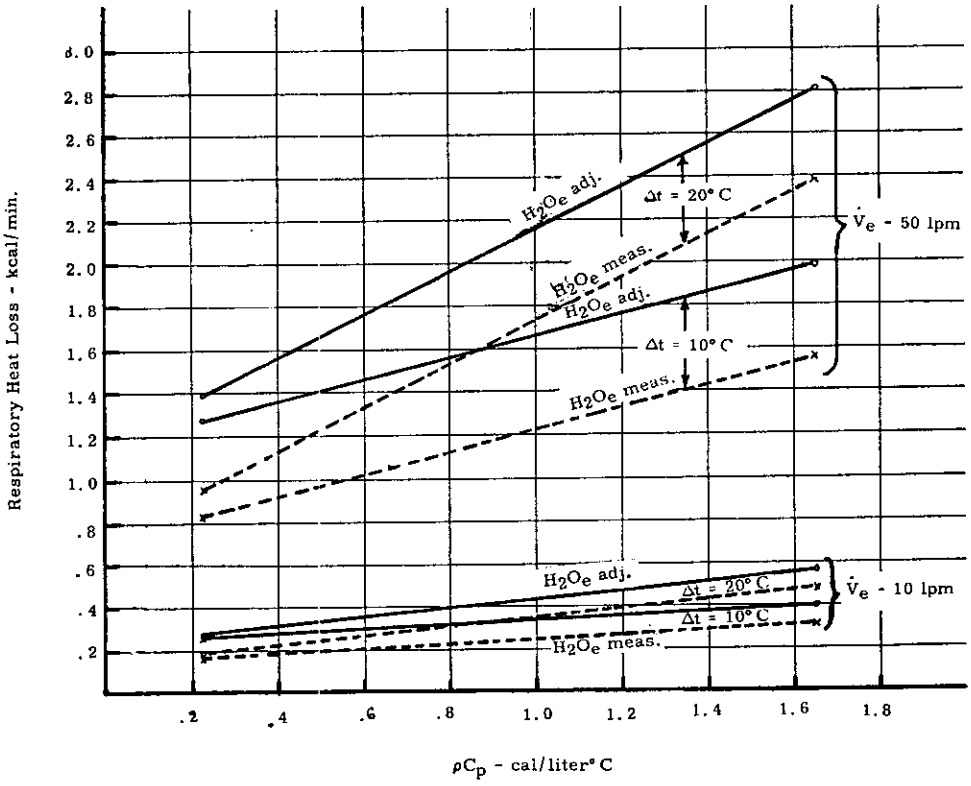
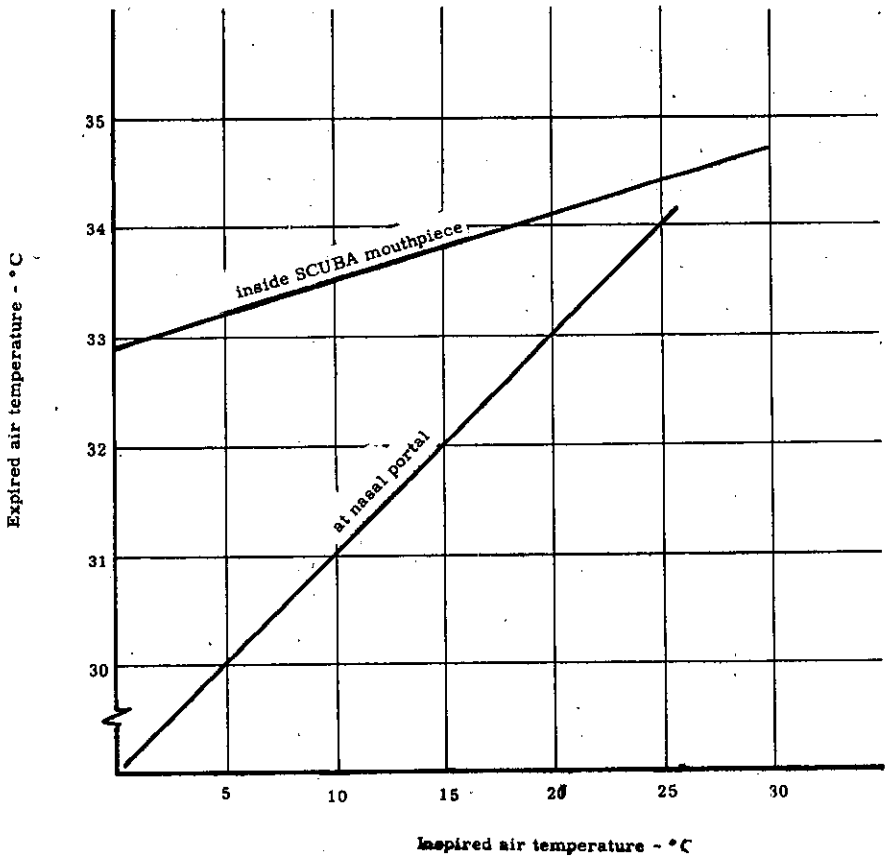


Figure 17 - The temperature of expired air as a function of the temperature of inspired air for measurements made at the nasal portal (Webb, 1951) and for measurements made inside a SCUBA mouthpiece. Air is at 1 atmosphere and dry.



To emphasize the importance of knowing how to find respiratory heat loss using the formula we have presented in this report, we have made a calculation of the respiratory heat loss during a 48 hour saturation dive to 650 feet at the Ocean Systems laboratory, as reported by Hamilton, et al (1966). In that experiment the gas mixture at depth was He 98.31%, and O_2 1.69%. The total pressure was 15,732 mm Hg. The ρC_p of this mixture at 1 atmosphere and 20° C is 0.2097 cal/liter °C, and at 650 feet and 30° C it is 4.198 cal/liter °C. The mean resting $\dot{V}_e$ was 12 lpm (BTPS), the mean chamber temperature 30.25° C, and the mean vapor pressure 25.6 mm Hg. We estimate expired air to have been at 34.5° C and saturated. The respiratory heat loss is calculated to have been 15.5 kcal/hr. The mean resting metabolic rate was 101 kcal/hr, so that respiratory loss was 15% of the total. (If the men had been breathing dry gas through a mask, with an assumed inspired temperature of 20° C, the respiratory heat loss would have been 41.2 kcal/hr or 41% of the total heat loss.)

Finally, we might comment on the problem of conserving body heat in cold water, and particularly on the protection of the respiratory avenue of heat loss. Is there a way of reducing respiratory heat loss ? The answer is certainly yes.

Heat conservation is clearly possible and in fact probable when external breathing apparatus is used and this passive conservation may be increased rather simply. A heat exchanger may be placed in the airway which is common to both inspiration and expiration, namely between the inspiration and expiration check valve. This space can be filled with a ball of copper shavings (like a Chore Girl pot scrubber). The copper becomes warmed by the expired air and the heat in turn is given up to the inspired air resulting in a net reduction of heat loss for the man. Active heating is also possible but probably not necessary. Finally, closed and semi-closed breathing apparatus greatly reduces the heat loss.

Our study has dealt only with the case of an open respiratory apparatus, and the results are valid for this kind of apparatus with the pressures and ρC_p's given. In diving practice an open system becomes less and less feasible at greater and greater depths, since the mass of gas respired increases with depth while $\dot{V}_e$ does not change. The amount of gas stored in portable cylinders is limited and the time of free swimming becomes greatly reduced as the depth increases. For free swimming at depths greater than 200 feet, closed or semi-closed breathing apparatus is essential if the swimmer is to have a significant period of time away from a fixed gas supply.

Respiratory water loss is greatly curtailed in a closed or semi-closed system since the airway becomes moist from condensate and keeps the inspired gas moist. In addition, the closed breathing apparatus contains a carbon dioxide absorber which is almost always exothermic, adding heat to the recirculated gas stream. Thus both temperature and water vapor of the inspired air are raised and respiratory heat loss is thereby reduced. If the water in which the man is swimming is still so cold that inspired air temperature and water content are low enough to cause sizable heat loss, especially at high ρC_p's, the simple heat exchanger described above plus additional heating if necessary would both serve to protect the swimmer from excessive heat loss. Also insulating the exposed parts of the breathing apparatus would help, since the heat drain has now become one of loss from the apparatus to the water rather than the loss to the exhaled air.

Perhaps of more interest is the estimation and perhaps necessity for measurement of respiratory heat loss when men are living in shelters kept at high pressure, as in the Sealab experiments and in the Ocean Systems saturation dive just described. There are some suggestions that thermal balance is a problem already, and it becomes important to be able to accurately access each avenue of heat loss in exposures such as these. The data reported here for t_e, and the methods of calculation for ρ, C_p, and respiratory heat loss should serve this purpose well.

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Body Heat Loss in Undersea Gaseous Environments

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WEBB, P. *Body heat loss in undersea gaseous environments.* Aerospace Med. 41(11):1282-1288. 1970.

Men who spend days in undersea hyperbaric gas environments require warm gas temperatures, typically above 29°C (85°F). They lose heat mostly by convection, despite a narrow skin-to-fluid temperature gradient. Empirical data in comfortable temperatures are arranged on a scale of "convective character" for fluids ranging from air at 1 Ata to water, which is 167 times more convective. Respiratory heat loss is greatly increased when breathing hyperbaric gases; during dives to 600 feet and deeper, the heat drain from the respiratory tract may become large enough to require heated breathing equipment. Prolonged stays in hyperbaric environments produce slight but consistent increases in resting metabolism, heart rate, and internal temperature, accompanied by loss in body weight despite adequate food intake. It is postulated that a chronically increased convective and respiratory heat drain is matched by a persistent increase in metabolic heat production.

WHEN MEN ARE CONFINED at several times atmospheric pressure in environments that are typically high in helium content, they are far more closely coupled thermally to their environment than men living in air at 1 atmosphere absolute (Ata). This tight thermal connection changes the usual modes of body heat loss, and it produces a different definition of thermal comfort, and very possibly a mild but sustained increase in metabolic rate.

The varied observations which tell us that hyperbaric gas is different thermally include the fact that men in hyperbaric helium environments are comfortable in rather warm temperatures, and they are quick to sense a small change in temperature.[2,4,6-8] The aquanauts in Sealab II were comfortable in 29 to 32°C helium-oxygen at 7.2 Ata as long as they were awake and active, but cold and often shivering in the same environment in their bunks.[8] In a similar situation but at greater pressure, the two subjects of a 650-ft chamber dive[7] were noted to shiver occasionally while asleep although their environment was kept between 29° and 31°C. In another situation, divers in unheated pressurized personnel transfer chambers complain bitterly of being cold. These men incur a heat debt before entering water, and when they return to the capsule following a cold water excursion, the heat drain continues and makes matters worse, both thermally and for the decompression to follow. Finally, there are small but apparently real changes in body temperature and heart rate which accompany prolonged stay in hyperbaric helium environments, a small but real increase in oxygen consumption, and weight loss despite high food intake.

Clearly, the hyperbaric gaseous environment is different from the air environment we are accustomed to. This presentation will review what evidence we have of the effects of close thermal coupling between men and hyperbaric gas, both in terms of the transfer of heat from the body surface and in terms of the heat loss by respiratory gas exchange, and will review the present evidence for a metabolic response to this loss.

COMFORT TEMPERATURES

A lightly clad man, wearing only shorts, shoes, and T-shirt, who is moving around the confines of an envir-

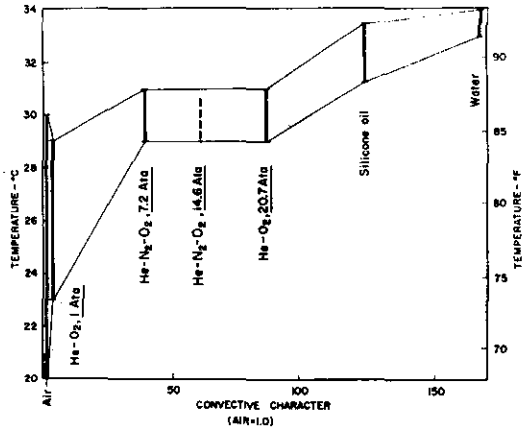

Fig. 1. Comfortable temperatures for prolonged stay in various fluids by men lightly dressed and mildly active. Based on data of Epperson et al.,[5] Hamilton et al.,[7] Hock et al.,[8] Raymond et al.[18] and Webb and Annis.[18]

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onmental chamber at sea level, is comfortable at air temperatures between 20 and 30°C. If he goes to sleep, he prefers to have the temperature in the higher end of that range. If he is continuously active, he prefers cooler temperatures. When the gas composition is changed, and when its pressure is raised, different ranges for comfort temperature have been described by various workers. Figure 1 summarizes this experience for environments ranging from those with the convective character of air to others many times more convective. At the high end of this comparative scale, water is shown as a fluid environment with very great heat removing (convective) power.

To explain the derivation of the scale in Figure 1, each fluid used in previous prolonged immersion projects has been characterized in terms of its density, specific heat, thermal conductivity, and viscosity. Table I shows these properties for seven fluids at a temperature of 28°C.

The scale on the graph has been normalized to air as a reference point, so that environments with greater cooling power than air are shown as higher than 1. Thus the Sealab II environment of 78% He-18% N_2-4% O_2 at a pressure of 7.2 Ata gave a ratio of 28 to 1 compared to air. The four physical constants of the fluids used do not represent a complete description of its convective heat transfer characteristics. Velocity was omitted as a variable by assuming something like free convection to make the various environments comparable; and there are other terms that go into a complete convective description of each environment. Nevertheless, the four physical properties chosen have permitted what looks like a sensible ordering of the thermal effects of these several media.

The wide range used in the figure is justifiable on the grounds that research is proceeding toward 1000-ft dives and deeper. In recent chamber experiments simulating 1000-ft depths (31 Ata),[5,12,14] gas mixtures contain 97-99% helium and the convective character is 127.5, which is higher than silicone oil. At 1500 ft (45 Ata) the convective character would be 185, which is higher than water. Bühlmann et al.[3] controlled the temperature of the gas at 31 Ata in their chamber to 31.6°C on the average, which falls within the band shown on Figure 1.

Undersea shelters have extremely high humidity. Convective heat loss becomes the main avenue for surface heat loss, even in "dry" chambers.[6,13] The effect this has on subjective feelings of comfort is not clear, but the convective pathway is worth examining further.

CONVECTIVE HEAT LOSS

Heat loss by convection from the body surface is a major pathway in normal air environments, but it becomes the dominant pathway in hyperbaric and helium-rich environments. It is possible to discuss convective heat loss from a straight theoretical standpoint, and examples of such analyses are given by Epperson et al.,[5] Nevins et al.,[11] Raymond et al.,[13] and Tauber et al.[15] But the analysis is complex and a number of important assumptions are often made which are true in normal air environments but unfortunately are not true in highly convective ones. For example, heat loss by convection is generally expressed as the product of the convective transfer coefficient (h_c) multiplied by the temperature gradient between the surface and the fluid. Not only is h_c affected by all the terms mentioned above (density, specific heat, conductivity, viscosity, and velocity), but also the skin-to-fluid gradient is not what one would expect from experience in air. As a general rule, it appears that the more strongly convective the environment, the smaller is the skin-to-fluid gradient. This is evident from the data presented in Figure 2. Here we show on the same scale used in Figure 1 that the more

TABLE I. CONVECTIVE CHARACTER OF SEVERAL FLUIDS AT 28°C

	Convective Constants*	Convective Character**
Air at 1 Ata	0.61	1
80% He-20% O_2 at 1 Ata (1 day exposure; Epperson et al.[5])	1.57	2.6
78% He-18% N_2-4% O_2 at 7.2 Ata (Sealab II; Hock et al.[8])	17.2	28.2
90% He-8% N_2-2% O_2 at 14.6 Ata (450-ft saturation dive in chamber; Raymond et al.[13])	36.6	60.0
98.3% He-1.7% O_2 at 20.7 Ata (650-ft saturation dive in chamber; Hamilton et al.[7])	52.0	85.2
Silicone oil at 1 Ata (96-hr submersion; Webb and Annis[18])	75.3	123
Water at 1 Ata	102	167

*The convective constants for each fluid are shown as the product of density (ρ) in gm/liter, specific heat (C_p) in cal/gm-°C, and thermal conductivity (K) in cal/min-cm-°C, divided by viscosity (η) in centipoises.

**The convective character is a ratio which normalizes the fluids to air by dividing the convective constants of the fluid by the convective constants of air at 1 Ata, or:

$$\frac{\rho C_p K \text{ fluid}}{\eta} \Big/ \frac{\rho C_p K \text{ air}}{\eta}$$

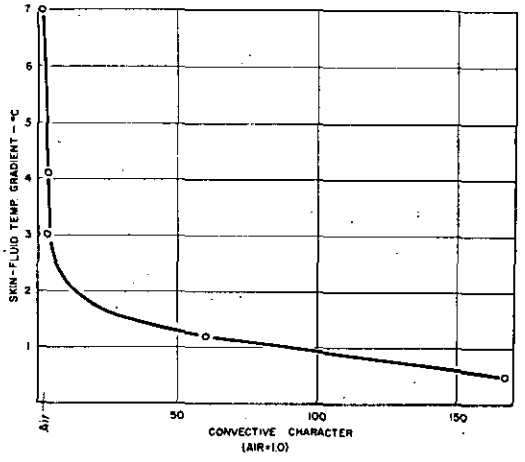

Fig. 2. Skin-to-fluid temperature gradients for mildly active men in various fluids at comfortable temperatures. Based on data from Bowers and Fox,[2] Epperson et al.,[5] Fox et al.[6] and Raymond et al.[13]

highly convective the fluid the smaller the temperature gradient.

We also know that the skin-to-fluid gradient is small in the special case of an air environment at 1 Ata where convection is increased by very high wind speed.[1] In this situation the term that was omitted from the convective character, velocity, can, when high, produce high convective heat transfer, even though the convective character of the fluid is 1.

We have then several important difficulties with predicting convective cooling in the absence of specific empirical data. Some empirical data exist, and these are plotted in Figure 3, using the same scale as in the previous two figures. *Notice particularly that these figures* for convective loss are for mildly active men in fluid environments which they find to be comfortable for days of exposure. The more convective the environment, the more of their total heat production leaves by this pathway.

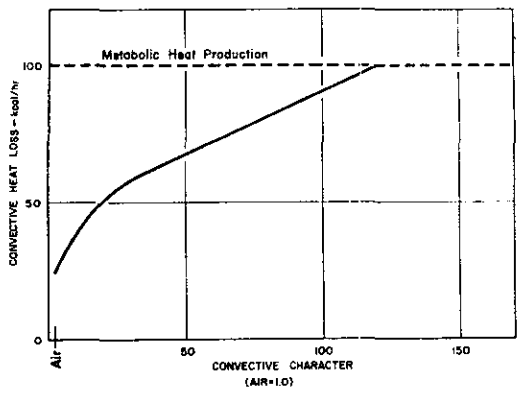

Fig. 3. Convective heat loss from mildly active men in various fluids at comfortable temperatures. Based on data from Epperson et al.[5] and Raymond et al.[18]

If we presume to extrapolate the curve of Figure 3 beyond its intercept with the standard level of metabolic heat production at 100 kcal/hr, it would appear that metabolism would have to increase in order to balance the convective heat drain. Suggestive evidence for this kind of metabolic effect is discussed below.

The data shown in Figure 3 are for hyperbaric helium-oxygen environments where the temperature is kept in the comfort zone. If the temperature happens to be lower, as it might well be in a personnel transfer chamber, convective heat loss would be extremely high and represent a serious drain of body heat. This situation has been analyzed by Tauber et al.[15] who estimate that divers in personnel transfer chambers in water temperatures around 4°C (40°F) at a depth of 600 feet would lose about 740 kcal/hr (more than seven times the resting metabolic level) by free convection alone, and this occurs even though the men are wearing two 3/16" foamed neoprene wetsuits. If one then adds radiant heat loss, the heat drain goes up by 5-30%, or 777-962 kcal/hr. Their conclusion is that men in this situation require heat replacement at a rate of 1500 watts (1290 kcal/hr) per man. Their analysis also includes the unusually high heat loss from the respiratory tract which this environment would impose, as discussed next.

RESPIRATORY HEAT LOSS

The loss of heat in warming cool dry inspired air at 1 Ata is determined by the heat needed to warm the air and to evaporate moisture from the lining of the upper airway. As gas density and specific heat increase, the warming of the gas becomes the dominant element, especially since undersea hyperbaric environments are humid. The only unknown is the temperature of the air as it leaves the oronasal portal in expiration. It is not correct to assume that gas leaves at body temperature (37°C), since heat absorbed by the inspired air is re-

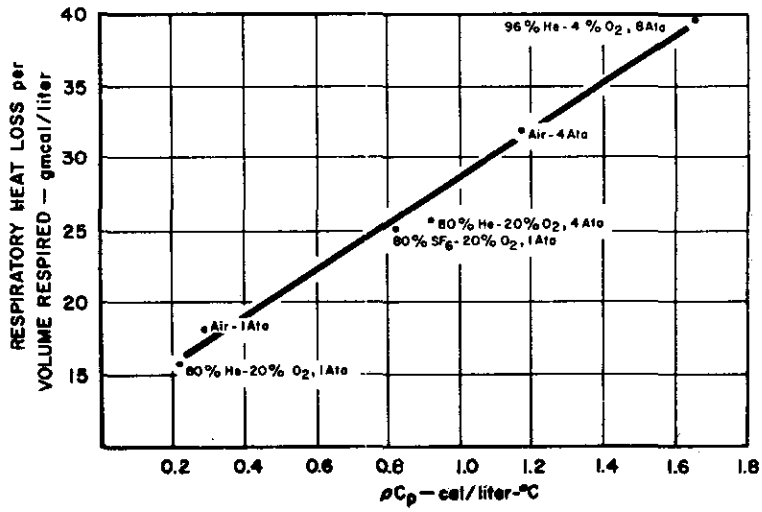

Fig. 4. Respiratory heat loss per unit volume of gas breathed, for gas mixtures with different ρC_p products. Redrawn from Webb and Annis.[17]

turned to the respiratory tract as the warm moist air exits over the previously cooled tissues. This has been studied for some hyperbaric environments by Webb and Annis.[17]

The quantity of respiratory heat loss depends upon how cold the air is, how dense it is, its specific heat, and the man's respiratory minute volume. The basic expression is:

$$H_{resp} = \dot{V}_e \rho C_p (t_e - t_i) + \dot{V}_e 0.058 (W_e - W_i)$$

where H_{resp} is the rate of respiratory heat loss in kcal/min; $\dot{V}_e$ is respiratory minute volume in liters/min (STPD); ρ is the density of the gas in gm/liter; C_p is the specific heat of the gas in kcal/(gm · °C); t_e and t_i the temperatures of expired and inspired gas in °C; 0.058 the latent heat of vaporization in kcal/gm; W_e and W_i the water contents of expired and inspired gas in gm/liter. Notice that only density and specific heat, not thermal conductivity or viscosity, are needed to describe the gas character here.

One graph from our earlier study is reproduced in Figure 4. The product of density and specific heat is seen to directly determine respiratory heat loss per unit quantity of air breathed. In other words, the denser the gas, the higher its specific heat, and the more gas respecific heat of the gas in kcal/(gm · °C); t_e and t_i the respiratory heat losses at greater depth and for higher ventilation rates than we tested, and showed very high calculated losses for divers working in cold water at 500-1000 feet. Their calculations, however, contain the assumptions that the gas is expired at body temperature and that it is inspired dry. Further experimental data in deeper dives will help to pin down the correct values for respiratory heat loss.

Other values for the quantity of heat lost by respiration are shown in Figure 5, where we assume a mildly active man with a respiratory ventilation of 10 lpm in fluids having the same range of convective character as used in Figures 1-3, but three different temperatures. It is evident that respiratory heat loss is a sizable avenue

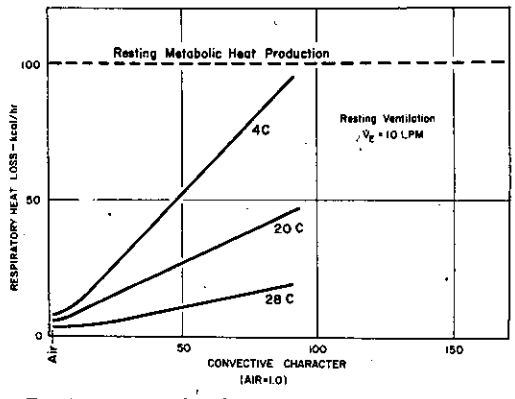

Fig. 5. Respiratory heat loss during mild activity while inspiring gases at several temperatures. Based on Tauber et al.[15] and Webb and Annis.[17]

for escape of body heat, especially when the environment is cooler than the comfort band shown in Figure 1.

It is relatively simple to reduce respiratory heat loss by including in breathing equipment a heat exchanger which would retain some of the heat in the warm expired gas and deliver it back to the cold inspired gas. While this approach makes sense in breathing equipment used for divers, it might be an annoying complication to wear such a piece of respiratory apparatus for prolonged stay in an underwater habitat.

In deep dives it may be necessary to heat the respired gas. Tauber et al.[15] have estimated that 250 watts would be needed to block serious respiratory heat drain in a diver at 650 feet breathing He-O_2 and working hard enough to have a respiratory minute volume of 25 lpm. Incidentally, should liquid breathing ever become a practical technique, respiratory heat loss would be enormous if the liquid breathed were just a few degrees less than 37°C.

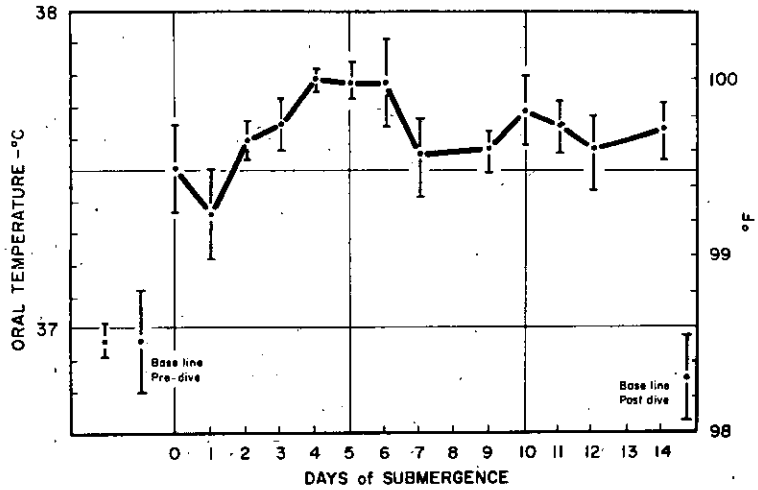

Fig. 6. Oral temperature of Sealab aquanauts plotted against time of exposure. Means are connected by straight lines, and standard errors are shown with vertical bars. Redrawn from Hock et al.[8]

POSSIBLE METABOLIC EFFECTS

Animals during long stays in helium-rich and hyperbaric environments have generally shown a slightly elevated body temperature and, in some cases, an elevated oxygen consumption, but conflicting data are easy to find. Referring to metabolic and other effects, Raymond et al.[13] clarify some of the confusion by saying: "Others have shown that by varying such factors as environmental temperature they could magnify or minimize the helium-related phenomena." Human experience is limited, but there are some strong suggestions of a metabolic response in comfortable temperatures. Let us review the evidence.

In the early days of saturation diving, three men spent 12 days in a 90% helium-oxygen environment at 7 Ata in a chamber at the Submarine Medical Center in a project called Genesis E. The men consumed an average of 4200 kcal/day, and despite confinement in the chamber, they lost a little weight—between 0 and 2 lbs. No increase in oxygen consumption was observed. (Bond, personal communication.)

In accounts of Sealab II, Hock et al.[8] and MacInnis and Bond[10] reported a persistent elevation in the men's oral temperature of approximately 0.5°C, as illustrated in Figure 6. At the same time the men had a mildly elevated pulse rate, suggesting that if oxygen consumption had been measured it would have been somewhat higher than normal. The men lost from 3-7 lbs in weight (mean approximately 2 kg or 4.4 lbs) despite a rather generous food intake which Bond estimates (personal communication) to have been more than 4000 kcal/day.

There was a suggestion of elevated body temperature in the two men making a 650-ft saturation dive in a chamber, as reported by Hamilton et al.[7]

Raymond et al.[13] observed a slight increase in resting metabolism in their five subjects after they had spent 12 hours or more in helium-rich hyperbaric environments. The effect was progressive, that is, at successively higher pressures over the range of 7-15 Ata, the metabolic rate was progressively higher. The control value in air was 47.8 kcal/($m^2 \cdot hr$), while at 14.6 Ata it was 51.6 kcal/($m^2 \cdot hr$). These men showed no increase in rectal temperature.

Even in the less hyperbaric environment of Tektite I, where four men lived for two months in an air environment at 38 feet (2.15 Ata), measurements made of oral temperature were higher than normal. The Medical Officer's log showed 96 readings on the four men, taken every second or third day at about the same time in the afternoon. The mean was 38.8°C (101.26°F) with a range of 38-39.4°C. However, the thermistors used to record these temperatures were suspect, since after the dive they were found to be reading high when compared with mercury thermometers at 1 Ata. The impression remains that the oral temperatures were elevated by about 0.5°C. As for body weight, the men lost 0, 2, 4 and 8 lbs, respectively (mean of 3.5 lbs), despite adequate food supplies. (These unpublished temperature and weight loss data were kindly made available by the Office of Naval Research and by the Medical Officer, Dr. T. Markham.)

On the other hand, the men in the Sealab (helium) and Tektite (nitrogen) projects were physically active and diving in cold water, so that a high caloric expenditure from both exercise and cold exposure was to be expected. This might explain their weight loss, but it would not explain the milder weight loss seen in the confined subjects in Genesis E. Nor do exercise and cold usually cause weight loss in healthy men who have adequate food supplies. In heli-oxygen chamber dives at Duke University, Saltzman (personal communication) has observed slight but consistent increases in resting oxygen consumption levels at 4, 7.8 and 8.5 Ata. And from the same laboratory, Overfield et al.[12] have reported slight increases in resting oxygen consumption after 24 hours in He-O_2 at 31 Ata, but interestingly enough, they reported no increase in oral temperature, which was measured sublingually with a thermistor probe. Bühlmann et al.[8] observed occasional increase in oral temperatures in two of their three subjects, but ascribed this to mild upper respiratory infections. They also saw weight loss in their relatively short saturation dive—81 hours at 31 Ata—which was not correlated with fluid balance data.

To summarize: oxygen consumption data from relatively short exposures in dry chamber dives show a small but consistent increase in resting metabolism; body temperatures appear to be slightly but consistently increased in two long saturation dives in the water; and there is loss of body weight despite adequate food and apparently high food consumption.

What causes the small but apparently real metabolic increase in response to hyperbaric environments? The most likely explanation is that there is a chronically increased heat production to match a persistently high heat drain, which is present despite apparent thermal comfort. If heat production (and loss) are persistently high, the effect on body temperature might be like that of steady low level exercise in which the higher the work rate the higher the rectal temperature. One might also liken the situation to the clinical picture of low grade fever or of mild hyperthyroidism.

More pertinently, the effect may be similar to what we know of chronic cold exposure, where, in animal experiments at least, there is a definite increase in metabolic heat production labeled non-shivering thermogenesis. Human data in prolonged cold exposure are less definite, but it can be argued that men really do not tolerate being cold for long, and in normal cold situations they find ways to avoid prolonged periods of increased heat loss.

A clear human metabolic response to repeated cold water exposure was reported by Kang et al.[9] who showed a significant (35%) increase in basal heat production in Korean diving women, the Ama, during the winter months when the water temperature was 10°C (50°F). These women dive until they have lost some 5°C in mean body temperature, meaning a loss of heat content of over 200 kcal—a remarkable degree of adaptation to or tolerance for cold.

In the hyperbaric environment where the warm gas feels comfortable, the high heat loss is not sensed as being cold. When the extra heat drain continues for days and weeks, it would seem entirely reasonable that

there should be a matching increase in metabolic heat production. This may be another clear case of human thermogenesis, with or without shivering.

Other explanations come to mind—the increased work of breathing dense gases, a specific pharmacological effect, or some unknown effect of pressure—but the thermal balance argument is quite plausible.

DISCUSSION

Having seen that convective heat loss from the body surface as well as loss from the respiratory tract is unusually high in hyperbaric environments, it is clear why the helium-containing habitats like Sealab II had to be kept quite warm in spite of being very humid. It is also easy to agree with Tauber et al.[15] that men in a personnel transfer chamber in cold water must be heated directly or else the chamber must be heated.

One can also explain why the comfortable temperature for mildly active men is distinctly too cold for men who are asleep in these hyperbaric environments. If the heat drain continues high, then when metabolic heat production is reduced during sleep, by 20 to 40% of the standing resting level, a definite imbalance occurs, shivering results, and men wake up feeling cold.

To improve on present convective heat loss data, it is important that whenever saturation dives are undertaken, either in experimental chambers or in the water, enough measurements be taken that one can directly calculate convective heat loss. This requires measurements of the gas temperature, pressure, viscosity, vapor pressure, and velocity, plus the wall temperature; and on the human side, skin temperature, internal temperature, and metabolic rate. When sufficient data of this kind have been gathered, it will be possible to predict convective loss rates in untried environments from reasonable estimates of h_c and skin-to-fluid temperature gradients.

Respiratory heat loss is becoming more critical as diving activities go deeper. This is simply the result of increasing gas density, hence greater heat carrying capacity. We can hope for new empirical data on expired air temperatures in the regions of 600 ft and deeper to confirm the present guess that at such depths the entire metabolic heat production can be lost from the respiratory tract.

New information about metabolic levels during prolonged sojourns in undersea shelters will be needed to show whether there is in fact an increase in heat production to match an increased heat drain. If there is such an effect, it will be an interesting demonstration of human non-shivering (?) thermogenesis. And further, such information should be useful in specifying dietary caloric levels, what clothing should be worn in the shelter, and what special provisions need to be made in sleeping areas.

To relate the discussion of heat balance in shelters to divers in the water, we can start with the observation that men who dive are usually cold when they return. Since we now suspect that the comfortable environment in an underwater habitat represents a continuous drain of body heat, the returning diver will have a hard time rewarming—that is, getting his body heat content back up to its initial level. Hot showers are fine, but a diver probably stays in the shower just long enough to feel comfortable. It is likely that at the end of the shower he has not fully recovered thermally. If he then dives again after only a few hours in the "comfortable" shelter, he probably starts out with a lowered body heat content. This is important; he will have an even shorter time in the cold water before reaching a critical stage of body cooling.

The difficulty here is in knowing mean body temperature, or body heat content. The proper way to measure change in body heat content is by direct calorimetry. While such measurements may be impractical for projects in the water, laboratory studies of this kind are entirely feasible using a water-cooled wetsuit.[16]

A repeat dive without complete rewarming may well have important dangers, just as repeat dives have when previously absorbed inert gas has not been fully evolved. Perhaps another kind of repetitive dive table will be needed, this one thermal, with probably as many complexities in derivation as the present table for avoiding decompression sickness. But with carefully done research on heat content and rewarming, simple yet useful techniques might be found for determining when a man is back to normal, or how much less time he should spend in cold water.

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DECOMPRESSION THEORY

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4

DECOMPRESSION THEORY

B. A. Hills

The formulation of decompression tables really started at the turn of the century with work at the British Admiralty under the direction of J. S. Haldane. The subsequent publication (Boycott, Damant, and Haldane, 1908) set the basis for most calculation methods used today. Not only is this the single most important paper in decompression formulation, but it also contains the first comprehensive series of observations of bubbles in the tissues of sacrificed animals. These authors anticipated correctly some of the limitations of their own calculation method and went on to make suggestions under serious considerations today, e.g., asymptomatic bubbles and querying whether bubbles are "carried through the lung."

Although the proposed model was criticized by many subsequent workers, the "Haldane" approach has survived as a "calculation method" whose innumerable empirical modifications have now deviated into incredible complexity. The changes are too many to list, but the names of Workman, Schreiner, Hamilton, Smith, and Bühlmann are prominent in the evolution of current computational methods. It is difficult to single out individual contributions, but the state of the art is well described by Workman (1965). Distinct milestones in decompression include: (1) realization of the advantages of substituting oxygen for inert gas in preventing "the bends" (Hawkins, Shilling, and Hanson, 1935) and treating them (Behnke and Shaw, 1937); and (2) the first demonstrated advantages of the use of helium in diving by End, and Behnke and coworkers in the U.S. Navy, leading to Keller and Bühlmann (1965), who formalized the rationale for switching inert gases in the proper sequence. The latter paper also predicts what would happen if gases were switched in the inappropriate direction, as seen in what is now known as transient supersaturation counterdiffusion.

The first to break away from the neo-Haldanian concept of ever-proliferating multiple-tissues was Hempleman (1952) who pointed out that, from scientific and clinical evidence, there was really no reason to justify involing more than one anatomical tissue type as responsible for limb bends. Hempleman deviated from conventional thinking even further by postulating that the uptake of inert gas was controlled by diffusion rather than circulation, and produced interesting results comparing air and heliox bounce dives to support this approach (Hempleman, 1967).

The single-tissue, partially diffusion-limited concept was adopted by Hills, who went on to challenge the popular concept of pressure ratios (M-values) as "trigger points" to bubble formation, assumed in neo-Haldanian calculation methods, with results indicating that such diving tables were really treating bubbles rather than preventing their formation (Hills, 1968). He also pointed out that the importance of subsymptomatic gas was not so much the presence of bubbles as the effect of their formation in greatly reducing the driving force for inert gas elimination. This driving force for resolving "dumped" gas can be derived from inherent gas unsaturation of living tissue, as demonstrated by Hills and LeMessurier (1969), and later termed the "oxygen window" by Behnke. The fact that this driving force increased with pressure for air diving led those authors to advocate deeper initial decompression stops and so explain the remarkable efficiency of schedules derived purely by trial and error by Okinawan pearl divers many years before their techniques were recorded (LeMessurier and Hills, 1965).

The tendency to go to physiologic models also led to considerations of pain, with Nims and Hills recalling the studies of Inman and Saunders (1945). They had shown that when hypodermic needles were placed in certain tight connective tissues, especially tendon, a pain indistinguishable from limb bends was produced when a pressure threshold for the injection of Ringer's solution was exceeded. This concept was quantified by Nims and then by Hills (1969), who went on to relate the pressure threshold differential of the bubble to dumped gas and so derived the concept of a critical volume contributed by all gases present in the tissue. More elegant derivations have subsequently been published and more cases covered by Hempleman and Hennessy, but the general qualitative interest in bubble volume can be traced back to Boycott et al. (1908).

DECOMPRESSION THEORY

B. A. Hills

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CHAPTER III

Decompression Sickness Following Exposure to High Pressures

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INTRODUCTION

It has long been known that too rapid decompression of divers and compressed-air workers causes the formation of bubbles in the blood stream and fatty tissues which give rise to painful symptoms if the bubbles are sufficiently numerous and are located in critical areas. The studies sponsored by the Subcommittee on Decompression Sickness, however, have added extensive and valuable quantitative data relative to the influence of exercise, age, degree of fatness, and diurnal and environmental conditions on the incidence of symptoms; procedures have been validated for the selection of individuals relatively resistant to decompression sickness; principles underlying formation and growth of bubbles have evolved from meticulous experiments; histologic studies have shown precisely the location of bubbles, and two new findings have been presented—the watery vacuoles in liver cells following too rapid decompression, and (of most immediate application) the indisputable fact that denitrogenation prevents altitude decompression sickness.

Despite these studies, it has not been possible to demonstrate the manner in which intravascular bubbles cause symptoms, although ischemia, distention of the vascular wall, and other possible mechanisms have been analyzed, nor is the relation of extravascular bubbles to symptomatology certain. On the other hand, from studies of diving and caisson decompression sickness beginning with the fundamental investigations of Paul Bert, Heller, Mager and von Schrötter, and Boycott, Damant and Haldane, there is good evidence that under conditions in which men are usually decompressed (in contrast to the rapid decompression frequently applied to lower animals) characteristic manifestation of pain (bends), asphyxia (chokes), and paralysis can be attributed to intravascular bubbles. It is my purpose to present pertinent quantitative data relative to decompression sickness as a basis for further experiments and for the formulation of better decompression procedures. The graphical representation of decompression tabular data initiated by Van Der Aue and the evaluation of the treatment of decompression sickness by Naval Medical Officers are felt to be especially valuable contributions.

PRIMARY PRESSURE PHENOMENA

Effects of Compression Applied Equally to All Parts of Body. The body can be compressed to almost 18 atmospheres (equivalent to a diving depth of 550 feet) without demonstrable physiologic change attributable to the compression itself provided that air has free access to all surfaces of the body, e.g., the membranous linings of the frontal sinuses and the ethmoid and mastoid air cells. Although the absolute cerebrospinal fluid and blood pressures are increased by 18 atmospheres, the relative pressure readings may not be altered by as much as 1 mm. Hg. Insofar as the pressure force operates, the brain is not in a "closed box" but is subject to the same compressive force as is the skin. That considerable pressure—in fact, up to hundreds of atmospheres—is well tolerated by protoplasm has been shown by McKeen Cattell.[65] Similarly, a decrease in ambient air pressure, equivalent to altitude of 50,000 feet, will not in itself cause injury although metabolic changes attributed to low pressure have been reported by Cook.[325] This tolerance implies equal distribution of pressure to preserve unaltered the structure of tissues and the body as a whole.

The rate of accommodation to additional pressure depends upon the ease with which air is introduced into the middle ear spaces by swallowing and upon freedom of sinal openings from obstruction.[17]

Effect of Unequal Pressure Application. If the pressure is not equally distributed over all body surfaces, a pressure difference between tissues and the ambient atmosphere of less than 50 mm. Hg (1 lb./sq. in.) will alter the shape of tissue and induce congestion, edema, hemorrhage and pain. The effect of compression and of pressure differences acting on the body is illustrated by the native pearl diver who is subjected to an additional compressive force of 1 atmosphere for every 33 feet of descent. At a depth of 100 feet, for example, the total pressure acting on his body is of the order of 4 atmospheres. At this depth the air in the diver's chest (at the surface, let us say, 6000 cc.) is compressed to one fourth or 1500 cc. This amount approximates the residual air volume. Should the diver descend deeper, hydrostatic pressure acting to compress the rib cage to a volume less than that occupied normally by residual air produces a condition known as a "squeeze." The effect of the "squeeze" is to force blood and tissue fluid into the respiratory passages where the residual pulmonary air is under less pressure than the pulmonary membranes due to the limitation caused by the ribs and contracted diaphragm.

Effect of Pressure Differences on Ears, Sinuses and Teeth. In a similar manner, aural and sinal membranes are injured by a "squeeze" if the corresponding ostia of the lined spaces do not permit the free ingress of air. During the past twelve years, thousands of our submarine personnel have been subjected to 50 pounds per square inch gauge pressure in naval recompression chambers in connection with the submarine escape drill. From 5 to 25 per cent of the trainees, at any given time, have been unable to accommodate readily the excess pressure, chiefly because of "colds" or varying degrees of infection of the respiratory tract which act through edema of lymphoid and other tissue to seal the openings of the auditory tubes and, less frequently, the sinal meatus.

In aviation during descent from altitude, the increased pressure similarly

affects individuals to create a condition termed by Armstrong and Heim[3a] "aero-otitis media." In civilian aviation, the stipulation that passenger aircraft must descend at a rate not greater than 300 feet per minute was based upon the difficulty generally experienced in the auditory tubes of apparently healthy individuals as indicated by an incidence of about 10 per cent failure at any given time to accommodate rapidly to pressure changes.[18] About 1.5 per cent of individuals experience sinal pain and another 1.5 per cent are subject to pain in one or more teeth. The pain elicited by unequalized pressure is felt in the area involved. Dental pain suggests the presence of small gas bubbles in the pulp or in a part of the tooth where soft tissue can be "squeezed." It is probable that bubbles form more readily in inflamed pulp than in healthy tissue. With reference to the ear, the pain may be felt over the mastoid area as well as in the auditory canal, indicating that the entire membranous lining of the middle ear and mastoid cells is involved.

Effect on Hearing. Following acute trauma, the audiogram reflects diminished perception of sound over the whole frequency range. As the pathologic disturbance undergoes resolution, however, hearing returns to the initial level of acuity. The rarity or absence of proved cases of deafness arising from injury incident to pressure trauma stands in contrast to the permanent aural damage caused by gunfire. Complications of suppurative otitis media, moreover, are infrequent if the traumatized tissues do not come in contact with water. The spread of infection from the nasopharynx by air passing into the auditory tubes during compression is not established.

Overdistention of Lungs (Traumatic Air Embolism). To escape from a sunken submarine, an individual may breathe compressed air or oxygen by means of a rebreathing bag such as the Momsen lung. The speed of his ascent can be regulated by a buoy line previously released from the submarine. In this manner ascents have been made routinely in submarine escape training tanks from depths of 100 feet and occasionally in the open sea from depths of 200 feet. During such ascents, the compressed gas in the lungs and in the breathing bag escapes through a relief flutter valve located on the bottom of the breathing appliance. In this manner, the intrapulmonic pressure closely approximates ambient hydrostatic pressure.

If the individual, instead of breathing freely, holds his breath and ascends to the surface, the intrapulmonic pressure becomes higher than the hydrostatic pressure and the difference in pressure of the order of 80 mm. Hg[22] overdistends the lungs, ruptures the alveolar sacs and blood vessels, and gas may be forced or aspirated into the blood stream. The gas emboli subsequently produce symptoms referable to the central nervous system and the circulation. The following description of symptoms produced by too rapid ascent combined with breath-holding is typical: "About a minute after reaching the surface the diver collapsed. The extremities and body were cold and the muscles rigid. Breathing was shallow and rapid and the pupils were dilated, but reacted to light. The radial pulse was absent and the heart beats slow and weak. After about fifteen minutes, the diver began to make sounds and to roll his eyes about. He was then dressed, but gave no assistance to this act and made thrashing, and apparently hysterical, movements with the arms and legs. When seen about a half hour later, he

complained of loss of vision, even to light, and anesthesia of the left foot and leg."

If, in tests, one purposely holds his breath during ascent, a sensation of substernal distress and a feeling of actual stretching of the lungs forces exhalation at periodic intervals. A condition of fright, however, apparently can cause a spasm of the glottis to bring about overdistention of the lungs. In this manner death has occurred in ascent from depths of only 15 feet. On the other hand, without any escape appliance ascents can be made from depths of 100 feet provided the individual exhales periodically. The application of these observations to the problem of explosive decompression is apparent.

Spontaneous Pneumothorax. Either with or without air embolism during rapid decompression, spontaneous pneumothorax may occur in the distended lung. The following description of an accident in submarine escape training illustrates this complication: "An individual 'blew up' from a depth of 20 feet in the submarine escape training tank. Examination revealed loss of consciousness, stertorous, gasping respiration, blood froth on the lips, and dilated pupils with fixation of eyes to the left. During recompression consciousness was regained at a pressure equivalent to a depth of 15 feet and the patient felt all right at '50 feet.' Following the completion of this treatment, the patient complained of substernal soreness and was again compressed in the chamber to '100 feet.' He strained considerably during the compression in order to 'clear' his ears. Upon subsequent decompression to the 40-foot level, a condition of pneumothorax was found on the left side. At the 20-foot level the patient was cyanotic and excited. The pulse was irregular and weak; respirations were rapid and shallow. Oxygen administered intermittently provided some relief for a period of twenty hours. It was necessary, however, at the 10-foot level to remove 2250 cc. of air from the thorax on the left side before the ambient pressure could be reduced to normal barometric pressure. Resolution of the pneumothorax occurred during the next few days."

It appears likely that the pneumothorax occurred primarily as a result of previous overdistention of the lungs during the second recompression and was precipitated by the patient's straining to "clear" his ears. The mechanism of this type of injury has been outlined by Gersh.[436]

Overdistention of Abdominal Viscera. In ascent from deep diving depths, the expansion of gas swallowed under pressure, in the stomach and segments of the large bowel, is a serious restraint to further decompression. A viscus, once having been distended with gas, appears to lose much of its motility. In distention of the stomach, for example, the cardiac and pyloric sphincters remain contracted and prevent immediate elimination of gas.

SECONDARY PRESSURE PHENOMENA INDUCED BY INCREASED GAS PRESSURES

Narcotic Action of Nitrogen. The phenomena previously described have arisen primarily from differences in pressure which have acted to distend and rupture blood vessels and membranes. On a wholly different basis are those pressure phenomena associated with disturbances in gaseous equi-

libria. When the air pressure is raised to 4 atmospheres or higher, the gaseous nitrogen induces a narcotic action manifest by decreased ability to work and changes in mood, frequently a euphoria. A slowing up of mental activity and fixation of ideas are observed.[25, 250] Recollection requires greater effort and concentration is difficult. Frequent errors may be made in arithmetical calculation and in the recording of data. Motor performance is impaired. The responses are, in fact, similar to those associated with anoxia or alcoholic intoxication. Although all individuals are to some extent narcotized at deep diving depths, stable persons react to the stress by increased effort and carry out their tasks until consciousness is lost. The unstable individual, on the other hand, is incapable of purposeful effort.

The substitution of helium which has a lower oil-water solubility ratio than nitrogen[31] diminishes the narcotic effect of high air pressures. In a simulated dive to 550 feet in which helium-oxygen mixtures were breathed, the diver remained in good condition throughout and subsequent to the period of the dive.[21] In an air atmosphere divers may lose consciousness at depths of about 350 feet.[152] Case and Haldane[61] have confirmed the finding that air at high pressures (8.6 atmospheres) has an intoxicating effect and that this effect can be abolished by substituting helium or hydrogen for nitrogen.

Although the young Swedish engineer, Arne Zetterström, was killed in a diving accident involving a mishap in decompression, he successfully demonstrated the value of hydrogen-oxygen mixtures in deep-sea diving. Zetterström kept the oxygen percentage at 4 or less in order to prevent formation of explosive mixtures at high pressure. The employment of hydrogen with its fairly high relative lipid solubility may serve to elucidate the possible role of molecular weight in contrast with lipid affinity in the etiology of narcotic action of chemically inert, elementary gases.

Oxygen. The oxygen "blackout" or sudden loss of consciousness without dyspnea when high CO_2-O_2 mixtures are breathed during exercise at pressures as low as 1 atmosphere contrasts with results found with air-CO_2 mixtures, and the confirmation of Campbell's finding[57] that high CO_2 pressures in tissues are associated with high oxygen pressures in the lungs is important.[538, 539] Even at atmospheric pressure the inhalation of pure oxygen was found by both British and German investigators to be associated with an increase in tissue CO_2 tension. It would appear that the hypothesis of Gesell,[115] as expounded in a polemic by Bean,[8] that CO_2 transport is impaired because of the failure of oxyhemoglobin to be reduced could at this time be better evaluated. The mechanism of CO_2 accumulation in tissues still remains unexplained and the solution of this problem no doubt will reveal the cause of oxygen poisoning. Stadie and his coworkers[261] have summarized the results of studies of the inhibitory action of oxygen on enzymatic systems. The irritant level for prolonged inhalation of oxygen has been found to be the same for man as for lower animals, namely, about 60 per cent of 1 atmosphere (428 mm. Hg), and 100 per cent oxygen appears to be toxic (substernal distress, nose and throat irritation) after a period of about twelve hours.[22] No sharp limit can be set, however, since individual variation in response is marked, par-

ticularly when physiologic variables are not controlled. That partial pressure, as Paul Bert demonstrated, is the important consideration rather than percentage is emphasized by one continuous experiment in which pure oxygen at ground level produced some pulmonary irritation (substernal distress) after four hours of inhalation but was well tolerated for a succeeding period of twenty-four hours when the pressure was decreased to 0.25 atmosphere (34,000 feet).[315]

At a pressure of 3 atmospheres absolute, pure oxygen can be inhaled by most individuals at rest for a period of about three hours. Symptoms indicative of pulmonary irritation do not arise but during the fourth hour of inhalation there may occur a rise in blood pressure, increase in pulse rate and a contraction of the visual fields. Pallor may be extreme. Periodic waves of nausea constitute the most common subjective manifestation of oxygen toxicity. In diving operations, therefore, the working pressure for oxygen is limited to 2.5 atmospheres. If pure oxygen is inhaled during exercise at 3 atmospheres pressure, the tolerance time is greatly reduced. Pedaling a bicycle at a rate sufficient to increase normal oxygen consumption threefold limited the inhalation of oxygen to a period of about ten minutes at a depth of 60 feet. At a pressure of 4 atmospheres, oxygen usually can be safely breathed by men at rest for a period of fifteen minutes. Beyond this period convulsive seizures or syncope may occur. While the nervous manifestations of oxygen toxicity are alarming, apparently complete recovery follows when air is again inhaled.

Of prime importance is the fact that exercise increases the toxic effect of oxygen. It is not surprising, therefore, that the administration of pure oxygen to divers working in depths exceeding 30 feet has been associated with symptoms of oxygen toxicity. By contrast, rarely do appreciable symptoms occur in the resting individual at depths up to 60 feet for periods of two to three hours. In the wet tank symptoms are also more prevalent than in the dry chamber, probably because of the factor of exercise and the accumulation of carbon dioxide. Despite these limitations, oxygen has proved to be of tremendous value in the later stages of decompression and in the treatment of compressed-air illness. It is unfortunate that tolerance times applicable to men at rest have been applied to men at work.

In the administration of oxygen proper humidification and comfortable masks are essential for prolonged inhalation. The greatest hazard in oxygen administration in chambers is the danger of fire. The proper precautions must therefore be strictly enforced.

Effect of Carbon Dioxide. Carbon dioxide enhances the toxicity of oxygen and the narcotic effect of nitrogen. In the diver's helmet the percentage of carbon dioxide must be reduced to a minimum. During rapid descent in deep-sea diving momentary vertigo and confusion are in part attributable to the accumulation of alveolar carbon dioxide as the air pressure rapidly rises in the lungs. With respect to work in compressed air, empirical evidence points to a higher incidence of bends in association with a rise in the carbon dioxide level. The *effective* carbon dioxide percentage should not exceed 1.5 per cent although percentages of carbon dioxide up to 5 are fairly well tolerated at normal barometric pressures for periods of at least sixty hours.[431]

SYMPTOMS AND SIGNS OF DECOMPRESSION SICKNESS

The major symptoms or signs of decompression sickness are pain (bends), asphyxia (chokes) and paralysis. Minor effects are pruritus, rash and fatigue. The parts of the body chiefly involved are the extremities (bends), the cardiorespiratory system (chokes) and the spinal cord.

Etiology. The primary role of bubbles in producing the symptoms of decompression sickness began to be known at the time of Robert Boyle in 1670.[50] Convincing experimental data, however, were not available until the work of Paul Bert, about 1880. Van Musschenbroek (1692–1761), professor in Leyden, believed[214] that gas bubbles block the blood vessels and interfere with the blood circulation, which is particularly damaging to the brain. Hoppe-Seyler[156] thought that he had first discovered the formation of bubbles in blood; the work of Boyle and van Musschenbroek was unknown to him. Comparing the symptoms of men who had worked in compressed air with those of animals under decreased pressure, he drew a clear picture of the blockage of pulmonary vessels by gas and the inability of the heart to propel the blood under these conditions. He found that the bubbles—consisting of N_2 and a little CO_2—formed when the normal atmospheric pressure was lowered and advocated the use of recompression in the treatment of decompression sickness in order to absorb the free gas and to reestablish circulation.

The mechanism by which intravascular and possibly extravascular bubbles produce symptoms is yet to be determined; ischemia, vascular distention and local irritation have been considered. That bubbles in subcutaneous fat tissue are not productive of pain is inferred from the following observations. If the procedure termed denitrogenation is employed for a period of one hour to remove most of the gaseous nitrogen dissolved in body fluids, an individual may be rapidly exposed to an altitude of 46,000 feet without developing symptoms. However, subcutaneous emphysema can be produced by the mild trauma incident to periodic inflation of a sphygmomanometer pressure cuff about the arm. The subcutaneous bubbles do not give rise to pain and the proof of their presence is that crepitus elicited by palpation will disappear with increase of ambient pressure, i.e., altitude descent.[315]

Further suggestion that the gas in fat does not cause symptoms is the observation that pain arising from too rapid decompression in helium atmospheres is similar to the pain occurring in compressed-air illness. Helium, as previously pointed out, is present in relatively small amounts in fat or diffuses rapidly out of fat. In helium diving care must be exercised to avoid too rapid decompression in the early stages of ascent. Bends have occurred at depths of 90 to 180 feet because of too rapid ascents from 400 feet.

Pathologic Changes. Permanent lesions attributed to intravascular or extravascular bubbles have been found in the spinal cord and in the shafts and epiphyses of long bones. The nervous symptoms, according to Heller et al.,[142] are the result of ischemic processes (as demonstrated first by Paul Bert) in the white substance of the cord. These authors considered that the formation of bubbles in the blood leads to circulatory disturbances analogous to those produced by compression of the aorta, by injection of

solids, or by "endarteritic changes either of a superficial nature or affecting the most sensitive nerve elements, or to changes of varying intensity designated earlier as myelitis although their origin clearly indicates that they have nothing to do with inflammatory processes." Boycott et al.,[49] however, concluded that areas of necrosis in the spinal cord were caused by extravascular bubbles. This matter of bubble location is of the greatest importance since, if bubbles form extravascularly in nervous tissue, every decompression holds the probability of serious consequences. With reference to the distribution of areas of injury, there is general agreement that the less vascular areas (lower thoracic and lumbar segments) and those high in fat (myelin) content are more often subject to injury.

With reference to osseous and arthritic lesions, Twynam[278] in 1888 reported bone necrosis in caisson disease and Bornstein and Plate[47] in 1911 pointed out that chronic arthritis could arise from repeated embolic and nutritional injury following too rapid decompression. Plate[224] also reported pathologic changes in bone demonstrated by x-ray. That bubbles can be present in marrow or within the cortex of bone is inferred from the pertinent observation that recompression, especially if it is too rapid, may intensify the pains of bends. This type of pain is believed to arise from a difference in pressure, or an actual "squeeze" of bone marrow tissue, resulting from compression of bubbles which is so rapid that body fluids cannot immediately replace the suddenly diminished gas volume within the bone cortex. Recent reports of characteristic lesions in bone[270] appearing in caisson workers support the view that the symptoms giving rise to bends originate, in part at least, from ischemic changes in bone. Kahlstrom et al.,[172] Coley and Moore,[69] and Rendich and Harrington[231] describe lesions in diaphyses and epiphyses of long bones complicated by joint involvement and attributed to aseptic necrosis of bone or interference with nutrition occurring secondary to the interruption of blood supply by liberated nitrogen gas.

However, the etiologic relationship between the presence of these lesions and embolic injury must be corroborated by additional findings and animal experiments before final conclusions can be drawn. In divers suffering repeatedly from experimental bends, Commander Walter Welham and the writer found no characteristic lesions in a roentgenologic study at different periods following injury.

Macroscopic and Microscopic Observations. In dogs rapidly decompressed from high atmospheric pressure (60 pounds gauge), small bubbles can be observed, first circulating rapidly through cutaneous arteries and veins; later bubbles of gradually increasing size are found to slow down and eventually stop circulation.[24]

In monkeys fitted with lucite calvaria according to the method of Sheldon and Pudenz,[248] the formation and movement of bubbles in the cerebral blood vessels can be observed following rapid decompression. Similarly, Wagner,[453] at the Naval Medical Research Institute, has observed through a Forbes window the movement of gas bubbles in the pial blood vessels of cats. The bubbles always appeared first in the arteries, and later, as the blood flow decreased, in the veins. Sludge formation, or the close grouping in compact masses of red blood cells separated by zones of clear plasma,

accompanied the reduction in blood flow. This clumping of cells described previously by Swindle[268] is a phenomenon that Knisely[445] has demonstrated under a variety of conditions associated with slow circulation, plasma loss and cell packing.

In the histologic studies of Gersh,[113] intravascular gas bubbles occurred in all tissues and organs of rapidly decompressed guinea pigs but were far more numerous in those rich in fat. Extravascular bubbles were observed

Table 7. Percentage Incidence of Symptoms and Signs of Decompression Sickness [173, 192]

	Caisson Workers			Divers
	Heller, Mager, von Schrötter	Keays	Levy	U. S. Navy
Total no. of symptoms	245	3692		176
Number of patients	198		680*	159
Central nervous system:				
Brain:				
Hemiplegia		0.11		
Aphasia	0.4			1.14
Auditory disturbances				
Ménière's symptom complex	5.9			
Deafness	0.82			
Visual disturbances				5.11
Vertigo	1.63	5.33	6.5	2.27
Unconsciousness		0.46		1.14
Spinal cord			1.6†	
Sensory disturbances	4.2	1.00		
Motor paralyses	11.7	0.90		0.57
Combined		0.26		
Cardiorespiratory system:				
Chokes	5.6	1.62	0.1	3.98
Substernal distress				
Asphyxia				
Condition of shock, prostration		1.26		
Extremities, shoulders and hips:				
Pain (bends)	69.6	89.00	91.7	72.16
Numbness				
Weakness				
Skin manifestations:				
Rash, itching				13.64
Permanent injury (no. of men)	6		2	
Death (no. of men)	2	20	2	0

* 1,361,461 decompressions.
† Central nervous system involvement.

in tissue rich in fat and in the lipid matter of the adrenal cortex, in the myelin sheaths of nerve fibers, in bone marrow, and in the connective tissue surrounding the tendons of the long muscles. Following dives—especially helium dives—the upper extremities and shoulders are frequently afflicted with bends. Swelling of the arms is not uncommon and crepitus has been elicited along the brachial veins, suggesting blockage of venous return as the cause of the edema.

Incidence. Bends occur (Table 7) most frequently, followed by skin manifestations, vertigo, chokes and visual symptoms.[173, 192] Paralysis occurs

only occasionally in divers but was reported not infrequently in caisson workers about fifty years ago.[142] In the classification of symptoms, no attempt is made to define the part of the body primarily injured. Thus under "brain" are listed visual disturbances and unconsciousness which may have been caused by cardiorespiratory impairment rather than by emboli. There is likewise doubt as to whether the sensory disturbances listed under "spinal cord" arose primarily from spinal cord injury, and conversely pain designated as bends may be due to a central rather than to a peripheral lesion.

Distribution of Pain (Bends). In caisson workers, bends in the lower extremities, chiefly the knee, predominated. In a series of 131 Naval dives of comparatively short exposure, about 70 per cent of the painful symptoms were in the upper extremities and shoulders. In seventeen prolonged saturation exposures, however, bends occurred five times more frequently in the lower than in the upper extremities. Apart from the apparent influence of duration of exposure to compression on location of symptoms, it has been observed that an exercised part of the body may be more susceptible to bends.

Time of Onset of Symptoms. Keays[173] reported that 85.1 per cent of symptoms appeared within one hour after decompression. In 14.9 per cent, symptoms were delayed beyond one hour. The time of onset of symptoms in 547 cases was as follows:

1–2 hrs.	225 cases	10–11 hrs.	2 cases
2–3 hrs.	108 cases	11–12 hrs.	2 cases
3–4 hrs.	69 cases	12–13 hrs.	1 case
4–5 hrs.	38 cases	13–14 hrs.	1 case
5–6 hrs.	26 cases	14–15 hrs.	2 cases
6–7 hrs.	16 cases	15–16 hrs.	1 case
7–8 hrs.	13 cases	16–17 hrs.	1 case
8–9 hrs.	4 cases	17–18 hrs.	1 case
9–10 hrs.	6 cases	18–19 hrs.	1 case

In a series of forty-six Naval dives of less than fifty-five minutes' exposure, it is of interest to note that the onset of symptoms was delayed not infrequently beyond one hour, and in one case seven hours, despite the short decompression time of less than three minutes' duration.

Effect of Exercise and Other Variables Affecting Bubble Formation. After exposure to high pressure and high altitude, the factors responsible for bubble formation fall into two groups. In the first are conditions which increase gas content of tissues—namely, the amount of fat, the degree and duration of exposure to pressure, the amount of work performed and, in rapid ascent to high altitudes, exercise which (among other effects) serves to introduce more carbon dioxide into the circulation. In the second group are variables affecting the circulation of blood and the transport of gas from the tissues. Thus age, time of day, temperature, fright, injury of tissue and the post-alcoholic state, all affect what may be termed "effective blood flow" through tissue.

In the numerous exposures in the low-pressure chamber to simulated altitudes above 30,000 feet, the circulatory factors have been carefully evaluated. That age is a factor in the sense that the individual of 18 years

is less susceptible to bends than is an individual of 25 years emphasizes the importance of adequate circulation as inferred from metabolic rate. The findings that bends are more apt to occur in the morning than in the afternoon, that fright produces peripheral vasoconstriction to interfere with gas transport, and that bends frequently occur at the site of old injury, all tend to emphasize the importance of the factor of effective blood flow and serve to explain not only the variation between individuals but variation in the same individual when subjected to the stress of decompression. There are the same difficulties in ascertaining individual susceptibility to decompression sickness in divers as in aviators. In caisson work and diving, empirical data establish for man the importance of age, degree of obesity, post-alcoholic state, effect of temperature, and influence of exercise during the pressure exposure. No conclusions can be drawn in regard to other factors. Of greatest importance, however, is the question of the effect of exercise *during or following the decompression period.* Physicians[44] with experience in caisson work have, in fact, pointed out the value of exercise following decompression and divers routinely have taken some exercise on the "stage" during decompression. When it was proved that exercise definitely increased susceptibility to altitude bends and chokes, controlled tests were carried out at the Experimental Diving Unit by Van Der Aue and his coworkers.[451] The results of rapid decompression after prolonged exposure at a critical depth indicated that exercise following exposure increased susceptibility to bends.

DETAILED SYMPTOMATOLOGY

Bends. The most common manifestation of compressed air illness is a dull, throbbing type of pain, gradual in onset, progressive and shifting in character, and frequently felt in the joints, or deeply in muscles and bones. Pain or pains of this nature are referred to as "bends," a term established by usage to denote a well-recognized clinical entity. Prior to the onset of pain there may be—particularly in the joints—paresthesia frequently described as numbness or merely an awareness that "something is not right." Skin temperature may fall as the part involved becomes blanched in appearance. In association with bends and chokes, fatigue may take the form of an exhausting malaise combined with chills, fever and sweating. Minor symptoms as skin rash and pruritus occur with regularity if the skin is chilled during decompression.

Paralysis. The most serious complication of decompression sickness is paralysis. Dogs rapidly decompressed from high pressures and then only partially recompressed (to a degree that prevents death from asphyxia) frequently develop paralysis of the hind legs, foot drop, a spastic type of gait and paralysis of the bladder musculature.[23] In man a similar spastic paraplegia or monoplegia involving the lower extremities may be preceded or associated with knifelike pains around the chest, and pain in the abdomen and lumbar areas radiating toward the lower extremities. These sensory disturbances may be so severe as to cause sudden collapse. Immediate and prolonged recompression usually brings about rapid recovery even following paraplegia. Insufficient recompression may be followed by residual symptoms of many months' duration.

There is a remarkable lack of cerebral involvement even under conditions of widespread embolism. Vertigo, deafness, occasional aphasia and transient visual disturbances have been recorded. In contrast with spinal cord lesions, permanent impairment referable to lesions of the brain is rare. Clinical conditions manifesting symptoms similar to those associated with the presence of air emboli in the spinal cord are tabes dorsalis, and arteriosclerosis of the terminal aorta involving the lumbar segmental arteries.

Chokes and the Shock Syndrome. The most interesting manifestation of decompression sickness is a type of asphyxia designated most aptly by the early caisson workers as "chokes." In comparison with bends, chokes occur less frequently since they apparently require the accumulation of quantities of gas eliminated from the arterial circulation and extravascular tissues into the large veins, the right side of the heart and pulmonary vessels. Thus, several hours of complete well-being following decompression may elapse before the appearance of symptoms. The earliest symptom of chokes, namely, a sensation of substernal distress felt only during deep inspiration and especially during inhalation of tobacco smoke, serves to elicit paroxysmal coughing. This sign has proved to be invaluable. The sensation of substernal distress may be only transient or it may progress to frank asphyxia. Normal breathing becomes shallow, rapid and then dyspneic. The skin becomes cyanotic, or ashen gray, cold and clammy. The pulse beat, at first slow and pounding, becomes thready. Paroxysmal attacks of coughing or true "chokes" may precede loss of consciousness. The picture presented is one of "shock" and represents a transformation within a period usually of several hours from a state of health and vigor to one of incapacitation without any apparent trauma having been inflicted upon the individual. It is this condition that not only frequently supervenes in divers when the premonitory symptoms of bends are ignored and treatment delayed but that may also be responsible for circulatory collapse and deaths which occasionally occur following too rapid decompression in the low-pressure chamber.

COMPARISON OF DECOMPRESSION SICKNESS AT ALTITUDE WITH THAT FOLLOWING HIGH PRESSURE EXPOSURES

Two chief differences are absence or rareness of spinal cord involvement and the more rapid amelioration of altitude symptoms when ambient pressure is increased. The absence of residual symptoms referable to the spinal cord may be due in part to the immediate recompression from altitude to ground level following the first appearance of symptoms indicative of central nervous system involvement. The more rapid amelioration of altitude symptoms (more rapid absorption of bubbles) may be expected on the basis of a greater water and carbon dioxide content of the altitude bubbles as well as a smaller number of bubbles in comparison with those forming after high-pressure exposures.

With reference to the mild symptoms, bends and substernal distress, divers are unable to distinguish differences in the character of the pain induced in the low-pressure chamber or following diving.[16] Frequently bends occur in the same areas in divers subjected to both high and low pressures.

In the more serious manifestations of decompression sickness pertaining to vision, cardiorespiratory involvement, and the state of collapse and shock, there appears to be confusion not only as to the mechanism of injury but whether or not gas bubbles play an etiologic role. Thus, in a discussion of complications of decompression sickness, Engel et al.[327] stated, "The syndrome of scotomata and headache was characterized by homonymous scintillating scotomata with objective visual field defects followed by contralateral hemicranial headaches. It was always preceded by symptoms of decompression sickness, most often by chokes. Visual disturbances began more often after descent than at altitude; once initiated, the course, intensity and duration were independent of altitude. There was no relationship of this syndrome to syncope or anoxia. Evidence is presented to show that the syndrome is vascular in nature, possibly on a reflex or humoral basis; and that it is not due to the direct mechanical effect of bubbles, either intravascularly or in the tissues."

In a review of fifty-five cases of collapse reported from various altitude training units, Masland,[387] in consideration of the tremendous diversity of symptoms, concluded, "On no single point do all cases agree. They vary from cases of sudden loss of consciousness, developing with few associated symptoms, to cases in which profound circulatory collapse developed without any impairment of consciousness. In some instances, symptoms of aeroembolism were prominent, in others they were absent. It is certain that no single disease entity can be held responsible for such a varied group of physiological disturbances. The one common factor in them all is that the cases developed at high altitude or at least following an altitude chamber flight."

In view of the importance of the proper treatment of these patients, essentially the inhalation of oxygen and recompression, a summary of Masland's excellent classification and description of these cases is presented.

1. The first group comprises those cases in which reflex vasomotor collapse is a prominent feature. The usual picture is that of an individual who develops severe pain while at altitude. The painful stimulus is usually bends or chokes, but it may also be due to abdominal gas, sinusitis or aerotitis. As the pain becomes severe, the subject becomes pale, breaks into a cold sweat, and complains of faintness. When he gets up to move into the lock, he faints. At first the pulse is often unobtainable. Later it is found to be slow. There is a transient fall in the blood pressure. Recovery is rapid with the relief of pain, but the slow pulse (often 50, occasionally 40) may persist for as long as 24 hours before returning to normal. Doses of atropine, gr. 1/150, do not alter the pulse. Larger doses have not been reported. Ephedrine sulphate may elevate the blood pressure.

2. The second group of cases comprises those in which delayed circulatory collapse was a prominent feature. In each of the 14 cases in this group some symptom of aeroembolism preceded descent. In some cases, collapse was immediate and occurred in the chamber. In others, the chamber episode was minor in character, and shock developed following a relatively free interval of from two to four hours. Circulatory failure, accompanied by pronounced hemoconcentration, persisted in some cases for as long as twenty-four hours. The secondary shock picture differs markedly from the primary. In the latter, the pulse is slow; in the former, rapid. Whereas in primary shock the disturbance appears to be chiefly vasomotor in origin and any painful stimulus may be responsible, in secondary shock, loss of blood volume is the chief problem and the condition is seen only in those cases having symptoms of aeroembolism. In several instances, primary shock with slow pulse has been observed

immediately after descent. The subject improved from this but later developed rapid pulse, fall in blood pressure, and a secondary shock picture. An example of this is reported from Selman Field, 24 April 1943.

3. The third group of cases are those in which there is evidence of primary involvement of the nervous system. In most of the subjects this was accompanied by primary or secondary shock or both, but in a few, little general reaction was observed. Involvement of the nervous system was always associated with other evidences of aeroembolism (either bends or chokes) and was most frequently seen in association with chokes. The commonest symptom of central nervous system involvement was disturbance of vision. Figures as to the incidence of visual symptoms are misleading, chiefly because the symptoms are so evanescent that they are difficult to evaluate and are often overlooked. However, complaints of scotomata or blurred vision, with or without field cuts, are encountered in nearly one-third of all collapse cases requiring hospitalization (at the School of Aviation Medicine).

4. The fourth group of cases comprises those in whom the outstanding disturbance appears to be cardiac in origin. There are three cases in this group, one coronary occlusion, one paroxysmal auricular fibrillation and one "short PR, BBB" electrocardiographic syndrome. The diversity of symptoms noted again emphasizes the difficulty in explaining them on the basis of a common etiological factor.

Since these manifestations—if we exclude faintness and syncope caused by psychic instability, anoxia or pain in the sinuses and ears—are seen in divers and caisson workers following compressed air exposures and since many of the signs, particularly the progression from a state of well-being to a condition of shock, can be reproduced experimentally in dogs, it seems appropriate to review experimental data[18] obtained some years ago at the Harvard School of Public Health.

Anesthetized dogs in complete equilibrium (100 per cent saturation) with the partial pressure of nitrogen in air at 45 pounds gauge pressure can be decompressed in 10 seconds to atmospheric pressure without disturbances of respiration or blood pressure, indicating that either nitrogen bubbles have not formed in the blood or that they are not of sufficient size and number to cause symptoms. That bubbles can exist in the blood stream without producing symptoms is proved by numerous experiments in which small quantities of air have been introduced intravenously without harmful effects.

Rapid decompression, however, of dogs previously exposed for one and one-half hours at 60 pounds gauge pressure may be associated, after an interval of about one half hour, with a moderate increase in respiratory rate. The return of breathing to the initial rate indicated that the degree of bubble formation was within the dogs' range of tolerance and the gas in bubble form was eliminated in the lungs. At the same time that rapid breathing begins, bubbles may be seen moving through cutaneous arteries and veins. A second exposure, however, of two hours' duration followed by rapid decompression results in bubble formation of sufficient magnitude to fill the right ventricle and pulmonary blood vessels, thereby bringing about immediate asphyxial death. This acute asphyxia is not preceded by tachypnea. As asphyxial rise in blood pressure to 140 mm. Hg is observed, followed by a rather precipitous fall to 40 mm. Hg.

Relationship Between Rapid Breathing and Pulmonary Gas Embolism. The symptoms from multiple gas emboli as produced in these experiments are remarkably similar to those associated with pulmonary embolism arising from intravenous starch injections in goats, and from starch or seed

injection into dogs. Of particular interest is the mechanism underlying the production of rapid, shallow breathing. Binger and his associates were able to distinguish rapid breathing due to obstruction of the pulmonary arterioles and capillaries from that due to obstruction of the larger branches of the pulmonary artery. They concluded—with reference to the etiology of rapid breathing—that obstruction of arterioles and capillaries initiated

*Table 8A. Analysis of Oxygen Content of Blood from Anesthetized Dogs Rapidly Decompressed from High Pressure Atmospheres**

Exposure	Period	Volume Per Cent Oxygen Content		Arterial Venous Difference	Oxygen Capacity	Per Cent O_2 Saturation		Pressure CO_2 Arterial Blood
		Arterial	Venous			Arterial	Venous	
9†	Control	15.9	10.1	5.8	17.7	90	57	45
	Following decompression	5.4	0.5	4.9	22.4	24	.2	59
	Recompression	17.9	7.9	10.0	20.3	88	39	
	Following recompression	5.9	2.3	3.6	22.8	26	10	
10‡	Control	20.6	17.0	3.6	22.8	90	75	
	Following decompression	14.6	7.7	6.9	26.1	56	30	
	Recompression	31.7§	20.0	11.7	27.3	100	64	
	Following recompression	26.9	7.3	19.6	29.8	90	24	

* Data from Behnke et al.[12]
† Air inhaled during two-hour recompression period.
‡ Oxygen inhaled during two-hour recompression period.
§ 4.4 volumes per cent oxygen in physical solution.

Table 8B. Physiologic Effects of Too Rapid Decompression (5–6 Seconds) of Dogs Exposed to 65 lbs. sq. in. Gauge Pressure for a Period of 105 Minutes

	Arterial pCO_2 (1)	Resp. Rate (2)	% Sat. HbO_2 (3)	Blood Pres. (4)	Arterial Venous O_2 Dif. (5)	O_2 Capacity (6)
Control period	45	20	90	116	3.6	22.8
Post compression period	59	142	24	140 to 30	6.9	26.1
Recompression period	56	40	88	90	11.7	27.3
Period following recompression	59	125	26	100*	19.6	29.8

* Oxygen was inhaled during the two-hour recompression period.

reflex stimuli, while obstruction of the pulmonary artery and its branches produced anoxemia. The reflex stimuli were thought to be the result of a particular lesion in the lungs, namely, congestion and edema which through a limitation of lung expansion probably initiated impulses through the vagal nerve endings. The mechanism underlying anoxemia was thought to be a more quickened blood flow through a diminished vascular bed resulting in a change in the quantitative relation of blood flow to the vascular diffusion area in the lungs.

The results of our experiments, in contrast with the work of Binger and his associates, do not conclusively distinguish between anoxemia and the

mechanical effect of bubbles in producing rapid breathing since both factors are removed by the same treatment, i.e., bubble absorption by compression and oxygen breathing. The rapid breathing is, however, considered to result primarily from reflex stimuli arising from the mechanical action of gas bubbles in the pulmonary vessels, and from anoxemia. Thus a respiratory rate of 90 following decompression will return to 20 if oxygen is administered and the dog recompressed to 30 pounds gauge pressure. As the pressure is slowly reduced, the respiratory rate again increases. At atmospheric pressure, the rate rises to 40 and then to 52 if oxygen is replaced by air. The continuance of the experiment by a third period of compression reduces the rate to 22, from which, following a terminal decompression, it rises to 100.

The degree of tachypnea is of such magnitude as to indicate that reflex stimuli arising from the mechanical action of gas bubbles in pulmonary vessels play a more important role than does anoxia. The failure of a high concentration of carbon dioxide in the arterial blood (Table 8) to change the pattern of the rapid shallow breathing is further evidence of the powerful effect of these reflex stimuli. According to Heller et al.,[142] the effect of gas in the pulmonary vessels is to displace blood and to inflate the lungs intravascularly, producing a decreased alveolar ventilation. The shallow breathing may therefore be tentatively looked upon as primarily the result of reflex stimuli initiated by alternate distention and contraction of gas-containing vessels during inspiration and expiration respectively. Gersh has demonstrated the remarkable distortion that occurs in the gas-filled pulmonary vessels of the guinea pig.

In man, limitation of deep inspiration may be considered to be a sign pathognomonic of the presence of bubbles in pulmonary vessels. Both divers and aviators, following too rapid decompression, have been affected by restricted breathing. The sense of substernal irritation, tracheal dryness and pain accompanied by coughing when deep inspiratory effect is made stands in contrast with the absence of symptoms if breathing is shallow. The disappearance of symptoms with recompression or sometimes with oxygen inhalation and the presence of pulmonary bubbles in dogs in association with rapid, shallow breathing supports the view that the substernal distress in man is caused by bubbles. In divers and aviators exposed to pressure changes the limitation of respiration serves as a premonitory sign that asphyxia and circulatory collapse may be imminent.

Changes in Blood Pressure and Pulse Rate. During the period of tachypnea following rapid decompression both pulse rate and blood pressure fall (Fig. 19). That these asphyxial phenomena are in fact reversed by recompression, which serves to compress the obstructing bubbles, is apparent. A temporary rise in blood pressure usually preceded the precipitous fall. This rise may be due to increased peripheral resistance as a result of multiple embolism. The abrupt fall in blood pressure is certainly, in part, dependent upon impaired blood flow to the left ventricle when the pulmonary circuit becomes filled with gas. Not only is it probable that mechanical blockage of blood flow caused by bubbles takes place in the pulmonary circuit but the force of contraction of the right ventricle may be dissipated in compressing gas bubbles instead of propelling a fluid column.

The frequent precipitous fall in blood pressure is abruptly checked by the reapplication of pressure (Fig. 19) and a rise usually occurs, although seldom to the initial level. The incomplete recovery of blood pressure is not related to anoxemia or to the presence of bubbles since pressure combined with oxygen does not bring about an improvement. It is interesting to note that, after the period of recompression, blood pressure may be maintained at a fairly high level associated with a degree of anoxemia (oxygen saturation of the hemoglobin 26 per cent) which would appear to be incompatible with life (column 3, Table 8*B*). The subnormal blood pressure of the recov-

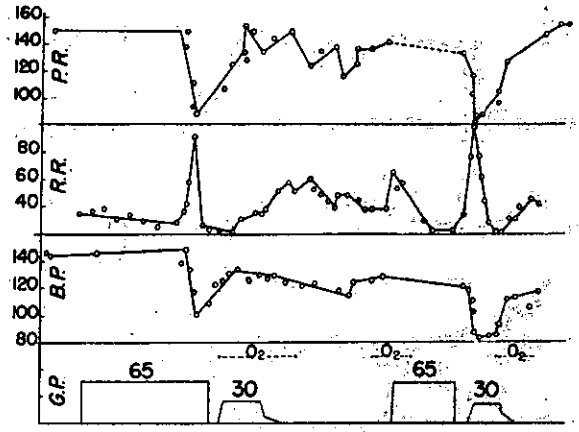

Fig. 19. Alterations in blood pressure, respiratory rate and pulse rate of dog decompressed in ten seconds from a gauge pressure of 65 lbs. after 1.5 hours' exposure followed by recompression (interval of ten minutes) to a pressure of 30 lbs. (oxygen) for twenty-five minutes. Pressure was then lowered to atmospheric in twelve minutes, and oxygen inhalation continued for seventeen minutes. Preceded by period of oxygen breathing (thirty minutes), compression of dog was again carried out at a pressure of 65 lbs. for period of forty-five minutes, followed by ten seconds' decompression. After interval of twelve minutes dog was recompressed to a pressure of 30 lbs. for twenty minutes (oxygen inhalation).[23]

ery period is conceivably accounted for by previous injury to the right ventricle (dilation) as a result of excessive resistance in the pulmonary circuit and of impaired circulation through the coronary vessels during the asphyxial period. Another possible factor in preventing complete blood pressure recovery is paralysis of splanchnic vascular tone from spinal cord injury. In the experiments of Heller, Mager and von Schrötter, spinal cord injury following a deprivation of blood supply was a frequent consequence of multiple gas emboli. Under the pressure conditions existing in our experiments, paralysis, usually of the hind legs, occurred regularly in unanesthetized dogs.

The maintenance of life under the conditions of these experiments depends, essentially, upon the integrity of the right ventricle, and upon its ability to propel blood through an obstructed pulmonary bed. The absorption of bubbles by compression and by oxygen inhalation leaves the animal in good condition as observed in experiments on unanesthetized

dogs, unless irreparable damage has been done to the heart by oxygen lack or increased pulmonary resistance, or to the spinal cord from ischemia.

Oxygen and Carbon Dioxide Content of Blood. Blood samples in these experiments were drawn from the femoral artery and from the right atrium or ventricle by means of a glass cannula inserted into the external jugular vein. Of particular interest was the occurrence of hemoconcentration shown by increased oxygen capacity of blood (Table 8*A*). In some tests it amounted to as much as a 30 per cent increase in cell volume. The hemoconcentration was thought to be due to a loss of fluid through capillaries damaged by asphyxia and possibly an increased mobilization of red blood cells from the spleen. The blood, moreover, was difficult to withdraw because of the tendency to clot. In histologic sections of the lungs, cell packing in blood vessels was a consistent finding. The increased arterial-venous oxygen difference is an indication of the slow circulation rate. The low values for arterial oxyhemoglobin reflect the derangement of pulmonary ventilation and circulation by the gaseous emboli. The phenomenon of especial interest is the continuance of cardiac contractions despite the presence of the greatly reduced hemoglobin in the arterial blood.

PRINCIPLES UNDERLYING PREVENTION OF DECOMPRESSION SICKNESS

The prevention of decompression sickness depends upon the elimination of nitrogen absorbed during exposure to increased barometric pressure by a procedure of decompression regulated to prevent excessive bubble formation in the blood and possibly other tissues.

Capacity of Body to Absorb Gases. The recognition by Haldane[49] and Vernon[281] that body fat absorbs about five times more nitrogen than the body fluids was the critical consideration with reference to the time required for saturation and desaturation of the body and hence for the formulation of a safe decompression procedure. The small amount of nitrogen taken up by hemoglobin does not affect appreciably the total gas content of the body but is obviously important in the transport of this gas. The ratio, then, of the solubility of a gas in water (blood) and in fat will be a major factor responsible for an increase in desaturation time of nitrogen (oil-water solubility ratio 5.3 to 1) compared with helium (1.7 to 1).

That fat constitutes a gaseous reservoir is apparent from measurements of nitrogen elimination. For example, the nitrogen content of a diver weighing 70 kilograms was 1076 cc. On the basis of his specific gravity (1.060) the body fat may be computed as 20 per cent of the total body weight from the formula[9]:

$$\text{Fat (per cent of body wt.)} = 500\,(1.100 - \text{sp. gr.})$$

The value 1.100 is taken as the density of the lean body mass. The body fluids may be estimated as 72.4 per cent of the lean body mass or 40.54 kg. (0.724). The nitrogen content, then, of the fluid and fat components of the body may be computed from the product of the solubility coefficients and component masses as:

$$\begin{aligned} 14.00 \times 55.7 &= 779.8 = N_2 \text{ in fat} \\ 40.54 \times 9.0 &= 364.9 = N_2 \text{ in body fluids} \\ \text{Total} \quad & 1144.7 = \text{Estimated total } N_2 \end{aligned}$$

Nitrogen Elimination Data. During the course of oxygen inhalation the dissolved gaseous nitrogen can be accurately measured for a period of six to nine hours following a short period (several minutes) of lung rinsing

Table 9. Nitrogen Elimination from a Diver Exposed to a Depth of 100 Feet for Seventy-five Minutes and Decompressed at Various Stops for a Period of Twenty-seven Minutes Compared with His Nitrogen Elimination after a Thirty-minute Exposure at 100 Feet[302]

Exposure	Stop	Tests	Nitrogen Eliminated (cc.)		
			At Stop 3–30 min.	Surface 33–90 min.	Total
75 min.: 100 ft	20	1	1478	834	2312
75 min.: 100 ft	50	2	1533	957	2590
75 min.: 100 ft	100	2	1415	739	2154
30 min.: 100 ft	44	1	1343	548	1891
30 min.: 100 ft	50	1	1312	565	1877
30 min.: 100 ft	66	1	1341	522	1863
			Surface	*Surface*	
30 min.: 100 ft	0*	1	626	401	1027
30 min.: 100 ft	0*	1	1191	499	1690
30 min.: 100 ft	0*	1	892	856	1748
30 min.: 100 ft	0*	1	1147	511	1658

* 2 minutes decompression from 100 feet to the surface.

Table 10. Maximal Exposure Time at Various Depths Followed by Minimal Decompression, i.e., Rate of Ascent not Less than 50 feet/min. Divers Were at Rest During Depth Exposure and Came to Surface (Wet Pressure Tank) Wearing the Submarine Escape Lung Charged with Air or Oxygen Two Minutes Prior to Ascent. (Data of Hawkins et al.[141])

Series	Depth of Dive (feet)	No. of Subjects	No. of Exposures	Length of Exposure (min.)	Theoretical Ratio of Ambient Pressure to Gas Pressures in Tissues with the Following Half Saturation Time				
					5 min.	10 min.	20 min.	40 min.	75 min.
2	100	8	600	34½					
7		8	56	36½					
9		8	46	39½					
11		8	408	42	3.8–1	3.8–1	3.3–1	2.6–1	2.0–1
10	150	8	4	18					
3		8	80	18½					
8		8	56	19½					
16		6	42	26					
15		5	408	27½	4.9–1	4.7–1	3.8–1	2.8–1	2.1–1
4	167	8	95	16½	5.1–1	4.3–1	3.2–1	2.3–1	1.8–1
5	185	8	56	13½	5.3–1	4.3–1	3.0–1	2.2–1	1.7–1
6	200	8	133	13	5.5–1	4.5–1	3.2–1	2.3–1	1.7–1

(Tables 11, 12). What we are especially interested in, however, is the time required for 99 per cent desaturation. Previous methods of analysis have enabled us to measure amounts not less than 5 cc. of gas per hour

diffusing from the body. Radio-gas technics, however, should provide a sharper end point for this important determination. Whether or not, for example, the slowest tissue half saturates or desaturates in 75, 90 or 120 minutes (98 per cent saturation in 450, 540 and 720 minutes) is the basis for the calculation of safe decompression tables for long exposures or for shorter exposures at deep diving depths.

Table 11. Treatment of Decompression Sickness and Traumatic Air Embolism

Stops		Bends—Pain Only				Serious Symptoms	
Rate of *descent*—25 ft. per min. Rate of *ascent*—1 minute between stops		Pain relieved at depths *less than* 66 ft. (29.4 lb.) Use column 1-A only when O_2 is not available.		Pain relieved at depths *greater than* 66 ft. (29.4 lb.). Use column 2-A only when O_2 is not available. If pain does not improve within 30 min. at 165 ft. (73.4 lb.) the case is probably *not* bends. Decompress on column 2 or 2-A.		Serious symptoms include any one of the following: 1. Unconsciousness 2. Convulsions 3. Weakness or inability to use arms or legs 4. Any visual disturbances 5. Dizziness 6. Loss of speech or hearing 7. Severe shortness of breath or chokes	
						Symptoms *relieved* within 30 min. at 165 ft. (73.4 lb.)	Symptoms *not* relieved within 30 min. at 165 ft. (73.4 lb.).
Lb.	Ft.	Column 1	Column 1-A	Column 2	Column 2-A	Column 3	Column 4
73.4	165	....	....	30(Air)	30(Air)	30(Air)	30 to 120(Air)
62.3	140	....	....	12(Air)	12(Air)	12(Air)	30(Air)
53.4	120	....	....	12(Air)	12(Air)	12(Air)	30(Air)
44.5	100	30(Air)	30(Air)	12(Air)	12(Air)	12(Air)	30(Air)
35.6	80	12(Air)	12(Air)	12(Air)	12(Air)	12(Air)	30(Air)
26.7	60	30(O_2)	30(Air)	30(O_2)	30(Air)	30(O_2) or (Air)	6 hr.(Air)
22.3	50	30(O_2)	30(Air)	30(O_2)	30(Air)	30(O_2) or (Air)	6 hr.(Air)
17.8	40	30(O_2)	30(Air)	30(O_2)	30(Air)	30(O_2) or (Air)	6 hr.(Air)
13.4	30		60(Air)	60(O_2)	120(Air)	12 hr.(Air)	1st 11 hr. (Air) Then 60(O_2) or (Air)
8.9	20	5(O_2)	60(Air)		120(Air)	120(Air)	1st 60(Air) Then 60(O_2) or (Air)
4.5	10		120(Air)	5(O_2)	4 hr.(Air)	120(Air)	1st 60(Air) Then 60(O_2) or (Air)
Surface							

Time at all stops in minutes unless otherwise indicated.

If symptoms return while breathing air *during* treatment with any of the above columns, recompress to depth of relief but never less than a depth of 30 ft. and then complete decompression from this depth according to column 4.

Analysis of Nitrogen Elimination Curve. Gaseous nitrogen elimination from the body as a whole during the course of oxygen inhalation follows a curve which can be conveniently expressed as a sum of exponential terms of the form

$$Y = Q(1 - e^{-kt}), \qquad (1)$$

which states that the quantity of nitrogen, Y, is eliminated at a rate which is a constant percentage of the amount present at any given time.[26] Q represents the nitrogen content of saturation value at the beginning of oxygen

inhalation. k governs the rate of change in the slope of the curve, and $(1 - e^{-kt})$ gives the percentage decrease of the total nitrogen during the time interval, t.

Table 12A. Manifestations of Decompression Sickness and Results of Treatment of 113 Divers Following the Procedures Outlined in Table 11. (Compiled by Duffner.[433])

Symptoms	Number of Patients Treated in Accordance with Each Table						Total Number of Patients with Each Symptom
	1	1A	2	2A	3	4	
Rash	4	0	4	1	0	0	9
Numbness	2	1	1	3	2	1	10
Localized pain	50	7	25	12	13	0	107
Chokes	0	0	0	0	1	0	1
Paralysis	0	0	0	0	0	0	0
Muscular weakness	3	0	1	2	3	1	10
Vertigo	0	0	0	1	3	0	4
Visual disturbances	0	0	0	1	7	0	8
Aphasia	0	1	0	0	1	0	2
Headache	0	0	1	0	1	0	2
Nausea	0	0	0	1	0	0	1
Unconsciousness	0	0	0	1	1	0	2
Number of patients exhibiting a single symptom	41	7	18	6	7	0	79
Number of patients exhibiting two of the above symptoms	9	1	7	5	6	1	29
Number of patients exhibiting more than two of the above symptoms	0	0	0	1	4	0	5
Number of patients in which pain was the only symptom	41	7	18	6	5	0	77
Number of patients in which localized pain was *not* a symptom	0	1	0	0	4	1	6

Table 12B. Results of Treatment

Subtable Number	Total Number of Patients Treated	Result of Treatment		
		Recovered	Recurred	Residual
1	50	47	3	0
1A	8	8	0	0
2	25	24	1	0
2A	12	12	0	1
3 (O_2)	7	7	0	0
3 (Air)	10	10	0	0
4	1	1	0	1

The value of Q, in terms of Y, can be expressed as

$$Q = \frac{(Y_1)^2}{2Y_1 - Y_2}, \qquad (2)$$

provided that the time interval t_2, corresponding to the value of Y_2, is twice that of t_1, corresponding to the value for Y_1.

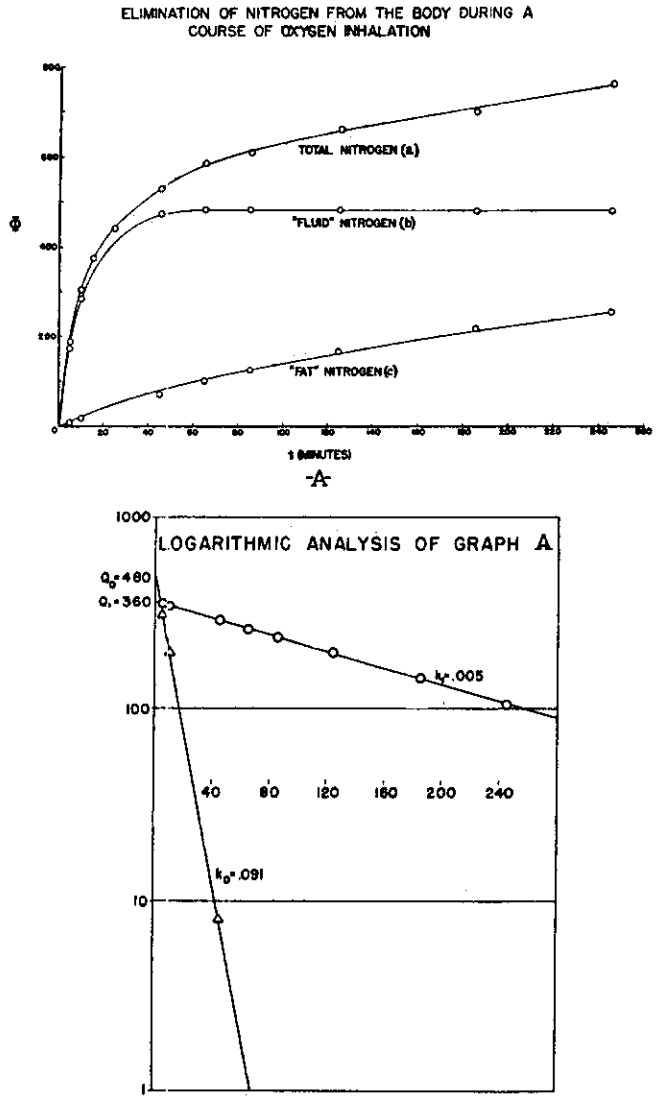

Fig. 20. Elimination of nitrogen from body during course of oxygen inhalation. Curve *a* is drawn through the experimental values. Curves *b* and *c* are hypothetical and represent the elimination of nitrogen from body solvents, "fluid" and "fat." Values of curve *a* are sum of corresponding values on curves *b* and *c*. If y values of curves *b* and *c* are subtracted from their corresponding Q values, log (Q — y) plotted against time is linear. Q value for curve *b* is 480 and k value 0.091. Corresponding values for curve *c* are 360 and 0.005. (From unpublished data of Behnke obtained in 1934–35.)

In terms of k, equation (1) becomes

$$k = \log_e \times \frac{A}{A - Y} \times \frac{1}{t}. \quad (3)$$

Interpretation of Exponential Curve. If the values for nitrogen elimination could be obtained from the single exponential expression (1), then blood flow, in order to carry away, let us say, 5 per cent per minute of the amount of nitrogen available for transport at any given time, must be distributed uniformly in relation to the nitrogen content of the body. This, however, is not the case for the body as a whole. Areas rich in fat and high in nitrogen content have relatively poor blood supply. Hence the blood, in the course of tissue desaturation, is not carrying equal amounts of nitrogen from the various tissues since the venous blood draining these tissues may, in some parts of the body, be saturated, and in other parts relatively nitrogen-free. The percentage of nitrogen removed in unit time in proportion to the amount present is highest at the beginning of nitrogen elimination and gradually decreases during the course of desaturation. If the experimental values for nitrogen elimination are substituted in equation (1), the value of k does not remain constant but progressively decreases during the course of five hours.

The curve for total nitrogen (Curve a, Fig. 20) can be more accurately represented by two exponential expressions on the basis of a high value for k during the first hour and a low value for k after the first hour. If that portion of the curve after the first hour is extrapolated to the left on the basis of its k value, then Curve c can be drawn. The difference in the nitrogen values for Curve c and those of Curve a is represented by Curve b. Curve a is thus the sum of two components, Curves b and c, or,

$$Y = 480(1 - e^{-0.09t}) + 360\,(1 - e^{-0.005t}).$$

The semilogarithmic plot of $(Q - Y)$ and t renders b and c straight lines (Fig. 20). Smith and Morales[259] have made accurate formulations to fit curves based upon experimental values, using three exponential expressions or one more than the number of gas solvents, i.e., fluid and fat (Fig. 21). Haldane's division of the body into five tissues implied that the nitrogen elimination curve for the body as a whole is the sum of five exponential expressions.

Interpretation Placed upon "Fat" and "Water" Curves. Curves b and c (Fig. 20) are only approximations of the manner in which nitrogen is absorbed by or eliminated from its chief body solvents.[11] They should not be interpreted to mean that fat and water exist as separated entities in the body, but rather that the lipids and water are so distributed that during saturation a large part of the nitrogen absorbed by fat diffuses from the body fluid. On decompression the reverse process is thought to occur. Thus, during decompression following partial saturation, the diffusion of nitrogen from the rapidly saturating body fluids into the slowly saturating fat tends to equalize the partial pressure of nitrogen in the different tissues of the body. With the exception of tissues with a high fat content (adipose tissue, bone marrow and spinal cord), the division of the body into tissues which saturate or desaturate at different rates is largely arbitrary and the body

can be regarded essentially as a unit. This fundamental concept can be made more clear by comparing the body to a beaker of water in which is

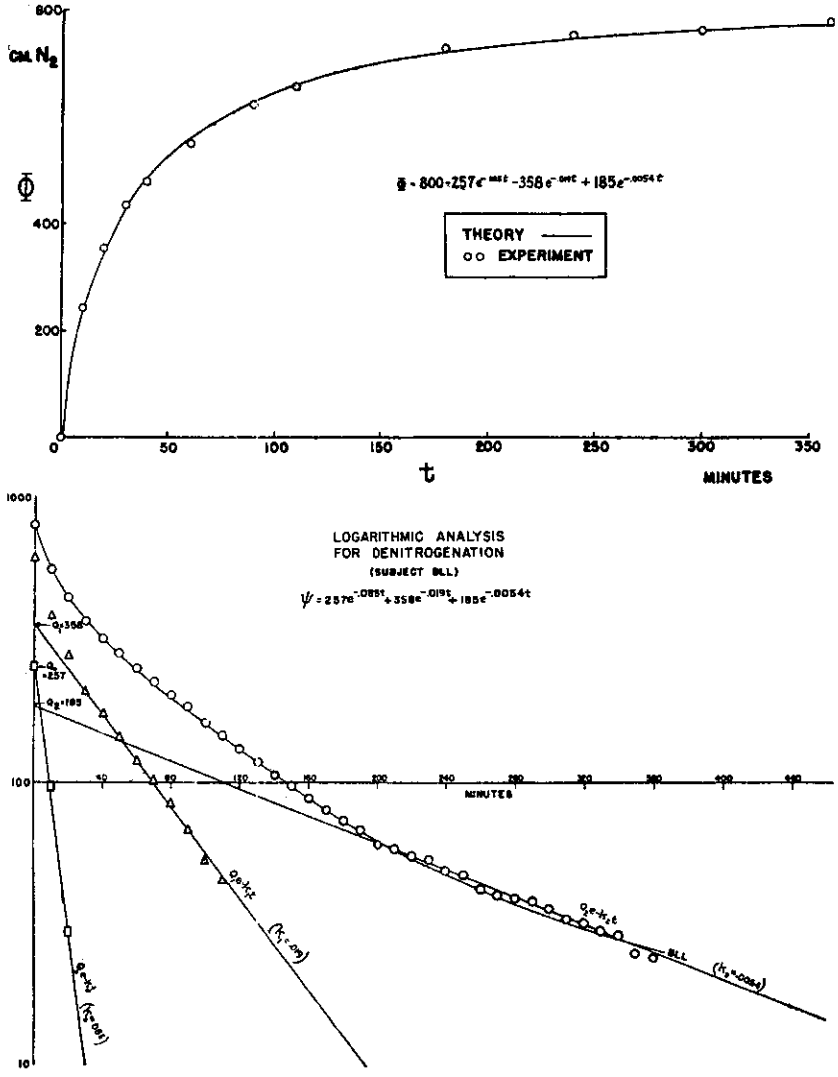

Fig. 21. Circles on upper graph represent experimental values for nitrogen elimination with exception of first five minutes (lung-rinsing period) for subject BLL. Curve is drawn from calculations on basis of equation. Total nitrogen eliminated is 800 cc. (Q). Lower graph is a semilogarithmic plot analysis of curve in upper graph. Values on original curve are sum of corresponding values of linear curves having respective Q and k values of 257, 0.085; 358, 0.019; and 185, 0.0054. (From data of Behnke as analyzed by Smith and Morales.[259])

distributed fat, with a greater concentration of fat in the lower portion. If the beaker is now exposed to a high nitrogen pressure for a short period

of time and then quickly returned to atmospheric pressure, diffusion of nitrogen will take place from the water into the surrounding air and also into the unsaturated water and fat present in the beaker. In the body, after short exposures (up to thirty minutes) to high pressure, the fat appears to act as a nitrogen absorbent during decompression and serves as a buffer against bubble formation in the blood stream. Remarkably high ratios, from 3.8 to 1 to 5.5 to 1, indicative of apparent gaseous supersaturation in rapidly saturating tissues, appear to be tolerated under these conditions. Thus an exposure at a depth of 100 feet for thirty minutes may be followed by a two-minute decompression to the surface without symptoms. A seventy-five-minute exposure at the same depth would be fatal if the same two-minute decompression period were applied. Nitrogen elimination measurements (Table 9) indicate that only about 600 cc. of additional nitrogen are taken up in the thirty to seventy-five-minute period.[302] Of special interest is the fact that nitrogen elimination, although interfered with (i.e., approximately equal amounts of gas eliminated during the first twenty-seven minutes compared with the succeeding sixty-minute period) in two tests following the rapid decompression, nevertheless followed an exponential type of curve in two other tests. The tabular data further indicate that the more slowly saturating part of the body is giving up most of the absorbed nitrogen in the thirty- to seventy-five-minute desaturation period.

Value of Helium-Oxygen Mixtures and Helium Elimination Curve. It is observed that in lean men (Fig. 20) about 75 per cent of the total body nitrogen is eliminated in about two hours. After exposures, at ordinary diving depths this nitrogen is eliminated with routine decompression without causing decompression sickness. It is a relatively small amount of gas, however, dissolved in fatty tissue that requires many hours for elimination. Thus, at a depth of 90 feet a 100-minute exposure requires a period of fifty-seven minutes for decompression; at the same depth a nine-hour exposure requires about twelve hours' decompression. By contrast, if helium-oxygen mixtures are used in place of air, there is very little more decompression time required for all exposures greater than 100 minutes. This is of fundamental importance in deep-sea diving and the empirical data relative to decompression time required for helium dives tie in well with quantitative data.

If the lipid substances are responsible for the prolongation of nitrogen absorption or elimination, then helium—possessing a low fat solubility coefficient and a more rapid rate of diffusion—should be eliminated in a shorter period of time. Following exposure in a helium-oxygen atmosphere, it is observed (Fig. 22) that the absorbed gas leaves the body in about one half the time required for nitrogen. Smith and Morales found, moreover, that two, rather than three, exponential expressions in the case of nitrogen elimination serve to predict accurately the curve of helium removal. In fact, the lowered oil-to-water solubility ratio and the more rapid rate of diffusion make it appear as though the helium were eliminated from one homogeneous solvent, the role of fat being obscured.

The reality of these considerations is apparent. Decompression following short exposures in a helium-oxygen atmosphere is actually longer than that required for air, possibly because of the tendency of helium to dif-

fuse more rapidly into the blood stream and thus make bubble formation more likely if the early stages of decompression are too rapid. Following saturation exposure, however, decompression time is increased from fifty to 638 minutes for air, and, by contrast, from seventy-five to seventy-nine minutes for helium.

Calculation of Decompression Tables. The problem of bringing a diver or caisson worker out of a compressed-air atmosphere has not been solved although there now has accumulated a mass of empirical data which have led to reasonably safe procedures. Attempts to formulate decompression tables on a more "rational basis" than the Haldane principles have proved to be a time-consuming but intriguing pastime. In computing his

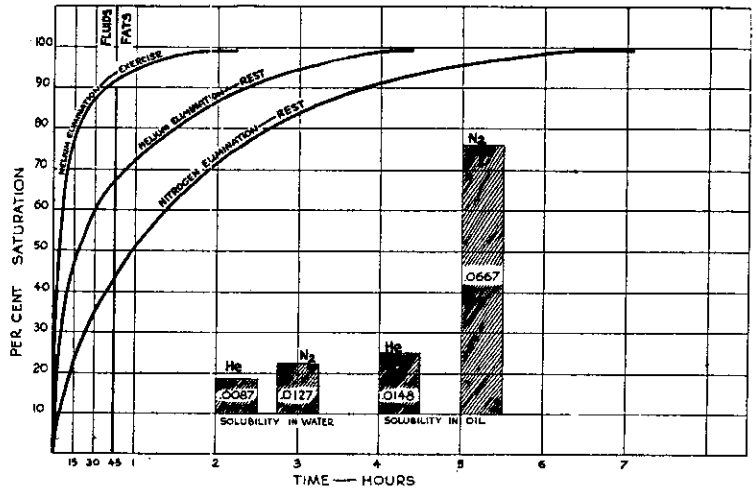

Fig. 22. Desaturation rate for man, comparing nitrogen with helium. During first forty-five minutes, gaseous removal takes place from body fluids, and subsequently mainly from body fat. Solubility coefficients for helium and nitrogen are expressed as cc. of gas, reduced to standard conditions, dissolved per cc. of solvent, temperature of 38° C. (From Behnke.[19])

decompression tables, Haldane postulated that since the body could be rapidly decompressed from 2 to 1 atmosphere, it would be safe to halve the absolute pressure at any level and to decompress divers according to a schedule which never allowed the nitrogen pressure in the tissues to exceed twice the nitrogen pressure in the lungs. The principle underlying the method of computing a decompression table may be illustrated by two examples showing the denitrogenation time required for prolonged stay at altitude. The nitrogen elimination curve for the body as a whole is practically an exponential form if experimental values only for nitrogen elimination are used, i.e., if the calculated quantity eliminated during the first five minutes is not included (Fig. 23).

If bubble formation is initiated in blood flowing through peripheral capillaries, the following gas pressures at sea level enter into the calculations:

Nitrogen	573	
Carbon dioxide	47	
Water	47	
Oxygen	40	(Variable)
	707	

If immediate ascent to 20,000 feet does not induce the bubble state, the ratio of gas pressure in venous blood to ambient pressure may for a short time be 707 to 349.1 or approximately 2 to 1.

The time required for denitrogenation with oxygen prior to an ascent to 30,000 feet may therefore be computed in the following manner: At 30,000 feet the barometric pressure is 225.6 mm. If the total pressure of gases in venous blood can safely be doubled, a value of 451 mm. (2 × 225.6 mm.) is obtained. Before rapid ascent can be made to 30,000

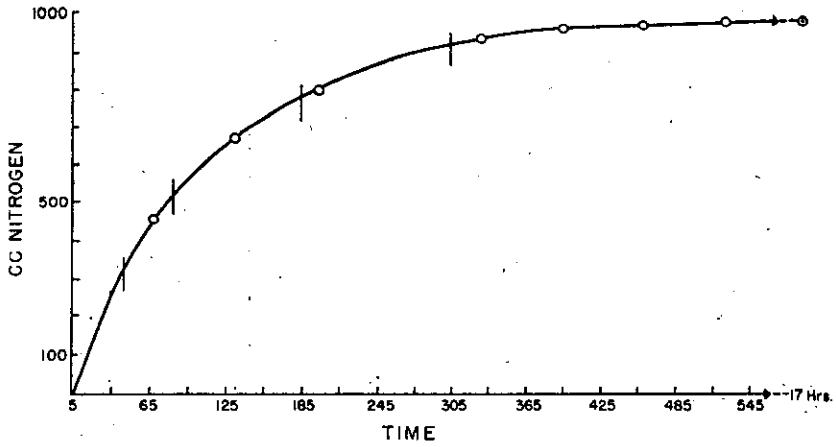

Fig. 23. Nitrogen elimination curve plotted from experimental data which does not include nitrogen eliminated during first five minutes (lung-rinsing period). End point of nitrogen elimination (within limits of experimental error, 5 cc./hr.) was reached at the end of 585 minutes. Total period of oxygen inhalation was seventeen hours. Cross lines indicate various periods of denitrogenation required for prolonged stay at altitudes between 30,000 and 40,000 feet for group of men, average age 33.

feet, the total gas pressure in venous blood must be reduced from 707 to 451 mm., a reduction of 256 mm. Of the total gases it is feasible to remove only nitrogen. In other words, the nitrogen pressure in the body must be reduced 256 mm. If the initial nitrogen pressure is 573 mm. at sea level, the body must lose 256/573 or 45 per cent of its nitrogen. From the nitrogen elimination curve (Fig. 23), 45 per cent desaturation requires sixty-three minutes, or the denitrogenation time required for immediate ascent to 30,000 feet followed by an indefinite exposure at the altitude without the occurrence of decompression sickness.

Calculation of desaturation time prior to an ascent to 35,000 feet followed by an indefinite period of exposure at altitude:

At 35,000 feet, barometric pressure = 178.7 mm.

2 × 178.7 = 357.4 mm., or upper limit tolerance based on 2 to 1 gas pressure ratio.

707—357 = 350 mm. = required pressure decrease in body.

350/353 = 61 per cent, or percentage of N_2 elimination required to reduce pressure to 350 mm.

From Figure 23 it is observed that 61 per cent denitrogenation requires 105 minutes. The time required for oxygen inhalation prior to immediate ascent to 35,000 feet is 105 minutes.

The 2 to 1 Ratio. Although for the diving depths and times of exposure with which Haldane was concerned the 2 to 1 ratio appeared satisfactory subsequent diving and caisson experience, particularly following saturation exposures or following dives to deep depths, have indicated with certainty that no one ratio is applicable for all tissues and that probably no degree of supersaturation is maintained in the body during decompression. Thus in the computation of decompression tables, ratios as high as 5.5 to 1 have been applied to rapidly desaturating tissues and as low as 1.7 to 1 for the slowest desaturating tissue.[141]

Although one may infer from the rapid changes in barometric pressure affecting divers and aviators that the body tissues including the blood are able to hold gaseous nitrogen in a state of supersaturation, it is difficult to use a set ratio that holds for the apparent degree of supersaturation tolerated by the body tissues in relation to ambient pressure. Thus the ratio derived from any single change of pressure in diving (e.g., 2 to 1 atmosphere) or in aviation does not appear to hold for a series of pressure changes or decompressions. It is necessary in practice to decrease the initial ratio either for an increase in exposure time or for an increase in diving depth. It may well be that bubbles form as soon as a state of supersaturation is initiated and that what appears to be a ratio of saturation tolerance is in reality an index of the degree of embolism that the body can tolerate.[223] What is important is that there are sharply demarcated limits of perhaps 5 feet in diving depth and several thousand feet in altitude ascent separating injury from a state of well-being.

Efforts to use a difference in pressure ΔP[11, 136] have not been translated into working out successful decompression procedures. It would appear that the underlying principle governing the initiation of bubbles and the maintenance of gas in supersaturation has not been formulated. A fixed ratio does not appear to hold, and, on the other hand, the concept of a constant value for ΔP may require the inclusion of some correction factor for pressure level (number of gas molecules) in order to be applicable to both diving and altitude decompressions.

EMPIRICAL DIVING DATA WITH REFERENCE TO DECOMPRESSION TIME

Exposure Time at Various Depths for Work Dives Followed by Continuous Ascent to Surface (Minimal Decompression). Divers may be exposed for appreciable periods of time to rather deep depths and not require any more decompression than that provided in continuous ascent to the surface at rates of 25 to 50 feet per minute. Thus, a diver may remain at a depth of 100 feet some twenty-five minutes or at 180 feet for five minutes and ascend rapidly to the surface. These values serve to define tolerance limits for exposure to high pressures followed by minimal decompression.

Exposure Time at Various Depths for Rest Dives. If conditions are altered so that the diver's activity underwater is minimal and if oxygen or oxygen-air mixtures are inhaled for a period of two minutes prior to and during ascent, the periods of exposure may be considerably increased. Thus a diver may remain for a period of thirty-four and one-half minutes at a depth of 100 feet compared with a stay of twenty-five minutes for a

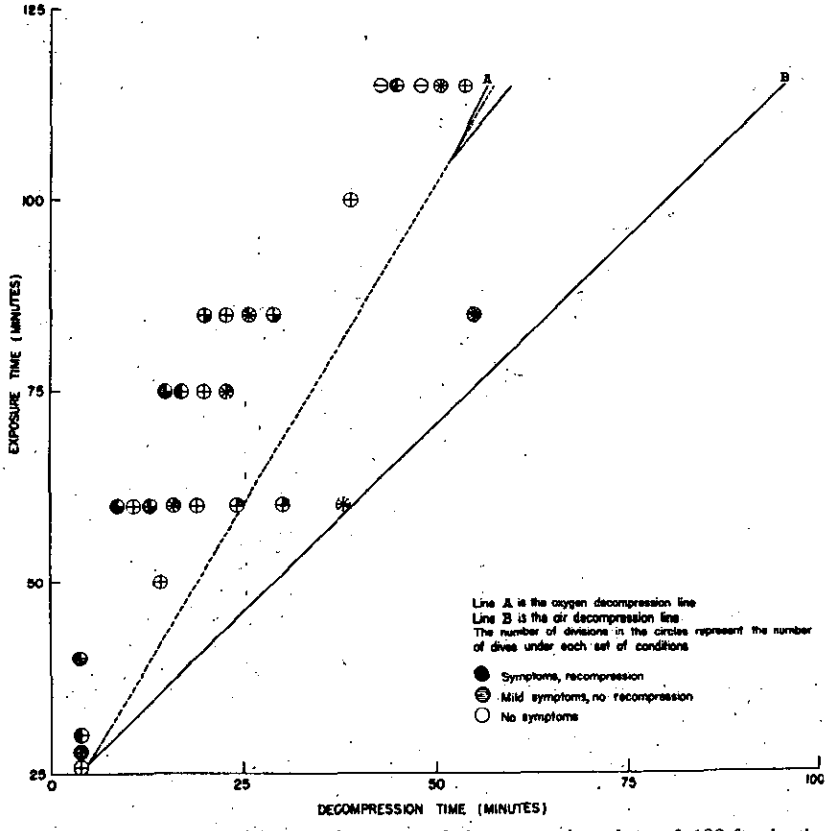

Fig. 24. Exposure time in relation to total decompression time of 100-ft. depth, showing effect of oxygen decompression in relation to air decompression and occurrence of decompression sickness when time is shortened, i.e., when points are to left of line A. (Plotted by Van Der Aue.[449])

work dive at the same depth. That the values are upper limits for the type of diving is evident from the data given by Harvey.[136] It is observed that only a few minutes' increase in exposure time gives rise to decompression sickness.

Exposures of Long Duration in Relation to Decompression Time. A depth of 38 feet (saturation? exposure of twelve hours) appears to be a critical depth with respect to the occurrence of decompression sickness following minimal decompression. In a susceptible group of men some individuals will develop decompression sickness following prolonged ex-

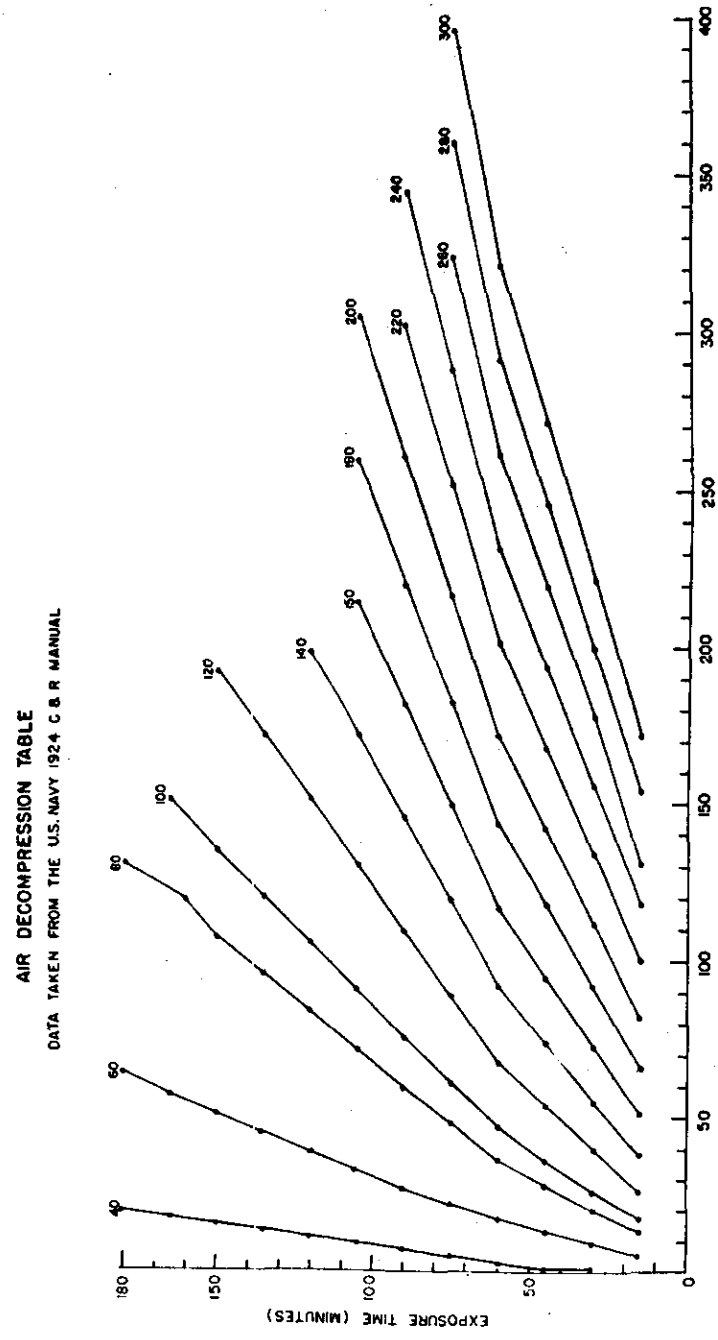

Fig. 25. Exposure time plotted in relation to decompression time for air dives at various depths, based essentially upon values from Haldane's tables as incorporated in the U.S. Navy Diving Manual.[147] Air is inhaled during entire decompression period.

posures at this depth. That this particular group was relatively susceptible to decompression sickness is shown by the fact that all of the divers except one developed bends at altitude (38,500 feet).[315]

Graphical Presentation of Data in Diving Tables. It is observed[449] that an exposure of twenty-five minutes at a depth of 100 feet requires minimal decompression (Fig. 24). If longer exposures are carried out at the same depth, the decompression time required increases linearly with exposure time. This graphic method used by Van Der Aue may prove to be the key for the ultimate formulation of correct decompression tables. It is observed that as depth increases the slopes of the lines decrease and the rate of decrease may eventually prove to be constant.

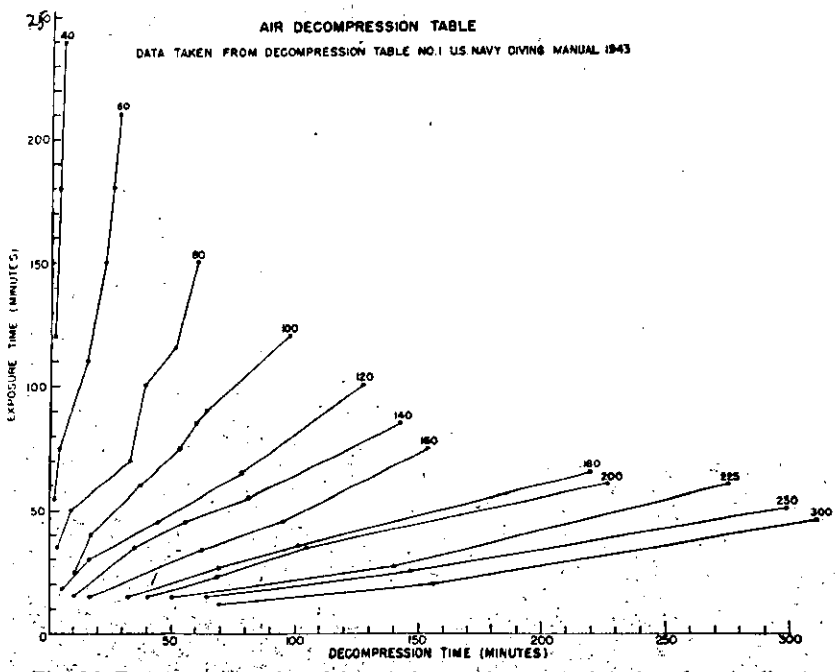

Fig. 26. Exposure time plotted in relation to decompression time for air dives at various depths, based upon values from U.S. Navy Diving Manual.[448] Air is inhaled during entire decompression period.

For any given depth, decompression sickness may occur if decompression time lies to the left of a given depth line (Fig. 24). Possible discrepancies in air diving decompression tables[447, 448] may be reflected in irregularities in the linear delineation. Further, as exposure time increases, a uniform safety factor may be applied by decreasing the slope of any given depth line. When the graph is completed by the addition of data derived from saturation exposures, the linear relationship may tend to be exponential. The graphic representation of Haldane's tables[447] and the U.S. Navy tables[448] is shown in Figures 25 and 26.

Graphical Presentation of Helium-Oxygen Decompression Tables. The fact that very little additional decompression time is required for exposures

greater than 100 minutes when helium-oxygen mixtures are inhaled is again emphasized by Figure 27 based on values from the Navy Diving Manual.[448] The contrast between air decompression data (Figs. 25, 26) is striking, and illustrates the practical application of the diffusion and lipid solubility properties of a gas.

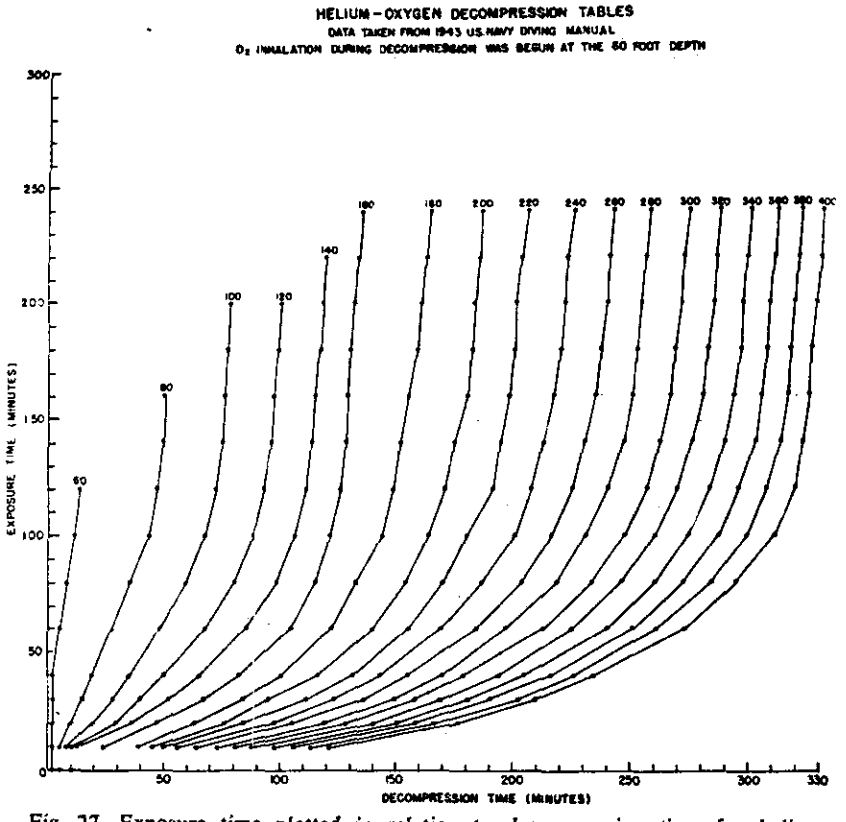

Fig. 27. Exposure time plotted in relation to decompression time for helium-oxygen dives at various depths, based upon values from U. S. Navy Diving Manual.[448] Oxygen is inhaled during decompression from 60-foot stop to surface.

Surface Decompression. Surface decompression is the procedure of bringing a diver from the sea bottom to the surface with decompression limited to the first stop in the water, followed immediately by recompression in a chamber, and subsequent decompression according to the diving tables beginning with and repeating the first stop.[450]

This procedure was first employed by Saunders in the salvage of the submarine S-51 in 1925, because cold water and tides rendered decompression in the open sea impractical. In 1939 it was extensively employed in the salvage operations required to raise the U.S.S. Squalus.[80, 450] Surface decompression permits the elimination of excess gas from the body tissues under ideal conditions—that is, with the diver warm, at rest, and under

observation. The danger of surface decompression lies in the formation of extensive gas embolism during the interval between the removal of the diver from the water and his subsequent recompression on the surface.

When standard decompression is followed, all decompression stops are made in the water. When surface decompression is followed, only the first stop of the standard decompression table is made in the water. The diver is then brought to the surface at the rate of 25 feet per minute where his shoes, helmet and belt are removed and he is recompressed in the chamber in as short a time interval as possible. In a dive to a depth of 100 feet for eighty-five minutes, the standard decompression stops are at 30 feet for six minutes, 20 feet for twenty-eight minutes and 10 feet for twenty-one minutes. In surface decompression the diver is brought to 30 feet at the rate of 25 feet per minute where he remains for six minutes. He is then brought to the surface at the 25-foot rate (which is now standard in the Navy for all continuous ascents), undressed and recompressed to 30 feet. A time interval not to exceed five minutes elapses from the beginning of the ascent in water from 30 feet to the beginning of recompression in the chamber at 30 feet. After repeating the time of first stop in the chamber, the diver is brought to 20 feet for twenty-eight minutes and then to 10 feet for twenty-one minutes. The total decompression time for surface decompression is greater than that for standard decompression by the duration of time spent at the first stop. The following results of depth and exposure for surface decompression are taken from the U.S. Navy Diving Manual.[448] Van Der Aue conducted a series of 282 dives to evaluate the safety of surface decompression for the recommended exposure periods. A total of 282 dives were made which included heavy work at bottom depth in which the subjects moved about as little as possible. The work (about 2500 ft. lbs. per min.) consisted of lifting a 58-pound weight (in water) from the submerged deck to a bench 26 inches high, ten times per minute. The results of these tests were a islightly greater incidence of bends in the control or standard decompression dives compared with surface decompression dives; in 98 work dives the incidence of bends was 12.3 per cent, in 103 rest dives the incidence of bends was 3.9 per cent. Bends occurred most frequently in the part of the body subjected to the most vigorous exercise under pressure (80 per cent of bends in upper extremities). That the "surface" interval may be prolonged as much as fourteen minutes is shown by the results of a series of tests conducted by Gouze.[119] He timed the "surface" interval from the appearance of the diver's helmet at the surface of the water to recompression at the first stop. In his series, there were no bends. The work of the divers consisted of routine tasks and may be graded as moderate exercise. The U.S. Navy Diving Manual[448] gives the following limits of depths and exposure for surface decompression:

Feet	*Minutes*
100	85
110	75
120	60
130	55
140	45
150	40
170	30

TREATMENT OF DECOMPRESSION SICKNESS

The prime objective in treatment of decompression sickness is the rapid restoration of normal blood supply by immediate recompression which serves to reduce the size of the gas emboli in proportion to the amount of pressure applied. Perhaps there is no therapeutic procedure more effective than recompression as applied to the asphyxiated, pulseless, cyanotic patient whose blood stream is filled with multiple gas emboli. Even patients presenting incipient lesions of the spinal cord have made complete recovery under immediate and prolonged recompression. Long periods of time, however, are required for the absorption and elimination of gas bubbles. The absence of symptoms in a patient under recompression treatment *does not signify freedom from* "silent" gas bubbles. The appreciation for the need of prolonged recompression underlies any regimen for successful therapy.

The tabular outline (Table 11) serves as a guide for recompression treatment and incorporates the following features developed from principles formulated by Behnke and Shaw[23] and Yarbrough and Behnke[14, 304]: (1) a thirty-minute period at maximal depth, (2) the use of oxygen when available, and (3) prolonged recompression for twenty-four or more hours in serious cases. It is emphasized that the condition of the patient governs therapy rather than rigid adherence to a tabular outline. The tables, however, represent the best practice at the present time on the basis of extensive experience gained at the Experimental Diving Unit, Navy Yard, Washington, D.C.

Treatment Procedures as They Apply to Manifestations of Decompression Sickness

Bends. In the mild cases of decompression sickness characterized by "bends" and comprising the majority of cases, the minimal pressure applied is 44.5 pounds per square inch (gauge) equivalent to a diving depth of 100 feet. Relief of symptoms may occur at a lower pressure but the additional compression reduces the size of bubbles to one fourth of their volume on the surface and facilitates their reabsorption.

Occasionally if recompression is delayed or extensive bubble formation is present, pressure in excess of 44.5 pounds per square inch may be required for relief of pain. The persistence of pain at a pressure depth of 165 feet indicates that some condition other than "bends" exists unless residual tissue injury is present. Some relief from "bends" pain as the pressure is applied is the almost invariable rule. The one exception to this rule is the occasional condition characterized by an increase in severity of symptoms as the pressure is applied. The basis for this aggravation of pain appears to be the too rapid application of pressure, resulting in the tendency of the bubbles in the bone marrow to be reduced faster than the blood and tissue fluids are replenished, with the consequent "squeezing" of the bone tissue. The aggravation of pain can be prevented by slow application of pressure.

Asphyxia, Circulatory Collapse and Paralysis. For the serious cases of decompression sickness recompression is limited to a pressure of 73.4 pounds per square inch (gauge) equivalent to a depth of 165 feet. At this

pressure the bubble has been reduced to 17 per cent of its volume at the surface. Higher pressures can do little to improve circulation as a result of decrease in bubble volume and will unduly delay decompression to levels at which oxygen can be safely breathed.

The practice of prolonged immersion in compressed air, colloquially termed the "overnight soak," has proved to be the conclusive method of terminating treatment. The patient is permitted to sleep and the bubbles have adequate time for absorption. Should there be any question of involvement of the central nervous system, the prolonged compression treatment is routinely put into effect.

For the moribund patient, the pressure level following the two-hour treatment at a depth equivalent to 165 feet is decreased in thirty-minute stages to 60 feet (Table 11, column 2). There should be no hesitancy in continuing treatment at the 60-foot level for a period of days if signs of severe circulatory impairment or paralysis persist. It is unlikely, however, that the time periods given in column 2 will be exceeded.

Air Embolism. This accident (in submarine escape) must always be regarded as serious. The symptoms are referable to the central nervous system and the circulation and therefore require treatment according to column 2. Symptoms have recurred when inadequate recompression has been given and individuals believed to be "cured" by the initial treatment have been rushed to the recompression chamber in a state of collapse.

Prior to ascending from any level the patient's ability to stand and walk the length of the chamber should be established. This test should be made routinely before leaving the maximal depth, at the completion of the 60- and 30-foot stops, and at the end of the recompression treatment.

Complications Arising During Treatment

Oxygen Toxicity. In the resting individual severe symptoms of oxygen poisoning rarely occur during the first two to three hours at a depth of 60 feet. If, however, during the course of oxygen inhalation, dizziness, nausea, muscular twitching, blurring of vision, tremor, extreme irritability or apprehension occurs, oxygen should be discontinued (see Table 11) and the following procedure should be put into effect: (1) If using treatment column 1, complete remaining stops of column 1A; (2) if using treatment column 2, complete remaining stops of column 2A; (3) if using treatment column 3, complete remaining stops of column 3 breathing air. At the discretion of the medical officer, oxygen breathing may be resumed at the 40- and 30-foot stops for a total of ninety minutes if using column 1 or 3 and 150 minutes if using column 2.

Spontaneous Pneumothorax. The sudden onset of thoracic pain accompanied by respiratory embarrassment as the chamber pressure is reduced suggests the complication of pneumothorax. Thoracentesis may be required in the pressure chamber in order to permit the completion of treatment. It is emphasized that vigorous employment of the Valsalva and other maneuvers in order to equalize pressure within the middle ear spaces must be avoided.

Recurrence of Symptoms. Should symptoms recur following treatment with column 1, 1A, 2 or 2A, recompress the diver to a depth giving relief.

If relief occurs at depths less than 30 feet, take the diver to 30 feet and then decompress from the 30-foot stop to surface according to column 3. If relief occurs deeper than 30 feet, remain at the depth of relief for thirty minutes and then complete the remaining stops, using treatment outlined in column 3 and air throughout. If symptoms recur after treatment according to column 3, take the diver to the depth necessary to relieve symptoms. If this depth is greater than 30 feet, keep him at this depth for thirty minutes and complete treatment according to column 4. If the depth of relief is less than 30 feet, take the diver to 30 feet and complete treatment according to column 4.

Adjuncts to Treatment

Judicious injection of glucose-saline and plasma may be required for the severely injured patients in order to counteract the effect of hemoconcentration. The specific gravity of blood and the hematocrit readings serve as a guide for this type of therapy.

The presence of appreciable quantities of gas in the blood stream places a severe load on the right ventricle and leads to dilatation. Following signs of circulatory embarrassment or collapse, it is imperative to consider that the right ventricle is weakened and all therapy must be directed toward the conservation of right ventricular cardiac function.

Large accumulations of gas in pulmonary vessels may lead to some degree of pulmonary edema. The probability of pneumonitis following severe decompression sickness and the presence of lung injury following accidents with the submarine escape appliance may require measures employed for the treatment of incipient pneumonia.

Frequent Errors in Diagnosis and Treatment

Diving history is replete with examples of avoidable errors in diagnosis and treatment. The fact that "bends" may occur only once in a series of 100 similar dives is not generally appreciated. Most of the errors can be attributed to:

1. Failure to apply the pressure test in doubtful cases. Although muscular and ligament injury unrelated to "bends," tenosynovitis, fractures and appendicitis have occurred during and immediately following recompression, it is safe practice to apply a pressure test of at least a few pounds per square inch in all doubtful cases to eliminate the possibility of "bends."
2. Delayed recompression. This mistake is usually due either to negligence on the part of the patient in reporting early symptoms or to failure of the diving supervisor or medical officer to keep divers in the vicinity of the pressure chamber. Apart from "bends" pain, substernal distress upon deep inspiration, and irritation caused by tobacco smoke are to be looked for as early signs of "chokes."
3. Failure to treat the serious cases adequately according to column 3 or 4 (Table 11) resulting in recurrence of symptoms and necessitating repeated recompressions. The apparently complete recovery of patients during the early stages of recompression may lead to the belief that the gas bubbles have been eliminated before this actually has been accomplished. Experience has emphasized that long periods are required for gas elimination once bubbles have formed. The "overnight soak" at pressures equivalent to depths of 30 to 60 feet has proved to be most effective.
4. Failure to keep the "treated" diver near the chamber for a twenty-four-hour period. This error has been responsible for the occasional collapse or death of divers who were considered to have had adequate treatment.

In Duffner's analysis[433] of 113 divers who developed decompression sickness, there was only one frank failure in treatment that required a second recompression. Of the four recurrences, two can be explained by a failure to recompress the patients according to the treatment outlined (Table 11). In one case, for example, symptoms were relieved at a pressure depth of 78 feet but the patient was recompressed to only 100 feet instead of a pressure depth of 165 feet. Another recurrence can be explained on the basis of faulty oxygen breathing equipment. The fourth recurrence is a frank failure of the treatment procedure. Residual symptoms were of a minor nature and may be explained by the delay in treatment, thirteen and one-half hours after the onset of pain in one case, and seventeen hours in the other.

THE USE OF OXYGEN IN THE TREATMENT OF COMPRESSED-AIR ILLNESS

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THE USE OF OXYGEN IN THE TREATMENT OF COMPRESSED-AIR ILLNESS [1]

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The early investigators (Bert, 1878; Zuntz, 1897; and Heller, Mager, and von Schrötter, 1900) concluded largely as a result of theoretical considerations that recompression combined with oxygen inhalation provided a rational and effective treatment for compressed-air illness. Oxygen inhalation, however, has been neglected probably for the following reasons: conclusive experimental evidence as to its value was lacking; man's tolerance for oxygen was not known; and facilities were not available for its economic administration. Thus, the treatment for compressed-air illness outlined in the Naval Diving Manual (1924) is essentially recompression with the patient breathing air. While this type of treatment affords relief in mild cases, it often fails in serious cases to prevent disability or death. It seemed worth while, therefore, to evaluate oxygen therapy on an experimental basis, and to determine the limits within which oxygen could be safely inhaled. In this paper are summarized the results of these studies.

The problem.—Rapid decompression after sufficient exposure to increased air pressure may result in the formation of nitrogen bubbles in the blood stream. These bubbles when sufficiently large and numerous mechanically obstruct blood flow, and deprive the tissues of their normal blood supply. Deprivation of blood supply gives rise to the characteristic symptoms of compressed-air illness, namely, asphyxia, paralysis, and pain. These symptoms occur either singly or in combination, and indicate that the areas for bubble formation and predilection are the right side of the heart and pulmonary vascular bed, the spinal cord, and probably the bone marrow. Treatment aims at the removal of bubbles from these areas in the shortest possible time in order to minimize injury particularly with reference to the spinal cord and the right ventricle.

Theoretical considerations.—The routine treatment of compressed-air illness, recompression with the patient breathing air, relieves symptoms immediately by reducing the size of bubbles, but accomplishes little in the way of bubble removal. This will be made clear by an example. If a dog in equilibrium with a gauge pressure of 60 pounds is suddenly decompressed to atmospheric pressure, the dissolved nitrogen in the blood will exist in a state of supersaturation, and diffusion of nitrogen from the blood stream into the lungs will

[1] From the Department of Physiology, Harvard School of Public Health, Boston, Mass. Received for publication Sept. 6, 1935. This research was aided by the Miriam Smith Rand fund.

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proceed with an initial pressure head of 60 pounds (3,040 mm.). Should bubbles form in the blood, the tension of nitrogen drops rapidly since the pressure in the bubbles is that of the surrounding medium (1 atmosphere) in addition to their surface energy. Since the percentage of nitrogen in a bubble is about

$$82\frac{(760-(47(\text{water vapor})+45\ (\text{carbon dioxide tension})}{760}$$
$$\frac{+40\ (\text{oxygen tension})}{\cdot\ 100),}$$

and in the alveolar air,

$$75\frac{(760-(47\ (\text{water vapor})+40\ (\text{carbon dioxide tension})\rightarrow}{760}$$
$$\frac{+100\ (\text{oxygen tension})}{\cdot\ 100),}$$

nitrogen diffusion proceeds at a pressure head (disregarding surface energy) of about 56 millimeters (7.3 percent .760). Nitrogen from the tissues, meanwhile, is diffusing into the peripheral capillaries at an excess pressure of 60 (−) pounds. Under these conditions the blood stream is rapidly filled with gas in bubble form. By the time that recompression is applied the quantity of nitrogen in bubble form is well in excess of the capacity of the blood to dissolve nitrogen at practicable pressures. Nitrogen in bubble form must be eliminated by passage either into the tissues through the peripheral capillaries, or into the lungs through the pulmonary capillaries. When air (79 percent nitrogen)[2] is breathed nitrogen diffusion from a bubble (82 percent nitrogen) proceeds with a negligible pressure head.

The futility of eliminating large quantities of nitrogen from bubbles in the pulmonary capillaries when air is breathed, is further emphasized by the results of clinical experience. Thus, Haldane (1927) states that bubble elimination is a slow process, and that it may be necessary to keep a patient in the pressure chamber 24 hours or more. Keays in 1912 reporting on 3,692 cases of compressed-air illness states that recompression, while an efficient means of treatment in mild cases often fails to prevent disability and death in severe ones. In the experiments of Boycott, Damant, and Haldane (1908) bubbles were found in the blood stream of a goat 2 days following decompression, and in the spinal cord 27 days after decompression.

The inhalation of oxygen, on the other hand, reduces the tension of nitrogen in the inspired air to a value approaching zero, and ensures not only a maximum elimination of nitrogen, but also an immediate relief of asphyxia (oxygen lack). At atmospheric pressure oxygen inhalation raises the pressure head for nitrogen diffusion from 7.3 percent to about 80 percent of 1 atmosphere, or an 11-fold increase as compared with air inhalation.

[2] Includes argon.

The questions are whether experimental evidence supports these theoretical considerations, and over what range of pressure oxygen breathing is feasible?

Experimental data.—Experiments, heretofore showing the advantage of oxygen inhalation compared with air, have been too few in number to be conclusive. In order to provide more extensive data with reference to the absorption of nitrogen bubbles, 26 experiments were performed on anesthetized dogs decompressed in 10 seconds from a pressure of 65 pounds after an exposure of 1 hour and 45 minutes. The results in detail and their physiologic implications are reported by Behnke and Shaw (1935). For this paper the essential findings, which apply specifically to the problem under discussion, are summarized.

The diagram shown in figure 1 represents the procedure in a typical experiment. The 10-second decompression from an excess pressure of 65 pounds led to the development of massive intravascular forma-

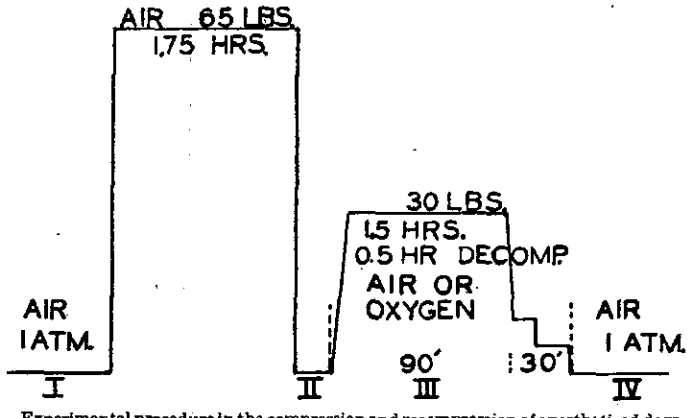

FIGURE 1.—Experimental procedure in the compression and recompression of anesthetized dogs. I, control period; II, asphyxial period following a 10-second decompression from 65 pounds gauge pressure after 1.75 hours exposure; III, recompression to 30 pounds pressure with the dog breathing either oxygen or air; IV, period following recompression, dog breathing air.

tion of bubbles in a period of 15 to 60 minutes unless recompression supervened. During period II (fig. 1) bubbles could be detected at the onset of symptoms in cutaneous arteries and veins. Pathognomonic of bubble formation was an increase in respiratory rate, a temporary rise followed by a fall in blood pressure, and a slowing of the pulse rate (fig. 2). Accompanying these symptoms were manifestations of critical arterial anoxemia and a slowing of the circulation. The tongue and mucous membranes and blood withdrawn from the femoral artery were cyanotic. Analysis of the oxygen content of arterial blood showed a reduction from the initial values as high as 66 percent. The reduction of mixed venous blood withdrawn from the right side of the heart was relatively greater, giving a 50 percent

or more increase in the arterial-venous oxygen-content difference. The low oxygen content of the venous blood indicated a remarkable slowing of the blood flow through peripheral capillaries. In addition, there was usually a concentration of red blood cells evidently as a result of plasma loss.

The clinical picture was, therefore, acute asphyxia with symptoms indicative of shock. The high degree of oxygen deficit in arterial blood was attributed to the blockage of the pulmonary vascular bed with nitrogen bubbles. These bubbles, presumably, not only inter-

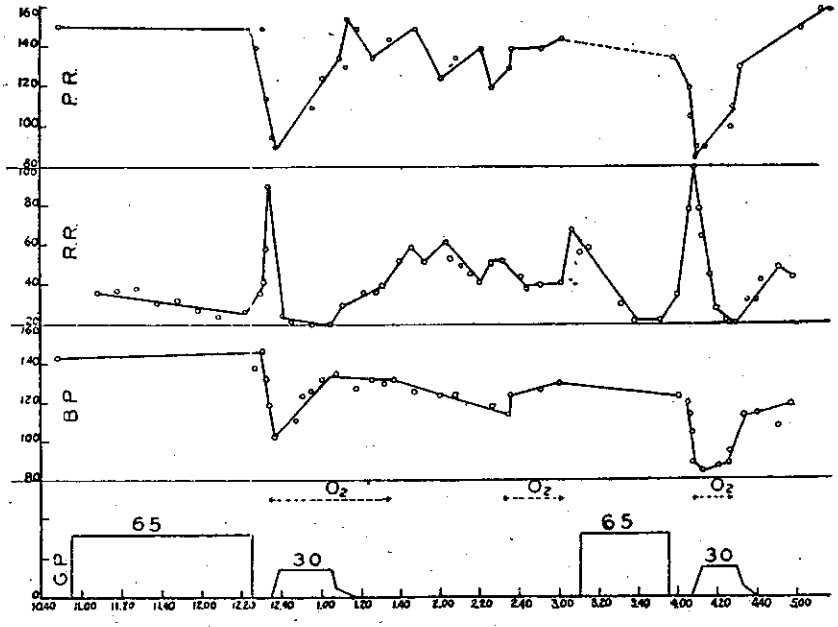

FIGURE 2.—Alterations in blood pressure, respiratory rate, and pulse rate of a dog decompressed in 10 seconds from a gauge pressure of 65 pounds after 1.5 hours exposure followed by recompression (interval of 10 minutes) to a pressure of 30 pounds (oxygen) for 25 minutes. Pressure was then lowered to atmospheric in 12 minutes, and oxygen inhalation continued for 17 minutes.

Preceded by a period of oxygen breathing (30 minutes) compression of the dog was again carried out at a pressure of 65 pounds for a period of 45 minutes followed by a 10-second decompression. After an interval of 12 minutes the dog was recompressed to a pressure of 30 pounds for 20 minutes (oxygen inhalation).

fered with pulmonary ventilation by limiting alveolar expansion but also restricted the circulating blood to comparatively few channels so that the volume of blood flowing through the lungs was diminished in relation to alveolar diffusion surface. Without recompression death occurred rapidly from respiratory, followed by circulatory, failure, usually with an interval between the two of a few seconds to several minutes.

Recompression to a gage pressure of 30 pounds (fig. 1, period III) with the dog breathing either air or oxygen relieved the asphyxia.

Respiratory rate returned to normal, blood pressure was improved, pulse rate increased (fig. 2), and the oxygen content of arterial blood was as high or higher than the initial values. It is important to note that at this stage apparent recovery was as rapid with either air or oxygen inhalation. It is during the period following recompression, however, that striking differences are noted.

One hour following recompression with air (fig. 1, period IV) the asphyxial symptoms (increased respiratory rate, anoxemia) reached their former degree of severity. The low oxygen values were almost the same as those of period II. Bubbles reappeared in cutaneous vessels, and were always present in large quantities in mixed venous blood. At autopsy this finding was verified by the presence of bubble accumulations in the large veins, right side of the heart, and pulmonary arteries. In the peripheral arterial bed bubbles were usually

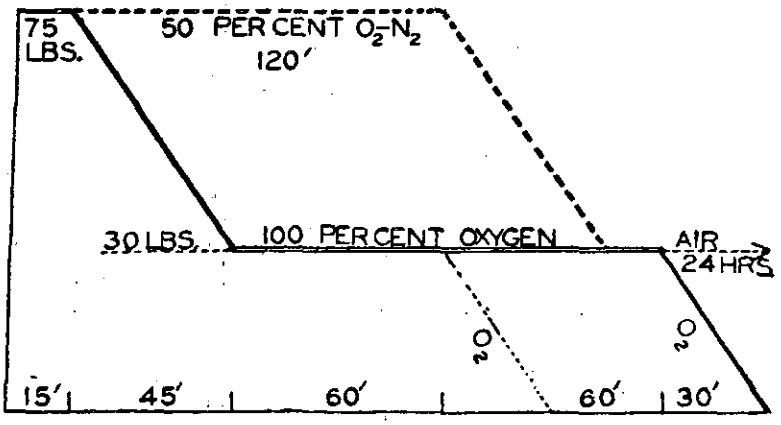

FIGURE 3.—The treatment of a serious case of compressed-air illness with oxygen and an oxygen-nitrogen mixture. Pure oxygen is breathed at or below a pressure of 30 pounds gauge, while the 50 percent oxygen-nitrogen mixture is inhaled between pressures of 30 and 75 pounds. The course of the treatment and the alternatives are clearly outlined.

present in the skin and in the extremities. The greatest amount of gas, however, collected in the venous side of the circulatory system.

In contrast with air recompression the period following oxygen breathing at a pressure of 30 pounds was characterized by a constant or only slight increase in the respiratory rate and by the maintainance of normal values for oxygen saturation of arterial blood. Bubbles when present at autopsy were confined to vessels of the extremities where the blood flow had been at a standstill during the recompression period. While recovery was usually not complete (subnormal blood pressure and circulatory rate) the advantage of oxygen over air was convincingly demonstrated by the permanent relief from asphyxia, and by the complete absorption of nitrogen bubbles from the circulating blood as determined by autopsy examination.

While the experimental evidence shows conclusively the value of oxygen in relieving asphyxia and in promoting bubble absorption it is essential to determine whether pressures higher than 30 pounds are necessary in recompression. Were asphyxia the only factor to consider, an excess pressure of 30 pounds combined with oxygen inhalation would be sufficient for all cases of compressed-air illness. Whether paralysis could be prevented by a pressure as low as 30 pounds, could not be determined in experiments on the anesthetized dog.

In order to determine the adequacy of a pressure of 30 pounds in preventing paralysis a second series of experiments was performed on intact dogs subjected to the same experimental conditions as were the anesthetized dogs. The results of these experiments are summarized in table 1. Dog 1, for example, was decompressed from 65 pounds excess pressure in 10 seconds after an exposure of 1 hour and 45 minutes. Three minutes following decompression the dog became excited and showed signs of pain (one of two experiments in which pain was a definite symptom). Four minutes later the dog was recompressed in an oxygen atmosphere to a pressure of 30 pounds for a period of 90 minutes. When the pressure was again lowered to 1 atmosphere (in 1 minute) paralysis of the hind legs was manifest. At autopsy bubbles were not visible in the blood stream. From this experiment it appeared that while bubbles were absorbed, recompression to 30 pounds pressure was insufficient to prevent the development of paralysis. This experiment showed the necessity of reestablishing the blood supply to the spinal cord in the shortest possible time. As a result of several similar experiments (dogs 2, 3, table 1), it was concluded that while the asphyxia was relieved and while the bubbles were absorbed, paralysis could develop during the breathing of oxygen at a pressure of 30 pounds.

In subsequent experiments the treatment was altered by raising the pressure to 65 pounds and then lowering it 5 pounds every 10 minutes until the level of 30 pounds was reached. Air was breathed during this period because a 50-percent oxygen-nitrogen mixture was not available. When the pressure was lowered to 30 pounds the chamber was filled with pure oxygen and the pressure maintained for 1 hour. A 1-minute decompression to atmospheric pressure completed the treatment. With this method of therapy paralysis either did not develop (during the recompression period), or the progress of the paralytic symptoms was stopped (dog 6, table 1). An exception to this statement may be the fact that in dog 5 paralysis of the hind legs developed after 24 hours following an apparently slight injury to the spinal cord.

TABLE 1.—*Treatment of compressed-air illness*

Dog	Date	Exposure	Following decompression (10-second decompression)	Recompression	Results
1	Apr. 23	1.75 hours, 65 pounds.	3 minutes, excitement, pain, outstanding symptom, no paralysis or asphyxia, 7 minutes, recompression.	30 pounds O_2 for 90 minutes.	Paralysis of hind legs. No bubbles in the blood stream.
2	Apr. 24	1.5 hours, 65 pounds.	No symptoms		
2	Apr. 29	1.75 hours, 65 pounds.	5 minutes, very active; 8 minutes, heart pounding; 9 minutes, slow heart rate (58); 10 minutes, languid, limping, left foreleg raised from floor; 14 minutes recompression.	30 pounds for 90 minutes (O_2). After 10 minutes, 30 pounds for 90 minutes (O_2).	Foot-drop. Dog able to stand but drags hind feet in walking. Unimproved by second recompression. Next day, paralysis and anesthesia of hind legs.
3	May 10	do	6 minutes, rigidity, left hind leg. Recompression.	30 pounds for 60 minutes (O_2). After 20 minutes 30 pounds for 60 minutes (O_2).	Limping; left hind leg rigid. Complete recovery after second recompression.
3	May 14	1.75 hours, 65 pounds.	9 minutes, limping, left foreleg off floor; 10 minutes recompression.	30 pounds, 60 minutes. After 2 minutes (O_2), 30 pounds, 60 minutes (O_2). After 9 minutes, 30 pounds, 60 minutes (O_2).	Right hind leg flexed. Spastic gait. Weakness hind legs. Spasticity and weakness increased. Autopsy, no bubbles.
4	May 22	do	4 minutes, collapsed	65 pounds air	Died in 26 minutes under 50 pounds pressure. Autopsy, bubbles in all blood vessels.
5	May 24	do	5 minutes, left hind leg raised off floor. Recompression.	65 pounds air [1] 70 minutes; 30 pounds O_2, 1 hour.	Recovery.
5	May 28	do	5 minutes, left foreleg flexed. Recompression.	do.[1]	Do.
5	June 11	do	8 minutes, stretched out, unable to move. Recompression.	do.[1]	Do.
5	June 18	do	12 minutes, no control over hind legs; 13.5 minutes, dyspnea. Recompression.	do.[1]	Weakness left hind leg. Ataxia left hind leg. Next day, dog able to walk but developed paralysis (hind legs) on the second day.
6	June 25	do	24 minutes; limping Recompressed.	O_2 30 pounds, 1 hour.	Recovery.
6	June 26	do	15 minutes, drags right hind foot; 17 minutes lying on side, hind legs useless.	65 pounds air [1], 70 minutes; 30 pounds O_2, 1 hour.	Right hind leg ataxic; 2 days later no improvement. 14 days later, recovery
7	do	1.75 hours, 65 pounds.	20 minutes, all extremities drawn up, dog in pain. Recompression.	65 pounds air [1], 30 pounds O_2 1 hour, 30 pounds O_2, 1 hour.	In good condition for 10 minutes, then vomiting, diarrhea. Active, in good condition.
7	June 28	1.77 hours, 65 pounds.	17 minutes, rigidity hind legs; 18 minutes, hind legs paralyzed, extended, priapism, dyspnea. Recompression.	65 pounds air [1], 30 pounds O_2, 1 hour.	Spastic paralysis of the hind legs. Reflex arc intact. Autopsy, distended bladder, spinal cord, lungs, normal. No bubbles. Petechial hemorrhages in fat.
8	June 29	do	27 minutes, cyanosis of mucous membranes and tongue. Left leg raised off floor.	65 pounds air [2] to 0 gage in 4 hours, 43 minutes.	Weakness, hind legs. Autopsy, a few bubbles in cutaneous vessels.

[1] Air pressure raised to 65 pounds, then lowered to 30 pounds at the rate of 2 minutes per pound; dog then breathed oxygen at 30 pounds pressure for 1 hour.
[2] Recompression essentially as outlined by the Diving Manual.

From these experiments it can be concluded that whenever bubble formation is massive (i. e., after a 10-second decompression from 65 pounds, 1.75 hours exposure) application of pressure to 65 pounds is necessary to prevent or to arrest the progress of incipient paralysis. While it is extremely doubtful if fully developed paralysis at the time of recompression will improve with the application of pressure, it is imperative in every case to compress the bubbles to a small size, and to secure their rapid absorption or removal from blood vessels in the spinal cord. The application of these findings clinically now depends upon the tolerance of man for oxygen at high pressures.

Tolerance of man for high oxygen pressure.—At atmospheric pressure healthy men can breathe oxygen for a period of 6 hours without symptoms indicative of pulmonary irritation. At higher pressures the effects of oxygen on the nervous system supersede those with reference to the lungs. At a pressure of 3 atmospheres, for example, pure oxygen can be breathed for a period of 4 hours without producing pulmonary injury (Behnke, Forbes, and Motley, 1935). It would appear that insofar as lung damage was concerned there was no direct relationship between the oxygen tension and the duration of exposure. The nervous symptoms, however, bear a direct relationship to the oxygen tension and the duration of exposure. At atmospheric pressure nervous manifestations of a minor character may accompany the breathing of oxygen (Behnke, Johnson, Poppen, and Motley, 1935). At a pressure of 3 atmospheres definite and sometimes apparently alarming symptoms occur during the fourth hour in every experiment. Preceded by a period of normality and with fairly abrupt onset, a rise in blood pressure, increase in pulse rate, and contraction of the visual fields with diminution in visual acuity point to the action of oxygen on the nervous system. Rapid and complete recovery invariably follows when air is again breathed. At a pressure of 4 atmospheres the limit of oxygen breathing is about 45 minutes. At this pressure convulsions or fainting may occur.

The mechanism underlying the action of oxygen on the nervous system is not known, but the significant fact is the reversibility of the nervous phenomena since complete recovery invariably follows the removal of oxygen. In experiments on 12 healthy men subjected (4 or 5 times) to oxygen tensions up to 4 atmospheres residual injury was not detected. While an oxygen tension of 4 atmospheres is to be regarded as a potentially convulsive level and hence to be avoided, a level of 3 atmospheres definitely represents a subconvulsive tension. The fact that pure oxygen at this pressure can be breathed for 3 hours permits oxygen therapy to form an essential part of the treatment for compressed-air illness. It should be remembered that a patient may tolerate oxygen for periods in excess of 3 or 4 hours in view of the probable anoxemia and slowed circulation, symptoms

which in dogs were associated with large quantities of bubbles in the blood stream.

Recompression based on oxygen therapy.—The fundamental principle underlying the treatment of compressed-air illness consists in the application of the fact that pure oxygen at a pressure of 30 pounds (3 atmospheres absolute) can be breathed for a period of 3 hours. If pressures higher than 3 atmospheres are used, the partial pressure of oxygen can be maintained at 3 atmospheres by adding air or nitrogen. For convenience, a 50 percent oxygen-nitrogen mixture could be made available for respiration between 3 and 6 atmospheres absolute. For pressures of 3 atmospheres or less pure oxygen would be breathed.

It is extremely difficult in view of the undetermined quantity of nitrogen in bubble form and of its undetermined distribution in the vascular beds of different organs to draw up a rigid outline of treatment for all cases of compressed-air illness. The condition of the patient, of course, is the criterion for guidance in treatment. The dog experiments (massive bubble formation in the blood stream), however, demonstrate the necessity of using comparatively high pressures (65 pounds) in order to prevent paralysis. These experiments in addition give an approximation of the time necessary for the absorption of bubbles.

For the serious cases of compressed-air illness in which the previous degree of pressure and duration of exposure, and in which the symptoms (asphyxia, paralysis, loss of consciousness) indicate extensive formation of bubbles, the reapplication of the pressure to 75 pounds with the patient breathing a 50 percent oxygen-nitrogen mixture ensures the immediate relief of asphyxia and the arrest of incipient nerve lesions. The pressure is then maintained at 75 pounds for a minimum period of 15 minutes with the understanding that the time can be extended to 2 hours for the moribund or paralyzed patient.

It may be well to consider what this initial stage in treatment will accomplish. The bubbles of nitrogen according to Boyle's law will be reduced to one-sixth of their volume at atmospheric pressure; as a result of compression the surface area of the bubbles in proportion to their volume is almost doubled, hence diffusion of nitrogen into the surrounding blood will be increased; the capacity of the blood and the tissues to absorb nitrogen will be increased six-fold; and if a 50 percent oxygen-nitrogen mixture is breathed, nitrogen will be eliminated from the body at a pressure head of 3 atmospheres. The quantity of nitrogen eliminated at 75 pounds pressure (with the respiration of a 50 percent oxygen-nitrogen mixture) can be approximately calculated as follows: With a pressure head of 1 atmosphere 35 to 50 cubic centimeters of nitrogen (NTP) are eliminated by a man at rest, weighing 60 kilograms. With a pressure head of 3

atmospheres and a normal circulatory rate a minimum of 105 cubic centimeters (NTP) of nitrogen per minute would be eliminated from the body as long as bubbles maintained nitrogen saturation in the blood stream (large veins and right side of the heart). Under these conditions it would be reasonable to expect the elimination of all or nearly all of the nitrogen in bubble form.

The second and final stage in treatment (patient conscious, respiratory rate normal) following 15 minutes' exposure to 75 pounds pressure, or at least 2 hours' exposure if paralysis is present, consists in the reduction in pressure to 30 pounds at the rate of 1 pound per minute. At this pressure pure oxygen is substituted for the oxygen-nitrogen mixture. The breathing of pure oxygen for a period of 1 to 2 hours serves to eliminate completely any residual bubbles following the first stage in treatment. This statement is based on the observation that in dogs dying from massive nitrogen bubble formation recompression to a pressure of 65 pounds and decompression in 70 minutes (in air) to 30 pounds pressure followed by 1 hour of oxygen inhalation resulted in the elimination of bubbles visible to the unaided eye. Since the circulatory rate in man is one-half that of the dog, the time for oxygen breathing is doubled (i. e., 2 hours at 30 pounds for the treatment of a previously moribund patient). If the patient is in good condition after 1 hour of oxygen breathing the pressure is lowered to that of the atmosphere over a period of 30 minutes. If, on the other hand, the condition of the patient indicates that bubbles are still present after the completion of oxygen breathing at a pressure of 30 pounds or its equivalent partial pressure for 3 hours, or if the return to atmospheric pressure is attended by increased respiratory rate, difficulty in breathing, and pain, air is substituted for oxygen and a pressure of 30 pounds maintained for 24 hours. At the end of 24 hours the inhalation of oxygen for 2 hours followed by a 30-minute decompression to atmospheric pressure completes the treatment. In figure 3 the therapy is represented in graphic form.

In order to summarize the main points in the treatment of a serious case of compressed-air illness it can be stated that recompression is simplified to two stages and utilizes oxygen breathing. In the first stage the patient breathing a 50-percent oxygen-nitrogen mixture is recompressed to 75 pounds pressure for a minimum period of 15 minutes. Symptomatic recovery and the absorption of all or nearly all of the nitrogen bubbles are the objectives in this procedure. Treatment at a pressure of 75 pounds can be prolonged for 2 hours, if necessary. In the second stage after the pressure has been reduced to 30 pounds, pure oxygen is breathed for a period of 1 to 2 hours. Treatment is completed by decompression in 30 minutes to atmospheric pressure. Unrelieved or partially relieved symptoms require treatment by prolonging the compression at 30 pounds (patient breathing air). At the end of 24 hours oxygen is breathed for 2 hours.

Toxic symptoms from oxygen should not occur (contraction of the visual fields, rise in blood pressure and pulse rate) with 3 hours of oxygen breathing in any 24-hour period.

Since 90 percent of the cases of compressed-air illness are mild and exhibit symptoms designated as "bends" (pain in the extremities), recompression to a pressure of 30 pounds with the inhalation of oxygen for 1 hour, followed by a 30-minute decompression, should be sufficient.

Concluding notes.—During the first stage in the recompression treatment the body should be maintained in a horizontal position with the head and shoulders inclined slightly downward. This procedure will protect the blood supply to the brain since bubbles tend to accumulate in the most elevated parts of the body (Van Allen, Hrdina, and Clark, 1929).

The follow-up treatment of the severe cases is designed to protect the heart and to prevent pneumonia. In patients afflicted with spinal cord injury retention of urine and the formation of decubitus ulcers are to be prevented. The concentration of red blood cells (plasma loss) associated with massive bubble formation (dogs) suggests the value of isotonic glucose-saline solution preferably administered subcutaneously, or if intravenously, very slowly (500 cubic centimeters in 30 minutes) and only after the completion of compression treatment.

The facilities for oxygen administration consists of cylinders and a spirometer to which is attached either a helmet or a mask. By adding a soda lime cannister, cooling coil, and blower oxygen can be rebreathed with a minimum loss of gas.

SUMMARY

On the basis of theoretical considerations and experimental evidence oxygen inhalation combined with recompression comprises the essential treatment for compressed-air illness.

Since pure oxygen can be breathed without discomfort by healthy men for 3 hours at a gage pressure of 30 pounds (3 atmospheres absolute), it follows that an equivalent tension (50-percent oxygen-nitrogen mixture) can be breathed at a pressure of 75 pounds (6 atmospheres absolute) for a corresponding period of time. These values for oxygen tolerance make possible the use of oxygen over the whole recompression period.

In the treatment of the severe cases of compressed-air illness (prostration, asphyxia, and paralysis) recompression consists of two stages (fig. 3). During the first stage the pressure is raised to 75 pounds and maintained for a period of 15 minutes to 2 hours. At this pressure a 50-percent oxygen-nitrogen mixture is breathed. The second stage consists in lowering the pressure at the rate of a pound

per minute from 75 to 30 pounds gage, and substituting oxygen for the oxygen-nitrogen mixture. Oxygen is breathed at a pressure of 30 pounds for a period of 1 to 2 hours, and treatment is completed by a 30-minute decompression to atmospheric pressure. Unrelieved symptoms require a prolonged stay at 30 pounds pressure for 24 hours and a second period of oxygen inhalation.

In the treatment of mild cases of compressed-air illness ("bends") oxygen inhalation at a pressure of 30 pounds for 1 hour followed by a 30-minute decompression should effect permanent relief.

The authors wish to express their thanks and appreciation to Capt. E. W. Brown, Medical Corps, United States Navy, and to Prof. Cecil K. Drinker, under whose direction this research was conducted. We also wish to express our thanks to Miss Anne C. Messer, Mr. Robert M. Thomson, and Mr. E. Preble Motley for assistance in the performance of the experiments.

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THE PREVENTION OF COMPRESSED-AIR ILLNESS.

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(*From the Lister Institute of Preventive Medicine.*)

[With 7 Figures and 3 Plates.]

CONTENTS.

INTRODUCTION.

MEN who have been working in compressed air, as in diving, preparing foundations of bridges, etc. under water, or making tunnels or shafts through water-bearing strata, are liable on their return to atmospheric pressure to a variety of symptoms generally known as "diver's palsy" or "caisson disease," but which may more conveniently be designated "compressed-air illness." It was shown experimentally by Paul Bert[1] that these symptoms are due to the fact that gas (chiefly nitrogen) which goes into solution in the blood and tissues during exposure to compressed air is liberated in the form of bubbles on too rapid decompression, and produces local or general blockage of the circulation or other injury. Subsequent investigations, for an account of which we must refer more particularly to the treatise on the subject by Heller, Mager and v. Schrötter[2] and to recent papers by Hill and McLeod[3] and Hill and Greenwood[4], have confirmed and extended Paul Bert's conclusions.

It was pointed out by Paul Bert that by means of very slow decompression the symptoms of caisson disease could be avoided, but his experiments were not sufficient to furnish data as to what rate of decompression would be safe. Nor has subsequent human experience in engineering undertakings solved this problem; and the risks attending work in compressed air at excess pressures of over $1\frac{1}{2}$ to 2 atmospheres are notorious. Heller, Mager and v. Schrötter have endeavoured to formulate rules as to safe decompression; and they express the belief that perfectly uniform decompression at the rate of 20 minutes an atmosphere would always be safe. Following this rule, which is based on a calculation, Hill and Greenwood decompressed themselves, without any serious symptoms, after short exposures at excess pressures of as much as five and even six atmospheres.

Although the rules formulated by the above-mentioned observers constituted a distinct step in advance, it appeared to us that, for reasons which will be explained below, there were grave doubts as

[1] *La Pression Barometrique*, 1878.

[2] *Luftdruckerkrankungen*, 1900; also v. Schrötter, *Der Sauerstoff in der Prophylaxie und Therapie der Luftdruckerkrankungen*, 2nd edition, 1906. The former work contains a very full abstract of all previous investigations on the subject.

[3] This *Journal*, vol. III. (1903), p. 401 (and references there given): see also *Recent Advances in Physiology*, 1906, pp. 233—255.

[4] *Proceedings of the Royal Society*, vol. LXXVII. p. 442, 1906; vol. LXXIX. p. 21, 1907; also *British Medical Journal*, July 7th, 1906, Feb. 16th, 1907, June 22nd, 1907.

to the safety of their recommendations, and particularly as to whether uniform decompression is desirable. The need for framing definite rules as to safe decompression in the shortest possible time presented itself in a very definite form in connection with the work of the Admiralty Committee on Deep Diving[1], of which one of us was a member. Our investigation, which was planned with the more particular object of furnishing information required for securing the safety of divers ascending from deep water, was rendered possible by the gift to the Lister Institute by Dr Ludwig Mond, F.R.S. of a large experimental steel pressure chamber and by substantial financial and other help from the Admiralty, Messrs John Aird and Son, the late Mr Basil Ellis, Messrs S. Pearson and Son, Ltd., and Messrs Price and Reeves.

The formation of gas bubbles in the living body during or shortly after decompression evidently depends on the fact that the partial pressure of the gas or gases dissolved in the blood and tissues is in excess of the external pressure. But it is a well-known fact that liquids, and especially albuminous liquids such as blood, will hold gas for long periods in a state of supersaturation, provided the supersaturation does not exceed a certain limit. In order to decompress safely it is evidently necessary to prevent this limit being exceeded before the end of decompression. Whether or not the decompression is free from risk will depend on the degree of supersaturation which can be borne with safety, the extent to which the blood and tissues have had time or opportunity to become saturated, and the extent to which they have had time to become desaturated again during decompression. In carrying out our investigations we have kept these three factors constantly in view, and it is necessary to discuss them in some detail before proceeding further.

[1] The Report of this Committee, which has recently appeared as a blue-book, contains a full account of the experimental investigations on Diving, carried out under its auspices at Portsmouth, off the West Coast of Scotland, and elsewhere, during the last two years: also a short summary of the experiments detailed in the present paper, and many data as to the occurrence of compressed-air illness in connection with diving and other work in compressed air. The conclusions and recommendations of the Committee are summarised at the beginning of the Report.

PART I. THEORETICAL.

A. *The rate of saturation of the body with nitrogen during exposure to compressed air.*

When a man or animal is placed in compressed air, the blood passing through the lungs will undoubtedly take up in simple solution an amount of gas which will be increased above normal in proportion to the increase in partial pressure of each gas present in the alveolar air. The experiments of Haldane and Priestley[1], which have since been extended by Hill and Greenwood[2], show that the partial pressure of CO_2 in the alveolar air remains constant with a rise of atmospheric pressure: hence there can be no increase in the amount of CO_2 present in the blood during exposure to compressed air. As regards oxygen, the amount in simple solution in the arterial blood will certainly increase in proportion to the rise in alveolar oxygen pressure; but as soon as the blood reaches the tissues this extra dissolved oxygen, which (except with exposures to enormous pressures) is only a small part of the total available oxygen in the arterial blood, will be used up, so that in the tissues and venous blood there will be at most only a very slight increase in the partial pressure of oxygen. For practical purposes therefore we need only take into consideration the saturation of the body with nitrogen.

In view of what is known as to the ease and completeness with which the blood becomes aerated in its passage through the lungs, there seems no reason to doubt that in compressed air the blood reaching the lung capillaries must become instantly saturated with nitrogen at the partial pressure existing in the alveolar air (see p. 351). At the commencement of exposure to compressed air this blood, on being carried to the tissues, will by diffusion share with them its excess of nitrogen and then return to the lungs for a fresh charge. By the constant repetition of this process the tissues, and the venous blood leaving them, will gradually become more and more saturated with nitrogen at the partial pressure of the nitrogen in the alveolar air, which will be practically the same as in the inspired air. Since the rate of blood supply and the solubility of nitrogen per unit mass of tissue vary greatly in different parts of the body, the rate of saturation

[1] *Journal of Physiology*, vol. XXXII. (1905), p. 229.
[2] *Proc. Roy. Soc.*, B, vol. LXXVII. p. 442.

will vary correspondingly. We may however form some rough general idea of the average rate of saturation by assuming as a basis of calculation that the blood is evenly distributed throughout the body, and that the tissues are similarly constituted in all parts.

According to the figures adopted by Bohr[1], 100 c.c. of blood take up in simple solution at the body temperature 0·87 c.c. of nitrogen for each atmosphere of air pressure. This is only 8 % less than would be taken up by water under the same conditions. Blood contains nearly the same percentage of solids as the semi-liquid tissues (apart from fat) in most parts of the body, and we may assume that these tissues will take up nearly the same proportion of nitrogen as blood. The earthy constituents of bone (about 3 % of the body weight) probably take up no nitrogen. On the other hand the body fat, as was recently shown by Vernon[2], who made a number of determinations at the body temperature with special reference to our investigations, takes up about six times as much nitrogen as an equal weight of blood. The body of a well-nourished man probably contains fully 15 % of its weight as fat or fatty material. Hence it may be estimated that it will, when saturated at any given pressure, on an average take up, weight for weight, about 70 % more nitrogen in simple solution than the blood under the same conditions, and that the whole body of a man weighing 70 kilos will take up about one litre of nitrogen for each atmosphere of excess pressure.

Now the weight of the blood in man is about 4·9 % of the body weight[3]: hence the amount of nitrogen held in solution in the body, when it is completely saturated at any given pressure, will be about $\frac{170}{4{\cdot}9}$, or 35 times as great as the amount present in the blood alone. If therefore the blood distributed itself evenly and at the same rate throughout the body, the latter would have received, at the end of one complete round of the blood after sudden exposure to high pressure of air, one thirty-fifth of the excess of nitrogen corresponding to complete saturation. The second round of the circulation would add one thirty-fifth of the remaining deficit in saturation, *i.e.* $1/35 \times 34/35$ of the total excess: the third round would add $1/35 \times (34/35 \times 34/35)$ of the total excess, and so on. On following out this calculation, it will be found that half the total excess of nitrogen would have entered the body

[1] *Nagel's Handbuch der Physiologie*, vol. I., 1905, p. 63.

[2] *Proc. Roy. Soc.*, vol. LXXIX. B, 1907, p. 366.

[3] Haldane and Lorrain Smith, *Journal of Physiology*, vol. XXV., 1900, p. 340.

after 23 rounds of the circulation, three-fourths after 46 rounds, seven-eighths after 69 rounds, and so on. The progress of the saturation of the body with nitrogen is thus a logarithmic curve of the form shown in Figure 1[1].

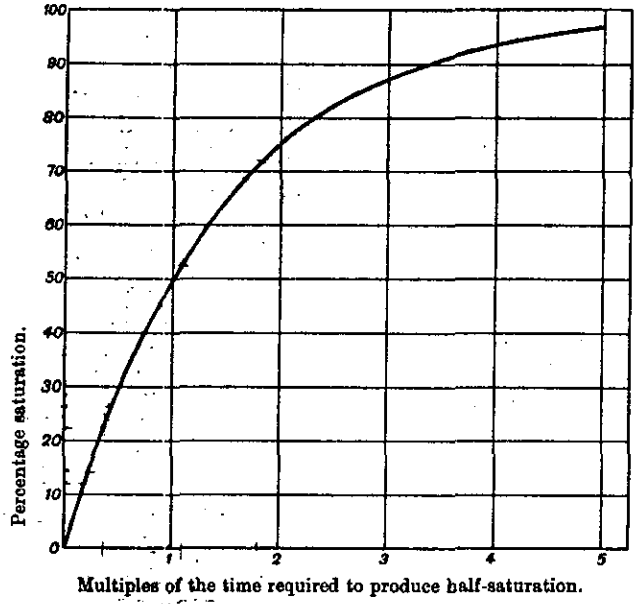


Fig. 1. Curve showing the progress of saturation of any part of the body with nitrogen after any given sudden rise of air pressure. The percentage saturation can be read off on the curve, provided the duration of exposure to the pressure, and the time required to produce half-saturation of the part in question, are both known. Thus a part which half-saturates in one hour would, as shown on the curve, be 30 % saturated in half-an-hour, or 94 % saturated in 4 hours.

Experiments on animals have shown that the venous blood entering the lungs contains about two-fifths less of oxygen than the arterial blood. If we assume that the same proportion holds good for a man at rest, and that very little oxygen is used up in the lungs themselves, the percentage of oxygen gained by the blood in the lungs must be about 8 %, or about double the percentage diminution in the expired

[1] This calculation is in principle similar to that made by Zuntz (*Fortschritte der Medizin*, 1897, No. 16), and worked out more fully by Heller, Mager and v. Schrötter (*loc. cit.*). On account, however, of the discovery that fat has a very high coefficient of absorption for nitrogen, and that the blood volume in man is considerably less than was formerly supposed, our calculation gives a much slower rate of saturation per round of the circulation.

air as compared with the inspired air. The volume of blood passing through the lungs is therefore about double the volume of air breathed. Since this volume of air (measured dry and at standard pressure and temperature) averages about seven litres per minute[1] for a man of 70 kilos during rest, the volume of blood passing through the lungs may be estimated at about 3·5 litres per minute[2]. The total blood volume is however also about 3·5 litres, so that a volume of blood equal to the total blood volume probably passes through the lungs about once a minute during rest. We may therefore substitute minutes for rounds of the circulation in the above calculation of the rate of saturation of the body with nitrogen, so that, if the assumptions made for the purposes of the calculation held good for a man exposed to compressed air, his body would be half saturated with the excess of nitrogen in 23 minutes, three-fourths saturated in 46 minutes, etc.

In reality, however, this calculation affords at best only a very *rough* general idea of the actual rate of saturation, since it is known that the distribution of blood per unit of body weight through various parts of the body varies greatly, and that the rate of circulation through any given part varies according as the part is at rest or in a state of activity. The proportion of fat and fatty material is also very different in different parts of the body, so that the capacities of different tissues for taking up nitrogen must vary *accordingly*. We should expect therefore that some parts of the body will saturate much more rapidly than the calculation shows, and other parts much more slowly. Direct experimental evidence of far more rapid saturation in some parts of the body has recently been furnished by Hill and Greenwood[3]. Their method was to determine the free nitrogen in samples of urine secreted shortly after exposure to high pressure, and shortly after return to normal pressure. A sufficiently copious secretion of urine was produced by previously administering large drinks of water to the subject of the experiment; and they found that, within about ten minutes of exposure to high pressure, samples of urine secreted were saturated at this pressure. Conversely, on lowering the pressure to normal, the excess of nitrogen disappeared within a few minutes.

[1] Haldane and Priestley, *loc. cit.*, p. 245.

[2] As a result of numerous experiments on man with the lung catheter Loewy and v. Schrötter (*Untersuchungen über die Blutcirculation beim Menschen*, 1905, p. 90) infer that the average rate of blood flow during rest is slightly faster. At present, however, there is some doubt as to the interpretation of results obtained by the lung catheter method.

[3] *Proc. Roy. Soc.* B, vol. LXXIX., p. 21, 1907.

These results seem to show conclusively that the kidney substance became saturated with nitrogen at a rate about ten times as great as would correspond to the above calculation. From the data given it appears, however, that urine was being secreted with great rapidity during the experiments. For instance, 135 c.c. were secreted in five minutes in one observation where the quantities and times are recorded. This is about thirty times the average rate of secretion, so that the circulation of blood through the actively working kidneys must have been greatly increased.

Equally clear evidence of the existence of a far slower rate of saturation is afforded by the experience of men working in compressed air, particularly in caissons and tunnels at moderate pressures. It is well known to those practically familiar with such work that the risk of symptoms occurring on decompression depends on the duration of the exposure. There is very little risk on rapid decompression after short exposures of less than an hour to an excess pressure of two atmospheres or even somewhat higher pressure; but as the duration of exposure increases hour by hour, so do the risks on decompression increase. We are assured by Mr E. W. Moir (of the firm of Messrs S. Pearson and Son, Ltd., Westminster), who has had an exceptionally large experience of tunnelling work in compressed air at excess pressures up to about $2\frac{1}{2}$ atmospheres, that the maximum of risk is not reached after even three hours, so that a limitation of working shifts to three hours markedly diminishes the frequency of compressed-air illness. Hence in some parts of the body saturation with nitrogen must still be incomplete after three hours. Another observation pointing in the same direction is that when the daily working period was $8\frac{1}{2}$ hours under pressure with two intervals of about $1\frac{1}{2}$ hours each for meals at ordinary atmospheric pressure, cases of caisson disease usually occurred after the last decompression in the evening and not when the men came out for meals[1].

Our own observations on animals afford fresh evidence bearing in the same direction. We found that in goats the risks on decompression increase with the length of exposure to pressure up to from two to three hours (see below, p. 396).

In different warm-blooded animals the rate of respiratory exchange varies, roughly speaking, according to the ratio of body surface to weight. The smaller the animals, therefore, the greater is the respiratory exchange per unit of body weight, and the more rapid must be the

[1] G. W. M. Boycott, *Trans. Inst. of Civil Engineers*, vol. CLXV., 1906.

circulation. In consequence small animals, when placed in compressed air, must saturate their tissues more rapidly in proportion to their more active respiratory exchange; and, conversely, they will free themselves more rapidly, during or after decompression, from the excess of nitrogen. Hence results obtained with small animals as to the time required for complete saturation, or for safe decompression, are not directly applicable to man. We selected goats for our experiments as they were the largest animals which could be conveniently used; but their weights averaged only about one-fourth to one-third of the weight of an adult man. As the surfaces of different mammals are roughly as the cube roots squared of their weights, we should expect that in goats of this size the respiratory exchange per kilo of body weight would be about two-thirds greater than in man. Direct determinations showed that this was the case (see p. 381). Hence if it required three hours exposure to a high pressure to effect practically complete saturation[1] of the more slowly saturating tissues of a goat with nitrogen, about five hours would be required for a man. An inspection of Fig. 1 (p. 347) will show that if these tissues became 50 % saturated in about 45 minutes in goats and 75 minutes in man, they would be 94 % saturated in three hours for goats, and in five hours for man. A higher degree of saturation than this would scarcely be appreciable, and we have concluded that for practical purposes any slower rate of saturation than this, and correspondingly slower rate of desaturation, need not be allowed for, unless the percentage of fat in the body is abnormally high. We must admit, however, that there is some evidence, both from our own experiments and from practical experience in work in compressed air, that in the parts of the body which are the seat of "bends" a still slower rate of saturation may exist.

B. *The rate of desaturation of the body with nitrogen during and after decompression.*

If the pressure is rapidly diminished to normal after exposure to saturation in compressed air, and no gas bubbles are liberated in the body, it is evident that for each part of the body the curve of desaturation will be similar to that of saturation, provided the physiological conditions are constant. The venous blood will give off practically the

[1] The only method apparently available to determine the time of complete saturation in normal animals is to subject them to a series of experiments in which the pressure and decompression are kept constant and the time of exposure varied, and to observe when the effects cease to become any worse. The method is open to obvious limitations.

whole of its excess of dissolved nitrogen during its passage through the lungs[1], and at each round of the circulation will bring back a fresh charge of nitrogen (at the partial pressure existing in the tissues) to be given off. The parts which become half desaturated by this process in a given time will be three-fourths desaturated in double the time, and so on. The slowest saturating tissues will thus, in accordance with our previous calculation, take one and a quarter hours to become half desaturated in man.

The normal combined gas pressure of nitrogen, oxygen and CO_2 in the tissues and venous blood may be estimated as about 90 % of an atmosphere, so that if the nitrogen pressure be more than an eighth above normal the total gas pressure will be above atmospheric pressure. Supposing therefore that before decompression the most slowly saturating parts of the body (*i.e.* those half saturating in one and a quarter hours) had been saturated to an excess pressure of two atmospheres of air, it would take about five hours at atmospheric pressure to reduce this excess pressure to a sixteenth (or an eighth of one atmosphere) and so bring down the total gas pressure in the parts in question to about atmospheric pressure. The slowness of desaturation must be as clearly borne in mind as the slowness of saturation, in connection with all the phenomena of compressed-air illness.

If gas bubbles are formed in consequence of too rapid decompression, they will naturally tend to increase in size by diffusion into them, in whatever part of the body they may be except the arteries, for some time after the end of decompression. They may thus easily cause blocking of small vessels, and even if they are carried to the right side of the heart or the pulmonary arteries, and lodge there, they will increase in bulk until the total gas pressure in the mixed venous blood falls to one atmosphere. The same remark applies to bubbles which

[1] In view of the enormous surface (probably more than 100 square metres) presented by the lung alveoli for diffusion it seems hardly possible to doubt that the blood during its passage through the lungs becomes saturated or desaturated to almost exactly the pressure of nitrogen in the alveolar air. According to the calculations of Loewy and Zuntz (*Die physiologischen Grundlagen der Sauerstoff-Therapie* in Michaelis' *Die Sauerstofftherapie*, Berlin, 1904), a difference in partial pressure of oxygen of less than 1 mm. of mercury would account for the diffusion of 250 c.c. of oxygen per minute through the alveolar walls. With a difference in partial pressure of nitrogen of two atmospheres, or 1520 mm. of mercury, between the blood and the alveolar air only about 70 c.c. of nitrogen would require to pass per minute in order to establish complete saturation, or desaturation, of the blood. The conditions are thus enormously more favourable for the taking up or giving off of this nitrogen than for the taking up of oxygen by diffusion during normal respiration.

lodge in the branches of the portal veins. If small bubbles are carried through the lung capillaries and pass, for instance, to a slowly desaturating part of the spinal cord, they will there increase in size and may produce serious blockage of the circulation or direct mechanical damage. Apart from this increase of size the air bubbles passing along the arteries are probably too small to cause any harm. Once formed they will under ordinary conditions take a long time to become reabsorbed, since even after the gas pressure in the blood and tissues has fallen to normal, the excess of nitrogen pressure in the bubbles over that in the blood and tissues will only be about a tenth of an atmosphere at most. In one case we found bubbles in the veins of an animal which died two days after suffering from severe decompression symptoms (see below p. 421).

In order to avoid the risk of bubbles being formed on decompression, it has hitherto been recommended that decompression should be slow and at as nearly a uniform rate throughout as possible. We must therefore carefully consider the process of desaturation of the body during slow and uniform decompression. For convenience in calculation we may imagine the process as occurring in a series of time-intervals, the first half of each of which is spent at the pressure existing at the beginning of the interval, and the second half at the pressure existing at the end. Let us suppose, for instance, that the body has been completely saturated with nitrogen at an excess pressure of five atmospheres of air, and that decompression occurs at a rate of one atmosphere in 20 minutes. The process may be divided into five periods of 20 minutes, during each of which the pressure falls one atmosphere. We can then easily calculate how far desaturation will have gone at the end of each period, and from these data construct a desaturation curve.

Let us first consider the mean desaturation rate of the whole body, assuming that, when the pressure is suddenly raised or diminished to a certain level, the tissues will on an average saturate or desaturate themselves by 50 % in 23 minutes, which was shown above to be a probable average rate. A reference to the curve (Fig. 1) shows that ten minutes' exposure to the reduced pressure of four atmospheres in excess will reduce the saturation by 28 % of the difference between five and four atmospheres, *i.e.* by 0·28 of an atmosphere. Hence at the end of 20 minutes the tissues will on an average be saturated to 4·72 atmospheres. Ten more minutes at four atmospheres will reduce the saturation to 4·5 atmospheres, and ten minutes at three atmospheres

will further reduce it by 28% of 4·5 − 3, *i.e.* by 0·42 atmosphere. Hence at the end of the second twenty minutes the saturation of the tissues will be 4·08 atmospheres. Continuing this calculation we get the desaturation curve shown in Fig. 2, from which it will be seen that when atmospheric pressure is reached the tissues are still saturated to an excess pressure corresponding to 1·4 atmospheres of air.

Fig. 2 also shows a similar curve for the parts which saturate and desaturate most slowly, and which, according to our previous calculations, take one and a quarter hours to become half saturated. At the end of decompression these slowly desaturating parts, as shown on the curve, are still saturated to 3·15 atmospheres. This of course represents a most formidable excess; and, as will be shown below (p. 401), uniform decompression at this rate is dangerous even to goats, and would certainly be extremely dangerous to men, who desaturate a good deal more slowly than goats.

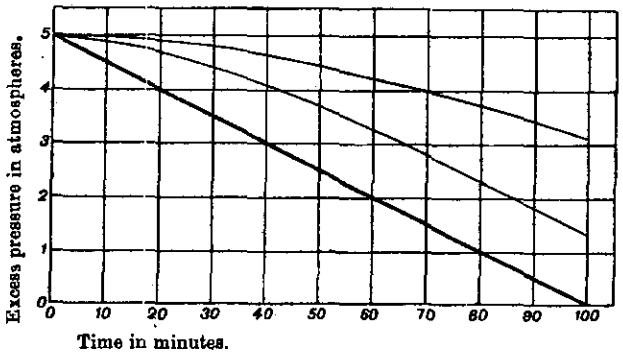


Fig. 2. Desaturation during uniform decompression after complete saturation at 5 atmospheres excess pressure. The thick line represents the air pressure: the upper and lower thin lines represent respectively the progress of desaturation in *parts of the body which half saturate in 75 and 23* minutes.

Inspection of Fig. 2 shows that with uniform decompression the nitrogen pressure in the body lags behind that of the air, and that (in the case of the slowly desaturating parts) the amount of the lag increases during the whole time of a decompression lasting 100 minutes. No other result seems possible, and actual experiments point strongly in the same direction, as will be shown presently. We must emphatically dissent from the conclusion drawn by Heller, Mager and v. Schrötter that decompression at the uniform rate of 20 minutes an atmosphere prevents any dangerous retention of gas in the body. To

prevent a maximum lag of more than one atmosphere, it would be necessary to decompress at a rate of over one and a half hours an atmosphere if the decompression were uniform and from an excess pressure of five atmospheres[1].

The examples given will be sufficient to illustrate the extreme slowness with which desaturation must occur with a uniform rate of decompression. This slowness has never hitherto been recognised, but must evidently be reckoned with in devising measures for the prevention of caisson disease.

It is clear that the rate of desaturation might be hastened by either (1) increasing the difference in nitrogen pressure between the venous blood and the air in the lungs, or (2) increasing the rate of blood circulation. In either case the blood would give off through the lungs an increased amount of the excess of nitrogen in a given time.

In order to increase the difference in nitrogen pressure between the venous blood and the alveolar air it has been proposed to give a diver oxygen to breathe during, or before decompression. As long, however, as the pressure was above about one atmosphere in excess, or 15 lbs., it would be impossible to do this safely, since, as will be explained more fully below, the effects might be rapidly fatal owing to oxygen poisoning. The possible applications of oxygen are thus somewhat limited, while the complications involved would be very considerable. The same end can, however, be attained in another way, as will be shown in the following section.

The rate of blood circulation can be increased considerably by muscular exertion. Quite moderate exertion is sufficient to increase the respiratory exchange to three or four times the normal; and the rate of blood flow through the lungs must be increased to something approaching to a corresponding extent. Unfortunately, the increased blood flow is chiefly through the muscles which are working, but probably many parts of the body participate to a greater or less extent in the extra blood supply. Muscular work must correspondingly increase the rate of saturation of the body with nitrogen. For this reason it seems desirable that where work has been done in compressed air, so that the muscles and associated tissues have probably become rapidly saturated with nitrogen, there should also be muscular exertion

[1] It is evidently a mistake to assume that a given rate of uniform decompression, such as 20 minutes per atmosphere, is either necessary for safety in all cases, or would be actually safe except from some limit of pressure. From a pressure below this limit the rate will be unnecessarily slow, and from above it dangerously fast.

during decompression. The rate of desaturation will thus be increased so as to compensate for the increased rate of saturation. In the case of short exposures to compressed air, as in diving work, this is specially important. Even, however, when there has been no special muscular work in the compressed air movements of joints and massage of the skin etc. will probably hasten desaturation. This has been clearly pointed out by Hill and Greenwood[1].

Another method which can be employed for increasing the circulation in the case of divers is to restrict the air supply, so that the partial pressure of CO_2 in the air of the helmet may rise sufficiently to stimulate the respiration and circulation. Both methods are now used in the Royal Navy during the ascent of divers.

C. *The limits of safety in decompression.*

It is a fact well known to those practically acquainted with work in compressed air that even with very rapid decompression there is no risk of caisson disease unless the pressure has exceeded a certain amount. It seems perfectly clear that no symptoms occur with less than one atmosphere[2] of excess pressure, however long the exposure may be. Whether any distinct symptoms ever occur with less than about 1·25 atmospheres (18½ lbs. per square inch or 41 feet of sea water) seems very doubtful: at any rate they are very exceptional. At pressures a little above 1·25 atmospheres occasional slight cases begin to be observed, and their frequency and gravity rapidly increase with higher pressures unless the time of exposure is limited or slow decompression is resorted to. The lowest pressure at which we have been able to find any record of a death occurring from caisson disease is 23 lbs. or 1·6 atmospheres[3]. As will be seen below, we were able to obtain slight symptoms on rapid decompression in 1 out of 22 goats after long

[1] *Proc. Roy. Soc.* B, vol. LXXVII., p. 449, 1906.

[2] One atmosphere or 760 mm. of mercury = 14·7 lbs. per square inch, about 1 kilogram per square centimetre, 34 feet of fresh water, 33 feet of sea water. In this paper where pressures are defined in pounds or atmospheres without qualification, reference is intended to the excess over atmospheric pressure as shown on gauges, not to the absolute total pressure.

[3] Babington and Cuthbert, *Dublin Quarterly Journal of Medical Sciences*, vol. XXXVI., 1863, p. 312. In the list of fatal cases given by Heller, Mager and v. Schrötter (*Luftdruckerkrankungen*, p. 1072), are entered two deaths at a pressure of 1·4 atmospheres. A perusal of Paul Bert's original account (*La Pression Barometrique*, p. 401) shows that both the pressure and the cause of death are quite uncertain.

exposure (four hours) to 1·36 atmospheres or 20 lbs. With 25 lbs. (1·7 atmospheres) two cases of slight illness occurred out of 23 animals.

If the risks of rapid decompression depended simply on the extent to which the blood and tissues are supersaturated with nitrogen on decompression, we should expect to find that even a short exposure to such an excess pressure as two atmospheres would be risky with rapid decompression: for there can be no doubt that within, say, half an hour or forty minutes the tissues, and the blood returning from them, must be for all practical purposes fully saturated in many parts of the body, and particularly in parts of great physiological importance which are richly supplied with blood. Nevertheless it seems to be well established that a man may stay without serious risk for forty minutes at a pressure which would involve great danger on rapid decompression if he remained in it for several hours.

Parts of the body with a rapid circulation will become very completely saturated in a comparatively short time, but the highly supersaturated blood which first returns from them on rapid decompression can remain but a very short time supersaturated during each round of the circulation, and on reaching the large veins will mix with less highly saturated blood from other parts of the body. It would seem that the state of high supersaturation in any portion of blood lasts for too short a time to enable bubbles to form.

If this interpretation of the facts is correct, we should expect to find with small animals, which rapidly saturate and desaturate, that a higher pressure would be required to produce symptoms on rapid decompression after a long exposure than in the case of larger animals. The general experience of previous observers is in accord with this, and our own experiments (see below p. 402) showed that we could produce no obvious effects in mice, and very few in rabbits, rats, and guinea-pigs, by sudden decompression after exposures at pressures which were invariably or frequently fatal to goats.

Since supersaturation to the extent of about 1·25 atmospheres above normal atmospheric pressure can be borne with impunity, though a greater degree of supersaturation is risky, it seems clear that, in decompressing after prolonged exposure to high pressures, the rate of decompression should be sufficiently slow to prevent any greater excess of saturation than this in any part of the body at the end of decompression. On the other hand decompression should evidently be as rapid as is possible, consistently with safety. A pressure of 1 to 1·25 atmospheres above normal corresponds to from 2 to 2·25 times the

normal atmospheric pressure; but the *volume* (not the *mass*) of gas (measured at the existing pressure) which would be liberated if the whole excess of gas present in supersaturation were given off is the same whether the absolute pressure is reduced from two to one atmospheres, or from four to two, or from eight to four. Hence it seemed probable that, if it is safe to decompress suddenly from two atmospheres of absolute pressure to one, it would be equally safe to decompress from four atmospheres absolute to two, from six atmospheres absolute to three, etc. Our experiments, which are detailed below (p. 398), have shown that this is the case[1]. The process of desaturation can therefore be hastened very greatly by rapidly reducing the absolute pressure to half, and so arranging the rest of the decompression that the saturation in no part of the body shall ever be allowed to correspond to more than about double the air pressure. The main advantage of this plan is that the discharge of nitrogen from the tissues is from the outset of decompression increased to the greatest rate which is safe. The rate of discharge evidently depends on the difference in partial pressure of nitrogen between the venous blood and the alveolar air; and by keeping this difference at the maximum consistent with safety a great saving of time is effected. Detailed investigations have completely justified the adoption of this principle: they are described below, and comprise, besides a series of observations on animals, a number of experiments in which Lieut. Damant and Mr Catto were exposed to excess pressures up to 80 pounds, or 6·4 atmospheres of absolute pressure, in the experimental chamber and to 93½ pounds, or 7·4 atmospheres, in actual diving. The method greatly simplifies the problem of safe decompression, and gets rid of many practical difficulties, particularly in connection with deep diving. It may be conveniently referred to as the method of "stage decompression," and is so described in the sequel, though its essential peculiarity does not lie in the decompression being done in stages but in its being rapid till the absolute pressure is halved and slow afterwards.

[1] Whether the law holds good for pressures much exceeding six atmospheres is still doubtful, as no experimental data exist.

D. *Practical measures for avoiding Compressed-air Illness.*

From the foregoing discussion the general nature of the measures needed to prevent compressed-air illness will be evident enough. The risks may best be avoided by properly calculated stage decompression, or by cutting down the period of exposure to a safe limit, or by both methods combined. In the case of work in compressed air in caissons, tunnels, etc., it is for economic reasons very undesirable to greatly reduce the period of exposure. In diving work, on the other hand, the periods of exposure are generally short in any case, and they can, without great inconvenience, be confined within limits which largely reduce the risks of compressed-air illness. Long periods of decompression are also very undesirable in diving, since changes of weather or tide or other causes may render a return to the surface necessary without any long delay in coming up, and since very prolonged stays under water are exhausting, and the diver's hands may become benumbed by cold.

As our investigations were in the first instance made with the object of securing safety from compressed-air illness in diving work, we may first consider the precautions desirable in connection with diving.

(1) *Diving work.*

The ordinary diving dress (Plate IV) consists of a copper helmet screwed to a corselet, the latter being in its turn connected water-tight to a stout water-proof dress covering every part of the body except the hands, which project through elastic cuffs. Air is supplied through a non-return valve on the helmet from a flexible pipe connected with an air-pump on a boat or ship. The air escapes through an adjustable spring valve at the side of the helmet. The arrangement is thus such that the pressure of the helmet air breathed by the diver is always at least equal to, and usually slightly greater than, the pressure of the water at the valve outlet. At a depth of 33 feet or 10 metres the diver is therefore breathing air at an excess pressure of one atmosphere, or at an absolute pressure of two atmospheres; and every additional 33 feet will add another atmosphere to the pressure. To enable the diver to sink, the dress and boots are suitably weighted. He is usually in connection with surface by a life-line containing a telephone wire, as well as by the air-pipe.

In descending or ascending a diver usually makes use of a rope attached to a heavy sinker at the bottom. He can thus easily regulate the rate of his ascent or descent, and take care that this rate is not so rapid as to cause any discomfort or pain in the ears owing to incomplete opening of the Eustachian tubes. A too rapid descent or ascent might cause mechanical injury followed by middle ear inflammation.

As explained above, there appears to be practically no risk of symptoms occurring from liberation of gas bubbles on rapid decompression if the pressure has not exceeded 1·25 atmospheres, corresponding to a depth of about seven fathoms or 42 feet of sea water. Up to this depth therefore no special precautions against caisson disease need be taken[1]. At greater depths precautions depending on the duration of exposure are evidently needed. The precautions which we have calculated to be desirable are embodied in the table given below (Appendix IV.); and the principles and experimental results on which this table is based must now be discussed.

It will be convenient to consider first the case of diving to a very great depth, and we shall take as an extreme example the case of exposure at a depth of 35½ fathoms (213 feet) of sea water, corresponding to an excess pressure of nearly 6·5 atmospheres, or an absolute pressure of 7·5 atmospheres.

Let us first suppose that the body of a diver is completely saturated with the nitrogen of air at this pressure, and that it is required to conduct his ascent to surface as rapidly as possible but without any risk of symptoms due to bubble formation, *i.e.* in such a way that, in accordance with the principles already laid down, the nitrogen pressure in no part of the body shall ever be more than double that of the air breathed at the same time.

The first step would obviously be to reduce the absolute pressure to about half, *i.e.* from 7·5 atmospheres absolute to 3·75 or from 6·5 atmospheres in excess to 2·75. This would be *ex hypothesi* the greatest initial drop in pressure which would be perfectly safe. The remainder of the decompression would evidently need to be conducted in such a way that the maximum partial pressure of nitrogen in any part of the body should diminish at double the rate of the fall in absolute pressure of the air. The ascent of a diver can be conveniently regulated from

[1] Heller, Mager and v. Schrötter recommend that at all depths decompression should be at a rate of at least 20 minutes per atmosphere. This would imply a delay of 25 minutes in coming up from 42 feet. Both common practical experience and our own experiments show that this excess of caution is quite unnecessary at small depths.

the surface by signalling to him to stop or come on at every ten feet as indicated on the pressure gauge attached to the pump. We may therefore divide the ascent into stages of ten feet, and the short periods occupied in the actual ascents may be neglected.

Since the depth was 213 feet, corresponding to 246 feet of water in absolute pressure, it would be safe to come up at once to a depth corresponding to 123 feet of absolute water pressure, *i.e.* to 90 feet of actual depth. Consequently the first stage would be a rapid ascent of 123 feet, and it would be necessary to wait here before the next ascent of 10 feet until the maximum partial pressure of nitrogen in the body had fallen to that of the nitrogen in air at $2 \times (80 + 33) = 226$ feet of absolute water pressure. The difference between 246 and 226 is 20, and this is 16 % of $213 - 90 = 123$, the difference between the original and the reduced pressure. The most slowly desaturating parts of the body will, according to our previous calculations, take 75 minutes to give off half of any excess of nitrogen which they may contain at any given air pressure; by inspection of the curve (Fig. 1) it will be seen that they will take about 19 minutes to lose 16 % of the excess. Hence a delay of 19 minutes would be necessary at 90 feet before coming up to 80 feet. At 80 feet the partial pressure in the body would require to fall an amount corresponding to 20 feet, which is about $17\frac{1}{2}$ % of $193 - 80 = 113$, the new difference in relative pressure between the nitrogen in the body and in the air. This would necessitate a delay of 21 minutes before ascending to 70 feet. The further delays needed would be 23 minutes at 70 feet, 26 minutes at 60 feet, 30 minutes at 50 feet, 35 minutes at 40 feet, 42 minutes at 30 feet, 51 minutes at 20 feet, and 62 minutes at 10 feet. It would thus take 309 minutes, or more than five hours, to reach surface.

This calculation is represented graphically in Fig. 3. It will be noticed from the figure that the time required for safe decompression does not increase proportionally to the increase in depth. For instance, an increase in depth of 15 feet from 50 to 63 feet necessitates an increase of 45 minutes in the time required for safe decompression; but the same increase in depth from 198 to 213 feet only requires an increase of 15 minutes in the time of decompression.

A somewhat more rapid rate of stage decompression could probably be adopted without appreciable risk to life, but the occurrence under water of even one of the less serious decompression symptoms might be extremely unpleasant or indirectly dangerous, so that a factor which we believe to be thoroughly safe in this respect has been used in the

calculation. The possible occurrence of slight symptoms after surface had been reached would not, however, be a serious matter: for this reason half of the last stop at 10 feet from surface might be dispensed with, which would save half an hour. The most slowly desaturating tissues would, according to the calculation, still be only saturated to an excess pressure of 1·3 atmospheres—a safe enough limit perhaps, but leaving no great margin to spare.

Fig. 3 also shows the maximum excess of saturation with uniform decompression in the same time and in 10 hours. It will be seen that uniform decompression in about five hours would leave at the end of decompression an excess saturation within the body of 2·1 atmospheres; and even if uniform decompression were extended to ten hours the excess saturation would still exceed one atmosphere. It is also perfectly clear that uniform decompression is an unsuitable way of bringing a man out of compressed air. Where a sufficiently safe rate of uniform decompression is employed (as, for instance, with 10 hours in the case under consideration), it is only at the very end (when the nitrogen pressure inside the body becomes more than double that of the air) that there is any risk of symptoms occurring; and for the sake of safety at the end the whole process is made quite unnecessarily long. Increased safety at the end is only secured in combination with useless delay at the beginning[1].

As will be seen in Part II, the results of our experiments, allowance being made for the difference between goats and men, fully confirm the foregoing mode of calculation. Not only has stage decompression in the calculated time proved safe where uniform decompression in the same total time was unsafe, but shorter periods of stage decompression than those calculated have been proved to involve risk of symptoms, increasing in gravity and frequency with the shortening of the time, though always less than the risk from uniform decompression in the same time.

If the whole body of a diver were allowed to become saturated at any great depth, it is evident that the time needed for safe decompression would be impracticably long. To reduce the time of de-

[1] The regulations of the Dutch Government make the following method of decompression obligatory for work in caissons, &c. The pressure is to be lowered at the rate of not more than $\frac{1}{10}$th of an atmosphere in 3 minutes till 3 atmospheres of excess pressure is reached: then at not more than $\frac{1}{10}$th of an atmosphere in 2 minutes till 1½ atmospheres excess pressure is reached; and finally at not more than $\frac{1}{10}$th of an atmosphere in 1½ minutes till normal pressure is reached. This method is still more unsuitable than uniform decompression, and would be very unsafe with high pressures.

compression to within limits practicable for divers, it is evidently necessary to greatly reduce the period of exposure to high pressure[1]. At great depths limitation of the exposure is also necessary in order to avoid toxic effects from the high pressure of oxygen (see p. 371). Calculation of the mode and period of decompression required after a limited exposure to pressure is a somewhat complicated matter, but the principles already laid down render it quite possible.

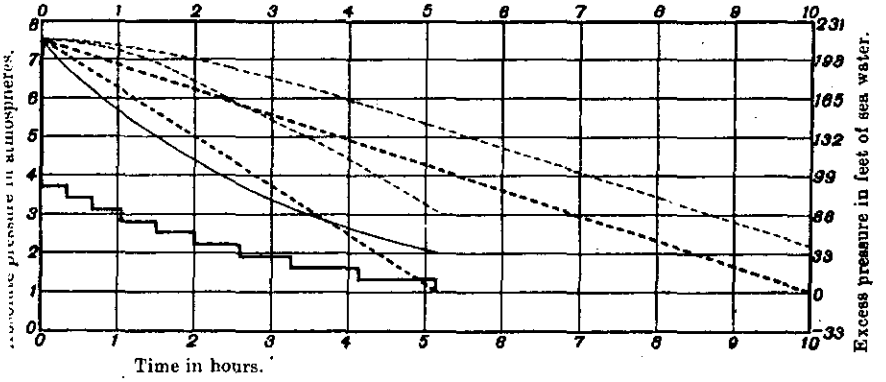


Fig. 3. Theoretical ascents of a diver after a prolonged stay at 213 feet of sea water. Stage decompression in 309 minutes compared with uniform decompressions in 309 minutes and in 10 hours. Continuous lines = stage decompression: interrupted lines = uniform decompression. Thick lines = air pressure: thin lines = saturation with atmospheric nitrogen in parts of the body which half saturate in 75 minutes.

When a diver goes down for a very short time, we have to take into consideration not only the time which he spends at the maximum pressure on the bottom but also the time occupied in the descent and the ascent. During the descent he is all the time saturating himself with nitrogen, and during most of the ascent he may be doing so also. Calculation will show that, if he descends and ascends at a uniform rate, the time spent in this process will be nearly equivalent, as regards the saturation of the body with nitrogen, to half the same time spent at the maximum depth. It is therefore clear that in deep diving the diver should descend as rapidly as is practicable, and should also ascend at once, on completion of his work, as far as he safely can. The rate of descent may be limited either by pain in the ears or by an air supply insufficient to keep the upper part of the dress full of air.

[1] This was fully realised by Catsaras who recommended a stay on the bottom of only 1 minute at 30 fathoms.

Both these causes are avoidable, and an experienced diver, with his Eustachian tubes well opened and a proper supply of air, can get to an excess pressure of six atmospheres (198 feet) in two minutes. This time was found sufficient in experimental dives up to 210 feet made by Lieut. Damant and Mr Catto (Appendix II). The recommendation commonly made that the rate of both ascent and descent should be slow is evidently quite unsound. A man who spent half an hour in descending to 30 fathoms, and an equal time in ascending at a uniform rate, would run a considerable risk of perishing on his return to the surface.

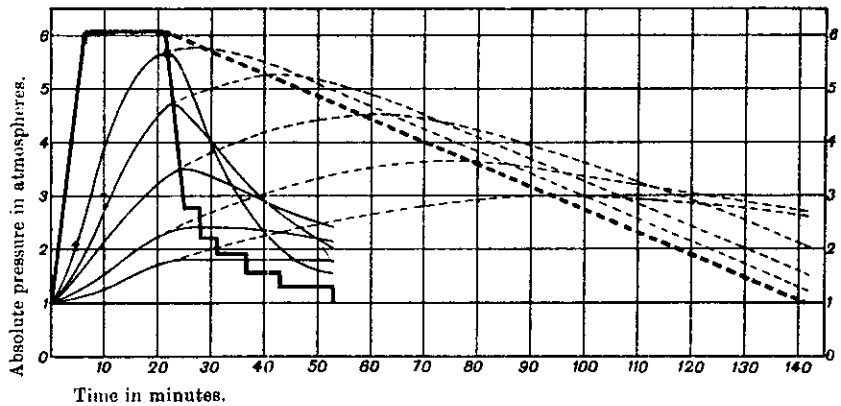


Fig. 4. Desaturation during stage decompression in 32 minutes and uniform decompression in 2 hours, after exposure for 15 minutes at 75 lbs. pressure with compression in 6 minutes. Thick lines = air pressure: continuous lines = stage decompression: dotted lines = uniform decompression. The curves from above downwards represent respectively the variations in saturation with nitrogen of parts of the body which half saturate in 5, 10, 20, 40, and 75 minutes.

In order to illustrate the method by which we have calculated safe modes of ascent in the minimum period of time we may take as an example the case of exposure for 15 minutes to a pressure of 75 pounds (6·1 atmospheres absolute or 28 fathoms = 168 feet). Many of our experiments on goats were made with this pressure and exposure. It took about six minutes to raise the pressure in the experimental chamber to 75 pounds, so that the total virtual exposure till decompression began was about 18 minutes. Fig. 4 shows graphically the variations of pressure during this period: also the calculated partial pressure of nitrogen in different parts of the body, as compared with the nitrogen pressure in the air. The first stage was from 6·1 to 2·8

atmospheres absolute (corresponding to an ascent in sea water from 168 to 60 feet) and occupied four minutes. The subsequent stoppages were:—

2	minutes	at	2·8	atmospheres	(60 feet	of sea water),
3	„		2·2	„	(40	„),
5	„		1·9	„	(30	„),
7	„		1·6	„	(20	„),
10	„		1·3	„	(10	„).

It will be seen from the figure that this rate of decompression was slightly faster than what was calculated above to be desirable. At the end of decompression the nitrogen pressure in those parts of the body which became half saturated in about 20 minutes under pressure would be equivalent to that of air at about 1·4 atmospheres, or 20·6 pounds per square inch. If the circulation in one of these parts were less vigorous during decompression than during exposure to the high pressure, it might well be that the nitrogen pressure in this part at the end of decompression would be higher than corresponded to the calculation. As a matter of fact minor symptoms ("bends") were observed five times in 34 decompressions of 18 goats, although no serious effects occurred. We concluded that the period of virtual exposure (18 minutes) was slightly longer than is desirable with stage decompression in 31 minutes: in the table below (p. 442) the limit has been set down at 15 minutes.

Fig. 5 shows the calculated nitrogen pressure in different parts of the body during uniform decompression in 31 minutes after the same exposure at 75 pounds. It will be noticed that at the end of decompression there is a dangerous excess of saturation in all parts of the body except those which half saturate in less than about seven or eight minutes, and that this supersaturation corresponds to an excess pressure of as much as 2·1 atmospheres of air. The goats used for the stage decompression experiments were on alternate occasions subjected to uniform decompression in the same time and with the same exposure. The result was that, in 36 decompressions, one died, two were paralysed, one had indefinite general symptoms of a severe character, and in 11 other cases "bends" occurred, besides two doubtful cases. This was entirely in accord with what the calculation would lead us to expect; and uniform decompression in 31 minutes is evidently dangerous under the conditions given.

It might be supposed that safety would be secured by extending to

a moderate degree the length of uniform decompression. It must be remembered however that the more the duration of uniform decompression is extended, the longer is the period during which the body is exposed to high pressure. Fig. 4 shows the calculated effects of uniform decompression extended to two hours. Although the quickly saturating parts of the body are desaturating during the greater part of the decompression, the slowly saturating parts are, on the other hand, becoming more and more saturated, so that at the end of decompression the parts which half saturate in from 40 to 75 minutes are saturated to an excess pressure of about 1·7 atmospheres, although at the beginning of decompression they were only saturated to from 0·7 to 1·3 atmospheres and could consequently have given no trouble.

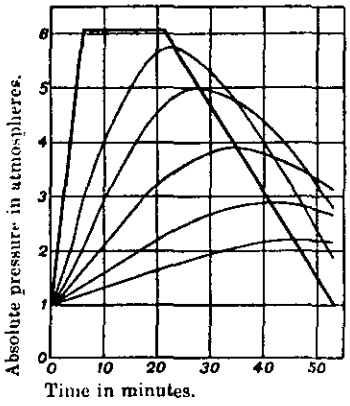


Fig. 5. Desaturation during uniform decompression in 32 minutes after exposure for 15 minutes at 75 lbs. pressure with compression in 6 minutes. Thick line = air pressure. The curves from above downwards represent respectively the variations in saturation with nitrogen of parts of the body which half saturate in 5, 10, 20, 40 and 75 minutes.

Very prolonged uniform decompressions are extremely tedious, and it seemed scarcely worth while to make any extensive series of such experiments. We found however that out of 12 goats uniformly decompressed in 90 minutes after 18 minutes virtual exposure at 75 pounds (6·1 atmospheres of absolute pressure) three developed symptoms of bends after decompression. The proportion of illnesses was thus greater than with stage decompression in a third of the time. With men the results would certainly be much worse, and we calculate that for a man, after the same exposure, several hours would be needed for uniform decompression in order to escape all risk of

symptoms occurring. The time would in fact require to be nearly as long as if the body had been completely saturated at the maximum pressure.

With very short exposures to high pressure, rapid decompression is probably safer than uniform decompression at a moderate rate. There is a considerable human experience on this point: divers working at great depths would seem to consider it fairly safe to go rapidly to the bottom at a depth of 160 or 180 feet and return equally rapidly, provided the time spent on the bottom does not exceed six or eight minutes and provided also that the dives are not repeated at short intervals. It is reported of the skilled Greek divers of the Mediterranean that, in case their gear becomes entangled on the bottom, they will cut their air-pipe and line and blow themselves up to the surface *in less than a minute from* a depth of 30 fathoms or the like rather than stop more than about ten minutes on the bottom. Our experiments on goats are in accordance with this practice. We found that no symptoms were produced by sudden decompression in less than a minute after virtual exposures at 75 pounds up to four minutes, and even in some trials up to six minutes (see below, p. 394).

With exposures exceeding a very few minutes, or such brief exposures frequently repeated, so that during the intervals the body has not time to become desaturated, we have little doubt that slow and uniform decompression—the slower the better—is at any rate preferable to sudden decompression. Uniform decompression must however be extremely slow to make it entirely free from risk of death or very serious symptoms, and the time required is so great that this method seems to *us quite impracticable in connection with diving work.* There appears to be very little human experience of slow uniform decompression. Divers usually come up in a few minutes at most, and even half an hour spent in the ascent would appear to be quite exceptional. Almost the only definite observations are those of Hill and Greenwood, who recently experimented on themselves at very high pressures. Fig. 6 shows the variations of pressure and the calculated saturations of different parts of the body during the experiment in which Greenwood went to a pressure of 91 pounds (7·1 atmospheres absolute). This experiment appears to have been a very risky one. After decompression he had bends in both arms, and Hill also had symptoms pointing towards blockage of vessels in the subcutaneous fat after similar experiences at 75 pounds pressure.

In Appendix IV two tables are given for the safe decompression of

divers after exposure for varying periods of time at different depths. These tables are the same as are now in use for divers in the Royal Navy, on the recommendation of the Committee on Deep Diving. In Table I the period of virtual exposure is so limited that the diver can return to surface by stages in half an hour or less. It will be noted that the maximum periods of exposure are from the time of leaving surface, so that there should be no chance of increased danger from undue delay in descending. The stoppages during the ascent are so calculated that, until surface is nearly reached, the excess of nitrogen pressure in any part of the body should never be more than double the nitrogen pressure of the air breathed, and not more

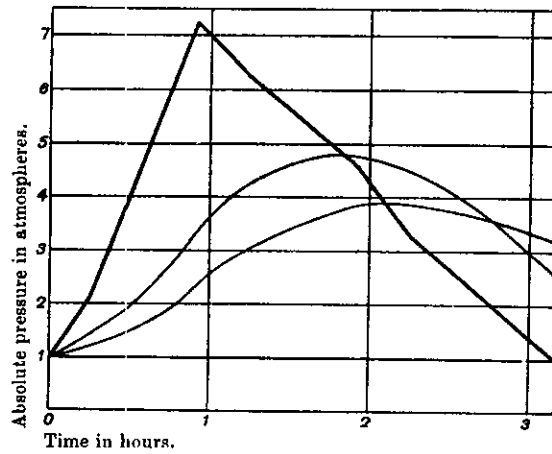


Fig. 6. Showing calculated variations in saturation with nitrogen during Dr Greenwood's experiment on himself. Thick line=air pressure: the two curves from above downwards represent respectively the variations in saturation with nitrogen of parts of the body which half-saturate in 40 and 75 minutes.

than two and a quarter times this pressure when surface is reached. The only case in which these limits are allowed to be slightly exceeded is with short exposures in comparatively shallow water. This slight excess is, however, only in parts of the body which saturate and desaturate very rapidly, and, as already explained, give rise to no danger. As an additional safeguard the diver is directed to keep his arms and legs constantly moving during each stoppage, so as to increase the rate of circulation and guard against the chance of the rate of desaturation during his ascent being proportionally less than the rate of saturation during his stay on the bottom while he was doing work.

The second table provides for the case of exceptionally long stays under water. A diver may be delayed by his air-pipe or life-line being fouled, or by other exceptional circumstances, against which it is necessary to provide. Where the fouling has been complicated by the action of tide the delay on the bottom has occasionally amounted to several hours, until the tide has slackened or turned. If the diver is at a great depth the calculated time required for safe decompression after so prolonged a stay is very long. On the other hand the dangers from cold and exhaustion have to be considered, and the difficulties caused by a strong tide during the diver's ascent. In view of these difficulties the time allowed for decompression after very prolonged exposures is somewhat curtailed, but not so much as to permit of risk of more serious symptoms than "bends," in so far as experiments on animals, and human experience, render it possible to calculate. In the case of men of exceptionally heavy build, and inclined to obesity, the time allowed after very prolonged exposures ought to be increased by about a third, although such men, particularly if over about 45 years of age, ought not to expose themselves to the risk of a prolonged stay in very deep water.

It might appear as if the rate of stage decompression recommended after prolonged exposures was slower than is actually required. A very unfortunate accident which occurred recently has shown only too clearly that this is not the case. In connection with the work of raising a torpedo boat which had sunk in 25 fathoms (150 feet or 46 metres) several divers were employed. They were working in 20 minute spells, and returning to surface by stages in 32 minutes, in accordance with the first table, which was the only one then in use. No symptoms of any kind were observed after the divers' return to surface under these conditions, nor have any symptoms ever been observed hitherto among divers working according to the table. One of the divers, however, became fouled in a very exceptional manner. His life-line was fixed in one direction over a spar or rope belonging to the sunk vessel, and his air-pipe was fixed in the other direction. He was thus prevented from going to free either his air-pipe or life-line. A second diver at once went down, but was unable to free him owing to the drag caused by the tide; and it was only after two and a half hours, when the tide had slackened, that he got free. He was then brought up by stages under the direction of Staff Surgeon Rees and Lieut. Damant. For the decompression two and a half hours were allowed, which we then believed would be a sufficient time in case of a diver being badly fouled

at 25 fathoms. The diver was, however, a man of heavy build with much fat in his body, and aged 49. Owing to his exhausted condition he did not come up on the ordinary rope, but had to be pulled up, hanging motionless on the life-line during the long stoppages. On reaching surface he was very exhausted and could hardly have been safely kept longer in the water. He had no paralysis or other definite symptoms of caisson disease. A bed was arranged for him on deck, and hot bottles &c. applied. After a time he complained of some pain in the legs, but this soon subsided; and as he seemed much better in the morning he was removed to hospital, since there was no suitable accommodation for him on the gun-boat where he was. The moving made him worse, and he gradually became restless and delirious in spite of administration of oxygen at intervals, showed signs of cardiac failure, and died somewhat suddenly about 24 hours after he had been brought up. At the post-mortem examination 12 hours later a moderate number of bubbles were found in the right side of the heart, the veins of the liver and intestines, while scattered bubbles were present in vessels elsewhere, including the coronary vessels, though none were seen in the vessels of the brain. The mesenteric fat, which was very abundant, was in places distended with small bubbles. There was about an inch of subcutaneous fat over the trunk, but no bubbles were seen in this layer. There seemed no reason to doubt that death was largely due to the bubbles, although the more usual symptoms of caisson disease were absent. There were no signs of pneumonia.

This is the only known case of prolonged exposure of a man to such a high excess pressure as four and a half atmospheres; and although his age, heavy build, and exhausted condition combined to make the circumstances very unfavourable, the fact of his death shows that the long decompression periods recommended in the second table after prolonged exposures are none too long, even for a man of ordinary build. Every precaution should be taken to guard against such long exposures at high pressures.

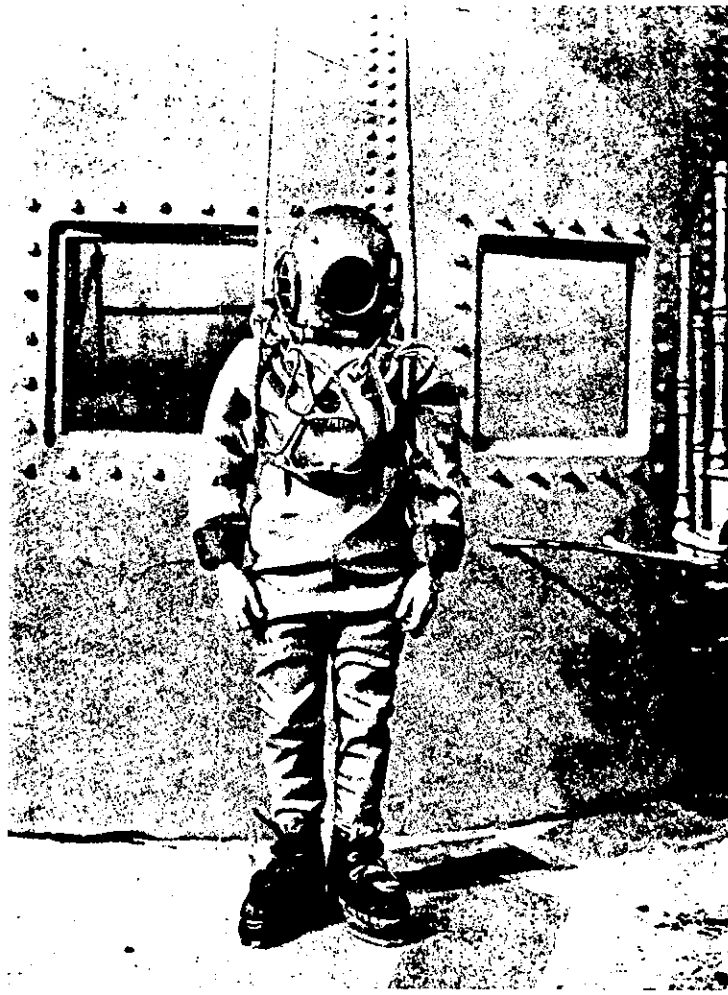
A diver has often to descend twice or oftener at short intervals. At the beginning of the second descent the more slowly desaturating parts of the body will not have had time to lose their excess of nitrogen, and consequently they will be more highly saturated at the end of the second descent than would otherwise have been the case. This will be clear from a study of Figs. 2 or 3. To meet the increased risk in decompression it is desirable, in calculating the proper stoppages, to add together the two periods of exposure, and adopt the corresponding rate

of decompression shown in the tables. For the first half of the stoppages this is not necessary, but for the second half, including the longer stoppages needed to meet the case of the more slowly desaturating parts, the rule should be carried out. The increasing danger after successive short dives by pearl divers, &c. without any precautions in decompression is notorious. This danger does not mount up to the same extent with stage decompression, but nevertheless exists. As the interval between successive dives increases the added danger on decompression diminishes. With an hour's interval the extra precautions might be halved, and with two or three hours' interval they might be omitted.

It may be remarked that the precautions recommended in the tables are greatly in excess of those which have hitherto been commonly employed in either diving work, or work in caissons, tunnels, &c. We have endeavoured to leave a clear margin beyond everything which either human experience or experiments on animals, or calculation, has shown to be risky. In connection with diving, the practice hitherto recommended in the British and other navies has been that the diver should both descend and ascend at a uniform slow rate. By abolishing the slow descent and ascent, and substituting stage decompression, it has been possible to combine greater safety with a clear saving of time under water for a given working period on the bottom. Where the air supply to the diver is managed in accordance with the recommendations of the Diving Committee there is also very greatly increased working efficiency in deep water. For a discussion of the air supply to divers, and many other practical points relating to diving, we must refer to the Committee's Report; and to the "Diving Manual," which has just been re-written and issued to the Royal Navy.

A possible complication to which we have not hitherto referred in connection with compressed-air illness arises from the fact that at very high pressures of air the partial pressure of oxygen begins to be so high as to be capable of producing serious effects. Paul Bert discovered that oxygen at a partial pressure exceeding about three atmospheres (corresponding to 14·3 atmospheres of air) causes animals to go into convulsions and die, even a short exposure being often fatal. More recently, Lorrain Smith, who experimented on mice, and whose results have been confirmed and extended by Hill and Macleod, showed that oxygen at high pressure acts on the lungs, producing pneumonia[1]. He

[1] Lorrain Smith, *Journ. of Physiology*, vol. xxiv., p. 19, 1899; Hill and Macleod, *Journ. of Hygiene*, vol. iii., p. 401, 1903.



Diving dress, front view, with air-pipe and life-line, which are connected with the helmet behind.

found that fatal pneumonia may be produced after four days' exposure to an oxygen pressure of as little as 75 % of an atmosphere, corresponding to air at an absolute pressure of 3·6 atmospheres (88 feet of sea water). At a pressure of about 1·25 atmospheres of oxygen (6 atmospheres of air, or 165 feet of water) death from pneumonia was produced in about 48 hours. At about 1·8 atmospheres of oxygen (eight and a half atmospheres of air, or 250 feet of water), marked symptoms usually occurred in about 12 hours, and death in 20 hours, though in one case death followed in seven hours. At about 2·8 atmospheres of oxygen (13·3 atmospheres of air, or 406 feet of water) marked symptoms were observed in about three hours, and death in nine hours.

The steel chamber at the Lister Institute was not made to withstand such high pressures as would produce within a short time symptoms of oxygen poisoning if air alone was pumped into the chamber. We have, however, made a few observations in the chamber when the oxygen pressure of the air breathed was raised by other means. In one experiment seven goats were placed in the chamber, and the oxygen pressure raised by opening three large cylinders of oxygen, and at the same time pumping in air to 81 pounds pressure. The total oxygen pressure was thus raised to 2·3 atmospheres, corresponding to a depth of 55 fathoms, or 330 feet, or 100 metres. After three hours one animal had died of pneumonia in the chamber, and most of the others seemed more or less affected, though they rapidly recovered on decompression[1]. We also tried on ourselves the effects of breathing nearly pure oxygen from a bag while we were in the chamber at an absolute pressure of two atmospheres; but we could not detect any effects after a few minutes with an oxygen pressure of 1·7 atmospheres, corresponding to about 40 fathoms (240 feet or 73 metres). In a number of goats which were exposed to 75 pounds' pressure (168 feet or 51 metres of water) for three hours, no symptoms indicative of oxygen poisoning were observed.

To judge from these data there is no immediate risk to a diver from oxygen poisoning at depths up to 40, or perhaps 50 fathoms (73 to 90 metres) if ordinary air is breathed, provided the stay is not long. With stage decompression the diver could rapidly return to a perfectly safe oxygen pressure; but, as already remarked, we do not yet know with

[1] One animal showed bends after decompression which was effected in 133 minutes by stages. After exposure at +75 lbs. for 3 hours in air this decompression gave 2 bends in 14 goats. There is therefore no evidence that the exposure to high pressure oxygen increased the susceptibility to caisson disease.

certainty whether it is perfectly safe to rapidly reduce the pressure to half after exposure to such very high air pressures.

(2) *Work in caissons, tunnels, and diving bells.*

In connection with various kinds of engineering work under water, or in soft water-bearing strata, compressed air is commonly used for keeping water out of the working place and preventing collapses. The men have thus to work continuously in compressed air.

In tunnels or 'tubes' through soft water-bearing strata, where a steel lining has to be erected to keep water out and resist pressure, the working face, or blind end of the tunnel under construction, is kept free of water by the air pressure with the help of a circular shield with a cutting edge which is advanced as each section of steel lining is erected into position. The soil is excavated by hand labour, and passed out on trucks through an air-lock.

In constructing foundations for the piers of bridges over rivers, caissons are employed. A caisson is a steel tube, which ultimately forms the lining of the pier, and is shaped accordingly. Near the lower end there is a steel diaphragm, forming a working chamber. An inner steel tube passes through this diaphragm, and serves for ingress and egress, and for passing up the material excavated. At the top of this inner tube there are air-locks for allowing the passage of men and material without escape of the compressed air contained in the working chamber. The latter is kept free from water by the air pressure, and the excess of air escapes beneath the cutting edge of the caisson. When a secure foundation for the pier has been reached this chamber is filled up with concrete. In constructing mine shafts through soft water-bearing strata the same principle may be employed. For work of a simpler kind on river or harbour bottoms diving bells are often used, the bell being simply lowered to the bottom at any required place, so that the men can work on the area covered by it and are kept dry by the air pressure.

The circumstances connected with work in compressed air in caissons, tunnels, &c., differ in certain respects from those associated with diving work.

In the first place the duration of exposure is far longer. A caisson or tunnel worker is usually in compressed air for six or eight hours daily, or even longer. The conditions of the work render any great limitation of the periods of exposure very difficult and expensive.

Usually, however, the workman comes out for meals at intervals of about three hours.

A second difference is that the very high pressures to which a diver may have to go are not needed in caisson or tunnel work. An excess pressure of about 3¼ atmospheres, or 48 lbs., is, we believe, the extreme limit hitherto employed; and usually the excess pressure does not exceed about two atmospheres or 30 lbs. Decompression seems to be usually effected in 10 to 20 minutes, or even, with the lower pressures, in three to five minutes.

With properly arranged air-locks for men and material there should be no need for hurry in coming out; and undue hurry is specially undesirable if the workman leaves the works at once, since he would be liable to develop symptoms when he was so far away that he could not be readily recompressed. To obviate this risk as far as possible, it is customary to endeavour to keep men for half to one hour on the works after they come out; and with the usual rates of uniform decompression this precaution is very necessary. Evidently, however, it is greatly preferable to prevent *all* practical risks of serious symptoms.

In order to attain this end stage decompression as recommended for divers in the tables in Appendix IV may be employed. An accurate and easily read pressure gauge, visible from both inside and outside the air-lock, is of course essential; and a reliable man should be in charge of the tap. As a further control it would be desirable to have an automatic graphic record of the variations of pressure each time the lock for men is used. As any very sudden drop in pressure might cause mechanical injury, the outlet tap should be so arranged as to prevent decompression at a maximum initial rate of more than about one pound in five seconds[1]. With this arrangement and an ordinary tap, the rate of decompression would diminish considerably as the pressure fell, and the proper point for interrupting the decompression could be accurately reached.

The tables in Appendix IV have been calculated with special regard to the comparatively short periods of exposure to pressure in diving work;

[1] The delivery of the inlet tap should also be restricted, and the man in charge should have strict directions to take care that the rate of admission or discharge of air does not cause pain in the ears, &c. of any of the men in the lock. To avoid pain a very slow rate of air admission may sometimes be needed, but with practice a rise of pressure of one atmosphere per minute is often not too much, so that any definite rule, limiting the rate to much less than this, seems scarcely desirable.

and the stoppages recommended during the divers' ascent after exceptionally long periods of exposure are somewhat shorter than would be desirable apart from the risks entailed by the long stay under water. In the case of caisson and tunnel workers, on the other hand, it is only in exceptional cases that the exposure to pressure lasts less than three hours; and usually the exposure during the day lasts at least six hours.

With such long exposures and only moderate pressures the calculated theoretical rate of safe decompression after the first rapid stage is nearly uniform; and the rules for decompression may be greatly simplified by adopting uniform slow decompression or uniform stages[1].

The following table shows the rate of uniform slow decompression calculated to be safe after the initial diminution of absolute pressure in the proportion of 2 : 1. Suppose, for instance, that men were working at a pressure of 24 pounds in 3-hour spells, with an hour's interval between for a meal. In coming out they would be rapidly decompressed to an absolute pressure of $\frac{24+15}{2} = 19{\cdot}5$ pounds or 4·5 pounds of excess pressure. After the first 3-hour spell of work the slow decompression would be at the rate of one pound in three minutes, or $3 \times 4{\cdot}5 = 13\frac{1}{2}$ minutes in all. After the second spell the rate would be one pound in five minutes, corresponding to $22\frac{1}{2}$ minutes in all. If they stayed for the whole period in the compressed air the rate of slow decompression would be one pound in seven minutes corresponding to $31\frac{1}{2}$ minutes in all. To take another example, if the work were at 40 pounds excess pressure the men could be rapidly decompressed to $\frac{40+15}{2} = 27\frac{1}{2}$ pounds of absolute pressure, or $12\frac{1}{2}$ pounds excess pressure. After a first 3-hour spell of work the period of slow decompression would therefore be $12\frac{1}{2} \times 7 = 87$ minutes: after a second spell (with an interval of 30 or 45 minutes outside the lock) $12\frac{1}{2} \times 8 = 100$ minutes; and after a continuous exposure of six or seven hours, $12\frac{1}{2} \times 9 = 112$ minutes[2].

[1] With the lock air-tight, and no ventilation, uniform decompression at any required rate could be easily secured by means of a reducing valve on an outlet, with a graduated tap beyond it, the arrangement being similar to the reducing valve and tap usually connected to a cylinder of compressed oxygen or gas used for limelight. If the delay in the lock is so long that ventilation is required, or if ventilation is needed in order to compensate for accidental leakage, it would be best to have an adjustable safety valve on the outlet, and adjust this by one pound at a time at the proper intervals.

[2] We have some doubt as to whether the increased slowness of decompression after very long exposures would be altogether sufficient to meet the increased tendency to slight symptoms ("bends"). These are, however, of minor importance if all serious symptoms

TABLE I.

Table showing rate of decompression in caisson and tunnel work.

Working pressure in pounds per square inch	Number of minutes for each pound of decompression after the first rapid stage		
	After first three hours' exposure	After second or third three hours' exposure, following an interval for a meal	After six hours or more of continuous exposure
18—20 pounds	2	3	5
21—24 ,,	3	5	7
25—29 ,,	5	7	8
30—34 ,,	6	7	9
35—39 ,,	7	8	9
40—45 ,,	7	8	9

It will be evident from the last example that in order to avoid waste of time in the lock it would be preferable with pressures exceeding about 25 pounds to keep the men under pressure continuously during each shift. Thus with two 3-hour spells of work separated by a decompression, the time spent in the lock would be $87 + 100 = 187$ minutes; whereas if the meal were taken in the compressed air, the two 3-hour spells would only imply 112 minutes in the lock.

With working pressures exceeding about 25 pounds the air-lock should be roomy and comfortably arranged, and large enough to take the whole of a shift of men. It should be provided with an electric heater, telephone, and if possible some sort of lavatory accommodation.

With pressures up to 45 pounds, or four atmospheres of absolute pressure, there appears to be no substantial objection to keeping men for six hours, or even more, continuously under pressure, provided that the mode of decompression is thoroughly safe. With pressures exceeding about 40 pounds, the practice has hitherto been to limit the exposure to about one hour, and employ rates of decompression which are dangerously rapid. This plan implies greatly increased risk and expense, since for the accomplishment of the work the number of decompressions is six times as great, and the men are idle most of the day. The actual increase in risk must be very great.

In tunnel work, or any other kind of work where plenty of space is available, there would be great advantage in providing a large air-lock, or section of tunnel, in which the pressure was constantly maintained at a little less than half the absolute pressure in the working section.

are prevented. We also think that with long shifts, exceeding a total of about 3 hours, still slower decompression would be needed for any men inclined to obesity. Such men should, therefore, be excluded in the medical examination which all men working in air at high pressures ought previously to undergo.

The men could then pass rapidly (in two or three minutes) from the working section into this intermediate lock or section, where they could take their meals, wash, and change their clothes. After a sufficient delay (dependent on the working pressure) they could then pass out rapidly. If, for instance, the working section was at a pressure of 30 pounds, the intermediate or "purgatory" lock could be kept at an absolute pressure of about $\frac{30+15}{2{\cdot}2} = 20{\cdot}5$ lbs., or $5\frac{1}{2}$ pounds of excess pressure[1]. At the end of the day's work there would be a delay of about 50 minutes in this large lock, during which the men could wash and change, or take a meal. With this plan all delays during actual decompression would be obviated, so that ingress and egress would be free at all times, and the men could use the locks employed for material. For persons going in for only short periods the delay in the "purgatory" lock could be curtailed in accordance with the tables in Appendix IV. The movement of the men while employed in washing, changing clothes, &c. would hasten the process of desaturation, and this would be a further advantage.

In any case where it was specially desirable to reduce the period of delay in the air-lock to a minimum, recourse could of course be had to breathing oxygen during the period of slow decompression. This would about double the rate of desaturation, and therefore halve the delay. The oxygen could be breathed from a bag, and the CO_2 absorbed by a purifier, so that very little oxygen would be needed. By so arranging the mouthpiece that part of the expired CO_2 was rebreathed, and the respiration and circulation thus stimulated, a still better result would be attained.

The results of some of our experiments seem to indicate that even the very slow rate of stage decompression which has been recommended above would be insufficient to completely obviate the risk of "bends" occurring after prolonged exposure. The rate of saturation and desaturation of some of the tissues which are the seat of "bends" is possibly slower than we have provisionally assumed. What we have aimed at is to completely obviate the risk of any serious symptom, while at the same time reducing the chances of "bends" to a minimum.

[1] A comparatively rapid fall in absolute pressure in the proportion of 2·2 to 1 is within practically safe limits, particularly if the previous period of continued exposure has not exceeded three or four hours.

Part II. Experimental.

1. *Apparatus.*

We owe the large pressure chamber (Plate V) in which both human and animal experiments were conducted to the generosity of Dr Ludwig Mond, F.R.S. It is a short segment of a boiler of $\frac{3}{8}$ inch plate resting on its side; the ends are slightly dished steel plates $\frac{1}{2}$ inch thick. Inside it measures $7\frac{1}{2}$ feet long by 7 feet wide and high, and has a capacity of 9500 litres (336 cubic feet). It is thus large enough to hold 3 or 4 persons comfortable and can be used for animal experiments lasting several hours without the necessity of ventilating. There are two doors: one, an oval manhole (24 × 15 inches), is easily removed and is in common use; at the other end is a large rectangular plate (28 × 24 inches) which can be unbolted for the admission of bulky articles. There are a number of spring and simple valves; the largest is in the floor of the chamber and serves also as a drain; when fully opened it reduces the pressure from 100 lbs. to atmospheric pressure in rather less than a minute. Besides this there are four spring and three simple valves so arranged that the pressure can be completely controlled either from inside or outside. The front is also furnished with an air-lock, by means of which small articles can be passed in or out of the chamber during an experiment. Three windows are provided of stout glass; as a precaution for safety these are fitted with an arrangement whereby the breaking of the glass releases a solid metal rubber-faced plug which falls into the hole. Wiring for lights, a telephone, electric heaters and a motor to drive a fan, kymograph, &c., is introduced through fibre plugs.

The pressure is raised or reduced by a simple compressor driven by a gas engine. While this has proved quite satisfactory for negative pressure experiments, the rate at which the pressure can be raised by its means is only about 2 lbs. per minute. This was a serious obstacle to the examination of the effects of exposure to high pressures of short duration. Accordingly after the preliminary experiments, a multitubular compressed air reservoir was placed at our disposal by the Admiralty. This reservoir has a capacity of about 22 cubic feet, and by charging it to about 70 atmospheres with a two-stage liquid-air compressor and also another steel bottle to 180 atmospheres we were enabled to suddenly blow the contents into the chamber and so reach a pressure of 60 lbs. in

4 minutes, and 75 lbs. in 5½—6½ minutes according to the temperature. The pressure is indicated by two Schaffer spring gauges (one of which is visible from within the chamber) for positive pressures, and one spring gauge outside and a mercurial barometer inside for negative pressures. The spring gauges show a lag of nearly 2 lbs. up to about half an atmosphere, but above one atmosphere they are concordant and, as far as could be ascertained, correct.

The chamber and accessory apparatus have now been frequently used during eighteen months for experiments at pressures varying from 100 lbs. above to 8 lbs. below atmospheric pressure, and have been found very satisfactory and convenient.

2. *Choice of experimental animals.*

A few experiments were made with rabbits, guinea-pigs, rats, and mice, but for regular use goats were selected chiefly because they were the largest animals which could be conveniently dealt with and which could be obtained in considerable numbers. The questions under consideration depend in a very fundamental way upon the rate of circulation in the animal under investigation. Among the ordinary mammals this must vary with the rate of the respiratory exchange per unit of body weight and is therefore proportional to the ratio between body surface and body weight. The susceptibility of any animal to caisson disease after sufficiently long exposure to compressed air must depend in the main upon the rate at which its respiration and circulation removes the excess of dissolved nitrogen on decompression.

Not only is this excess removed more rapidly in small animals, so that the time during which bubbles might be formed is correspondingly less, but, as already pointed out, there is every reason to believe that the time during which the venous blood remains in a supersaturated state during each round of the circulation largely determines the formation of bubbles. This time is so short in small animals that no bubbles at all are formed, in spite of the temporary existence of very great supersaturation in the blood and tissues. The susceptibility of any species of animal then varies enormously with the size. Thus a mouse, weighing 20 grammes and with a CO_2 production of about 8 grammes per kilo per hour, is much less susceptible than a goat, weighing 20,000 grammes and producing about 0·8 gramme CO_2. We have indeed failed to produce any symptoms at all in mice on decompression in less than a minute after one hour's exposure at 75 lbs., an experience

The steel chamber at the Lister Institute. Front end, showing the manhole for entering, the small air-lock for passing food, &c. into the chamber, an inspection window, a pressure gauge, and several valves, &c.

The steel chamber at the Lister Institute. View from outside, showing the back end of the chamber, with the large door and one inspection window.

invariably fatal to goats. In the same way dogs, with a respiratory exchange of some 1·3 gms. CO_2 per kilo per hour, are much less susceptible than men with an exchange of about 0·5 gms. Thus Heller, Mager and v. Schrötter observed no symptoms in dogs[1] on sudden decompression from any pressure less than about 60 lbs., while abundant illnesses are caused in man, and for the matter of that in goats also, by inappropriate release from 30 lbs. pressure. It therefore appears clear that it is necessary to use large animals for experiments which are designed to illustrate the incidence of caisson disease in man. Indeed *the quantitative factor by which the results obtained on quite small* animals might be translated into human experience is so large as to become qualitative in character.

Since pressures of some 100 lbs. or more are required to produce symptoms in a reasonable proportion of small animals, the use of animals such as goats is also very desirable in order to keep as far away as possible from the point at which the partial pressure of oxygen is high enough to cause toxic effects. We found that an exposure of three hours at 81 lbs. to an atmosphere containing 36 % oxygen (the oxygen pressure being thus equal to that of 150 lbs. excess air pressure) killed one goat out of seven with "pneumonia." Our experience shows that it is not necessary to exceed an air pressure of half this (75 lbs.) to produce symptoms which are sufficiently varied and severe to satisfy experimental requirements.

Experience also showed that goats were very suitable animals in that slight symptoms were presented to our notice in a definite objective form. The lesser symptoms of caisson disease cannot be neglected, and there are reasons for supposing that their occurrence is not exactly conditioned by those experimental circumstances which in a more severe form produce serious and fatal results. They cannot be properly detected in mice or guinea-pigs or even in rabbits. Goats, while they are not perhaps such delicate indicators as monkeys or dogs, and though they are somewhat stupid and definitely insensitive to pain, are capable of entering into emotional relationships with their surroundings, animate and inanimate, of a kind sufficiently nice to enable those who are familiar with them to detect slight abnormalities with a fair degree of certainty.

The animals, 85 in number, used in the present experiments were a mixed collection of ordinary English goats of no particular breed. They

[1] The weights are only given in a few instances; from these it may be surmised that the dogs were small (5 to 12 kilos).

were about equally distributed between the sexes, and varied in weight from 10 to 30 kilos, the average being rather less than 20 kilogrammes. All were apparently adult, judging from the fact that none showed any increase in weight while in our possession. One or two (XIII A, XXXII A) seemed to be quite aged, but the rest were fully active.

On the whole the herd remained healthy. Two died of apical pneumonia and two of diarrhoea, which was at one time epidemic in a severe form. The cause could not be determined, but the trouble became much less marked after the animals were placed on a more meagre diet and corn withheld. Three animals were under some suspicion of being infected with *M. melitensis*[1]; two of them seemed rather depressed (though not more so than appears to be natural in some goats), while the third showed no signs of ill-health. Various items of pathological interest were found in those which came to post-mortem: in the lungs various nematodes were found several times, *Linguatula* once, and a surgical needle once; a *Streptothrix* abscess in the stomach wall followed puncture with a needle to relieve distension; a bony tumour was found in an adrenal gland; in one old goat (XXXII A) the aorta was extensively atheromatous; flukes occurred in the liver once, while hydatids in the peritoneum were very common and intestinal worms abundant. None of these conditions (except possibly the arterial disease) can however be considered to have rendered the animals definitely abnormal as far as caisson disease was concerned, and none of them could be attributed to exposure to compressed air.

3. *Respiratory exchange of goats.*

The difficulties of measuring directly the circulatory activity of normal animals are almost insuperable. This must be however in general proportionate to the rate of respiratory exchange, and a number of determinations of the CO_2 production of our goats were made in order to get a line of comparison with other animals (and especially man) in respect of the rate at which air would be taken up by and discharged from the body.

[1] Of 22 animals whose blood was examined, 16 gave no reaction with *M. melitensis* at a dilution of 1:20, 3 gave some reaction at 1:20, while 3 animals gave complete agglutination up to 1:200 (XVIII A, XXVI A, XXIII A). Cultures from the blood during life were negative, and when they eventually came to autopsy cultures of blood, spleen, liver, inguinal, axillary, mesenteric and mammary glands were negative as regards *M. melitensis*. The exact history of these animals could not be obtained, but there is practically no doubt that they had never been out of England.

The observations were made by using the pressure-box as a respiration chamber. The animals were enclosed and hourly samples removed (after thorough mixing with an electric fan) and analysed in a delicate form of Haldane's gas analysis apparatus. The results were entirely satisfactory, the successive analyses showing a regular increase in the CO_2. The goats led a regular life, and all the observations were made at approximately the same time of day so that they are fairly comparable with one another in respect of the influence of food. The animals remained fairly quiet, though they seldom lay down.

The results of 27 experiments are given in the next table. The analyses have been calculated in grammes of CO_2 per hour per kilo of

TABLE II.

Number of experiment	Temp. °C.	Bar. mm.	Duration hours	Pressure lbs. positive	Goats					CO_2 gms. per hour		Remarks
					Number	Males	Females	Total weight kilos.	Average wt. kilos.	Per kilo body wt.	Per 1000 sq. cms. surface	
I	19	764	3	0	4	—	4	99·0	24·7	1·006	2·625	
II	13	763	2½	0	4	2	2	62·8	15·7	1·123	2·070	
III	15·5	765	1½	0	9	4	5	159·7	17·7	0·908	1·823	
IV	15	752	1½	0	9	3	6	171·1	19·0	0·727	1·749	
V	17	762	3	0	6	6	—	111·8	18·6	1·104	2·554	R. Q. 1·03.
VI	11	769	6	0	6	—	6	138·8	23·1	0·670	1·771	R. Q. 0·90.
VII	13	765	5	0	6	6	—	121·3	20·2	0·975	2·389	R. Q. 1·06.
VIII	13	754	4	45	7	7	—	142·7	20·4	0·887	2·187	
IX	13	740	4	45	8	—	8	193·7	24·2	0·627	1·682	
X	15	754	7	0	7	7	—	142·1	20·3	0·664	1·630	R. Q. 0·91.
XI	16	780	6	0	6	6	—	126·3	21·0	0·615	1·533	Fasting 20 hrs.: R. Q. 0·82.
XII	15	778	4	21	7	7	—	140·9	20·1	0·763	1·770	
XIII	15	774	7	0	8	—	8	193·7	24·2	0·548	1·469	R. Q. 0·82.
XIV	14	760	4	45	13	5	8	295·7	22·7	0·667	1·738	R. Q. 1·08.
XV	16	758	3½	25	6	6	—	127·9	21·3	0·959	2·367	
XVI	17	764	3¾	20	7	3	4	148·7	21·2	0·635	1·572	
XVII	15	762	4	0	6	6	—	127·9	21·3	0·669	1·652	
XVIII	17	762	1¾	45	6	—	6	122·1	20·3	1·020	2·504	
XIX	14	761	4	45	6	6	—	127·9	21·3	0·697	1·722	
XX	13	760	3	0	5	—	5	100·1	20·0	0·921	2·258	
XXI	16	760	4	45	5	—	5	100·1	20·0	1·104	2·701	
XXII	15	762	4	45	6	6	—	127·9	21·3	0·967	2·390	
XXIII	16	768	4	45	5	—	5	100·1	20·0	0·852	2·083	
XXIV	12	776	5	0	4	2	2	95·3	23·8	0·717	1·858	
XXV	14	775	5	0	4	2	2	95·3	23·8	0·751	1·941	
XXVI	14	775	5	0	4	1	3	76·9	19·2	0·624	1·501	
XXVII	13	766	5	0	4	1	3	76·9	19·2	0·704	1·693	

body weight and also per 1000 square centimetres of surface according to the usual formula $S \times 100 = \sqrt[3]{W^2} \times 11{\cdot}2$, where S = surface in square centimetres and W the body weight in kilogrammes.

The goats used belonged to Series II (Exps. 1—4), III and IV.

The results of these experiments are very variable; the averages are shown in the next table:

TABLE III.

	No. of experiments	CO_2 in grms. per hour: Per kilo body-weight	CO_2 in grms. per hour: Per 1000 sq. cms. surface
At *atmospheric pressure*	16	0·795	1·907
At 45 lbs. positive	8	0·853	2·126
At 20, 21 and 25 lbs. positive	3	0·786	1·903
All pressure experiments	11	0·834	2·065
Males only	10	0·830	2·019
Females only	8	0·843	2·137
Mixed experiments	9	0·762	1·771
All experiments	27	0·811	1·971
		(410 c.c.)	(997 c.c.)

One may conclude that goats produce about 0·8 grm. CO_2 per kilo per hour under conditions of incomplete rest, and that no great departure from this figure is occasioned by the animals being under pressure up to 45 lbs. or by sex. It is shown elsewhere[1] that something more than 10% of the total CO_2 produced by goats comes from the fermentation of the contents of the alimentary canal, and figures detailed below (p. 409) indicate that one-fifth of the body weight is contributed by these contents. In comparing the CO_2 production of goats with that of man, we may regard these two corrections as roughly balancing one another and may neglect them.

It appears that man produces under conditions of bodily activity comparable to that of our experimental animals, about 0·45 to 0·5 grm. CO_2 per kilo per hour. Goats therefore show a respiratory activity approximately 1·7 times that of man. This figure corresponds fairly well with that calculated from the size. If the respiratory exchange per unit of surface is the same, a goat of 20 kilos will produce 1·5 times as much CO_2 per unit of weight as a man of 70 kilos.

4. *Method of conducting the experiments.*

No animals were subjected to experiment when obviously ill. As a rule five to eight animals were put in at one time. The pressure

[1] *Journal of Physiology*, vol. XXXVI. (1907), p. 283.

having been raised to the desired point, the chamber was entirely closed and no ventilation given until decompression began. The average CO_2 production of goats is about 435 c.c. per kilo per hour at ordinary temperatures. The chamber usually contained 100 to 150 kilos of goat so that the CO_2 rose about 0·45 to 0·55 % (measured at atmospheric pressure) per hour. In this way it never attained a harmful partial pressure in experiments lasting from a few minutes to four hours. In the few observations made with an exposure of eight hours, the CO_2 was allowed to accumulate for four hours and afterwards the chamber was ventilated so that the CO_2 did not exceed a partial pressure of 2 % of an atmosphere. No experiments have been made to directly examine the possible influence of CO_2 upon the incidence of caisson disease. It appears to the authors that the effect must (1) in any case be very slight with partial pressures of less than 2 or 3 %, and the result, if any, of the increased respiratory and circulatory activity must be in the direction of diminishing the ill-effects of decompression after any but quite short exposures[1].

After the preliminary experiments (Series I), the animals were never used more than once on the same day, and, with rare exceptions, not on succeeding days. In many cases indeed individual goats rested for a week or more between the experiments.

During decompression the animals could be watched fairly satisfactorily through the windows of the chamber, though fog of course completely blocked the view during the actual moments of rapid decompression. At the end they were allowed to escape from the chamber and run about free in the yard. They were kept under continuous observation for half an hour or longer, and were frequently seen throughout the day. We found that practically all the symptoms which were going to appear declared themselves within thirty minutes, though a few slight signs were probably missed. We also found that slight signs were much more obvious when the animals were not distracted or excited by food or other causes. During the breeding season it is advisable to keep the males and females separate, and, by removing any sources of interest, to allow the animals to fall into a state of meditative boredom. Under these circumstances, trivial symptoms are easily detected which are not made the subject of objective demonstration by animals engaged with their appetites.

[1] Greenwood (*British Medical Journal*, June 22nd, 1907, Supplement, p. 409) has recently found that high percentages of CO_2 do not increase the liability to decompression symptoms.

No observations were made of the temperature within the chamber during an experiment. Very hot and very cold weather did not seem to influence the results. The air in the chamber was always warmed by compression and sometimes also artificially, while decompression was of course accompanied by sudden, often very severe, spells of cold. No account has been taken of variations in atmospheric pressure. The extreme readings of the barometer on record are 806 and 689 mm. at sea level, and in this country 790 and 695 mm.[1], giving ranges of 117 mm. and 95 mm. or about 2¼ and 1¾ pounds. Even this variation, though it occurs at an important part of the absolute pressure scale, cannot be of great significance.

Times of exposure of one hour, or less are, unless the contrary is directly specified, to be taken as indicating actual exposure to the given pressure, the time of compression (six minutes) being neglected. For longer exposures it was sometimes convenient to raise the pressure more slowly: in these cases therefore the times specified may indicate either the actual exposure *plus* four to six minutes compression or a virtual exposure calculated by adding the actual exposure to half the time of compression which is in minutes roughly one quarter of the pressure in pounds positive (see above, p. 362).

As will be gathered from the details given below, the general scheme of the experiments involved the examination of three variable factors—degree of pressure, duration of exposure and duration and mode of decompression. For the most part the degree of pressure was kept constant while the other two factors were varied. It soon appeared from the preliminary experiments that the individual variability of the animals was very large—larger indeed than the difference between many of the modes of decompression which it was desired to examine. It also appeared that the relative susceptibility of the different individual animals remained fairly constant so that after a time one could pick out goats which were known to be either susceptible above the average or definitely resistant to caisson disease. It was therefore clear that either an enormous number of animals had to be employed or the experiments had to be so framed as not to produce fatal results and so reduce the proportion of susceptible individuals in the herd. It appears probable that any 20 or 30 goats would give much the same results, but if many are lost it is necessary to discard the remainder and procure a fresh batch to be subjected to the comparative experience. Obvious reasons prevented this procedure. It was therefore necessary to be at

[1] *Nature*, vol. LXXV., 1907, p. 330.

some pains to secure that the deaths should be as few as possible so that the same individuals might pass through a number of different combinations of pressure, exposure and decompression. The animals were therefore first put through the experiments which we surmised would give least symptoms, and were subsequently exposed to circumstances of progressively increasing severity. Even so, each batch of animals became selected to a more or less considerable degree. Be it noted however that one may in this way obtain strong evidence of an *a fortiori* kind. For, if the selected resistant members of the herd show many symptoms in the severest experiments, so much the more would the whole original lot of average animals have been affected. This individual variability of the animals renders many of our experiments incomplete, and should be constantly borne in mind in considering the results obtained.

5. *The symptoms observed in goats.*

The symptoms observed in goats in sequence to decompression are protean in character. The majority may however be grouped under a few definite heads.

1. *Bends.* The commonest symptom which we have observed consists of the exhibition of signs indicating that the animal feels uneasy in one or more of its legs. The limb, most commonly a fore-leg, is held up prominently in the air and the animal is evidently loth to bear weight upon it (see Plate VI[1]). In mild cases such a limb is used normally in walking or running, but in other instances the animal limps more or less considerably when it is forced to use the affected member, and is often very anxious to lie down. No tenderness can be detected on pressure or manipulation of the leg and it is not altogether clear that the animal suffers definite pain. We have however noted that a goat may break its leg and immediately use it for progression without evincing any signs of pain. We may conclude from this that the response to stimuli which in many animals would be distinctly painful is largely suppressed in the goat to the level of the exhibition of a consciousness that the limb is somewhat abnormal and not well suited for active use. But it must be understood that this objective demonstration is a very conspicuous and definite symptom. There is little doubt that these symptoms observed in the legs of goats are the equivalent of the "bends" or "screws" which are the commonest

[1] We are indebted to Dr H. W. Armit for this photograph.

"Bends" of fore-leg in a goat.

symptoms in caisson workers; in human experience they are of course accompanied by definite pain, often of a severe character.

The following table shows the distribution of "bends" in the last 110 cases observed:

TABLE IV.

One hind leg	28
One fore leg	70
Both hind legs	1
Both fore legs	1
One fore and one hind leg	10
Total one leg	98
Total two legs	12
Total right	50
Total left	48

"Bends" may be seen immediately at, or indeed (but very rarely) shortly before the end of a long decompression. Most commonly however they come on after an interval of about 15 minutes; on the other hand they may be delayed still more. As might be expected, the period of delay varies with the duration of decompression: thus the average delay in a number of cases after rapid decompression (1 to 10 minutes) was 16 minutes, which was reduced by long decompression to six minutes. Their duration appears to be brief; all evidence of their presence has usually disappeared in one or two hours and it has been very exceptional for any trace of them to be present next day (16 to 20 hours).

"Bends" in parts of the body other than the limbs are very difficult to identify in animals; we have however occasionally noted symptoms which might well be bends in the trunk, though we are not prepared to definitely identify them as such.

2. *Temporary paralyses* may be of two kinds. In the first a general weakness is present accompanied with dyspnoea and there is dragging of the hind legs with foot-drop. These are clearly symptoms due to a general deficiency of oxygen from pulmonary embolism and are comparable to the paralyses seen in, *e.g.*, carbon monoxide poisoning in animals and men. In our records and the tables such cases are not classified as "paralysis" but as "dyspnoea." In the second group fall a series of cases which are obviously of nervous origin. The animal, while showing no signs of general illness, or in other instances having already had bends, exhibits foot-drop or a more extensive palsy in one or more hind- or fore-limbs. The paralysis does not usually come on till about 15 minutes after decompression, rapidly becomes more marked

for a few minutes after the first signs are noted, and then soon begins to mend, so that there is marked improvement in about half an hour, and by next day the animal is found quite well. This form of paralysis chiefly involves the hind legs (16 out of 19 cases).

3. *Pain.* In some cases the animals have shown signs of acute pain by urgent bleating and continual restlessness. Bleating in goats after decompression is usually a sign of distress such as is produced by cardiac and respiratory embarrassment and is often present in fatal cases. In other instances animals showing only severe bends bleat in a most distressing manner and are evidently in acute pain: at the same time they may gnaw at some part of their body (such as the testicles) as if localising the origin of the pain. In animals which have recovered, we have not had any instance where these signs persisted for more than 10 or 15 minutes.

4. *Permanent paralyses.* The onset is usually immediately after decompression, the condition is complete from the first and for at least several days there are no signs of improvement. In a few cases the first paralysis has passed off (to all appearances completely) in two or three hours and the animal has been found next morning to be again paralysed. This second paralysis is permanent. A similar history has often been noted in human cases. In 15 cases out of 16 the condition has been a paraplegia, and in one all four legs were affected more or less. In some there has been retention of urine, and one animal had to be killed on account of acute distension of the stomach which came on some 20 hours after the onset of the paraplegia. In the most severe cases the animals have been killed; others have however soon begun to mend and have lived for some months with a slight spastic paralysis of the hind legs.

5. A fair number of cases have occurred where the animal has been obviously ill, but in which it has been impossible to identify any definite local symptoms or any definite dyspnoea. The goat may lie down, refuse to move or to be tempted with corn (of which goats are inordinately fond), sometimes lying extended on the side, sometimes hurriedly rising, walking a few steps and then lying down again. On two occasions the most probable interpretation of the symptoms was that the animal was blind. The goat may run wildly about instead of becoming very apathetic and depressed. These and other such symptoms are on the whole somewhat persistent and the animal is often dull and poorly the next day. In one case (XXV A) the goat showed little but a marked apathy and distaste for food, but died 16 hours later.

6. *Dyspnoea* is usually the precursor of (7) *death* and only a minority of goats survived after showing clear dyspnoea. In these cases the condition has rapidly improved; more commonly however it progressively increases till the animal is moribund, when it is replaced by irregular, faint, gasping respiration. The mucous membranes become livid and pale and the animal lies for a short time unconscious before respiration stops. The heart continues to beat regularly throughout and the rate is not apparently much altered. Only on one occasion have we been able to hear gurgling in the heart on auscultation: it was then audible at some distance. Death ensues at varying periods after decompression; with very severe experiments (*e.g.* 100 lbs.: 1 hour: 1 minute)[1] it may follow in five or ten minutes: with more moderate conditions it is delayed for 20 or 30 minutes, or rarely for two or three hours: on three occasions it has followed still later, up to 40 hours. The delay in the onset of the first symptoms is often most striking; the animal may appear quite normal for as long as 10 or 15 minutes, dyspnoea then appears, the goat falls down helpless and in another 15 minutes is dead.

8. *Mechanical symptoms* are not important. We have not been able to satisfy ourselves that goats ever suffer materially during compression from the ear troubles which are so common in men. Abdominal distension is occasionally extreme, but the animal soon empties its distended stomach and seems to be little inconvenienced[2].

Our index throughout has been the presence of symptoms, not the presence of bubbles. Anticipating here a later section (p. 410) we may say we are in entire agreement with the view which attributes most of the severe symptoms of caisson disease to local or general blocking of the circulation by bubbles of gas. One might suppose in consequence that the incidence of severe symptoms, especially of paralyses, would be of a haphazard kind, since they would be to a large extent dependent on the chance distribution of bubbles by the blood stream. Some support for this view is perhaps to be found in the records of caisson workers given by von Schrötter; as far as can be ascertained from the details given, the cases of paralysis and dyspnoea were distributed through the whole range of pressure experienced by the men in about the same proportion to the total number of illnesses of all kinds, which latter increased greatly as the pressure became higher. It should however be noted that the range of pressure was small (up to 2·4 atmospheres positive), and

[1] *i.e.* pressure 100 lbs. positive; exposure for 1 hour; decompression in 1 minute.

[2] Post-mortem experience shows that the stomach alone is distended, not the bowels.

the general experience of caisson works as well as our own experiments with animals are distinctly at variance with these results. We have noted only two instances of what may be called "chance incidence" of paralysis: (*a*) goat XV (Series II) had a paraplegia after 15 minutes' exposure at 75 lbs. and decompression in 30 minutes uniformly, and afterwards lived for some time, passing through much more severe experiments without symptoms, and eventually being killed with some difficulty by 75 lbs: 2 hours: 1 min.: (*b*) goat XII A (Series III) after 45 lbs.: 1 hour: 10 min. uniform, had apparently very severe bends; it did not however recover in the usual way and became partially paraplegic, subsequently passing through many comparatively severe experiments without symptoms. The tables of our results seem to show quite clearly that as the conditions of experiment become more searching, not only does the frequency of symptoms increase but the proportion of severe to total symptoms becomes much greater.

It is necessary for comparative purposes to form some idea of the relative importance of these different symptoms, and to consider how far they may be classed as relatively dangerous or comparatively negligible. "Bends" are clearly a slight symptom; there is abundant evidence both in goats and men that their occurrence is no indication of urgent danger to life. At the other end of the scale we have death. Dyspnoea is not far removed in significance from death, and lasting paralyses are somewhat less serious than dyspnoea. Next in order come pain and those indeterminate conditions which we have grouped as "indefinite and various general": these may be followed by death and are much more indicative of danger than bends. Temporary paralyses are not so important and we are inclined to the view that they are not much more dangerous than bad bends. This classification is based for the most part on our experience as to the kind of experiment with which each group of symptoms is commonly associated, and the way in which the different groups are associated together in the same experiment. The individual variability of the animals introduces many difficulties, but it is certain that the more severe the conditions of pressure, exposure and decompression, the more likely it is that the animals will suffer from symptoms which we have classed as severe.

Immunity to symptoms. There is not the slighest ground, either theoretical or experimental, for supposing that animals or men, as the result of repeated exposure to compressed air, acquire any immunity to the formation of bubbles within their persons. It must be remembered in this connection that the susceptible individuals become eliminated,

so that those who have been through many decompressions necessarily show more than average resistance. The matter is not so clear with regard to the exhibition of symptoms resulting from such bubbling. We have a certain amount of evidence, too vague to be detailed, that some goats show slight bends rather more easily in their first few experiences, and it is not difficult to imagine that they might grow to neglect altogether those bubbles which evidently cause them no very great inconvenience at any time. With severe symptoms it is of course different: no one can suppose that a goat acquires immunity to extensive pulmonary air emboli or to infarction of the spinal cord.

TABLE V.

Series I. June—July 1906. Pressure 75 lbs. positive (=6 atmospheres absolute). Compression in 39—41 minutes. The details of the stage decompressions are shown in Table IX.

Decompression minutes		40—50 uniform			40–50 stages		
Actual exposure minutes....		12	15	30	12	15	30
No. of goat	Sex						
I	M	0					
Pa	M	0	bends	0		0	0
XIII	F	bends					
XVIII	F	bends + indefinite[1]	0	0			0
XXI	F	0+0[1]	bends				
XXII	F	0	bends				
X	F		bends	bends			0
XVI			bends	bends		0	
XX	F		bends	bends	bends		
XXIV	M		0	bends		bends	0
XXVII	F		0			0	0
XXIX	F		0	bends, dyspnoea		0	
XXX			bends			bends	
XXXII			bends				
III	M			0			0
IV	M			0			bends
VI	M			0			0
XXVI	M			bends			bends + bends[1]
XXVIII	F			bad bends			
VIII	M				0		
XIV					bends		
XIX					bends		
II	M						bends
XXV	M						bad bends

[1] Each of these experiments was repeated upon the same animal: both results are shown. XVIII was generally uneasy, lay down, nothing definite.

TABLE VI.

Series II. December 1906 to January 1907. Pressure 75 lbs. positive (6 atmospheres absolute); compression 6 *minutes*.
The details of the decompressions are shown in Table IX.

Actual exposure mins.			1	3	15				30			60		120[17]			240[17]	
Decompression mins.			1	10 uniform	10 uniform	31 stages	31 stages	31 uniform	31 stages	31 stages	31 uniform	31 stages	31 stages	31 stages	70 stages	70 uniform	31 stages	31 uniform
No. of goat	Sex	Weight kilos																
1	M	18·3		0		0	bad bends	0	0	bends	0		bends	0	bad bends	0	bends	
2	M	16·2	0			0	bends	sl. bends	para-plegia[5]	temp. paral.			0			bends	para-plegia[6]	bad bends, pain
X	M	16·4	0		bad bends[1]	0	0	0	0	bends	0		0	0	bad bends[1]	bends	0	bends
XI	F	17·1			bends	0	0	0	0	0	0	bad bends	bends	0	bad bends	0	bends	
XII	M	19·8			died[7]													
XIII	M	17·8			0	0	0	0	0	0	0		bends	0	bends	0	0	0
XIV	F	18·6		0		0	[14]	bends	bends									
XV[12]	M	16·8	0		0	sl. bends[18]	0	para-plegia[4]	0	bends			0			bends	bends	0
XVI	M	10·7	0		bends	0[18]	0	bends	0	bends	temp. paral.	bends	0	0	bends	0	bends	temp. paral.
XVII	F	24·8				0[18]	0	0	0	bends			bends, dyspnoea			0	temp. paral.	
XVIII	F	26·3	0			0	0	bends	0	0	bends	bends	0	obscure[3]	bad bends	0	0	bends
XIX	F	15·0				0	0	sl. bends	0	bends	0	bends	0	0	bends	0	bends	
XX	F	15·0				0	0	0	? bends	0	0	0	0	temp. paral.	bends	0	slight bends	died[10]
XXI[15]	F	29·7				0	bends	obscure[2]	bends	bad bends						bends, dyspnoea		
XXII	F	19·0				sl. bends	0	0	? bends	0					died[9]			
XXIII	F	21·4				0		bends	died[8]									
XXIV[16]	M	35 about																
XXV[13]	M	21·5	0		bends	0	0	bends	sl. bends	0		temp. paral.	0			bends	bends	bends
XXVI	F	17·5				0	0	0	0				bad bends					
XXVII	F	12·0				0	0	bends	0	temp. paral.			0			0	0	

[1] Animal also lay down and seemed generally ill: no dyspnoea. [2] Lay down, *grunted*, seemed *quite ill*: no definite bends or dyspnoea. [3] Lay down and refused to move: no definite local symptoms. [4] Could walk with feet dragging in 6 days; nearly well when killed 9 weeks later. [5] Well in 9 days. [6] Almost well in 48 hours. [7] Died in *15 minutes*. [8] Died in *30 minutes*. [9] Died in 76 minutes: bad bends, dyspnoea, no paralysis. [10] Pain, paralysis, dyspnoea; died 43 minutes. [11] Dyspnoea; died in 26 minutes. [12] 72 lbs., 4 hours, 40 seconds; convulsions, dyspnoea, died 20 minutes. [13] 75 lbs., 2 *hours*, 45 *seconds*; *bends*, convulsions, dyspnoea, died 17 minutes. [14] Injured shoulder: killed immediately after decompression: see p. 412. [15] 75 lbs., 1 hour, 1¾ minutes; died in 10 minutes without dyspnoea or any symptoms except collapse. [16] 80 lbs., 2 *hours*, 10 *minutes uniform*; bends, paralysis, dyspnoea; died in 12 minutes. [17] In some of these experiments slow compression in 39 minutes was used, in which case the actual exposure was reduced by half the time of compression. [18] A somewhat different decompression was used *in this experiment*, viz. 75 lbs. to 17 lbs. in 5 minutes, wait 5 minutes, then 5 minutes at 13 lbs., 10 minutes at 9 lbs., and 10 minutes at 4 lbs.

TABLE VII.

Series III. February to June 1907. Pressure 45 lbs. positive (4 atmospheres absolute). The details of the stage decompressions are shown in Table IX.

Exposure minutes			15	30	45		60			90	120				240			480
Decompression minutes ..			2	2	30 stages	30 stages	11	10 uniform	30 stages	52 stages	30 stages	1	10 uniform	30 stages	57 stages	10 uniform	30 stages	62 stages	10 uniform
No. of goat	Sex	Weight kilos																	
3	M	24·3	0	0	0	0	0	bad bends	bends	0		0	0		0	0		bends	0
4	M	19·6	0	0	0	0		0	0	0		para-plegia[4]	0	0	0	0	0	0	0
X A	M	17·0	0	0	0	0	bends	0	sl. bends	0		temp. paral.	temp. paral.	0	0	bends	0	0	temp. paral.
XI A	M	20·0	0	bends	0	0	0	0	0	0		0	bends	0	0	0	0	0	0
XII A	F	19·2	0	0				para-plegia[2]			0	0	0	0	0	0	0	bends	temp. paral.
XIII A[12]	F	28·2	0	0				bends	bends	0	bad bends		bends dyspnoea para-plegia[7]	0	0		0	0	
XIV A[8]	M	16·4	0	0	0	0		bends	0	sl. bends					0			bends	
XV A	F	15·5	0	0			0	0	0	0	obscure[3]	para-plegia[5]	bends	bends	0	bends	bends	bends	bends
XVI A	M	21·1	0	bends	0	0		bends	0	0		para-plegia[6]	0	0	0	temp. paral.	0	0	0
XVII A[9]	F	26·8	0	0					0	0	0			0	0		0	0	
XVIII A[11]	F	32·0	0	0			0	0	0	0	0	0	0	0	0	bends	0	0	bends
XIX A	M	22·4	bends	0	0	0	0	0	bends	sl. bends		bends	bends	0	bends	0	0	0	0
XX A[10]	F	19·8	0	0					0	0	0			0	0		0	bends	
XXI A	F	16·0	0	bends			0	bends	0	bends	bends	bad bends	bends	0	bends	bends	bends	bends	bends
XXIII A	F	26·3	0	0				0			0		0	0	0	0	0	0	0

[1] Six other animals had this experience also, of which 7, XXVII A, and XXIX A had bends, and XXIV A, XXX A and 9 showed no symptoms. [2] Never so completely paralysed that it could not walk, but no improvement occurred during 21 weeks. [3] Bleating, seemed lost and walked into objects as if blind: well in 2 hours. [4] Acute distension of stomach developed next day; goat killed. [5] Killed next day. [6] Hind legs and, to a less degree, fore legs also: could walk in 3 days; killed 15 days when much improved. [7] Killed 3 days. [8] Broke leg, killed. [9] Died of pneumonia: no reason to connect this with decompression. [10] Died, cause unknown. [11] 75 lbs., 3 hours, 58 seconds: died 12 minutes without showing dyspnoea or any symptoms except collapse. [12] Apparently elderly.

TABLE VIII

Series IV. January to June 1907.

Pressure lbs. positive							75						75	51	45	39	30	25	20
Exposure minutes			3	6	10	15	½	15	30		60	120		180	180	180	120	120	60	240	240
Decompression minutes			1	1	½	1	60 uniform	90 uniform	68 stages	68 uniform	86 stages	92 stages	100 uniform	134 stages	134 uniform	75 to 24 in 1½ mins., wait ½ hr., total 118 or 131(1)[1]	4	to – 6 lbs. in 6 mins.[7]	to – 6 lbs. in 6½ mins.[7]	10 uniform	2	2
No. of goat	Sex	Weight kilos[2]																				
3	M	19·2		0	0	bends			0	0		0	0	0	bends					0	0	0
4	M	20·0						0				0	0							0	0	0
X A	M	17·8		0	para-plegia[11]			0	0	bends		0	temp. paral.	0						0	0	0
XI A	M	23·0		0	0	0		0	0	0		0	0	0	sl. bends					0	0	0
XII A	F	19·2		0	0	0						0	0					bends		bends	0	0
XIII A	F	28·2						0				temp. paral.	paral., dyspnoea							0	0	0
XIV A	M	16·4						0														
XV A	F	15·5						bends	0	bends		0	0	0						bends	0	0
XVI A	M	22·6						0				0	bad bends					died[8]		0	0	0
XVII A	F	26·8						0														
XVIII A	F	32·0							0	0		0	0	bends	bends					0	0	0
XIX A	M	25·3						0	0	bends		bends	bends	0	? bends					0	0	0
XX A	F	19·8						bends				0	0							bends	0	0
XXI A	F	16·0		0	0	bends		bends	0	bends		0	0	0	0					0	0	0
XXIII A	F	26·3						0				0	0							bends	0	0
XXIV A	F	14·4	0		0	temp. paral.	0		0	bends	0	bends	temp. paral.	0		? *bends*	*bends*, dyspnoea	para-plegia[12]	0	0	0	0	0
7	M[14]	19·0	0				0		0	0				bends	bends	+ bends	bends		dyspnoea	1	bends	0
XXV A	M	14·6										0	died[4]									0
XXVI A	M	14·4	0								bends	0	0			0	0				0	
XXVII A	F	27·6	0	0	0	died[3]	0		0	bends	0	0	bad bends	0		0	bad bends[13]			0	bends	0
XXVIII A	F	21·1									0	bends	pain[9], temp. paral.	0	0	bad bends	died[14]				0	
XXIX A	M	18·5					0		0	bends	0	0	pain, dyspnoea	0	0	0	indefinite[10]		bends, dyspnoea	0	0	0
XXX A	M	20·6					0		0	0						+ 0	*0*		*bends*, dyspnoea	0	0	0
9	F	26·6	obscure[5]				0		0	0				0	0	+ bends	bends, dyspnoea			0	0	bends
XXXII A[15]	F	22·0					bends									+ 0	*died*[6]			0	0	0
XXVII	F	12·0					0		0	0				0	0	+ 0	bends					

[1] None of the animals in these two experiments showed any symptoms while watched for 1 hour at 24 lbs. and for ½ hour at 17 lbs. The results in the Table are those observed after final decompression. [2] Some of these weights differ from those in Series III, Table VII: several of the animals became somewhat thinner in the later part of the experiments. [3] Bleated, some convulsions, fore and hind legs paralysed, a little dyspnoea; found dead next morning; no bubbles. [4] Cried out, lay down, refused to move, evidently very ill but no local symptoms or dyspnoea; died between 17½ and 18 hours later; bubbles in heart. [5] Bleating, dyspnoea, died 27 minutes. [6] Paraplegia, dyspnoea, died 190 minutes after decompression and 130 minutes after returning to atmospheric pressure. [7] In these experiments the pressure fell to atmospheric pressure in 30—35 seconds, the thermal effect then produced a delay of about 2 minutes when the pressure began to fall further, reaching – 6 lbs. in about 4 minutes more: decompression was therefore in rough stages. The animals were maintained at – 6 lbs. for 1 hour. [8] No symptoms for 18 minutes, then cried out, was moderately convulsed and right fore leg appeared paralysed, no dyspnoea, seemed very ill for about 10 minutes but then recovered and showed no symptoms later. [9] Constant nystagmus also noted lasting about ½ hour. [10] Lay down, evidently ill, no definite symptoms. [11] No improvement, killed 4 days. [12] No improvement, killed 6 days. [13] On a second trial again showed severe bends. [14] Castrated, of male habit. [14] Paralysis, nystagmus, no apparent dyspnoea, died 24 minutes. [15] An aged animal.

6. *Results of goat experiments.*

The detailed results of the experiments on goats are set out in the accompanying tables. With the exception of those in Series I, these tables contain nearly all the experiments which were made. Read vertically the columns give the results of the different combinations of pressure, exposure and decompression: the records of individual goats can at the same time be read on the horizontal columns. The tables give however no indication of the chronological sequence of events. In Series I only a few experiments are given; the series actually comprised 164 experiments on 34 animals, but the procedures adopted were, through ignorance, so ill-devised that no very definite results were obtained, though we gained information which enabled us to devise more satisfactory experiments subsequently. We have therefore extracted from Series I only a few results which illustrate the difference between stage and uniform decompression. The four series roughly represent four batches of goats, except that the animals of Series IV are the remnant of Series III with the addition of a further small herd. When reference is made to individual goats of Series I, the series is noted; otherwise the goats of Series III and IV are distinguished by "A": this does not apply to hornless animals which are specified by Arabic instead of Roman numerals, no two goats having the same number.

TABLE IX. *Showing the decompressions of goats from 75 lbs. and 45 lbs. Times given in minutes, one minute being occupied in each drop after the first.*

	Decompressions from 75 lbs. +								Decompressions from 45 lbs. +			
Series	I	II	II	II	IV	IV	IV	IV	III	III	III	III
Columns..	4, 5, 6	4, 5, 8, 9, 11, 12, 13, 16	4 (part)	14	12	7	10	9	3, 4, 7, 9 12, 15	8	13	16
First drop in	4	4	5	2	3	3	3	4	1	2	2	2
Wait at 32							3					
,, 27	5	2		7	15	4	9	2				
,, 22½	4			5	19	4	14	4				
,, 18	4	2	5	5	19	9	14	16		4	9	14
,, 14	4	4	4	10	24	9	14	16	3	14	14	14
,, 9	4 or 9	4	9	15	24	14	14	19	9	14	14	14
,, 4½	10 or 14	10	9	20	24	19	14	19	14	14	14	14
Total time	41 or 50	31	36	70	134	68	92	86	30	52	57	62

In the next table (Table X) the results are condensed and grouped in a simpler way, and one or two more experiments are given from Series I.

TABLE X.

Pressure lbs. positive	Compression minutes	Actual exposure minutes	Decompression minutes	No. of goats	No symptoms		Bends				Temporary paralysis	Various indefinite	Paraplegia	Dyspnoea	Total severe symptoms	Death
					Number	Percent.	Slight	Bends	Bad	Total						
75	6	½	60 un.	8	7	87		1		1					0	0
		1	1	6	6	100				0					0	0
		3	1	5	4	80				0		1			1	0
		3	10 un.	2	2	100				0					0	0
		6	1	6	6	100				0					0	0
		10	1	7	6	86				0			1		1	0
		15	1	6	2	33	1		1	2	1				1	1
		15	10 un.	7	2	29			3	3		1			1	1
		15	31 st.	34	29	85		2	2	5					0	0
		15	31 un.	36	19	53	2	3	8	13		1	2		3	1
		15	90 un.	12	9	75			3	3						
		30	31 st.	23	12	52			7	1	8	3				3	0
		30	31 un.	6	1	17			3	1	4	1				1	0
		30	68 st.	14	14	100					0					0	0
		30	68 un.	14	7	50			7		7					0	0
		60	31 st.	22	15	68			3	1	4	1	1		1	3	0
		120	31 st.	9	0	0			4	3	7		1			1	1
		120	70 st.	14	9	64			4		4				1	1	0
		120	70 un.	13	4	31		1	6		7	1		1		2	0
		120	92 st.	19	15	79			3		3	1				1	0
		120	100 un.	19	10	53			1	2	3	2	1		2	5	1
		180	134 st.	14	12	86			2		2					0	0
		180	134 un.	10	5	50	1	1	3		5					0	0
		240	31 st.	8	2	25			3	1	4	1				1	1
		240	31 un.	4	0	0				2	2	1				1	1
51	6	180	4	10	2	20			2	1	3		1		2	3	2
45	6	15	2	15	14	93			1		1					0	0
		30	2	15	12	80			3		3					0	0
		45	30 st.	14	14	100					0					0	0
		60	1	13	10	77			4		4					0	0
		60	10 un.	13	7	54			4	1	5			1		1	0
		60	30 st.	13	9	69		1	3		4					0	0
		60	52 st.	13	10	77		2	1		3					0	0
		90	30 st.	8	5	62			1	1	2		1			1	0
		120	1	10	4	40			1	1	2	1		3		4	0
		120	10 un.	12	6	50			4		4	1			1	2	0
		120	30 st.	13	12	92			1		1					0	0
		120	57 st.	15	13	87			2		2					0	0
		240	10 un.	11	6	55			4		4	1				1	0
		240	30 st.	13	11	85			2		2					0	0
		240	62 st.	15	9	60			6		6					0	0
		480	10 un.	11	6	55			3		3	2				2	0
30	6	60	10 un.	19	15	79			4		4					0	0
25		240	2	23	21	91			2		2					0	0
20		240	2	22	21	95			1		1					0	0
75	39	1	7 un.	8	7	87					0			1		1	0
		10	10 un.	4	3	75					0					0	1
		12	45 st.	4	1	25			3		3					0	0
		12	45 un.	6	4	67			2		2					0	0
		15	45 st.	6	4	67			2		2					0	0
		15	45 un.	12	4	33			8		8					0	0
		30	45 st.	11	7	64			3	1	4					0	0
		30	45 un.	12	5	42			5	1	6				1	1	0
		30	10 un.	4	0	0					0					0	4
		30	10 un.[1]	4	4	100					0					0	0
		30	10 un.[2]	4	0	0			2		2			1		1	1
		60	75 un.	4	2	50			1		1					0	1

[1] Recompressed at once to 15 lbs. for 32 minutes.

[2] Recompressed to 15 lbs. for 37 minutes 18 minutes after decompression.

un. = uniform decompression: st. = decompression by stages.

The following tables give in the simplest form the experimental evidence on certain points which are of especial importance.

(I) *Experiments showing that a certain minimum pressure is required to give symptoms in goats, and that the results vary with the pressure.*

TABLE XI.

Pressure in lbs. positive	Exposure in minutes	Decompression in minutes	No. of goats	No symptoms	Bends	Severe symptoms	Death
20	240	2	22	21	1	0	0
25	240	2	23	21	2	0	0
30	60	10 uniform	19	15	4	0	0
45	60	10 ,,	11	7	3	1	0
60[1]	45	15 ,,	4	1	3	0	0
75	15	31 ,,	36	19	13	3	1
75[2]	50	10 ,,	4	0	0	0	4

[1] Experiment in Series I: compression 30 minutes, exposure 30 minutes.
[2] Series I: compression 40 minutes, exposure 30 minutes.

These experiments show that the effects become more severe as the pressure increases although the duration of exposure was at the same time diminished and the duration of decompression increased. It was necessary to arrange the experiments in this way to prevent an inconvenient mortality among the animals.

(II) *Experiments showing that the duration of exposure to high pressures is of great importance.*

TABLE XII.

Pressure 75 lbs. positive, reached in 6 minutes.

Exposure in minutes	Decompression in minutes	No. of goats	No symptoms	Bends	Severe symptoms	Death
1	1	6	6	0	0	0
3	1	5	4	0	1	0
6	1	6	6	0	0	0
10	1	7	6	0	1	0
15	10 uniform	7	2	3	1	1
15	31 stages	34	29	5	0	0
30	31 ,,	23	12	8	3	0
60	31 ,,	22	15	4	3	0
120	31 ,,	9	0	7	1	1
240	31 ,,	8	2	4	1	1

These experiments show that goats have taken up enough air in 15 minutes to give severe symptoms on decompression in 10 minutes, while, if the exposure is less than 10 minutes, nearly all the animals escape, even with sudden decompression. Note too that with short

exposures and rapid decompressions such symptoms as appear are more frequently severe, and that bends are proportionately less common than with longer exposures and slower decompressions. Beyond 15 minutes exposure the results are somewhat irregular, but on the whole there is a progressive increase of bad symptoms up to two hours exposure. The results after four hours exposure are about the same, but the animals used (see Table VI, Series II) were to a large extent selected by previous experiments, so that it would appear that goats are practically saturated in about three hours[1].

TABLE XIII.

Pressure 45 lbs. positive.

Exposure in minutes	Decompression in minutes	No. of goats	No symptoms	Bends	Severe symptoms	Death
15	1	15	14	1	0	0
30	1	15	12	3	0	0
60	1	14	10	4	0	0
120	1	10	4	2	4	0
60	10 uniform	11	7	3	1	0
120	10 ,,	11	6	4	1	0
240	10 ,,	11	6	4	1	0
460	10 ,,	11	6	3	2	0

These figures show that with a duration of exposure up to about three quarters of an hour, no severe symptoms follow even sudden decompression. The series with sudden decompression shows that the results after two hours are much worse than after one hour. This is not clear from the series with 10 minutes decompression, which, however, show that the results do not become distinctly worse even after

[1] The following figures have been compiled from the records of Helier, Mager and von Schrötter as illustrating the saturation time for dogs of about 10 (?) kilos. The corresponding data for other animals do not seem to have been determined. Pressure 62—69 lbs., compression in 5—16 minutes, decompression ½ to 1 minute.

Exposure minutes	Number of experiments	No symptoms	Mild paralysis and bends	Lasting paralysis	Paralysis and asphyxia	Asphyxia
Less than 10	1	1	0	0	0	0
10—29	6	5	1	0	0	0
30—59	12	0	6	2	3	1 (lived)
60—120	19	2	2	2	3	10

Four of the group "paralysis and asphyxia" died, and the other two would probably have died if they had not been killed. All but one in the "asphyxia" group died, but in none of the rest was the decompression immediately fatal. These results seem to show pretty clearly that dogs require more than an hour to become saturated. It is strange that the authors conclude (*Luftdruckerkrankungen*, p. 806) that saturation is so far complete in about 38 minutes *in man* that no further intake of nitrogen is of any practical importance.

eight hours exposure. Note that of the nine severe symptoms, five were temporary and four permanent paralyses: only one case of dyspnoea was seen in the whole of the experiments at 45 lbs. (Series III) and the one case of severe illness of obscure nature was suggestive of temporary local cerebral anaemia. At 75 lbs., out of 26 severe cases, four had dyspnoea, four permanent and 12 temporary paralysis, and six indefinite: seven died.

(III) *Experiments to show that the duration of decompression is of great importance.*

TABLE XIV.

Pressure 75 lbs. positive, reached in 6 minutes.

Exposure	Decompression	No. of goats	No symptoms	Bends	Severe symptoms	Death
15	10 uniform	7	2	3	1	1
15	31 ,,	36	19	13	3	1
15	90 ,,	12	9	3	0	0
30	31 stages	23	12	8	3	0
30	68 ,,	14	14	0	0	0
120	31 ,,	9	0	7	1	1
120	92 ,,	19	15	3	1	0

(IV) *Experiments to show that the absolute range of pressure through which decompression occurs may be of less importance than the relative range of absolute pressure.*

TABLE XV.

Pressure in lbs. +	Exposure in minutes	Decompression to lbs.	Fall of pressure in lbs.	Relative reduction of absolute pressure	Duration of decompression in minutes	No. of goats	No symptoms	Bends	Severe symptoms	Death
75	180	+24	51	2·3 : 1	1½	10	10	0[1]	0	0
51	180	0	51	4·4 : 1	4	10	2	3	3	2
45	120	−6	51	6·7 : 1	6	3	0	1	1	1
39	120	−6	45	6·0 : 1	6	4	1	0	3	0
45	120	0	45	4·0 : 1	1	10	4	2	4	0

[1] There were three cases of bends at the ultimate end of a two hours' decompression.

A sudden drop of about 50 lbs. from 75 lbs. positive to 27 or 24 lbs. positive has been made about 200 times altogether in the course of these experiments without producing any symptoms, and about two-thirds of the animals showed no symptoms at the end of the stage decompression. The animals were however only left a short time at 27 lbs. before proceeding with the further decompression. In the

present series the animals were left for one hour at 24 lbs. and watched very carefully, and afterwards suddenly decompressed to 17 lbs. and again observed for half an hour. The same goats were subsequently dropped suddenly from + 51 lbs. to atmospheric pressure with very disastrous results, and a drop of 51 lbs. from + 45 lbs. to − 6 lbs. was even worse. The details of these experiments are given in Appendix III. Owing to the cooling effect of rapid decompression, the falls from + 45 and + 39 to − 6 lbs. were interrupted by a delay of about two minutes at atmospheric pressure so that they were in a rough way stage decompressions.

(V) *Experiments showing the importance of the mode and spacing of decompression.*

The next table shows in brief the results of seven groups of experiments undertaken with the purpose of directly testing the results of stage decompression in comparison with those of uniform decompression in the same total time. The only exceptions to the parallelism of the experimental conditions are (1) in group ζ the time of uniform decompression was extended from 92 to 100 minutes in order that it might correspond to the supposed safe rate of 20 minutes an atmosphere[1]; and (2) in group β stage decompression, three animals were decompressed by stages in an abnormal way (see Table VI and note, Series II); since these stages were certainly not more favourable to the animals than those used for the rest of the group, we have included the results.

In considering these results it must be clearly understood that the stage decompressions used were not in most cases intended to be safe for the particular exposure to which they were attached. The only two groups which were intended to be safe (δ and η) gave fairly satisfactory results; with 30 minutes exposure (+ 6 minutes compression) at 75 lbs. and 68 minutes stage decompression, we obtained no illnesses in 14 goats, and with three hours exposure and two and a quarter hours stage decompression only two cases of bends in the same number of animals. For comparative purposes it was desirable that the stage decompressions should produce symptoms of some kind, and they were intentionally designed so to do in so far as our knowledge allowed[2].

[1] The details of the experiments in this group are given in Appendix III.

[2] The stage decompressions from 45 lbs. pressure are likewise all shorter than what we calculate to be safe. The stoppages are also imperfectly spaced. The proper spacing and duration of stoppages could not be calculated till the results of the experiments were known, and we realised the extreme slowness of saturation and desaturation.

TABLE XVI. *Showing the comparison between the results of stage and uniform decompression. Pressure 75 lbs. positive.*

A. *All experiments.*

Group	Exposure minutes[1]	Decompression, minutes	Decompression, method	Number of animals	Number of decompressions	No symptoms	Per cent.	Bends: Doubtful	Bends: Slight	Bends: Bends	Bends: Bad	Bends: Total	Temporary paralysis	Various general	Paraplegia	Dyspnœa	Total severe	Death
α	12–30	45	stages	18	22	12	55			9	1	10					0	
β	15	31	,,	18	34	29	85		2	2	1	5					0	
γ	30	31	,,	15	23	12	52			7	1	8	3				3	
δ	30	68	,,	14	14	14	100					0					0	
ε	120	70	,,	14	14	9	64			4		4				1	1	
ζ	120	92	,,	19	19	15	79			3		3	1				1	
η	180	134	,,	14	14	12	86			2		2					0	
Total					140	103	74	0	2	27	3	32	4	0	0	1	5	0
α	12–30	45	uniform	19	32	14	44			15	1	16		1		1	2	
β	15	31	,,	18	36	19	53	2	3	8		13		1	2		3	1
γ	30	31	,,	6	6	1	17			3	1	4	1				1	
δ	30	68	,,	14	14	7	50			7		7					0	
ε	120	70	,,	13	13	4	31		1	6		7	1		1		2	
ζ	120	100	,,	19	19	10	53			1	2	3	2	1		2	5	1
η	180	134	,,	10	10	5	50	1	1	3		5					0	
Total					130	60	46	3	5	43	4	55	4	3	3	3	13	2

B. *Experiments on identical animals.*

β	15	31	stages	18	34	29	85		2	2	1	5					0	
γ	30	31	,,	6	6	4	67			2		2					0	
δ	30	68	,,	14	14	14	100					0					0	
ε	120	70	,,	13	13	9	69			4		4					0	
ζ	120	92	,,	19	19	15	79			3		3	1				1	
η	180	134	,,	10	10	8	80			2		2					0	
Total					96	79	82	0	2	13	1	16	1	0	0	0	1	0
β	15	31	uniform	18	36	19	53	2	3	8		13		1	2		3	1
γ	30	31	,,	6	6	1	17			3	1	4	1				1	
δ	30	68	,,	14	14	7	50			7		7					0	
ε	120	70	,,	13	13	4	31		1	6		7	1		1		2	
ζ	120	100	,,	19	19	10	53			1	2	3	2	1		2	5	1
η	180	134	,,	10	10	5	50	1	1	3		5					0	
Total					94	46	49	3	5	28	3	39	4	2	3	2	11	2

[1] Group α compressed in 39 minutes; the rest in 6 minutes or, with long exposures, in 39 minutes and half the time of compression deducted from the actual time of exposure.

The results are given in two forms: (*A*) shows the fate of all the animals tested to obtain the direct comparison between stage and uniform decompression, while in (*B*) the figures are confined to the effects (in the same experiments) on animals which were exposed to both stage and uniform decompression in each group. This emendation removes the only very severe symptom and three out of four of the temporary paralyses caused by stage decompression. Goat XXI (Series II) was advancing in pregnancy and, after having nearly died as the result of quick stage decompression, was excluded from the experimental troupe; the effect of the corresponding uniform decompression on this animal can therefore be only surmised. The effects of 31 minutes stage decompression after 30 minutes exposure were so bad that, not wishing at this stage to risk losing any animals, the parallel experiment with uniform decompression was limited to the more resistant animals. In group β (*B*) two of the animals were only decompressed once by stages. One had died from uniform decompression, and the other had broken a leg and had to be killed.

The figures show that the ratio of animals showing no symptoms with stage decompression to those escaping after uniform decompression in the same total time is about eight to five. Be it noted too that the difference between the two methods is in the same sense, *i.e.* in favour of stage decompression, in each of the seven groups, including group α (Series I) where the stages were less well arranged than afterwards. The difference between the two methods appears still more strikingly in the quality than in the quantity of the symptoms produced. For while but one animal had symptoms which can be called distinctly severe after stage decompression, as many as eleven were materially ill after the corresponding uniform decompressions, and one died.

This difference may perhaps obtain more definite expression if we assign numerical values to the different symptoms. Making bends = 1, temporary paralysis = 2, and so on up to death = 6, we obtain the following results, showing a ratio of nearly five to one (*B* grouping) in favour of stage decompression:—

Group	Stages	Uniform
β	5	30
γ	2	6
δ	0	7
ϵ	4	13
ζ	5	26
η	2	5
Total	18	87

This method is of course very rough. "Death" is worth more than six times "bends," and bends should have different values according to the sort of experiment. Bends arising from short exposures and relatively rapid decompressions (*e.g.* group β) indicate that the exposure has been long enough to allow material saturation and are very significant, while if bends show merely the extreme slowness with which the tissues in which they arise get rid of the excess gas (*e.g.* group η), they are of much less moment.

If we exclude bends, and count only the more serious symptoms, or death, the comparison becomes still more striking, the ratio being then two for stage decompression, as compared with 50 for uniform decompression.

(VI) *Experiments illustrating the difference between different kinds of animals.*

(1) Five goats (XXIV A, XXVI A, XXVII A, 7 and 9), 10 small guinea-pigs (175 to 275 gms., average 230 gms.), 9 mice (average 20 gms.), 12 small rats (average 35 gms.), 9 medium rats (average[1] 85 gms.), 8 large rats (average[1] 200 gms.), and 4 rabbits (1285, 1450, 1850, 2850 gms.) were compressed to 72 lbs. in 7 minutes and left at that pressure for 3 more minutes and decompressed in 50 seconds. Goat 9 had a curious short seizure and rolled over on the ground 10 minutes after decompression; it seemed alright immediately afterwards and showed no after effects. One small rat became paraplegic at once, and two other small rats were found dead next morning; one of these had bubbles in the heart. The rest of the animals showed no symptoms. The incidence of illness on the young rather than on the old rats is curious in view of the demonstration of the general immunity of young animals by Hill and Greenwood[2]: it was perhaps correlated with the shortness of the exposure.

(2) Twelve small rats, 13 medium rats, 8 large rats, 59 mice, 7 rabbits, 10 guinea-pigs, and 1 old hen were raised to 72 lbs. in 10 minutes, left for 1 hour and then decompressed in 50 seconds. No goats were put in since it was well established that this experience would have killed all of them. The hen and the largest rabbit (weight 2800 gms.) died in 5 minutes, and 1 guinea-pig became paraplegic in 10 minutes and died in 20 minutes. All three were extensively

[1] The details were eaten by a goat. All the animals were about the same size.

[2] *British Medical Journal*, June 22nd, 1907, Supplement, p. 408.

bubbled; it is interesting to note that there were no bubbles in the avascular eggs of the hen. None of the other animals showed any symptoms.

(3) Five rabbits, 10 guinea-pigs, 23 mice, 10 small, 9 medium and 6 large rats were compressed to 51 lbs. in 7 minutes, left there for 2 hours 56 minutes and decompressed in 45 seconds. In similar experiments, out of 10 goats 2 died and only 2 escaped without symptoms (see above, p. 398). The largest rabbit, a very fat animal weighing 2·9 kilos, died 9 minutes after decompression: the rest showed no symptoms.

(4) Six goats (3, XI A, XII A, XXI A, XXIV A, XXVII A), 7 guinea-pigs and six rabbits were raised to 75 lbs. in 5½ minutes, left for 15 minutes and decompressed in 42 seconds. Goat XXVII A had dyspnoea and paraplegia and was found dead next morning: XXIV A had temporary paralysis of both hind legs without dyspnoea and was quite recovered in an hour: 3 and XXI A had bends, while XI A and XII A showed no symptoms. None of the small animals were affected.

(5) Seven goats (3, X A, XI A, XII A, XXI A, XXIV A, XXVII A), 7 guinea-pigs, 5 rabbits, 7 medium and 12 large rats and 37 mice were compressed to 75 lbs. in 6 minutes, left 10 minutes and decompressed in 48 seconds. Goat X A had paraplegia. The other goats and the small animals showed no symptoms.

(6) Guinea-pigs, mice and rats were compressed with ourselves to 30 lbs. in 15 minutes, and 1 guinea-pig, 1 mouse, 1 medium and 1 large rat were killed with chloroform after 33 minutes. After decompression in 26 minutes by stages, many bubbles were found in the heart and vessels of the guinea-pig, a few in the mouse's heart, a few in the great vessels of the large rat, but none in the medium sized rat.

7. *Individual variation among the experimental animals in their susceptibility to decompression symptoms.*

The variation in the individual susceptibility of different goats is very marked. The same variation has been noted constantly among both divers and caisson workers, and is apparent in most of the published animal experiments. As an example, the following figures have been extracted from the tables of experiments at 75 lbs. All four animals were males and very similar to one another in all obvious respects: two were resistant and two susceptible.

TABLE XVII.

Exposure	Decompression	XIII (17·8 kg.)	X (16·4 kg.)	2 (16·2 kg.)	XV (16·8 kg.)
15 mins.	31 mins. uniform	0	0	slight bends	paraplegia
15 ,,	31 ,, ,,	0	0	paraplegia	0
15 ,,	31 mins. stages	0	0	0	slight bends
15 ,,	31 ,, ,,	0	0	bends	0
30 ,,	31 ,, ,,	0	bends	pain, temporary paralysis	bends
60 ,,	31 ,, ,,	bends	0	0	0
120 ,,	70 mins. uniform	0	bends	paraplegia	bends
120 ,,	70 mins. stages	0	0	bends	bends

In all, therefore, goats X and XIII showed mild symptoms three times in 16 decompressions, while in the same experiments goats 2 and XV showed symptoms 11 times, and on 4 occasions these were of a severe character.

It might be supposed that this variation was only in the exhibition of symptoms, depending on individual susceptibility to pain, &c., and did not represent a variation in the amount and distribution of bubbles within the body. But post-mortem experience shows that the amount of bubbling present in two animals killed in the same experiment may be very different; and in living animals it is clear that on the whole susceptibility to bends involves susceptibility also to the more severe symptoms, which cannot be much altered by the temperament of the animal.

The complete explanation of this individual variation in susceptibility probably requires a knowledge of the details of caisson disease far beyond that which we at present possess. Data exist, however, on which the influence of several factors may be discussed.

(A) *Influence of sex.* The following table shows the sum of the results of the experiments grouped according to the sex of the animals. The groups defined as "selected" include only those experiments in which the animals examined were approximately representative: in Series II for example the figures given are the totals of those experiments in which 10 or more animals were examined, while in Series III and IV are summed only those observations which included both sexes about equally (Series III, expts. 1, 2, 5—8, 10—17, Series IV, expts. 18—20).

It would appear from this that there is no clear difference between the sexes in liability to decompression symptoms in general. The experiments suggested however that under certain circumstances there might be a marked difference in the susceptibility to death. In

Series I, of 5 deaths, 3 were in females, a distribution of fatalities corresponding to the numbers of the sexes (males 12, females 16) used, while in Series II are shown 1 death in 7 males and 4 deaths in 11 females. All these last four animals were to some degree advanced in pregnancy, and their mortality is very probably to be associated with this condition, which, in the goat, is accompanied by a marked increase in the subcutaneous and intra-abdominal fat. That the deaths in Series I did not fall more heavily upon the females is perhaps to be correlated with the fact that these experiments were made in the summer and none of the goats were found pregnant, while the autopsies of Series II showed that in the winter practically every female is pregnant.

TABLE XVIII.

	Males				Females			
	Number	Decompressions	Illnesses	Per cent.	Number	Decompressions	Illnesses	Per cent.
Series I:								
Total	12	78	25	32	16	71	35	49
Series II:								
Total	7	84	42	50	11	91	38	42
Selected	7	64	26	41	11	79	27	34
15 mins. exposures	7	28	9	32	11	42	13	31
1 and 2 hrs. exposures	7	25	11	44	8	24	10	42
Series III and IV:								
Selected	7	108	26	24	8	113	29	26
Total	26	270	93	34	35	275	102	37

Influence of size. In the same way the influence of size on susceptibility may be examined. In the next table the animals are grouped as above and below the average weight for each sex.

TABLE XIX.

	Above average weight			Below average weight		
	Decompressions	Illnesses	Per cent.	Decompressions	Illnesses	Per cent.
Series II:						
Selected	55	22	40	80	26	32·5
15 mins. exposure	27	9	33	39	9	23
1 and 2 hrs. exposure	20	9	45	26	12	46
Series III and IV:						
Selected	102	19	19	119	36	30
Total	157	41	26	199	62	31

The results are contradictory unless (which appears hardly possible) there is an essential difference between exposures to high (75 lbs.) and to low (45 lbs.) pressures. The sums of the whole show no material difference between large and small goats. Theoretically, with decompressions of moderate length such as were used in the experiments under consideration, small goats should be somewhat more susceptible than large goats with short exposures since they should saturate more quickly in proportion to their relatively greater gaseous exchange[1]. This is not borne out by the experiments, in which however the rate of decompression may not have been quick enough to bring out the difference. It is, on the other hand, obvious that the larger goats should be more susceptible after long exposures with any except very short or very long decompressions: this is confirmed by the experiments at 75 lbs. (Series II), but those at 45 lbs. (Series III) show a greater difference in the opposite sense.

In comparing the incidence according to sex with those arranged according to weight, it will be noted that in Series II the males are somewhat more susceptible though they are rather smaller, while the same experiments, arranged by weights, show that the heavier animals suffer more frequently. In Series III, in which the male group is again composed of smaller animals, the susceptibility of the sexes is equal, while the lighter animals are more susceptible if weight be taken as the criterion. The only conclusion to be drawn is that these figures do not indicate that either sex or weight was a determining factor in the incidence of decompression symptoms.

Influence of the activity of gaseous exchange. General considerations suggest rather strongly that the susceptibility would be found to vary with the activity of gaseous exchange, directly as regards short exposures and inversely as regards long exposures. In most of our experiments, especially those of Series III, the incidence of symptoms has been conditioned rather by the mode of decompression than by the duration of exposure. As a whole, then, the goats with the most active exchange should prove to be the least susceptible.

The respiration results already given have been analysed in reference to this point: the results are variable and inconclusive and need not be detailed. This is perhaps not very remarkable when we consider that the animals were not grouped for the respiration experiments according

[1] The respiratory activity per unit of body weight, being proportional to the ratio of surface to mass, would of course vary but little in the goats, and would only be about a fourth greater in a goat of 15 kilos than in one of 30 kilos.

to their susceptibility but by the bands into which they had been marshalled for the pressure experiments. A factor of considerable importance, which is to a large extent beyond control, is the activity of the goats at the moment. Some goats are naturally vivacious while others are almost constantly lethargic. These individual idiosyncrasies are no doubt of some moment in relation to susceptibility, but the customary habits of a group of animals may be altogether upset by an incompatible companionship in the chamber during an experiment.

One group of measurements gave for example the results shown in the following table. The CO_2 production of each group was determined on four separate occasions under conditions similar to those obtaining in the pressure experiments.

TABLE XX.

Females.						Males.					
No. of goat	Weight kilos	Expts.	Illnesses	Pressure lbs.	CO_2 gms. per kilo per hour	No. of goat	Weight kilos.	Expts.	Illnesses	Pressure lbs.	CO_2 gms. per kilo per hour
XII A	14·2	14	4	0	0·921	3	19·2	15	3		
XV A	15·5	17	8	45	1·104	4	20·0	16	1	0	0·669
XVIII A	31·4	17	2	45	1·020	X A	17·8	17	6	45	0·697
XXI A	17·0	17	11	45	0·852	XI A	23·0	17	2	25	0·959
XXIII A	22·0	13	0			XVI A	22·6	16	4	45	0·967
						XIX A	25·3	17	7		
Average	20·0	78	25 (32 %)	—	0·974		21·3	98	23 (23 %)	—	0·823

The average size in each group is about the same, and the sex incidence for all goats of Series III is the same. The results therefore appear to show that the males are 32 % less susceptible and produce 17 % less CO_2—a result which cannot be correlated with theory.

The only experiments made with the animals grouped according to their susceptibilities gave much more rational results. Great care was taken in this series to make the conditions as nearly identical as possible in all four observations; the animals were kept in the dark and remained quite quiet throughout. The results show a CO_2 production by the susceptible animals one-sixth less than that of the non-susceptible.

Influence of blood volume. The volume of the blood was determined in 8 goats, in 7 of which the susceptibility to caisson symptoms had been ascertained. The method used was the simple one of Welcker, in which, after taking a standard sample of arterial blood, the animal is bled to death and then thoroughly washed out with salt solution. The

TABLE XXI.

Non-susceptible goats.

Animals							Respiration					
			Total		Selected						CO_2 gms. per hour	
No. of goat	Sex	Weight	Decomp.[1]	Ill	Decomp.	Ill	No. of expt.	Temp.	Bar. m.m.	Duration in hours	per kilo	per 1000 sq. cms.
4	M	18·6	15	0	10	0						
XI A	M	20·8	16	1	11	1	I	12°	776	5	0·717	1·853
XVIII A	F	30·7	14	0	10	0	III	14°	775	5	0·751	1·941
XXIII A	F	25·2	12	0	8	0						
Average		23·8	57	1 (2 %)	39	(2½ %)					0·734	1·897
Susceptible goats.												
XV A	F	15·0	15	6	10	4						
XXI A	F	15·4	15	8	10	6	II	14°	775	5	0·624	1·501
XIX A	M	21·3	16	7	10	5	IV	13°	766	5	0·704	1·693
XIII A	F	25·2	16	5	11	2						
Average		19·2	61	26 (43 %)	41	17 (41 %)					0·664	1·597

[1] These figures are given up to the date at which the respiration experiments were made. Some time elapsed before the final susceptibilities were ascertained: these were 8 % for the non-susceptible group and 45 % for the susceptible animals.

tissues were not afterwards extracted with water: the red colouring matter so obtained is so small in amount that it can have little influence on the final result, and Douglas[1] has shown that additional difficulties are thereby introduced. For purposes of calculation the specific gravity of the blood has been taken as 1050. The results and the decompression records of the goats are given in the two following tables. The figures should be read in relation to the "clean" weight, *i.e.* the crude weight less the weight of the contents of the alimentary canal, which in these animals is very considerable.

The results seem to indicate that there are two types of blood volume in goats: one about 7½ % of the clean body weight and the other about 6½ %, the first type being also associated with a higher percentage of haemoglobin. No relation between blood volume and susceptibility is apparent; thus goats 2 and XIII, both males, have identical blood volumes and differ about as widely in their susceptibility as any two goats which have come under our notice.

Conclusions. Of the four factors considered in detail, it appears therefore that age, sex and blood volume were without appreciable influence. Pregnancy and a low rate of respiratory exchange seem to favour the occurrence of symptoms.

[1] *Journal of Physiology*, vol. XXXIII. (1906), p. 499.

TABLE XXII.

No. of goat	Sex	Whole weight kilos	Weight of contents of stomach and intestines: Total kg.	Weight of contents of stomach and intestines: Per cent. of whole weight	Volume of blood c.c.	Mass of blood per cent. of: Whole weight	Mass of blood per cent. of: Clean weight	Haemoglobin p.c. of human standard[1]
1	M	19·9	3·8	19·1	1006	5·31	6·56	74
XIII	M	18·9	4·3	22·7	883	4·91	6·36	—
2	M	18·0	3·7	20·5	874	5·10	6·42	64
X	M	17·0	3·0	17·6	833	5·14	6·25	72
XVI	M	11·3	2·3	20·3	592	5·50	6·91	64
A	F	31·2	5·2	16·7	1874	6·31	7·57	78
XVIII	F	27·1	4·6	17·0	1395	5·41	6·47	75
XVII	F	24·4	4·0	16·4	1520	6·54	7·83	84
Average		21·0	3·9	18·8	1122	5·53	6·80	73
Average of males		17·0	3·4	20·0	838	5·19	6·50	68·5
Average of females		27·6	4·6	16·7	1596	6·09	7·29	79

[1] The red blood corpuscles of goats are very small, about 4μ in diameter (Jolly, *C. R. Soc. de Biol.*, vol. LXIII (1907), p. 210).

TABLE XXIII.

Pressure 75 lbs.

Exposure minutes	Decomp. minutes	Goat 1	2	X	XIII	XVI	XVII	XVIII
15	30 un.	0	slight bends	0	0	bends	0	slight bends
15	30 un.	0	para-plegia	0	0	0	0	0
15	30 st.	0	0	0	0	0	0	0
15	30 st.	bad bends	bends	0	0	0	0	0
30	30 st.	bends	temp. paral.	bends	0	bends	bends	0
60	30 st.	bends	0	0	bends	0	dyspnoea	0
120	70 un.	bends	para-plegia	0	0	bends	temp. paral.	0
120	70 st.	0	bends	bends	0	0	0	0
15	1	—	—	—	—	bends	—	—
15	10 un.	—	—	bad bends	0	bends	—	—
30	30 un.	—	—	—	—	bends	—	bends
30	30 st.	0	—	0	0	temp. paral.	—	bends
60	30 st.	0	—	0	0	0	—	obscure
120	30 st.	bad bends	—	bad bends	bends	bends	—	bad bends
240	30 st.	—	bad bends	bends	0	temp. paral.	—	bends
240	30 un.	—	—	temp. paral.	—	—	—	—

But there are doubtless other particulars which, alone or in combination, are of fundamental importance. Such other factors we have not yet been able to examine in detail. Fatness for example can be gauged only in the dead, and, though we have the distinct impression that the goats which die easily (*i.e.* under circumstances of pressure, exposure and decompression which cause very few severe symptoms and deaths) are fatter than those which are killed with difficulty, we have had no means of extending our observations on this head to the great majority of our animals[1]. Fatness also involves a low rate of respiratory exchange per unit body weight. There are grounds in human experience for holding that age may have an important share in the production of symptoms and Hill and Greenwood have recently shown[2] clearly that young animals (rats, rabbits and cats) are far less susceptible than adults of the same species. All the goats used by us appeared to be adult; in the two cases (XIII A, XXXII A) in which old age had obviously set in, the susceptibility seemed to be somewhat above the average, but the ages of the animals as a whole were unknown. In any case such a factor as old age must be reduced to simpler components before it can be correlated with the theory of decompression.

8. *The pathology of caisson disease in goats.*

We have hitherto dealt exclusively with the symptoms exhibited by the experimental animals rather than with the actual or possible presence of bubbles within them. We have however made a number of observations on the post-mortem appearances of goats after decompression, which may be shortly dealt with here. Most of the animals had died from caisson disease but in other instances they were killed at varying periods after decompression.

The presence of bubbles *in vivo* must be inferred from their discovery post-mortem with considerable caution. The supersaturation of the body may be such that the separation of the gas as bubbles may take place after death. There are reasons for supposing that the living body presents nothing in the way of points or surfaces on which bubbles might arise in the blood and tissues as they do upon the glass and dust in soda-water, and a remote analogy may perhaps be drawn

[1] We have since examined this point by direct analysis of rats and guinea-pigs divided into susceptible and non-susceptible groups by decompression experiments. The results, which will be published in detail later, show that fatness is a very important factor in individual susceptibility to death.

[2] Meeting of Physiological Society, Nov. 1906.

with the relations of the vessels to the separation of fibrin *intra vitam*. Death may well alter this condition in some degree, and in any case the time factor is of importance as well as the foreign manipulation which examination involves. During life no portion of the blood remains in a supersaturated state for more than the time required for it to return from the tissues to the lungs. We have already seen that the duration of this period is probably of very great importance as regards risk of bubble formation. On cessation of the circulation the blood remains in a supersaturated state for an indefinite period. In one instance at least we have actually observed such post-mortem separation of bubbles: a rabbit was killed immediately after 75 lbs., 2 hours, 31 minutes stages, opened up at once and no bubbles found[1]; an hour later a few bubbles were found in the inferior *vena cava*. In another case bubbles in the bladder were seen to increase considerably in number and volume during the progress of the examination.

The possibility of air being introduced from without into the veins must also be considered. Ewald and Kobert showed that air might be forced into the pulmonary capillaries by an increase of intra-pulmonary pressure such as may occur in severe dyspnoea. We have seen bubbles in large quantities in the meningeal veins, and in small numbers in the superficial veins of a fore-foot, under circumstances which left no reasonable doubt that they had been sucked into the vessels during the somewhat violent manipulations used in opening the skull and skinning the leg respectively.

There is not much doubt that some of our animals which showed no symptoms must have had bubbles present in the blood. Catsaras decompressed a dog in 1 minute after 2 hours exposure at 65 lbs.: it showed no symptoms and was killed 6 hours later, when fine bubbles were found in the blood. Heller, Mager and von Schrötter (pp. 790, 882) record two dogs which were killed 10 minutes after sudden decompression after 65 and 52 minutes at 15 and 18 lbs. respectively: in both cases bubbles were found in the heart[2], though there is abundant evidence to show that dogs never show any symptoms after decompression from such low pressures. In our own animals attempts were made to see bubbles in the retinal vessels during life. Though an

[1] The vessels and bladder in the rabbit are so thin-walled that bubbles can be seen with certainty if they are present.

[2] On the other hand dogs (showing no symptoms) killed after sudden decompression after 16 minutes exposure at 2·8 atmospheres, 5+ at 3·5, 12 at 4·5 and 5 at 4·7, showed no bubbles in the blood: these were however found in three other dogs after 10+ minutes at 4·0 atmospheres, 16 and 72 at 4·5.

excellent view of the fundus may easily be obtained, no bubbles were ever seen even in animals with severe dyspnoea, so that the method cannot be taken as giving any indication of the absence of bubbles in the blood. Some of these animals died and plenty of free gas was found in the retinal vessels post-mortem. Four animals which showed no symptoms were killed within ten minutes after decompression with the following results:

TABLE XXIV.

Series and number of goat	Pressure lbs.	Exposure (actual) minutes	Decompression minutes	Bubbles in blood	Results of similar experiments in other goats			
					Number	Bends	Severe symptoms	Death
3 : XXVI A	25	120	½	absent	23	2	0	0
1 : II	45	26	6	absent	15	3	0	0
2 : XIV	75	19	31 stages	present	29	5	0	0
1 : 1	78	30	9	absent	4	0	0	1

These goats were killed before the expiration of the appropriate period for the development of bends. The experience of similar experiments indicates that they might have shown symptoms if they had not been killed. Yet three out of four had no bubbles in the blood. A few observations on rabbits on the other hand gave rather different indications. Seven rabbits in seven different experiments were exposed to 75 lbs. for periods of from 15 to 120 minutes and killed immediately after decompression in 31 minutes by stages. There is no question but that it would be the very rarest occurrence for a rabbit to have any symptoms under these circumstances, but in four of the animals we found bubbles in the heart or great veins. These may however have been formed post-mortem, and in one such case they were observed to appear some time after death.

The post-mortem appearances observed may now be shortly described. It should be remembered that most of the animals dealt with here died under circumstances of experiment less severe than those of other observers. The pressure was in almost all cases 75 lbs. and in a majority of instances the decompression was not instantaneous. These considerations probably afford the explanation of the somewhat less emphatic changes which we have noted. The naked eye appearances were in nearly every case supplemented by microscopical examination of many of the organs.

Lungs. The amount of blood in the lungs depends upon the condition of the heart: in severe cases, with the pulmonary artery choked with bubbles and the right heart distended, they are pale and bloodless; in other instances the quantity of blood appears about normal.

Haemorrhages may occur and small blood clots are not infrequently found in the trachea. A very marked, scattered, lobular emphysema is almost constant; the only explanation appears to be that some bronchioles are more or less impervious during decompression. Examination of fresh material showed that bubbles may burst out of the capillaries into the interstitial tissue of the lungs, and presumably therefore also into the alveoli. The same was found in rabbits which were killed by the injection of small quantities of air into the veins. Nothing resembling the exudative process seen in oxygen poisoning was ever found in animals exposed to simple air pressures.

In all fatal cases (with one exception) more or less abundant bubbles were found in the blood. In severe, rapidly fatal cases, the right heart is much distended with bubbles, the pulmonary vessels plugged with froth and the left heart nearly empty. The block in the pulmonary artery may indeed be so complete that the left auricle is collapsed and puckered up. In other animals, which have lived for 20, 30 or 60 minutes or longer, the two sides of the heart are equally full of blood and the right heart is not distended. The immediate cause of death, in all but three cases, which died many hours after decompression, was clearly pulmonary air embolism, and this is doubtless the cause of the urgent dyspnoea already noted. In two cases death ensued without any dyspnoea. Both these animals were intentionally killed by very severe experiments, viz. 75 lbs. for 1 hour (goat XXI) and 3 hours (XVIII A) with decompression in $1\frac{3}{4}$ and 1 minutes. Both showed no symptoms for 5 minutes and collapsed and died quietly in 10 and 12 minutes respectively. Such animals must be regarded as being so overwhelmed by sudden asphyxiation that they exhibit only the symptoms of deficiency of oxygen and not those of the accumulation of carbon dioxide.

The fatal case in which no bubbles were found in the blood post-mortem was in goat XXVII A. After 75 lbs., 15 minutes, 42 seconds it showed pain, ate part of a note-book, and became paraplegic. It was *found dead next morning*[1]. In several other cases of delayed death, and in one (XVI A) in which the animal died in 3 hours[2], the quantity of bubbles found seemed to be altogether inadequate to produce a fatal result. One may suppose that they had been previously more

[1] Heller, Mager and v. Schrötter (p. 852) record a case in a dog fatal in 6 hours after decompression in which no free gas was found in the vessels.

[2] This animal had however been recompressed and died under a state of recompression: see protocol *e*, Appendix III.

numerous and that oxygen starvation resulted in death at a time when the aeration of the blood had been restored. This form of delayed death from deficiency of oxygen is well-known in *e.g.* carbon monoxide poisoning. It might be for instance that temporary obstruction of the coronary arteries or portal capillaries caused fatal degenerative changes in the heart muscle or liver cells.

The distribution of the bubbles in the different parts of the vascular system shows several peculiarities. If only a few are present, all may be collected in the smaller branches of the pulmonary artery with none in the right heart. The left heart generally contains a few bubbles; the amount there and in the arteries roughly varies inversely with the rapidity of death unless decompression has been very quick. Smallness in the amount of bubbling affords the heart the best chance of being able to pass on the froth to the arteries, and cases which die slowly seem to show distinctly more arterial bubbles than those which expire almost at once. The veins contain variable quantities of bubbles, but always more than the arteries. They are especially abundant in the mammary, mesenteric, spermatic and portal veins, coronary vessels, and notably few in the veins on the surface of the stomach and in those of the brain and spinal cord. In several instances we have noticed great accumulations of froth in the liver while the spleen at the same time showed no bubbles in the blood flowing out on section. This massive portal embolism is probably the cause of the multiple small capillary haemorrhages which are frequently seen in the omentum and mesentery. Blocking of the portal circulation might also give rise to general symptoms of a very serious character.

It should be noted that the liver is particularly badly situated for getting rid of excess gas during and after decompression; nearly all the blood reaching it is already partly saturated by passing through the intestines, &c. The liver also contains much fat.

Lymph. The lymph in the thoracic duct has been noted to be full of froth on several occasions.

Other liquid areas. Bubbles have very seldom been found in the *aqueous humour*; the blood supply is considerable, so that their absence is probably to be attributed to the excess gas being carried off during decompression and the period which the supersaturation phenomenon adds, for practical purposes, to the actual time occupied in reducing the pressure to normal. The *vitreous humour*, on the other hand, has a poor blood supply and its consistence is such that any bubbles forming there would remain *in situ*. On only one occasion have bubbles been found

(goat XXVI, 75 lbs., 2 hours, 31 minutes stages), when they were seen in a layer close against the ciliary body. Their absence is explicable on the ground that the vitreous humour would take a very long time to saturate. The *bile* often contains bubbles: they were noted in one goat exposed at 75 lbs. for 15 minutes and killed immediately after decompression in 31 minutes stages, and in 8 animals exposed to the same pressure for 1—4 hours, but not in two animals exposed for 15 minutes which died 30 minutes after decompression in 10 minutes and 30 minutes uniformly respectively. The *urine* found in the bladder *post-mortem is remarkably free from bubbles*; on two occasions only has free gas been found. We have evidence here that the phenomenon must be due to supersaturation and the absence of "points," since we have very frequently observed goats pass urine after decompression which frothed freely on coming into contact with foreign surfaces. This *is often seen in animals which show no symptoms.* Thus in one experiment, seven goats were exposed at 45 lbs. for one hour and decompressed in 30 seconds. One had bends 19 minutes later. Within 24 minutes after decompression four animals passed urine; in two cases this frothed up freely as it ran over the pavement while in the other two (including the goat which had bends) *no bubbles could be observed.* It is somewhat striking to observe the transparent bladder of the rabbit containing urine quite free from bubbles while the vesical veins coursing over its surface are full of froth. The *cerebro-spinal fluid* rarely shows any bubbles: they have been seen only three times, in all cases after long exposures (1 to 3 hours) at 75 and 51 lbs. with sudden decompression. *Synovial fluid* is almost always full of bubbles; exposure for 15 minutes at 75 lbs. is sufficient to cause their presence, while decompression in 100 minutes uniformly is not enough to prevent their formation. In animals which have died within 3 hours of decompression, we have found them in every case. *Amniotic fluid* is dealt with below. Bubbles have been seen after very severe experiments in the *pericardial* and *peritoneal fluids* when present, and in the serous contents of a mammary cyst, but not in the milk. We have not seen any accumulations of gas in the serous cavities.

Solid organs. Fat commonly shows bubbles, *often in extreme* abundance. They are more numerous in the abdominal than in the subcutaneous fat; the latter is much more vascular. Other solid organs for the most part show no bubbles outside the blood vessels; a few are sometimes found in the liver and the spinal cord may contain large numbers. In the liver it is very difficult to determine whether any

bubble is inside a capillary or not, and we have failed to find clear evidence of bubbles outside blood-vessels, still less actually within tissue cells, in cardiac or skeletal muscle, spleen, kidney, suprarenal, salivary glands, thymus, thyroid and parathyroid, pancreas, lymphatic glands, haemolymph glands, nerves, posterior root ganglia, testis, ovary or mammary gland, though an extensive systematic histological examination has been made of more than 20 goats exposed at 75 or 45 lbs. for from 10 minutes to 4 hours and decompressed in from 30 seconds to 100 minutes.

This condition has no very obvious explanation. It is curious, for instance, to see the spermatic vein (and sometimes artery as well) full of froth and yet find no evidence of bubbles in the tissues which it drains: the same thing is also shown most strikingly in the mammary gland and vessels. There can be no doubt that these tissues must be fairly completely saturated in 4 hours and it is impossible that the excess should be removed from the tissues more quickly than from the blood. It follows that the blood must stand in an unfortunate relation towards bubbling in that it effervesces with a smaller difference of pressure, within and without, or with the same difference of pressure in a shorter time, than do the more solid organs. It seems unlikely that this difference depends on the motion of the blood. Rhythmical pulsating circulation through a smooth elastic system can hardly function as a shaking which would be efficient in bringing out free gas. Even if it did, it is not easy to see why the tissues are not affected by the pulsations in the same way, though perhaps not to the same degree, since isolated collections of fluid, as in the joints, may bubble very easily. One can only suppose that the dissolved particles of gas find in the tissues obstacles, visible and invisible, more obstructive to their aggregation into bubbles than those occurring in the blood.

Bubbles once formed in the blood will also increase in size more readily, since their movement will continuously keep them in contact with fresh portions of supersaturated liquid.

Among the solid organs, bubbles outside the vessels are found most frequently in the central nervous system. The fatty nature of this tissue is probably important in this respect. The brain is singularly free, both by direct examination and by the study of secondary degenerations. The cord may however contain numerous bubbles, and a study of their occurrence and distribution gives interesting results. In the first place they may occur in areas of softening after comparatively mild experiments (*e.g.* 45 lbs., 2 hours, 10 minutes): in this case

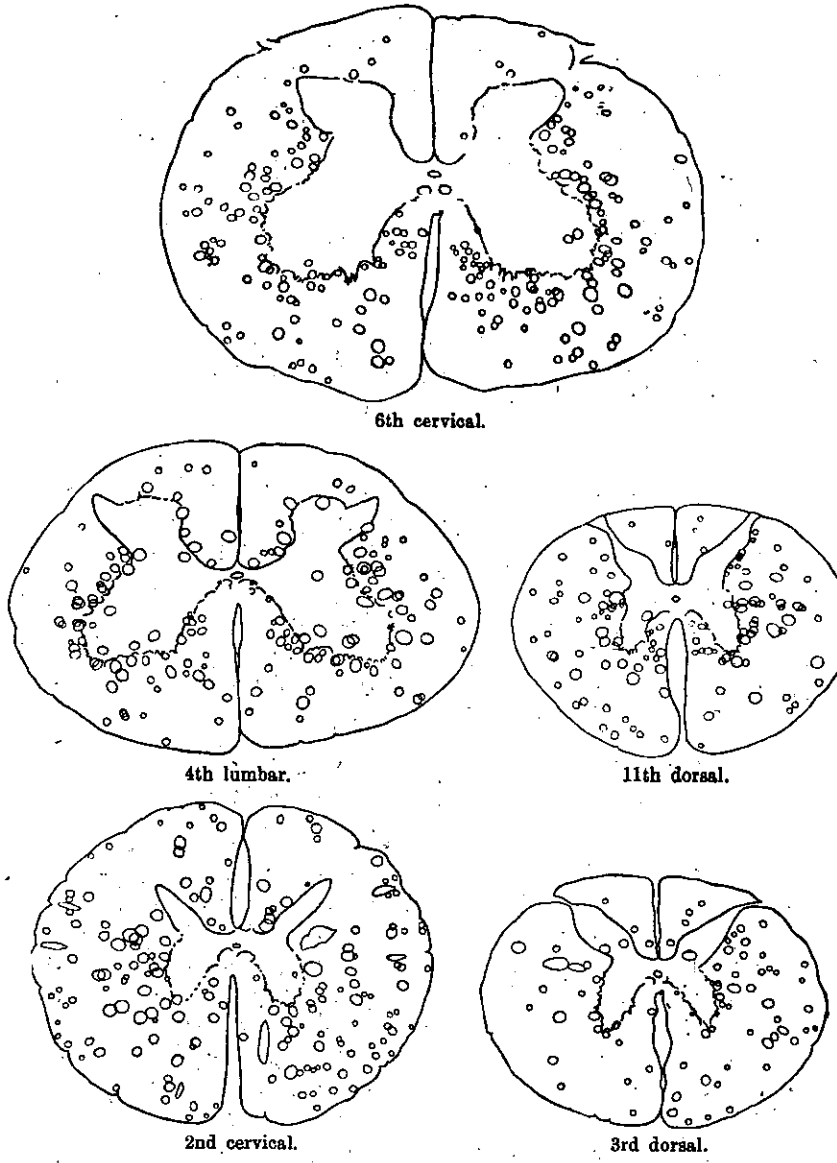


Fig. 7. Shows the distribution of extravascular bubbles in five regions of the spinal cord of goat 3 (series IV). The animal died of oxygen poisoning soon after the beginning of a decompression of 133 minutes duration by stages after 3 hours exposure at 81 lbs. in an atmosphere containing 36 % oxygen. The bubbles are practically confined to the white matter and are there especially concentrated in the boundary zone where the circulation is least good. Each diagram is a composite drawing showing all the bubbles in 0·4 mm. length of cord.

they are confined to the area in which the circulation has been brought to a sudden standstill by a collection of gas. On the other hand they may be found in the cords of animals which have died immediately after a drastic decompression. This is however rather exceptional. Thus the cords of three animals decompressed in less than a minute after 1 hour at 100 lbs. and 1 and 2 hours at 75 lbs. contained numerous bubbles, while in two animals treated in the same way after exposure at 75 lbs. for 1 and 3 hours respectively, none were found.

The distribution of the bubbles when numerous is in harmony with the theoretical conclusions derived from the blood supply. They are for instance least numerous in those segments with an abundant blood supply (lumbar enlargement), and are almost confined to the white matter, those found in the grey substance being distributed along its periphery towards the boundary zone between the superficial and deep vessels. Thus one cord (goat XXI: 75 lbs., 1 hour, 1¾ minutes) contained the following bubbles in 412 cubic millimetres in different parts:

Segment	Grey matter	Posterior columns	Ant.-lat. columns	White matter	Total
2nd cervical	14	141	215	197	175
5th dorsal	11	23	95	87	79
1st lumbar	0	32	161	140	140
4th lumbar	2	15	37	28	19
Average	7	53	127	113	103

Fig. 7 shows the distribution of bubbles in another case: note the paucity of bubbles in the grey matter and their concentration in the boundary zone.

The distribution of the areas of softening is also important. With one exception, these are most marked in, and usually confined to, the lower dorsal and upper lumbar segments where the blood supply of the cord may on many grounds be surmised to be at its minimum. They affect only the white matter. Now the only parts of the body in which we have found appearances resembling embolic infarction are the white matter of the spinal cord and the fat. The latter has on several occasions been found to contain large and small areas of necrosis. We have obtained no evidence of infarction of the spleen, kidney, heart-muscle, &c. The distribution of small bubbles by the arterial blood stream must be universal. They probably lodge in many places: while they are rapidly pushed forward in the grey matter and in most other tissues, if they lodge among the fatty surroundings of the capillaries of the white matter, or in actual fat, they quickly increase in size to such

an extent that their removal becomes impossible. It is also clear that in consequence of the slow circulation in the white matter, and especially in such inactive parts as the lower dorsal segments, bubbles have plenty of time to increase in size in the circulating blood. The condition of supersaturation will also last much longer in the white than in the grey matter. The cause then of these areas of softening in the cord is not ordinary embolism, but embolism which becomes effective to produce infarction by reason of the effect on the size of the embolus of the local conditions of the circulation rather than from any of those peculiarities in the resistance of the different tissues to lack of oxygen, or in the freedom of collateral circulation, which determine the topography of common infarcts.

The presence of bubbles in the uterine contents. We may group together here a number of casual observations which have been made on the distribution of bubbles in the foetus and amniotic fluid of pregnant goats dying of caisson disease. The pressure was in all cases 75 lbs.

TABLE XXV.

Number of goat	Exposure minutes	Decompression minutes	Time of death after decompression minutes	Bubbles present in the maternal blood	Bubbles present in the foetus	Bubbles present in the amniotic fluid	Development of foetus
XXIII	15	31 stages	30	+	0	0	advanced
XXII	120	31 ,,	75	+	0	+	,,
XX	240	31 ,,	40	+	live + dead 0	+ +	6 inch 4 inch
XXI	60	1¾	10	+	+	+	advanced
XI	240	31 uniform	25	+	0	0	1 inch
XIV	15	31 stages	killed at once	+	0	0	½ inch
XVIII A	180	1	12	+	+	+	advanced
XXVIII A	180	4¼	24	+	0	0	½ inch
XXXII A	180	4	27	+	0	0	4 inch (dead)

These observations seem to be fairly concordant. In 15 minutes the uterine contents have not taken up much excess of gas (XXIII), nor does a dead foetus absorb any (XX, XXXII A). In one hour both foetus and amniotic fluid have taken up abundant excess (XXI), which may, if death be long delayed after a rather slow decompression, be discharged from the foetus more quickly than from the amniotic fluid (XXII)[1]. With a very young foetus, the circulation is probably too

[1] Two pregnant guinea-pigs were exposed for 1 hour at +100 lbs. and decompressed in 34 minutes by stages: they showed no symptoms. On being killed 5 hours later, numerous bubbles were found in the amniotic fluid but nowhere else.

active and the bulk of fluid too small to favour bubbling (XI, XIV, XXVIII A).

The amniotic fluid, which contained in this case only a faint trace of proteid, may show the phenomenon of supersaturation to an exquisite degree. In goat XXI it was especially noted that a large bubble was present in the amniotic fluid on removing the uterus from the body. After free shaking to bring out any more gas, the uterus was opened and the contents poured into a glass vessel. Contact with this foreign surface immediately produced a great froth of fine bubbles.

The free gas runs together into one large bubble. Advantage was taken of this convenient circumstance in two instances to make analyses. The samples were collected over water and in XXII analysed at once; in XX they were kept for 20 hours over water before examination and in this case therefore the figures for CO_2 represent minimal and those for oxygen maximal values.

	XXII	XX Live foetus	XX Dead foetus
Total gas c.c.	16	27	10·5
CO_2 per cent.	16·23	5·55	2·73
O_2 ,,	1·10	2·14	0·85
N_2 ,,	81·90	94·14	96·21
Combustible gas (calculated as CH_4 and H_2)	0·77	0·17	0·21

These results correspond with those of Bert (pp. 955, 961) of the free gas in the heart: they are not in accord with those of Heller, Mager and von Schrötter (p. 800) who found 15·31 and 7·18 per cent. of oxygen in the free gas collected from the hearts of dogs. It is somewhat significant that if this excess of oxygen is calculated as an air leak, the figures of Schrötter correspond exactly with those of Bert and our analysis XXII.

Duration of bubbles. It is difficult to say how long bubbles may remain in the vessels and tissues after their first formation in animals which survive[1]. The question is much complicated by the fact that we have reason to believe that bubbles may continue to form for a long, and quite unknown, time after decompression. This is probably especially marked in cases in which either local blocking of the blood supply has occurred, or the circulation has been slowed generally by a greater or less degree of cardiac and pulmonary obstruction. It would

[1] Zografidi (*Revue de Médecine*, 1907, p. 159) records the finding of numerous bubbles in the peripheral vessels, but not in the heart, of a diver who was paralysed and died 33 days after decompression!

appear likely that bubbles once lodged in the lungs would probably stop there for a considerable time, since their gaseous composition would quickly approximate to that of the alveolar air and there would be no considerable difference of tension to encourage their removal. Such results as we have which bear on the matter are collected in the next table. It will be seen that bubbles have been found in the blood of one animal which died two days after decompression (and that in an animal which had shown no dyspnoea) and in the joints up to 26 hours. In the substance of the spinal cord bubbles may persist far longer: in two cases we have found them 15 days after the last exposure to pressure and in one 27 days after the last occurrence of symptoms.

TABLE XXVI.

Goat	Pressure lbs.	Exposure minutes	Decompression minutes	Result hours	Bubbles present in: Blood	Bubbles present in: Joints
XXII (Series I)	75	35	40 stages	died 39	+	−
XXV A	75	120	100 uniform	,, 16½	+	0
XXVII A	75	15	½	,, 15*	0	0
XV A	45	120	½	killed 24	0	0
4	45	120	½	,, 26	0	+
XIII A	45	120	10 uniform	,, 72	0	0
X A	75	10	½	,, 96	0	0
XXIII A	45 to −6	180	6	,, 144	0	0

* Found dead next morning.

A histological point of some practical importance arises in connection with the size of the bubbles found in the blood. The bubbles soon run together into large bullae after death so that it is necessary to make the examinations immediately after death in order to observe approximately the true state of affairs. It will then be found that there are no bubbles so small as to be of strictly microscopic dimensions. Nor are any very small bubbles found in the spinal cord; in any one case all the bubbles are about the same diameter, commonly some 25 microns. The same is true of the bubbles given off on decompressing water, salt solutions, serum, blood, and even such thick solutions as gelatine or agar. At the same time however it is possible to produce bubbles which are truly microscopic and which last some hours in some sticky solutions such as gum and treacle. The energy required to aggregate particles of dissolved gas into a bubble is evidently considerable, and there is the same difficulty in the formation of free gas bubbles from solution in liquids as there is in the separation of liquid particles from solution in gases and of solid particles from solution in liquids.

Extremely minute bubbles are unstable in the same way as extremely minute droplets of water condensing from supersaturated air, or salt crystals forming in a supersaturated solution in water: in all cases the tendency is to reduce the free energy (surface tension) by reducing the ratio of surface to mass, and accordingly the smallest bubbles, droplets or crystals as the case may be, are rapidly, in the case of bubbles practically instantaneously, abolished to produce macroscopic masses. This is well seen on watching under the microscope a stream of bubbles coming off some "point" in soda water. It follows that if the concentration of dissolved molecules of gas is not higher than some unknown point, bubbles will not be formed. It is possible that the absence of bubbles from most of the solid tissues is to be explained by this non-existence of very small bubbles and the mechanical difficulties of the rapid aggregation of a sufficient number of molecules to produce large bubbles. It is also doubtless connected with the period of delay in bubble formation whereby an animal, for practical purposes, gains several minutes over the actual time of decompression.

It is reasonable to suppose that the temporary paralyses are due to temporary ischaemia from air bubbles in the vessels. The more lasting palsies are undoubtedly caused by obstruction sufficiently complete to produce softening and necrosis. As already mentioned, the change is confined to the white matter and in nearly all instances affects only the lower dorsal or upper lumbar region. In these segments the bulk of cord destroyed may be very extensive: thus in goat XXIII A fully three-quarters of the lateral columns were destroyed from the eighth dorsal to the second lumbar segment over a length of rather more than five inches, and in goat XV A the softening involved nearly the whole of the lateral columns and parts of the anterior and posterior columns for a length of four and a half inches. Such cases may recover to a remarkable degree, and eventually show objective signs of paralysis so slight as to be hardly perceptible except to those familiar with the individual animals.

The only other tissue in which we have found any signs of the results of circulatory obstructions is the intra-abdominal fat. Large masses of necrosed fat have been occasionally met with, especially in the fat lying below the kidneys. Only late stages have been seen: the necrosed areas are then surrounded by a well-marked ring of giant-cell reaction, and the surface layers are mostly converted into a calcium soap.

No evidence of infarction in other organs has been seen: the rarity

of such changes seems to afford pretty good evidence that the duration of any obstruction in such organs as the spleen or kidney cannot be very long.

The pathological changes underlying the chief symptoms have been already sufficiently noticed except as regards bends. The exact cause of bends is not known. They have been attributed to bubbling in the central nervous system, chiefly on the ground that human experience shows that they are very frequently bilaterally symmetrical. This fact however cannot be taken as indicating any such origin in view of the complete symmetry of the limbs (where the symptoms occur) and the uniform symmetry of the causative agent throughout the body. In two animals which were killed soon after decompression when they showed bends only, we could find nothing abnormal in the cord, posterior root ganglia, or nerves, and there is abundant evidence from a number of goats that the cause of bends does not produce such lesions in the nervous system as are followed by secondary degeneration which can be revealed by the methods of Marchi or Weigert. The two following goats may be cited in detail as to this point: in neither was any degeneration found. Goat XXI (Series II) was used in seven experiments between November 26th and January 18th: it had bends on December 5th, 11th and 18th (the last being noted as "bad bends"), and dyspnoea, nearly fatal, on January 2nd: it was killed on January 18th. Goat XV A (Series III) was exposed 27 times between February 2nd and June 10th: it had bends on February 2nd, 20th, 22nd, March 3rd, 5th, May 13th, 15th, 27th and June 6th: it was killed on June 11th. Thorough examination of the pons, medulla and cord showed no secondary degeneration in either animal. There are therefore reasons for thinking that the cause of bends is peripheral rather than central. The constant presence of bubbles in the joints has been already mentioned, and they seem to afford a fairly probable explanation of most of the cases. Even in those cases in which the muscles are the seat of pain, it is quite possible that a sensation actually originating in or around the joints is referred to other parts. The joint pains in man are often relieved by flexion, and goats evidently try to obtain ease in the same way (see Plate VI). This fact adds strong confirmation to the conclusion that the origin of the pain is in or about the joints.

We have already seen that bends, while not the first symptom to appear as the duration of exposure to high pressure is increased, are the last symptom to disappear as the decompression is extended, that bends in short arise in parts of the body which saturate and desaturate

rather slowly. The synovial fluid satisfies this criterion; on the other hand the tendons and other dense tissues about the joints are not in disagreement with it.

Bends occur with a lower degree of supersaturation with air than any other symptom of compressed-air illness. In goats they are readily produced after exposures to 30 lbs. or less. The fact that only a moderate degree of supersaturation is needed to produce them seems to explain the fact that although they are not the first symptom to appear as the duration of exposure to very high pressure is increased, yet a moderate duration of exposure suffices to produce them, in spite of the fact that they occur in parts of the body with a slow rate of circulation, as shown by the fact that they are the last symptom to disappear as the duration of decompression is prolonged.

Summary.

1. The time in which an animal or man exposed to compressed air becomes saturated with nitrogen varies in different parts of the body from a few minutes to several hours. The progress of saturation follows in general the line of a logarithmic curve and is approximately complete in about five hours in man and in a goat in about three hours.

2. The curve of desaturation after decompression is the same as that of saturation, provided no bubbles have formed.

3. Those parts of the body which saturate and desaturate slowly are of great importance in reference to the production of symptoms after decompression.

4. No symptoms are produced by rapid decompression from an excess pressure of 15 pounds, or a little more, to atmospheric pressure, *i.e.* from two atmospheres absolute to one. In the same way it is safe to quickly reduce the absolute pressure to one-half in any part of the pressure scale up to at least about seven atmospheres: *e.g.* from six atmospheres (75 pounds in excess) to three (30 pounds), or from four atmospheres to two.

5. Decompression is not safe if the pressure of nitrogen inside the body becomes much more than twice that of the atmospheric nitrogen.

6. In decompressing men or animals from high pressures the first part should consist in rapidly halving the absolute pressure: subsequently the rate of decompression must become slower and slower, so that the nitrogen pressure in no part of the body ever becomes mor-

than about twice that of the air. A safe rate of decompression can be calculated with considerable accuracy.

7. Uniform decompression has to be extremely slow to attain the same results. It fails because it increases the duration of exposure to high pressure (a great disadvantage in diving work), and makes no use of the possibility of using a considerable difference in the partial pressure of nitrogen within and without the body to hasten the desaturation of the tissues. It is needlessly slow at the beginning and usually dangerously quick near the end.

8. Decompression of men fully saturated at very high pressures must in any case be of very long duration: and to avoid these long decompressions the time of exposure to such pressures must be strictly limited. Tables are given indicating the appropriate mode and duration of decompression after various periods of exposure at pressures up to 90 pounds in excess of atmospheric pressure.

9. Numerous experiments on goats and men are detailed in proof of these principles.

10. The susceptibility of different animals to compressed-air illness increases in general with their size owing to the corresponding diminution in their rates of circulation.

11. The average respiratory exchange of goats is about two-thirds more than that of man; they produce about 0·8 gram. of CO_2 per hour per kilogramme of body weight.

12. The mass of the blood in goats is six and a half or seven and a half per cent. of the "clean" body weight.

13. The individual variation among goats in their susceptibility to caisson disease is very large. There is no evidence that this depends directly on sex, size or blood-volume: there is some evidence that fatness and activity of respiratory exchange are important factors.

14. Death is nearly always due to pulmonary air-embolism, and paralysis to blockage of vessels in the spinal cord by air. The cause of "bends" remains undetermined; there are reasons for supposing that in at least many cases they are due to bubbles in the synovial fluid of the joints.

15. In our experiments bubbles were found post-mortem most freely in the blood, fat and synovial fluid; they were not uncommon in the substance of the spinal cord, but otherwise were very rarely found in the solid tissues.

APPENDIX I.

Details of the experiments made on Lieutenant Damant and Mr A. Y. Catto, Gunner, R.N., in the pressure chamber at the Lister Institute.

These experiments were undertaken in July, 1906, as a preliminary to actual diving experiments in very deep water.

In the first three or four the decompression was controlled from inside the chamber; in the rest from outside. The subjects remained closed in the chamber for half an hour after each experiment, the engine being also kept running so that recompression could be at once begun if any serious symptom developed. In addition to the actual period of exposure to each pressure, we have noted the virtual period of exposure calculated on the assumption that about half the time occupied in compression must be added (see above, p. 362).

In view of the results with goats, the occurrence of decompression symptoms seemed probable in the more severe experiments. No symptoms were, however, observed, except considerable itching of the skin of the fore-arms where it was uncovered. In the compressed air the well-known alteration in the voice, and corresponding abnormal sensations about the lips and mouth, were very marked at pressures exceeding 60 or 70 lbs.

I. July 25th. Actual exposure to 39 lbs. for one hour. Virtual exposure 69 minutes, decompression in 24 minutes:

Compressed to	39 lbs.	in 17 minutes.		
Waited at	39 ,,	for 60 ,,		
Decompressed to	9 ,,	in 7 ,,		
Waited at	9 ,,	for 5 ,,		
Decompressed to	4 ,,	*in* 1 ,,	}	24.
Waited at	4 ,,	for 9 ,,		
Decompressed to	0 ,,	in 2 ,,		

II. July 26th. Actual exposure to 50 lbs., 27 minutes. Virtual exposure, 39 minutes. Started at 10.37 a.m. Decompression in 34 minutes:

Compressed to	50 lbs.	in 24 minutes.
Waited at	50 ,,	for 27 ,,
Decompressed to	17 ,,	in 4 ,,
Waited at	17 ,,	for 6 ,,
Decompressed to	13 ,,	in 1½ ,,
Waited at	13 ,,	for 3½ ,,
Decompressed to	9 ,,	in 2 ,,
Waited at	9 ,,	for 3 ,,
Decompressed to	4 ,,	in 2 ,,
Waited at	4 ,,	for 8 ,,
Decompressed to	0 ,,	in 4 ,,

III. Same day, 3.3 p.m. Exposure to 55 lbs. for 19 minutes. Virtual 33 minutes. Decompression in 31 minutes:

Compressed to	55 lbs.	in 28	minutes.
Waited at	55 ,,	for 19	,,
Decompressed to	17 ,,	in 4	,,
Waited at	17 ,,	for 5	,,
,, ,, ...	13 ,,	,, 5	,,
,, ,, ...	9 ,,	,, 5	,,
,, ,, ...	4 ,,	,, 10	,,
Decompressed from	4 to 0 ,,	in 2	,,

The time taken for decompressing from 17 to 13 lbs., &c., was counted as time at 13 lbs.

IV. July 27th, 10.29 a.m. Exposure to 60 lbs. for 20 minutes. Virtual exposure 36 minutes. Decompression in 37½ minutes:

Compressed to	60 lbs.	in 30½	minutes.
Waited at	60 ,,	for 20	,,
Decompressed to	22 ,,	in 5	,,
Waited at	22 ,,	for 5	,,
Decompressed to	17 ,,	in 1	,,
Waited at	17 ,,	for 4	,,
Decompressed to	13 ,,	in 1½	,,
Waited at	13 ,,	for 3½	,,
Decompressed to	9 ,,	in 1	,,
Waited at	9 ,,	for 4	,,
Decompressed to	4 ,,	in 1½	,,
Waited at	4 ,,	for 8½	,,
Decompressed to	0 ,,	in 2½	,,

V. Same day, 3.37 p.m. Exposure to 67 lbs. for 18 minutes. Virtual exposure 36 minutes. Decompression in 36 minutes:

Compressed to	67 lbs.	in 36	minutes.
Waited at	67 ,,	for 18	,,
Decompressed to	22 ,,	in 3	,,
Waited at	22 ,,	for 5	,,
Decompressed to	17 ,,	in 1	,,
Waited at	17 ,,	for 4	,,
Decompressed to	13 ,,	in 1	,,
Waited at	13 ,,	for 4	,,
Decompressed to	9 ,,	in 1	,,
Waited at	9 ,,	for 4	,,
Decompressed to	4 ,,	in 1½	,,
Waited at	4 ,,	for 8½	,,
Decompressed to	0 ,,	in 3	,,

VI. July 30th, 10.57 a.m. Actual exposure at 74 lbs., 15 minutes. Virtual exposure 35 minutes. Decompression in 42 minutes:

Compressed to	74 lbs.	in 39	minutes.
Waited at	74 ,,	for 15	,,
Decompressed to	26 ,,	in 4	,,
Waited at	26 ,,	for 5	,,
Decompressed to	22 ,,	in 1	,,
Waited at	22 ,,	for 4	,,
Decompressed to	17 ,,	in 1½	,,
Waited at	17 ,,	for 3½	,,
Decompressed to	13 ,,	in 1	,,
Waited at	13 ,,	for 4	,,
Decompressed to	9 ,,	in 1	,,
Waited at	9 ,,	for 4	,,
Decompressed to	4 ,,	in 1½	,,
Waited at	4 ,,	for 8½	,,
Decompressed to	0 ,,	in 3	,,

VII. July 31st, 11.0 a.m. Actual exposure to 80 lbs. for 12 minutes. Virtual exposure, 34 minutes. Decompression in 51 minutes:

Compressed to	80 lbs.	in 44	minutes.
Waited at	80 ,,	for 12	,,
Decompressed to	31 ,,	in 3	,,
Waited at	31 ,,	for 5	,,
Decompressed to	22 ,,	in 1	,,
Waited at	22 ,,	for 4	,,
Decompressed to	18 ,,	in 1	,,
Waited at	18 ,,	for 4	,,
Decompressed to	15 ,,	in 3	,,
Waited at	15 ,,	for 2	,,
Decompressed to	13 ,,	in 1	,,
Waited at	13 ,,	for 4	,,
Decompressed to	9 ,,	in 1	,,
Waited at	9 ,,	for 9	,,
Decompressed to	4 ,,	in 2	,,
Waited at	4 ,,	for 8	,,
Decompressed to	0 ,,	in 3	,,

APPENDIX II[1].

A DIARY OF THE DEEP DIVING EXPERIMENTS CARRIED OUT OFF ROTHESAY, ISLE OF BUTE, FROM H.M.S. *SPANKER*, AUGUST, 1906.

Monday, 20th August.

H.M.S. *Spanker* arrived at Rothesay about 7 p.m., and was met by Drs Haldane and Rees and Mr Catto, Gunner, R.N. Arrangements were made to commence experiments the following day.

Tuesday, 21st August.

All the pumps to be used in the experiments were tested up to a pressure of 200 feet, and the leakage at this pressure measured. The pressure gauges, which had been specially graduated for these experiments, were tested and found to give correct readings. The method of testing employed was to attach the free end of the diving hose to a lead line, and lower it over the side into the sea to the required depth. The pumps were then hove round until there was a free supply of air, and then stopped whilst the reading of the gauge was taken.

The re-compression chamber was tested on the Whitehead torpedo charging column, and it was found that the pressure could be brought up to 40 lbs. on the gauge in 3 minutes. There was a leak of 1 lb. per minute, or, roughly 3 cubic feet. Afterwards Drs Haldane and Rees were compressed up to about 30 lbs. in order to further test the working of the chamber.

In the afternoon both divers made a trial dive in 15 fathoms:

	Lieutenant Damant	Mr Catto
Time of descent	2 minutes	1¼ minutes.
,, on bottom	1 hour	1 hour.
,, of ascent	18½ minutes	17½ minutes.
No. 5-minute stops	1 at 30 feet	1 at 20 feet.
,, 10 ,, ,,	1 ,, 10 ,,	1 ,, 10 ,,

Two double pumps were used for each diver in these and the subsequent dives. The divers were perfectly comfortable in moving about on the bottom. It may be mentioned that Lieutenant Damant had not dived previously beyond about 19 fathoms, and had no experience in diving except what he had gained in his course of instruction as a gunnery officer and in experimenting at Portsmouth for the Committee. Mr Catto had much previous experience in diving work, but had never dived beyond 23 fathoms.

[1] Reprinted from the *Report of the Admiralty Committee on Deep Diving*, 1907.

Wednesday, 22nd August,

H.M.S. *Spanker*, off Rothesay.

In the forenoon Mr Catto descended in 23 fathoms, and in the afternoon Lieutenant Damant did the same:

	Mr Catto	Lieutenant Damant
Time of descent	2 minutes	2½ minutes.
,, on the bottom	20 ,,	20 ,,
,, of ascent	35½ ,,	32½ ,,
No. 5-minute stops	4 at 50, 40, 30, 20 feet	2 at 50, 40 feet.
,, 10 ,, ,,	1 ,, 10 feet	2 ,, 20, 10 ,,

Thursday, 23rd August,

H.M.S. *Spanker*, off Rothesay.

After testing the pumps each diver made a descent to 25 fathoms:

	Lieutenant Damant	Mr Catto
Time of descent	2 minutes	2 minutes.
,, on the bottom	18¾ ,,	19¼ ,,
,, of ascent	37¾ ,,	39¾ ,,
No. 5-minute stops	3 at 60, 45, 30 feet	3 at 50, 40, 30 feet.
,, 10 ,, ,,	2 ,, 20, 10 feet	2 ,, 20, 10 feet.

Friday, 24th August,

H.M.S. *Spanker* was taken through the narrows of the Kyles of Bute and anchored off the entrance of Loch Riddon.

In the morning, after the usual tests had been applied to the pumps, Mr Catto descended in 27 fathoms, and in the afternoon Lieutenant Damant went down in a similar depth:

	Mr Catto	Lieutenant Damant
Time of descent	2 minutes	1 minute 20 seconds.
,, on the bottom	16½ ,, ...	16¾ minutes.
,, of ascent	55½ ,, ...	44¼ ,,
No. 5-minute stops	4 at 60, 50, 40, 30 feet	4 at 60, 50, 40, 30 feet.
,, 10 ,, ,,	1 at 20 feet. (Diver was employed just under the ship's bottom in examining a propeller which had been slightly injured, for 19½ minutes before coming up.)	2 ,, 20, 10 feet.

Saturday, 25th August,

H.M.S. *Spanker*, off Loch Riddon.

The *Spanker* shifted her position slightly, and, after the usual tests of the pumps, both divers descended in 29 fathoms of water:

	Mr Catto	Lieutenant Damant
Time of descent	3 minutes	1½ minutes.
,, on the bottom	14½ ,,	13½ ,,
,, of ascent	46 ,,	48½ ,,
No. 5-minute stops	4 at 70, 50, 40, 30 feet	4 at 66, 54, 40, 30 feet.
No. 10 ,, ,,	2 at 20, 10 feet	2 at 20, 10 feet.

Monday 27th August,

H.M.S. *Spanker*, off Loch Riddon.

Thirty fathoms of water were obtained. Mr Catto was the diver in the morning. The pumps used were Nos. 3604 and 3593. Six men were told off for each pump, in reliefs of 5 minutes. Details of the descent:

Time	Remarks
11.22	Glass screwed up. Depth by lead line 30½ fathoms.
11.23½	Diver under water.
11.23½	,, down 50 feet.
11.23¾	,, ,, 70 ,,
11.24¼	,, ,, 110 ,,
11.24½	,, ,, 150 ,,
11.24¾	,, ,, 180 ,, on the bottom. 1 min. 30 secs. in descending. Revolutions averaged 32 per min., but fell to 24 for a short time, owing to the great exertions that were necessary to keep the pumps going at the higher speed. Diver quite comfortable while moving about on the bottom.
11.36¾	Diver called up.
11.38½	,, started up.
11.39¼	,, at 160 feet.
11.39¾	,, ,, 140 ,,
11.40¼	,, ,, 120 ,,
11.41	,, ,, 100 ,,
11.41½	,, ,, 70 ,, 1st stop. Diver employed in gymnastic exercises. One pump stopped.
11.46½	Diver at 50 feet. 2nd stop.
11.51½	,, ,, 40 ,, 3rd stop.
11.56½	,, ,, 30 ,, 4th stop.
12.1½	,, ,, 20 ,, 5th stop.
12.11½	,, ,, 10 ,, 6th stop. There were no ill-effects. Water jackets gained 20 degrees F.
12.22½	Diver called up.
12.23¾	Glass off.

Afternoon. Lieutenant Damant.

2.14½	Screwed up glass.
2.15¾	Diver under water.
2.16	,, down 70 feet.
2.16½	,, ,, 120 ,,
2.16¾	,, ,, 160 ,,
2.17	,, ,, 186 ,, on the bottom. 1 minute 20 seconds in descending. Revolutions averaged 30 per minute.
2.29	Diver called up.
2.30	,, started up.
2.31	,, at 170 feet.
2.33	,, ,, 120 ,, Diver stopped 1¼ minutes.
2.33½	,, ,, 70 ,, 1st stop.
2.38½	,, ,, 50 ,, 2nd ,,

Time	Remarks
2.43½	Diver at 40 feet. 3rd stop.
2.48½	,, ,, 30 ,, 4th ,,
2.53½	,, ,, 20 ,, 5th ,,
3.3½	,, ,, 10 ,, 6th ,,
3.13½	,, called up.
3.15¼	Glass off. There were no ill-effects. Later in the afternoon the pumps were tested at different temperatures of the water jacket, to see how the leakage was affected.

Tuesday, 28th August.

In the same locality, Lieutenant Damant made a second descent in 30 fathoms in order to obtain samples of the air in the helmet. The pumps used were Nos. 3588 and 3592:

Time	Remarks
10.18½	Diver under water.
10.20¼	,, on the bottom, 1 minute 40 seconds in going down.
10.34½	,, started up.
11.21½	Glass off. Whilst on the bottom, diver took two samples whilst at rest. There was a distinct tide on the bottom, which affected the diver.

Analysis of Samples.

No. of sample	CO_2 per cent.	O_2 per cent.	CO_2 production in cubic feet per minute
1st	·32	20·86	·025
2nd	·50	20·43	·041 (? tide)

In the afternoon Mr Catto was in the dress. Pumps Nos. 3588 and 3592 were used:

Time	Remarks
2.17	Glass screwed up.
2.18¼	Diver down 60 feet.
2.19	,, ,, 100 ,,
2.19¾	,, ,, 180 ,, on the bottom. The diver took down with him a wire hawser to shackle on to a sinker.
2.31¾	Diver called up, but could not come up as he was foul, until—
2.48½	,, started up.
2.50½	,, at 140 feet.
2.53	,, ,, 100 ,, 1st stop.
2.56	,, ,, 80 ,, 2nd ,,
3.1	,, ,, 60 ,, 3rd ,,
3.7	,, ,, 50 ,, 4th ,,
3.12	,, ,, 40 ,, 5th ,,
3.22	,, ,, 30 ,, 6th ,,
3.37	,, ,, 20 ,, 7th ,,
3.52	,, ,, 15 ,, 8th ,,
4.0	,, ,, 10 ,, 9th ,,
4.18½	,, on the surface.

Mr Catto attempted to shackle a hawser on to the sinker. He found the sinker without the slightest difficulty, and then, having tied his distance line to it, went back to the hawser. He found this in bights, and he seems to have got within the coils, and in trying to find the end of the wire to have fouled his life line. When called up he could not get away, and it was 20 minutes before he could clear himself. In all he was down 28¾ minutes in 30 fathoms of water. The rate of the pump could not be kept up above 24 revolutions per minute, and the supply of air was not adequate to his exertions to free himself, so that he was almost overcome by the excess of CO_2. On account of his long exposure during heavy work, great care was taken in decompressing him, 1½ hours being allowed. There were no ill-effects.

Thursday, 30th August,

H.M.S. *Spanker*, off Loch Riddon.

Mr Catto made another descent under the same conditions, and shackled on the hawser to the sinker in 4 minutes after reaching the bottom. The revolution of the pump averaged 24 to 30 per minute. The day was very bright, with the sun shining on the water, so that the diver saw with comparative ease in the water.

In the afternoon Lieutenant Damant, at the same depth, took three samples of the air in the helmet, and the pumps were tested at 180 feet pressure. He suffered from no ill-effects:

	Mr Catto	Lieutenant Damant
Time of descent	3 minutes	1 min. 20 secs.
,, on the bottom	12¾ ,,	13 minutes.
,, of ascent	46¼ ,,	46¼ ,,
No. 5-minute stops	4 at 70, 50, 40, 30 feet	4 at 70, 50, 40, 30 feet.
,, 10 ,, ,,	2 at 20, 10 feet	2 at 20, 10 feet.

Analysis of Samples obtained by Lieutenant Damant.

Per cent.	First sample	Second sample	Third sample
CO_2	·43	·39	·36
O_2	20·56	20·52	20·47
Deficiency of oxygen	·48	·52	·57
CO_2 produced in cubic feet per minute	·035	·029	·027

Friday, 31st August,

H.M.S. *Spanker* moved down to the entrance of Loch Striven, where 35 fathoms of water could be obtained.

In the morning Lieutenant Damant was the diver. Pumps Nos. 2593, 3604 and 3592 were tested and used. Six hands were told off for each pump in reliefs of 5 minutes:

Time	Remarks
11.8	Glass screwed up.
11.8½	Diver under water.
11.9	,, down 80 feet.
11.9¼	,, ,, 120 ,,
11.9½	,, ,, 150 ,,
11.9¾	,, ,, 180 ,,
11.10¼	,, ,, 200 ,,
11.10½	,, ,, 216 ,, on the bottom. Revolutions kept at 30 per minute, and the diver had a good supply of air.
11.13½	Diver took samples seated on the shot at the bottom of the rope.
11.15½	,, called up.
11.16½	,, started up.
11.17	,, at 190 feet.
11.18	,, ,, 110 ,, Diver stopped to blow off sampling tube.
11.20½	,, ,, 90 ,, 1st stop.
11.23½	,, ,, 70 ,, 2nd ,,
11.28½	,, ,, 52 ,, 3rd ,,
11.33½	,, ,, 42 ,, 4th ,,
11.39½	,, ,, 32 ,, 5th ,,
11.44½	,, ,, 22 ,, 6th ,,
11.54½	,, ,, 11 ,, 7th ,,
12.4½	,, called up.

There was no light on the bottom, which was of soft mud. The depth by the shot rope was 210 feet. Pressure was 93½ lbs. The gauge showed a pressure of 216 feet of fresh water with the pumps stopped, and 220 feet whilst they were heaving. The actual depth, as carefully measured on the shot rope against the ship's standard measure, was just over 35 fathoms, 210 feet.

In the afternoon Mr Catto made the same descent, and reached 35 fathoms. He found that the air supply was more than ample. He walked out to the end of his distance line, and then took a sample of the air in his helmet:

Time	Remarks
2.12	Screwed up glass. Same pumps as last.
2.12¾	Diver under water.
2.14¾	,, on the bottom. Revolutions reduced to 24, as the diver found the supply too much. He proceeded to the end of his distance line before taking his sample.
2.20½	Diver started up.
2.27¾	,, at 90 feet. 1st stop.
2.30⅛	,, ,, 70 ,, 2nd ,,
2.35¾	,, ,, 50 ,, 3rd ,,
2.40¾	,, ,, 40 ,, 4th ,,
2.45¾	,, ,, 30 ,, 5th ,,
2.50¾	,, ,, 20 ,, 6th ,,
3.0¾	,, ,, 10 ,, 7th ,,
3.10¾	,, called up.

Analysis of Samples.

	Lieut. Damant	Mr Catto
CO_2 per cent.	·14	·53
O_2 ,, ,, ...	20·89	20·34
Deficiency of O_2 per cent	·15	·70

Monday, 3rd September.

Experiments on rest and measured work were carried out, by means of an arrangement of rope and pulleys by which the diver on the bottom raised and lowered a 56 lb. weight suspended in view of those on deck. The heavy rope and blocks used caused great friction and resistance.

Time	Remarks	
2.26	Diver, Mr Catto, descended.	
2.27½	,, on bottom, 142 feet.	
2.31	,, *took sample sitting on the shot.*	(No. 1.)
	Two pumps at 30 revolutions per minute.	
	Raised the weight 4 times 5 feet, at the rate of one lift per minute.	
2.36	,, took sample.	(No. 2.)
	Raised weight 7 times 5 feet in 5½ minutes.	
2.42	,, took sample.	(No. 3.)
2.45	,, started up.	
3.23	,, on surface, no ill-effects.	

3.3½	,, Lieutenant Damant, started down.	
3.4½	,, down 100 feet.	
3.5	,, on bottom, 139 feet.	
4.0	,, took sample sitting on the shot.	(No. 4.)
	Two pumps at 26 revolutions.	
	Raised weight 5 times in 1¾ minutes.	
4.3	,, took sample.	(No. 5.)
	Raised weight 3 feet 18 times in 6¼ minutes.	
4.10	,, took sample. Pump 24 revolutions.	(No. 6.)
4.13½	,, started up.	
4.52½	,, at the surface. No ill-effects.	

Analysis of Samples.

CO_2 ... ... ·30 per cent. O_2 ... ... 20·72 ,,	} Mr Catto.	Sample No. 1.
CO_2 ... ... ·70 ,, O_2 ... ... 20·29 ,,	} ,,	,, No. 2.
CO_2 ... ... ·71 ,, O_2 ... ... 20·23 ,,	} ,,	,, No. 3.
CO_2 ... ... ·18 ,, O_2 ... ... 20·73 ,,	} Lieutenant Damant.	Sample No. 4.
CO_2 ... ... ·73 ,, O_2 ... ... 20·12 ,,	} ,,	,, No. 5.
CO_2 ... ... ·81 ,, O_2 ... ... 20·36 ,,	} ,,	,, No. 6.

Tuesday, 4th September.

The *Spanker* was anchored in six fathoms of water, and experiments were made on the bottom by Dr Haldane, Lieutenant Damant, and Mr Catto on the risks of blowing up. After being compressed in the air chamber to teach them to open their Eustachian tubes, Lieutenant and Commander E. V. F. R. Dugmore, Lieutenant G. N. Henson, Jack Haldane (age 13) all made descents in six fathoms of water. This was the first time that these had ever dived in a diving dress, which illustrates the usefulness of the re-compression chamber in the practical teaching of divers.

Wednesday, 5th September.

Exhaustive tests were made as to the leakage of the pumps and composition of the air, with the water jackets at various temperatures. The results are embodied in the Report. These experiments concluded the work undertaken for the Committee.

APPENDIX III.

We give here some illustrative protocols of certain important animal experiments.

1. *Comparison of stage* (93 *minutes*) *and uniform* (100 *minutes*) *decompression after* 2 *hours exposure at* 75 *lbs.*

(*a*) 15.3.07. Goats 3, 4, X A, XI A, XVI A, XIX A, XXV A.

Started up	10.23	
Reached 75 lbs.	11.3	
Started from 75 lbs.	12.43	Stage decompression. Total = 93 mins.
,, 31½ ,, ...	12.49	
,, 27 ,, ...	12.59	
,, 22 ,, ...	1.14	
,, 18 ,, ...	1.29	
,, 13½ ,, ...	1.44	
,, 9 ,, ...	1.59	
,, 4½ ,, ...	2.14	
Reached 0 lbs.	2.16	

XIX A had bends left hind-leg at 2.20. X A passed urine not frothy at 2.27. Rest nil.

(*b*) 18.3.07. Goats XII A, XIII A, XV A, XVIII A, XX A, XXI A, XXIII A.

Started up	10.53	
Reached 75 lbs.	11.35	
Started from 75 lbs.	1.14	Stage decompression. Total = 93 mins.
,, 31½ ,, ...	1.20	
,, 27 ,, ...	1.30	
,, 22 ,, ...	1.45	
,, 18 ,, ...	2.0	
,, 13½ ,, ...	2.15	
,, 9 ,, ...	2.30	
,, 4½ ,, ...	2.45	
Reached 0 lbs.	2.47	

XX A urine no froth at 2.54. XIII A at 2.55 seemed uneasy in hind-legs and lay down but nothing definite; at 3.0 right hind-leg slight limp and foot-drop; foot-drop very marked at 3.10 and could hardly walk; alright at 4.0. Rest nil.

(*c*) 14.3.07. Goats XXIV A, XXVI A, XXVII A, XXVIII A, XXIX A.

Started up	10.35	
Reached 75 lbs.	11.14	
Started from 75 lbs.	12.55	Stage decompression. Total = 93 mins.
,, 31½ ,, ...	1.1	
,, 27 ,, ...	1.11	
,, 22½ ,, ...	1.26	
,, 18 ,, ...	1.41	
,, 13½ ,, ...	1.56	
,, 9 ,, ...	2.11	
,, 4½ ,, ...	2.26	
Reached 0 lbs.	2.28	

XXIV A showed bends left fore-leg during decompression from 4½ to 0; XXVII A passed urine no froth at 2.32; XXVIII A bends left hind-leg at 2.40. Rest nil.

(*d*) 12.3.07. Goats XXIV A, XXVI A, XXVII A, XXVIII A, XXIX A.

Started up	12.53	
Reached 75 lbs.	1.1	
Started from 75 lbs.	3.0	Uniform decompression. Total = 100 mins.
Reached 60 lbs.	3.20	
,, 45 ,, ...	3.40	
,, 30 ,, ...	4.0	
,, 15 ,, ...	4.20	
,, 0 ,, ...	4.40	

XXIX A bleated at about 1 lb., gnawed side, lay down; both fore-legs completely paralysed and hind-legs unsteady; kept head bent round on left side; bleated continually; no dyspnoea till 4.55, when it was moderate; seemed like to die. At 5.10 no dyspnoea, stopped bleating, could just stand. Could walk at 5.35. XXVII A passed very frothy urine at 4.41; both hind-legs bad bends at 4.50, right fore-leg at 5.10. XXIV A left hind-leg partial foot-drop and bends at 4.50; left fore-leg bends at 5.0. XXVIII A bad bends right fore-leg, won't stand up; at 5.0 could not stand, had constant nystagmus, bleated; at 5.10 left hind-leg bad bends, nystagmus stopped, no bleating; walked very badly at 5.30. XXVI A no symptoms.

(*e*) 19.3.07. Goats 3, 4, X A, XI A, XVI A, XIX A, XXV A.

Started up	10.30	
Reached 75 lbs.	11.14	
Started from 75 lbs.	12.52	Uniform decompression. Total = 100 mins.
Reached 60 lbs.	1.12	
,, 45 ,, ...	1.32	
,, 30 ,, ...	1.52	
,, 15 ,, ...	2.12	
,, 0 ,, ...	2.32	

XVI A came out with bad bends left hind and right fore-legs; could hardly walk and kept head twisted round to left; much better at 2.50. XIX A urine at 2.34 full of froth; bends right fore-leg. X A began bleating at 2.38 but showed nothing till 2.44 when he had complete foot-drop right fore-leg and bends left hind-leg; at 2.50 right fore-leg paralysed, could not stand up, left fore-leg also weak; urine at 2.50 a little froth. XXV A cried out a bit, belly very tight, refuses to move, *evidently far from well: died between 8 and 8.30 a.m. next day: a good* many bubbles in right heart. Rest nil.

(*f*) 20.3.07. Goats XII A, XIII A, XV A, XVIII A, XX A, XXI A, XXIII A.

Started up	11.5	
Reached 75 lbs.	11.47	
Started from 75 lbs.	1.26	Uniform decompression. Total = 100 mins.
Reached 60 lbs.	1.46	
,, 45 ,, ...	2.6	
,, 30 ,, ...	2.26	
,, 15 ,, ...	2.46	
,, 0 ,, ...	3.6	

A goat unknown aborted two foetuses 2 in. *long; they were quite* warm when found, so probably during decompression. XXIII A very

frothy urine at 3.8. XIII A dyspnoea, both hind-legs dragging; at 3.25 lying down, moaning bleat, tongue and lips getting cyanosed, dyspnoea not violent. Made sure it was going to die, but at 3.55 it got up and showed only bends right fore-leg and weakness in both hind-legs. At 5.0 seemed all right. Rest nil.

(2) *The effects of a sudden drop of* 51 *lbs. in different parts of the scale of absolute pressure.*

(*a*) 26.3.07. Goats XXIV A, XXVI A, XXVII A, XXVIII A, XXIX A.

Started up	10.0	
Reached 75 lbs.	10.46	
Left 75 lbs.	1.23	
Reached 24 lbs.	1.24½	
Left 24 lbs.	2.25	
,, 14 ,,	2.55	
,, 8 ,,	3.18½	
Reached 0 lbs.	3.21½	Total = 118½ mins.

No symptoms during decompression. XXVIII A passed frothy urine at 3.23; at 3.31 had bad bends, evidently very uneasy generally; better at 4.0. XXIX A urine no froth at 3.31. Rest nil. (The immediate object of the experiment having been attained, an unwise quickening of the end of decompression gave XXVIII A bad bends.)

(*b*) 23.5.07. Goats 7, 9, XXX A, XXXII A, XXVII.

Start up	9.55	
Reach 75 lbs.	10.35	
Left 75 lbs.	1.15	
Reach 24 lbs.	1.15.40"	
Left 24 lbs.	2.15	
,, 14 ,,	2.45	
,, 8 ,,	3.5	
,, 4 ,,	3.25	Total = 131 mins.

No symptoms during decompression. 7 limped right hind-leg on coming out; urine 3.30 no froth. 9 right hind-leg bends at 3.35. XXXII A urine 3.35 no froth. Rest nil.

(*c*) 27.3.07. Goats XXIV A, XXVI A, XXVII A, XXVIII A, XXIX A.

Started up	11.0
Reached 51 lbs.	11.30
Left 51 lbs.	2.16
Reached 0 lbs.	2.20¼

XXVIII A very unsteady on hind-legs at 2.25, passed urine full of froth; legs gave way; at 2.30 lying down grunting, constant nystagmus, mucous membranes not pale; at 2.38 respiratory movements almost stopped; died 2.44 p.m. Ordinary moderate bubbling. XXVII A bends left fore-leg at 2.27, bad; a little left next day. XXIV A left hind-leg bends at 2.29; had pretty marked dyspnoea at 2.40. XXIX A urine 2.40 no froth, seemed uneasy, kept lying down but could make out nothing definite. XXVI A no symptoms.

(*d*) 24.5.07. Goats 7, 9, XXVII A, XXX A, XXXII A, XXVII.

Started up	...	...	...	...	**9.51**
Reached 51 lbs.	...	...	...	...	**10.15**
Started down	...	...	...	...	**1.3**
Reached 0 lbs.	...	...	...	...	**1.7**

XXX A, urine 1.10 much froth, no symptoms. XXVII A, bad bends left fore-leg, jumpy hind-legs. 7, bends right fore-leg. 9, bends right fore-leg; slight dyspnoea, bends bad, both hind-legs wobbly; dyspnoea gone by 1.40 and legs alright. XXXII A bleating, won't stand up, dyspnoea; died 1.34 p.m. Bad general bubbling. XXVII bends right fore-leg.

(*e*) 5.6.07. Goats XII A, XVI A, XXIII A.

Started up	...	...	...	...	**9.52**
Reached 45 lbs.	...	...	...	...	**10.14**
Left 45 lbs.	...	...	...	...	**12.3**
Reached 0 lbs.	...	...	...	...	**12.3.33"**
,, −6 lbs.	...	...	...	...	**12.10**

XVI A uneasy at −5 lbs., paraplegic at 12.10, struggling and bleating, dyspnoea. XII A bends right fore-leg 12.19, bleating at 12.28. XXIII A tried to get up at 12.25 but failed once; then got up, right hind-leg paralysed; both gone just afterwards, could just crawl across tank; dyspnoea at 12.28. Raised pressure to atmospheric and opened tank at 1.10. XII A got up and seemed alright. XXIII A and XVI A lay log-like, conscious, breathing slightly and slowly. At 1.40 XXIII A could rest on fore-legs, hind-legs completely paralysed, ate hay; seemed pretty well except for paraplegia at 4.0. (Condition did not improve and it was killed six days later.) XVI A died at 3.20 p.m. A few small bubbles in right auricle and right femoral vein.

(*b*) 12 . 6 . 07. Goats 7, XXIV A, XXIX A, XXX A.

Started up	9.55
Reached 39 lbs.	10.13
Left 39 lbs.	12.4.20″
Reached 0 lbs.	12.4.50″
Left 0 lbs.	12.6.10″
Reached −6 lbs.	12.11.5″

XXX A bends right fore-leg at 12.13, dyspnoea at 12.30. XXIX A bends right fore-leg at 12.14, lay down, dyspnoea at 12.24. 7 lay down, dyspnoea at 12.14. XXIV A no symptoms. Raised pressure to normal and opened up at 1.15. 7 showed bends left fore-leg and had slight dyspnoea. XXX A seemed alright. XXIV A and XXIX A were very quiet but no definite symptoms. All alright at 3.30.

APPENDIX IV.

TABLE I.

Stoppages during the ascent of a diver after ordinary limits of time from surface.

Depth		Pressure	Time from surface to beginning of ascent	Approximate time to first stop	Stoppages in minutes at different depths*						Total time for ascent in mins.
Feet	Fathoms	Pounds per square inch			60 ft.	50 ft.	40 ft.	30 ft.	20 ft.	10 ft.	
0–36	0–6	0–16	No limit ...	—	—	—	—	—	—	—	0–1
36–42	6–7	16–18½	Over 3 hours	1	—	—	—	—	—	5	6
42–48	7–8	18½–21	Up to 1 hour	—	—	—	—	—	—	—	1½
			1–3 hours ...	1½	—	—	—	—	—	5	6½
			Over 3 hours	1½	—	—	—	—	—	10	11½
48–54	8–9	21–24	Up to ½ hour	—	—	—	—	—	—	—	2
			½–1½ hours ...	2	—	—	—	—	—	5	7
			1½–3 hours ...	2	—	—	—	—	—	10	12
			Over 3 hours	2	—	—	—	—	—	20	22
54–60	9–10	24–26½	Up to 20 mins.	—	—	—	—	—	—	—	2
			20–45 mins. ...	2	—	—	—	—	—	5	7
			¾–1½ hours ...	2	—	—	—	—	—	10	12
			1½–3 hours ...	2	—	—	—	—	5	15	22
			Over 3 hours	2	—	—	—	—	10	20	32
60–66	10–11	26½–29½	Up to ¼ hour	2	—	—	—	—	—	—	2
			¼–½ hour ...	2	—	—	—	—	—	5	7
			½–1 hour	2	—	—	—	—	3	10	15
			1–2 hours ...	2	—	—	—	—	5	15	22
			2–3 hours ...	2	—	—	—	—	10	20	32
66–72	11–12	29½–32	Up to ¼ hour	2	—	—	—	—	—	2	4
			¼–½ hour ...	2	—	—	—	—	3	5	10
			½–1 hour ...	2	—	—	—	—	5	12	19
			1–2 hours ...	2	—	—	—	—	10	20	32
72–78	12–13	32–34½	Up to 20 mins.	2	—	—	—	—	—	5	7
			20–45 mins. ...	2	—	—	—	—	5	10	17
			¾–1½ hours ...	2	—	—	—	—	10	20	32
78–84	13–14	34½–37	Up to 20 mins.	2	—	—	—	—	—	5	7
			20–45 mins. ...	2	—	—	—	—	5	15	22
			¾–1¼ hours ...	2	—	—	—	—	10	20	32
84–90	14–15	37–40	Up to 10 mins.	2	—	—	—	—	—	3	5
			10–20 mins. ...	2	—	—	—	—	3	5	10
			20–40 mins. ...	2	—	—	—	—	5	15	22
			40–60 mins. ...	2	—	—	—	3	10	15	30
90–96	15–16	40–42½	Up to 10 mins.	3	—	—	—	—	—	3	6
			10–20 mins. ...	2	—	—	—	—	3	5	10
			20–35 mins. ...	2	—	—	—	—	5	15	22
			35–55 mins. ...	2	—	—	—	3	10	15	30
96–108	16–18	42½–48	Up to 15 mins.	3	—	—	—	—	3	5	11
			15–30 mins. ...	3	—	—	—	3	7	10	23
			30–40 mins. ...	3	—	—	—	5	10	15	33
108–120	18–20	48–53½	Up to 15 mins.	3	—	—	—	2	3	7	15
			15–25 mins. ...	3	—	—	—	5	5	10	23
			25–35 mins. ...	3	—	—	—	5	10	15	33
120–132	20–22	53½–59	Up to 15 mins.	3	—	—	—	2	5	7	17
			15–30 mins. ...	3	—	—	—	5	10	15	33
132–144	22–24	59–64½	Up to 12 mins.	3	—	—	—	3	5	5	16
			12–25 mins. ...	3	—	—	2	5	10	12	32
144–156	24–26	64½–70	Up to 10 mins.	3	—	—	—	3	5	5	16
			10–20 mins. ...	3	—	—	2	5	10	12	32
156–168	26–28	70–75	Up to 10 mins.	3	—	—	2	3	5	5	18
			10–16 mins. ...	3	—	2	3	5	7	10	30
168–180	28–30	75–80½	Up to 9 mins.	3	—	—	2	3	5	5	18
			9–14 mins. ...	3	—	2	3	5	7	10	30
180–192	30–32	80½–86	Up to 13 mins.	3	—	2	3	5	7	10	30
192–204	32–34	86–91½	Up to 12 mins.	3	2	2	3	5	7	10	32

* During each stoppage the diver should continue to move his arms and legs.

TABLE II.

Stoppages during the ascent of a diver after delay beyond the ordinary limits of time from surface.

Depth		Pressure	Time from surface to beginning of ascent	Approximate time to first stop	Stoppages in minutes at different depths							Total time for ascent in mins.
Feet	Fathoms	Pounds per square inch			80 ft.	70 ft.	60 ft.	50 ft.	40 ft.	30 ft.	20 ft.	10 ft.	
60–66	10–11	26½–29½	Over 3 hours	2	—	—	—	—	—	—	10	30	42
66–72	11–12	29½–32	2–3 hours ...	2	—	—	—	—	—	—	10	30	42
			Over 3 hours	2	—	—	—	—	—	—	20	30	52
72–78	12–13	32–34½	1½–2½ hours	2	—	—	—	—	—	—	20	25	47
			Over 2½ hours	2	—	—	—	—	—	—	30	30	62
78–84	13–14	34½–37	1½–2 hours ...	2	—	—	—	—	—	—	15	30	47
			2–3 hours ...	2	—	—	—	—	—	5	30	30	67
			Over 3 hours	2	—	—	—	—	—	10	30	35	77
84–90	14–15	37–40	1–1½ hours ...	2	—	—	—	—	—	5	15	25	47
			1½–2½ hours ...	2	—	—	—	—	—	5	30	35	72
			Over 2½ hours	2	—	—	—	—	—	20	35	35	92
90–96	15–16	40–42½	1–1½ hours ...	2	—	—	—	—	—	5	15	30	52
			1½–2½ hours ...	2	—	—	—	—	—	10	30	35	77
			Over 2½ hours	2	—	—	—	—	—	30	35	35	102
96–108	16–18	42½–48	40–60 minutes	2	—	—	—	—	—	10	15	20	47
			1–2 hours ...	2	—	—	—	—	5	15	25	35	82
			Over 2 hours	2	—	—	—	—	15	30	35	40	122
108–120	18–20	48–53½	35–60 minutes	2	—	—	—	—	5	10	15	25	57
			1–2 hours ...	2	—	—	—	—	10	20	30	35	97
			Over 2 hours	2	—	—	—	—	30	35	35	40	142
120–132	20–22	53½–59	½–1 hours ...	3	—	—	—	—	5	10	15	20	53
			1–1½ hours ...	3	—	—	—	5	10	20	30	30	98
			Over 1½ hours	3	—	—	—	15	30	35	40	40	163
132–144	22–24	59–64½	25–45 minutes	3	—	—	—	3	5	10	15	25	61
			¾–1½ hours ...	3	—	—	—	10	10	20	30	35	108
			Over 1½ hours	3	—	—	—	30	30	35	40	40	178
144–156	24–26	64½–70	20–35 minutes	3	—	—	—	3	5	10	15	20	56
			35–60 minutes	3	—	—	—	7	10	15	30	30	95
			Over 1 hour ...	3	—	—	20	25	30	35	40	40	193
156–168	26–28	70–75	16–30 minutes	3	—	—	—	3	5	10	15	20	56
			½–1 hour ...	3	—	—	3	10	10	15	30	30	101
			Over 1 hour	3	—	5	25	25	30	35	40	40	203
168–182	28–30	75–80½	14–20 minutes	3	—	—	—	3	3	7	10	15	41
			20–30 minutes	3	—	—	2	2	3	10	15	25	60
			½–1 hour ...	3	—	3	3	7	10	20	30	35	111
			Over 1 hour	3	—	15	25	30	30	35	40	40	218
182–194	30–32	80½–86	13–20 minutes	3	—	—	—	3	3	7	15	15	46
			20–30 minutes	3	—	—	3	3	5	10	15	25	64
			½–1 hour ...	3	—	3	5	10	12	20	30	35	118
			Over 1 hour	3	5	20	25	30	30	35	40	40	228
194–206	32–34	86–91½	12–20 minutes	3	—	—	3	3	5	7	10	20	51
			20–30 minutes	3	—	3	3	3	5	10	20	20	67
			½–1 hour ...	3	3	3	5	10	15	20	30	35	124
			Over 1 hour	3	15	20	25	30	30	35	40	40	238

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A SUGGESTED CHANGE IN CALCULATING DECOMPRESSION TABLES FOR DIVING[1,2]

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Men who have been working in compressed air, either in diving suits or caissons, are liable upon their return to atmospheric pressure to a variety of symptoms variously classified as "diver's palsy", "compressed-air illness" or "caisson disease." Paul Bert (1878) showed that these symptoms were due to the fact that gas (chiefly nitrogen) which goes into solution in the blood and tissues during exposure to compressed air is liberated in the form of bubbles on too rapid decompression, and produces local or general blockage of the circulation or other injury. Subsequent investigators have confirmed and extended Paul Bert's conclusions. Paul Bert (1878) pointed out that

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[2] We wish to express our appreciation for the suggestions and advice given by the Advisory Committee—Capt. E. W. Brown, Medical Corps. U. S. Navy; Commander E. L. Gayhart, Construction Corps, U. S. Navy; and Commander H. E. Saunders, Construction Corps, U. S. Navy, formerly a member of the committee.

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by means of very slow decompression caisson disease could be avoided, but he did not furnish any definite method. V. Schrötter (1906) suggested a uniform decompression at the rate of 20 minutes an atmosphere. Boycott, Damant, and Haldane (1908), in a most comprehensive study, established the stage method of decompression which is the basis for the present method of calculating the decompression tables of the Diving Manual of the United States Navy.

The data to be presented in this paper were accumulated during experimental escapes from various depths using the submarine escape appliance—"lung"—in an attempt to determine how long a subject could remain at a given depth and then come to the surface without any decompression and yet not develop caisson disease.

Apparatus—Submarine escape appliance.—The submarine escape appliance, described by Mankin in 1930, is a bellows-type, collapsible, stockinette-covered rubber bag, 9½ inches wide and 12 inches long with a capacity of 5.5 liters. It is fitted with a special-type rubber mouthpiece which provides a watertight seal at the lips and is connected to the bag by two ¾-inch hollow metal arms joined by a metal cylinder containing two 1-way mica disk valves directing the gas flow. The exhaled gas passes through the exhaust valve and metal arm directly into the bag, and the inhaled gas is drawn through a soda-lime cannister located inside the bag and immediately below the intake valve. A manually controlled master valve is provided adjacent to the mouthpiece which completely cuts off the flow of gas at the top of the submarine escape appliance to allow filling of the bag. A Schraeder charging valve is provided at the top of the bag for inflating with oxygen. A rubber flutter valve is fitted into the bottom of the bag to permit exhaust of excess gas and thus maintain an even pressure in the appliance. It is provided with suitable straps and snaps for holding it in place while in use. A nose clip is worn to prevent nasal breathing.

Diving tank.—The experiments were carried out in a vertical cylindrical diving tank, 10 feet 1 inch in height and 9 feet 10 inches in diameter with walls of 2-inch steel, tested to a pressure of 400 pounds per square inch. When in use the tank is filled with water to a height of 8 feet to allow an air pocket above the water. It is fitted with an airtight hatch on the upper end which opens downward into the tank. There are six 4½-inch ports in the side for observation purposes. The tank on the inside is well lighted by electric lights, and is equipped with loudspeakers and telephone.

Recompression chamber.—A recompression chamber developed by the United States Navy was available for the treatment of caisson disease. This chamber is a horizontal cylinder of 2-inch steel, 14 feet 7 inches long with an inside diameter of 6 feet 6½ inches. It is divided into two compartments by a bulkhead and door of the same gage steel.

The inner compartment is 9 feet 8 inches in length while the outer compartment is 4 feet 11 inches in length. It is possible to enter or leave the inner compartment without changing the pressure on the subject. Each compartment is provided with four 3-inch observation ports. The internal working pressure is 500 pounds per square inch. The recompression chamber is also equipped with electric lights, loudspeaker, and telephone. Air pressure can be controlled from either inside or outside, and accurate gages are provided for determining the pressure. In these experiments, the recompression chamber was used only for the treatment of caisson disease.

Method.—Subjects were exposed in the diving tank to air pressures equal to various depths of sea water. During the exposure time they breathed in the air pocket and exercised by swimming and diving in the water. Prior to the end of the exposure, the subject put on the submarine escape appliance, charged it with oxygen or air, submerged completely in the water and breathed into the appliance for 2 minutes after which ascent was simulated at the rate of 50 feet per minute by reduction of the air pressure. This constituted the entire decompression received by the subjects. Each subject made daily dives 5 days a week until the series was completed. Usually eight subjects were used for each depth and time of exposure, and this was called a run. In each series the depth was kept constant while the time of exposure was increased either ½ or 1 minute for each succeeding run.

The end-point in each series was the production of caisson disease of severe enough nature to necessitate terminating the series. Competent personnel were on call at all hours to treat the subjects on the appearance of caisson disease, which was encountered in several subjects in each series except series 2.

Experimental results.—The basis for the suggested change in the decompression tables is the data obtained from 2,143 experimental dives made over a period of 3 years. They were divided into 12 series and were conducted at depths of 100, 150, 167, 185, and 200 feet. Table 1 gives the information concerning these experimental dives.

It is seen from table 1 that all subjects did not go the same length of exposure without incurring "bends." In the 4 series, run with different subjects at 100 feet the time when "bends" first appeared varied from 37½ to 43 minutes. In the same way the exposures following which caisson disease developed at 150 feet varied from 18½ to 28 minutes.

TABLE 1.—*Experimental results*

Series	Depth gage	Number of runs	Individual exposures	Initial exposure time	Increase of exposure time	Final exposure time	Caisson disease			
							First case exposure time	Number of cases	Number of exposures	
									Before first case	After and including first case
	Feet			*Minutes*	*Minutes*	*Minutes*	*Minutes*			
2	100	75	600	8½	1	34½	----------	0	600	0
7	100	18	75	14½	1	39½	37½	3	56	19
9	100	50	127	32½	1	51½	40½	5	46	81
11	100	59	429	3	1	48	43	5	408	21
10	150	28	70	18½	½	24½	18½	5	4	66
3	150	34	117	10½	1	22½	19½	3	80	37
8	150	18	71	9½	1	21½	20½	2	56	15
16	150	18	54	18	½	27	26½	2	42	12
15	150	74	214	10	½	28	28	5	206	8
4	167	38	141	6½	1	22½	17½	6	95	46
5	185	9	72	6½	1	15½	14½	3	56	16
6	200	23	173	7½	½	16	13½	2	133	40
Total	----------	----------	2,143	----------	----------	----------	----------	46	1,732	361

Discussion—Historical.—In order to clearly understand the theory of decompression of men following high-pressure air exposure it is necessary to consider the fundamental facts of saturation and desaturation of the tissues. Haldane (1922) says:

> The formation of bubbles depends, evidently, on the existence of a state of supersaturation of the body fluids with nitrogen. Nevertheless there is abundant evidence that when the excess of atmospheric pressure does not exceed normal by more than 1¼ atmospheres there is complete immunity from symptoms due to bubbles, however long the exposure to the compressed air may have been, and however rapid the decompression. Thus, bubbles of nitrogen are not liberated within the body unless the supersaturation corresponds to a decompression from a total pressure of more than 2¼ atmospheres. Now the volume of nitrogen which would tend to be liberated is the same when the total pressure is halved, whether that pressure be high or low. Hence it seemed to me probable that it would be just as safe to diminish the pressure rapidly from 4 atmospheres to 2, or 6 atmospheres to 3, as from 2 atmospheres to 1.

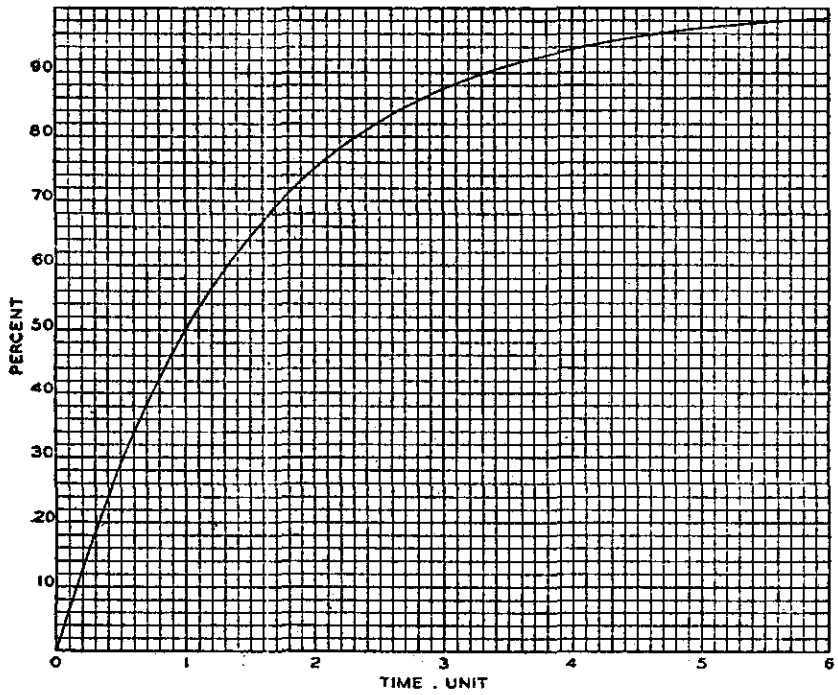
It was early shown that the degree of saturation of any part of the body depends not only on the pressure to which it is exposed and the duration of the exposure, but also upon its blood supply and its fat content. Thus, the blood itself is almost instantly saturated at the partial pressure of the gas in the lungs. Hill and Greenwood (1907) demonstrated that the kidney saturated and desaturated about 10 times as rapidly as the body as a whole. Vernon (1907) demonstrated that fat absorbed about six times as much nitrogen as blood; thus, fatty tissue would saturate and desaturate more slowly than non-fatty tissue. Haldane (1922) assumed that complete saturation of certain tissues is approached only after 5 hours exposure.

Whether or not the decompression is free from risks depends on the degree of supersaturation which can be borne with safety, the extent

to which the blood and tissues have had time or opportunity to become saturated, and the extent to which they have had time to become desaturated again during decompression.

On the basis of these facts, Boycott, Damant, and Haldane (1908) in calculating their stage decompression tables assumed the existence of 5-, 10-, 20-, 40-, and 75-minute tissues. In these tables they did not permit any of the tissues to exceed the ratio of 2.0 to 1 except at the last stage where the ratio might be as high as 2.3 to 1. This ratio was computed from the relative nitrogen saturation of the tissues in depth absolute to the nitrogen at normal atmospheric pressure.

FIGURE 1



Method of computation.—In order to permit a clearer understanding of the discussion to follow, the method of calculating a decompression table is given in detail. As an example, let us consider a diver at 108 feet (gage) for 30 minutes' exposure. Haldane (1922) states that the progress of saturation of the body with nitrogen is a logarithmic curve of the form shown in figure 1. From this figure the percentage saturation can be read off the curve, provided the duration of the exposure to pressure and the time required to produce half saturation of the tissues in question are both known. Thus the tissues which half saturate in 5 minutes (5-minute tissues) would in 30 minutes (6 time units) be 98 percent saturated. The 10-minute tissues would be 87 percent, the 20-minute tissues would be 65 percent, the

40-minute tissues would be 40 percent, and the 75-minute tissues would be 17 percent saturated.

According to Henry's law governing solubility of a gas, the tissues which are three-fourths saturated at 4 atmospheres absolute would contain as much nitrogen as if completely saturated at 3 atmospheres absolute. Thus in the present example the 5-minute tissues would contain as much nitrogen as if saturated at $0.98 \times 108 = 106$ feet gage. Similarly the other tissues are found to be saturated as if at 95, 70, 43, and 18 feet gage respectively.

We have found by use of the time unit and saturation curve that the most completely saturated tissues (5-minute tissues) are saturated to a pressure corresponding to 106 feet gage. We know from the work of Boycott, Damant, and Haldane (1908), we can safely ascend half of the absolute depth or to

$$\frac{106+33}{2}=69$$

feet absolute or 36 feet gage. But since desaturation also occurs during the 3 minutes of ascent, it is possible to bring the diver to 30 feet gage. During the 3 minutes of ascent he is subjected to an average pressure corresponding to

$$\frac{(108+33)+(30+33)}{2}=102 \text{ feet absolute.}$$

The difference between the pressure in his 5-minute tissues (139 feet absolute) and this average pressure during ascent to the first stop is $139-102=37$ feet absolute and he is subjected to this difference of pressure for 3 minutes or 0.6 time units. From the curve (fig. 1), we find that 0.6 time units is 34 percent. Thus the pressure in his tissues diminishes $0.34 \times 37 = 13$ feet and so when he reaches the first stop, the pressure in his 5-minute tissues is $139-13=126$ feet absolute. In a similar manner the saturations of the 10-, 20-, 40-, and 75-minute tissues are calculated. (See table 2.)

Since, in stage decompression, the diver is brought up in 10-foot stages, the next stop in this instance will be 20 feet (53 feet absolute). However, to maintain a 2-to-1 ratio, the diver has to remain at the 30-foot stop until the pressure in his most deeply saturated tissues (5-minute tissues at this stop) drops to twice the pressure of the 20-foot stop ($2 \times 53 = 106$). This drop will have to be $126-106=20$ feet. The difference in pressure to which the diver is subjected is $126-63=63$. If he remained long enough at this stop, the pressure in his body would drop to the pressure of the stop or 63 feet absolute, but he is to be desaturated only 20 feet at this point. So he will stay at this stop (30 feet) $\frac{20}{63}$ or 32 percent of the time required to desaturate

to the pressure of the stop. Applying this percentage to the curve (figure 1), we get 0.6 time unit and as 0.6×5 (minute tissues)=3 minutes, we know we keep the diver at 30 feet for 3 minutes in order not to exceed a 2-to-1 ratio. Actually we find when we calculate many of Haldane's tables (1922) that he often goes to a ratio of 2.1 or even 2.3 to 1, but this is well within the safety factor. As already shown, the pressure in his tissues drops 32 percent of the difference between the tissue tension at the start of the 3 minutes and pressure of the stop, i.e., in the case of the 5-minute tissues already figured 126—106 or 20 feet. By applying the time factor and percentage, all of the other tissues are calculated in the same manner.

By following the same method of calculating used to determine the length of stay at 30 feet, we find that it is necessary to stay 7 minutes at 20 feet. But in this case, it is the 10-minute tissues which are so deeply saturated as to be the governing tissues. That is, it is necessary to extend the time of this stop more than is required by the 5-minute tissues in order that the 10-minute tissues may not exceed a ratio of 2 to 1. In the same manner, it is the 20-minute tissues that determine the 10-minute stop required at 10 feet. All of these calculations are presented in table 2.

TABLE 2.—*Depth, 108; Time, 80—Decompression chart*

		Exposure	To first stop	First stop	Second stop	Third stop
Tissue	Depth	108	69	30	20	10
	Depth (absolute)	141	102	63	53	43
	Time	30	3	3	7	10
5	Time units	6.0	0.6	0.6	1.4	2.0
	Percent	0.985	0.34	0.34	0.621	0.75
	Difference in pressure	108	37	63	52	30
	Difference in saturation	+106	−13	−21	−32	−23
	Tissue saturation	139	126	105	73	50
10	Time units	3.0	0.3	0.3	0.7	1.0
	Percent	0.875	0.187	0.187	0.384	0.5
	Difference in pressure	108	28	60	59	46
	Difference in saturation	+95	−5	−11	−23	−23
	Tissue saturation	128	123	112	89	66
20	Time units	1.5	0.15	0.15	0.35	0.5
	Percent	0.646	0.098	0.098	0.215	0.293
	Difference in pressure	108	1	40	46	46
	Difference in saturation	+70	0	−4	−10	−13
	Tissue saturation	103	103	99	89	76
40	Time units	0.75	0.075	0.075	0.175	0.25
	Percent	0.405	0.05	0.05	0.113	0.158
	Difference in pressure	108	25	15	24	31
	Difference in saturation	+44	+1	−1	−3	−5
	Tissue saturation	77	78	77	74	69
75	Time units	0.4	0.04	0.04	0.093	0.133
	Percent	0.242	0.027	0.027	0.062	0.088
	Difference in pressure	108	43	3	7	17
	Difference in saturation	+26	+1	0	0	−1
	Tissue saturation	59	60	60	60	59

Interpretation of results.—Following the method just outlined, the saturation of each of the theoretical tissues upon reaching the surface was calculated for every case of caisson disease encountered during

the course of the experimental dives. These are all presented in figure 2 in which the abscissae represent the individual cases of caisson disease grouped according to the depth of exposure and the ordinates

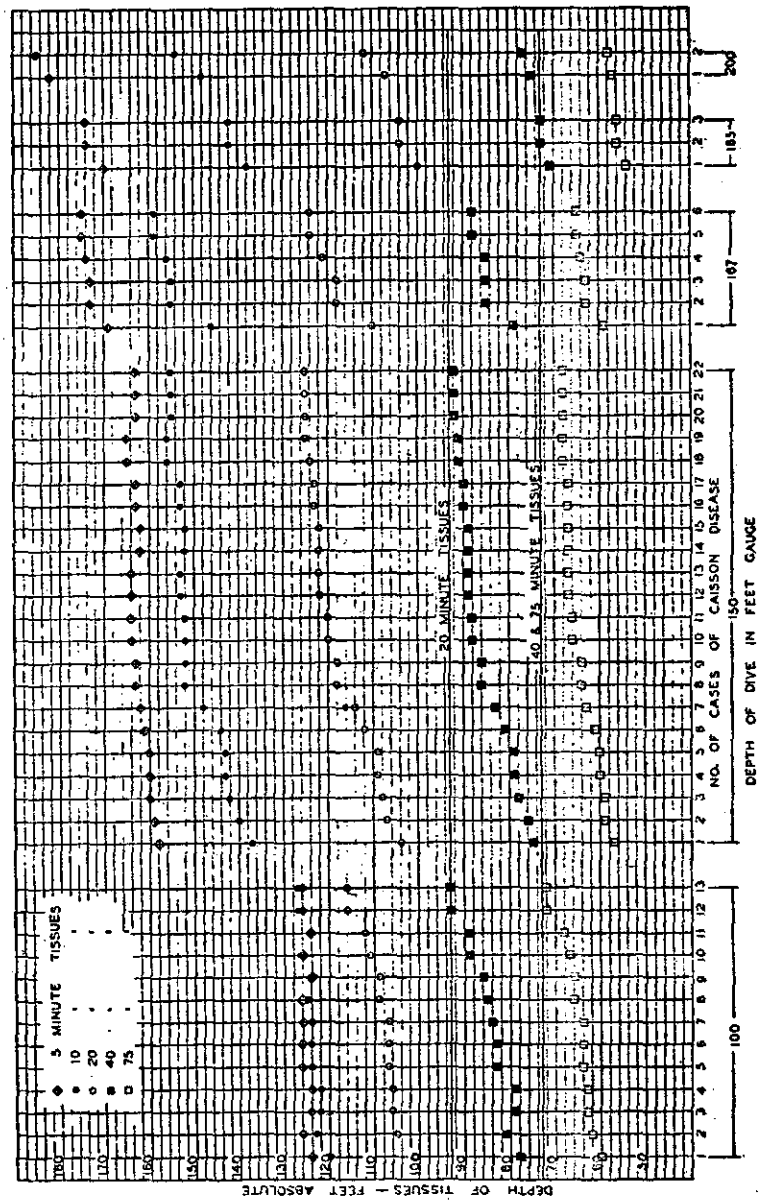


FIGURE 2

represent the saturation of each of the theoretical tissues in feet absolute upon reaching the surface. In order to determine the saturation ratio for any of the tissues thus plotted, it is only necessary to

divide the plotted depth in feet by 33. By doing this, we find that at a hundred-foot depth, the 5-minute tissues have a ratio of 3.8 to 1 while at 150 feet this ratio ranges from 4.8 to 1 to 5 to 1. At 200 feet, the ratio is as high as 5.6 to 1. As a matter of fact, the only tissues not exceeding a 2 to 1 ratio, i. e., plotted under the 66-foot level are the 75-minute tissues. The 10-minute tissues range from a ratio of 3.6 to 1 at 100 feet to 4.7 to 1 at 200 feet, the 20-minute tissues ranged from a saturation ration of 3.1 to 1 to 3.8 to 1, and the 40-minute tissues ranged from 2.3 to 1 up to 2.8 to 1. By looking only at figure 2, one would be forced to conclude that any of the tissues other than the 75-minute tissues might have caused the bubble retention which produced the caisson disease.

But by the same method of calculating, the saturation of each of the theoretical tissues was determined for the run prior to the caisson disease producing run, and again as shown by these results presented in table 3 the ratio for all of the tissues except the 75-minute tissues is high enough to have produced caisson disease. Yet we know that caisson disease did not develop until after a longer exposure, and thus a greater saturation than any reported in this table. In fact, in some instances diving operations were continued for from 10 to 14 runs after the development of the first case of caisson disease. Actually, as noted in table 1, of a total of 2,143 individual exposures, 1,782 were prior to the development of the first case of caisson disease in their respective runs while there were 361 including and following the first case. It is thus shown that in many individuals even greater ratios than those encountered in either table 3 or in figure 2 can be borne with impunity.

TABLE 3.—*Run prior to the run producing caisson disease in each series*

Series no.	Depth of dive feet gage	Number of subjects	Length of exposure	Depth of theoretical tissues in feet absolute (minute tissues)					Tissue saturation ratio (minute tissues)				
				5	10	20	40	75	5	10	20	40	75
			Minutes										
2	100	8	34½	126	121	102	78	60	3.8–1	3.7–1	3.1–1	2.4–1	1.8–1
7	100	8	36½	126	122	104	80	62	3.8–1	3.7–1	3.2–1	2.4–1	1.9–1
9	100	8	39½	126	124	107	83	64	3.8–1	3.8–1	3.2–1	2.5–1	1.9–1
11	100	8	42	124	124	109	85	65	3.8–1	3.8–1	3.3–1	2.6–1	2.0–1
10	150	8	18	158	136	103	74	57	4.8–1	4.1–1	3.1–1	2.2–1	1.7–1
3	150	8	18½	158	137	104	75	58	4.8–1	4.2–1	3.2–1	2.3–1	1.8–1
8	150	8	19½	159	140	107	77	59	4.8–1	4.2–1	3.2–1	2.3–1	1.8–1
16	150	6	26	162	151	121	88	67	4.9–1	4.6–1	3.7–1	2.7–1	2.0–1
15	150	5	27½	163	154	125	91	68	4.9–1	4.7–1	3.8–1	2.8–1	2.1–1
4	167	8	16½	168	143	107	75	58	5.1–1	4.3–1	3.2–1	2.3–1	1.8–1
5	185	8	12½	174	142	100	71	56	5.3–1	4.3–1	3.0–1	2.2–1	1.7–1
6	200	8	13	182	149	107	75	57	5.5–1	4.5–1	3.2–1	2.3–1	1.7–1

Depth (absolute) = depth (gage) + 33 feet.

It is conclusively shown by table 3 that all of the subjects were able to tolerate saturations in the 5- and the 10-minute tissues greatly in excess of the supposed safe ratio of 2 to 1. In fact, it is evident that the saturation of the 5- and the 10-minute tissues has no relationship to the production of caisson disease. These conclusions are based not only on the runs presented in table 3, for it should be borne in mind that in every series many of the runs preceding those presented in table 3 left the tissues saturated to a degree greatly exceeding the 2-to-1 ratio.

The 20-minute tissues appear to be the first ones it is necessary to consider in the production of caisson disease, for when these tissues reach a saturation of 63 feet (96 feet absolute) caisson disease begins to appear. By the same reasoning by which the 5- and 10-minute tissues were eliminated, the 20-minute tissues can be carried to a ratio of 3 to 1 without danger of caisson disease. Whether these tissues could go to a still higher ratio without trouble resulting cannot be proved from the dives made, as by the time the 20-minute tissues are left at 63 feet, the 40-minute tissues have reached a saturation of 41 to 43 feet, or a ratio of 2.3 to 1. Thus, it is impossible to determine whether the resulting attack of caisson disease was produced in the 20- or the 40-minute tissues.

Proposed change in tables.—From the foregoing results, it is seen to be safe to use a decompression table calculated without considering the desaturation rate of the 5- and 10-minute tissues and using a ratio of 3 to 1 for the 20-minute tissues, and 2.3 to 1 for the 40- and 75-minute tissues at the last stop. The time of decompression can thus be shortened considerably on dives of short duration where the 40- and 75-minute tissues do not become deeply saturated.

Tables have been calculated (see table 4) for certain depths and for various times of exposure in order to show the advantage in time saved in ascent, in which the 5- and 10-minute tissues are ignored, and carrying a ratio of 2.8 to 1 (3 to 1 would be safe) in the 20-minute tissues and 2.0 to 1 in the 40- and 75-minute tissues. These ratios are represented by the two horizontal lines labeled 30-minute tissues, and 40- and 75-minute tissues in figure 2. The saving in decompression time is large in many instances. For example, following a dive of from 20 to 30 minutes at 100 feet, the present tables require a decompression of 23 minutes while the proposed tables require but 4 minutes decompression. An exposure of from 30 to 40 minutes at 100 feet requires 33 minutes by the present tables and only 18 minutes by the proposed tables.

TABLE 4

Depth in feet	Time from surface to start of ascent	Diving-manual tables										Proposed tables				Total time of ascent	
		Time to first stop	Stops in feet									Time to first stop	Stops in feet			Diving-manual table	Proposed table
			90	80	70	60	50	40	30	20	10		30	20	10		
	Minutes	*Min.*										*Min.*				*Min.*	*Min.*
0 to 40	Over 180	1									5	1			5	6	6
41 to 50	0 to 60	2									5	1				7	1
	60 to 120	2									10	1			6	12	7
	120 to 180	2									10	1			10	12	11
51 to 60	0 to 60	2									10	1				12	1
	60 to 90	2									10	1			10	12	11
	90 to 120	2								5	15	1			17	22	18
	120 to 180	2								5	15	1		6	15	22	22
	Over 180	2								10	20	1		10	30	32	41
61 to 70	0 to 30	2								3	5	1				10	1
	30 to 60	2								5	12	1			7	19	8
	60 to 90	2								10	20	1			20	32	21
	90 to 120	2								10	20	1		12	20	32	33
71 to 80	0 to 30	2								5	15	2				22	2
	30 to 60	2								10	20	2			18	32	20
	60 to 90	2								15	30	2		14	19	47	35
	90 to 120	2								15	30	1		24	19	47	44
81 to 90	0 to 30	2								5	15	2				22	2
	30 to 40	2								5	15	2			9	22	11
	40 to 60	2							3	10	15	2			27	30	29
	60 to 90	2							5	15	25	2			27	47	29
91 to 100	0 to 10	3								3	5	2				11	2
	10 to 20	3							3	7	10	2				23	2
	20 to 30	3							3	7	10	2			2	23	4
	30 to 40	3							5	10	15	2			16	33	18
	40 to 50	2							10	15	20	2			18	47	20
	50 to 60	2							10	15	20	2		18	19	47	39
101 to 120	0 to 15	3							2	3	7	3				15	3
	15 to 30	3							5	10	15	2			14	33	16
121 to 140	0 to 15	3						2	5	10	12	3				32	3
	15 to 30	3					3	5	10	15	25	3		8	19	61	30
141 to 160	0 to 15	3					2	3	5	7	10	3			5	30	8
	15 to 30	3					3	5	10	15	20	3		19	19	56	41
161 to 180	0 to 15	3					3	3	7	10	15	4			8	41	12
	15 to 30	3				2	2	3	10	15	25	3	3	27	19	60	59
181 to 200	0 to 15	3				3	3	5	7	10	20	4			15	51	19
	15 to 30	3			3	3	3	5	10	20	20	4	12	27	19	67	62
201 to 225	0 to 15	8		3	5	7	7	10	15	20	20	4		5	20	95	25
226 to 250	0 to 15	4	2	3	5	7	10	10	15	20	30	5		16	19	106	40

Although these proposed changes in calculating decompression tables are based on the results of 2,143 experimental dives using the submarine escape appliance, yet it is hoped to further check them, both in suit dives at the experimental diving unit and in the open sea under service conditions.

SUMMARY

An analysis of 2,143 experimental dives has been made in which it is shown that the saturation of the 5- and 10-minute tissues has no bearing on the production of caisson disease. It is also shown that the 20-minute tissues may have a saturation ratio of 3 to 1 without the development of caisson disease.

The method of calculating a decompression table has been given, together with its relation to tissue saturation and desaturation in connection with the production of caisson disease.

The findings obtained from these experimental dives have been used as a basis for calculating decompression tables. These tables reduce the time of decompression following dives of short duration.

CONCLUSION

New decompression tables have been calculated without considering the desaturation of the 5- and 10-minute tissues, and allowing a ratio of 2.8 to 1 for the 20-minute tissues, and 2.0 to 1 for the 40- and 75-minute tissues.

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INVESTIGATION INTO THE DECOMPRESSION TABLES

REPORT III

PART A. A New Theoretical Basis for the Calculation of Decompression Tables.

by

H.V. Hempleman

PART B. A Method of Calculating Decompression Stages and the Formulation of New Diving Tables.

by

W.E. Crocker

and

H.J. Taylor.

From the
Royal Naval Physiological Laboratory

Report prepared for the
Decompression Panel
of the
Underwater Physiology Sub-Committee
of the
R.N.P.R.C.

June, 1952.

PART A. A New Theoretical Basis For The Calculation Of Decompression Tables.

by

H.V. Hempleman

SUMMARY.

A new theoretical treatment of the problem of nitrogen exchange in tissue is presented. The blood is considered as a well-stirred fluid and the tissues as immobile solvent layers.

Suggestions are made as to the way the theory may be used for the calculation of diving tables.

INTRODUCTION.

Boycott, Damant and Haldane (1908) proposed a method of stage decompression for divers working in compressed air. The success of this procedure has been amply demonstrated by the absence of serious cases of compressed air illness (bends or chokes) since the introduction of diving tables calculated according to Haldane's method. However, it was soon discovered that the permitted tissue partial pressure decompression ratio of 2:1 was dangerous when long periods of time elapsed at depths exceeding 120 ft. of sea water, and accordingly the permitted ratio of the assumed controlling tissue (a slowly saturating one) was modified to a decompression ratio of 1.75:1. In more recent investigations (Hawkins, Shilling, Hansen 1935) it has become apparent that the various tissues of the body will tolerate decompression ratios varying between 5:1 for a rapidly saturating tissue down to 2:1 for a slowly saturating one. The original theory of Haldane could in no way predict the possibility of such findings in any quantitative and useful way and it is clear that a different approach must be made to the problem of inert gas exchange in the tissues.

Early in the history of compressed air illness it was found that the cause of the illness was due to liberation in the blood and tissues of bubbles of gas consisting almost entirely of nitrogen. The cause of the bubble formation is evident. At raised air pressures used in diving procedures the blood in the lungs is exposed to greatly increased partial pressures of nitrogen and oxygen. Thus the blood and tissues of the body tend to become saturated and reach equilibrium with these new partial pressures. The longer the diver stays at a given pressure the more nearly will he approach complete saturation of all his tissues. When the air pressure is suddenly reduced, then unless the nitrogen can be transported rapidly out of the tissue a large excess nitrogen partial pressure will exist which will naturally find its outlet by degassing and forming bubbles in the tissue. It is now necessary to examine Haldane's theory of the way the nitrogen saturates the various tissues of the body. His theory has influenced all workers in compressed air illness and therefore, the reasons for rejecting a theory so apparently well supported by a mass of accumulated evidence will require some discussion. The fundamental postulate is that a tissue can be assigned a half saturation time, and that the tissue will saturate and desaturate exponentially with time. The basic equation governing this type of gaseous exchange is $\frac{dP_T}{dt} = K (P_B - P_T)$

where P_B = nitrogen partial pressure in the blood and P_T = nitrogen partial pressure in the tissue.

t = time in minutes. K = constant

Now this type of equation only applies to two well stirred solutions on either side of a permeable membrane. Indeed the equivalent of this situation has been used by Jones (1951) in order to calculate the relative diffusion rates of gases through a hydrated gelatin membrane. From the measurements thus made it is concluded that "diffusion and transcapillaric permeability are factors not limiting the gas exchange rate". These experiments help to prove the main point to be stressed in this contribution, namely that the body cannot be regarded as various well stirred fluids separated from the blood by a membranous layer, and that to talk of a tissue possessing a certain partial pressure of nitrogen is meaningless, except when equilibrium is reached. In the theory to be presented, the blood will be

regarded as a well stirred liquid, but the tissues as immobile solvent layers. It is inevitable that in any attempt to apply a physical analysis to a system as complex as the body certain simplifying assumptions have to be made.

ASSUMPTIONS OF THE THEORY

The assumptions to be made in the theory to be outlined are:-

(1) The equations of linear diffusion will apply. If one imagines at time t = 0 a blood capillary carrying nitrogen at a partial pressure in excess of that in the surrounding mass of tissue, then after a time t a given nitrogen concentration in the tissue will be distributed radially (Fig.1(a)). If one repeats this experiment with two closely parallel capillaries then after a time t the given concentration will be distributed as in Fig.1(b).

It is simple to see from this that with a large number of parallel capillaries as represented (in cross section) by Fig.1(c) that the given concentration is very nearly represented by two parallel planes equidistant from the plane of the capillaries. A piece of vascular tissue may thus be represented as thin layers of blood between layers of tissue.

(2) Blood circulation rate in normal animals is unimportant. This in effect means that when a tissue is exposed to high pressures of inert gas at time t = 0 then the blood will be assumed to be in equilibrium with the new pressure at t = 0, and again when decompression takes place the blood will be assumed to follow the external partial pressure exactly, moment by moment. This is obviously not true if one wishes to be strictly accurate, but figures given by Hill (1931) show that for men the alveolar partial pressure of nitrogen falls very rapidly on decompression and the error from this assumption will only be operating in the first two or three minutes.

(3) Only one type of tissue is responsible for the production of mild bends. No consideration will be given to the production of chokes or central nervous system bends which are the end result of rather drastic conditions of high pressure exposure and decompression.

If one exceeds the permitted partial pressure ratio on Haldane's system of calculation then a bend will result. This bend always has the same general manifestations (pain in or around a joint) whether one exceeded the ratio on a five minute tissue (e.g. five minutes at 300 ft. sea water and decompression to surface) or whether one exceeded the ratio on an eighty minute tissue (e.g. 4 hours at 40 ft. sea water and decompression to surface). Thus depending on the circumstances of the dive, a bend may result from a 5, 10, 20, 40 or 80 minute tissue and yet this bend has the same site (a joint) and the same associated pain. The situation would appear to be more satisfactory if only one tissue is postulated as being responsible, e.g. a "tight tissue" (Nims, 1951).

(4) The symptoms of decompression sickness are caused by extravascular bubbles. This assumption is based on two well known experimental facts:-

(a) Bends pain is always relieved by recompression.

(b) Once pain has appeared, recompression will relieve the pain, but on re-ascent the pain will reappear in the same site.

CORRECTION

Assumption (1) page 2. The last sentence should read:-

"A piece of poorly vascularisedtissue with a capillary plexus may thus be represented as thin layers of blood between layers of tissue."

Assumption (2) page 2. The first sentence should read:-

"Blood circulation rates can be neglected."

The equation with the integral on page 3 should read:-

$$Cx,t = C\left\{1 - \frac{2}{\sqrt{\pi}} \cdot \int_0^y e^{-y^2} dy\right\}$$

Experiments (Rodbard 1944) have shown that this immediate recurrence of pain is possible for periods up to three or four hours. This is extremely difficult to explain on an intravascular bubble theory.

(5) After decompression the tissue can only retain a fixed volume of excess nitrogen.

FORMULATION OF THE EQUATIONS TO BE USED.

With these assumptions the equations to be used will now be formulated. The notation and units are as follows:-

$C_{x,t}$ = Tissue concentration in mols./cc. at a distance x cms. from the blood layer t secs after compression has commenced.

C = Initial uniform concentration of nitrogen in the blood.

D = Diffusion coefficient for nitrogen. (cm^2/sec).

$y = \frac{x}{2\sqrt{D.t}}$ = a variable of integration.

Boundary conditions

$t = 0, \quad C_{x,o} = 0$
$t \to \infty \quad C_{x,t} = C$
} For tissue

$t = 0 \quad C$
$t \to \infty \quad C$
} For blood

The use of Ficks equation for linear diffusion, namely

$$\frac{\partial C_{x,t}}{\partial t} = D. \frac{\partial^2 C_{x,t}}{\partial x^2}$$

leads to the solution

$$C_{x,t} = C\left\{1 - \frac{2}{\sqrt{\pi}} \int_0^y e^{-y^2}\right\} dy$$

This of course, applies only to an infinitely thick sheet of tissue, but for the reason to be given later this is a satisfactory enough solution in practice.

At x = 0, $\frac{\partial C_{x,t}}{\partial x} = \frac{K}{\sqrt{t}}$ K = constant

i.e. rate of entry of nitrogen (per sq. cm) into tissue is proportional to $t^{-\frac{1}{2}}$. By integration it is therefore clear that the quantity of nitrogen present in a tissue after a time t is proportional to $t^{\frac{1}{2}}$

$$\text{or } Q = K_1.t^{\frac{1}{2}}$$

Q = quantity of nitrogen (moles)

K_1 = constant

Now tissue is only of a finite thickness and this square root law of entry and egress of nitrogen might be expected to hold for only short periods of time. However, in practice it is found that the tissue responsible takes a very long time to saturate completely and there are pressures of air to which one can be exposed for five hours and not get a bend on return to the surface, yet a six hour period of exposure will result in bends. (Davidson, Sutton and Taylor, 1950).

This means that the tissue concerned (due no doubt to its very low nitrogen diffusion constant) is behaving as an infinitely thick barrier for a considerable period of time (approximately 2 hours). As most practical diving exposes men to air pressures for periods much less than two hours, it becomes a very convenient working rule to use the square root as a basis for calculations. For exposures longer than about two hours duration the estimate of the quantity of nitrogen dissolved in the tissue at pressure will be in excess of the correct amount. This will result in a grossly safe decompression procedure after very prolonged exposure to pressure.

SOME EXAMPLES.

In order to calculate an air diving table a single definite piece of information is necessary, e.g. the maximum safe exposure time at 100 ft. of sea water followed by immediate surfacing is 22 mins. This fixes the volume of nitrogen, as measured at atmospheric pressure, which the susceptible tissue can retain without a bend being produced. In arbitrary feet of sea water-minute units this will be $100\sqrt{22} = 475$ units. It is now a matter of simple arithmetic to calculate the lengths of stay and first stops at any other depth, e.g. How long can one stay at 50 ft. sea water and surface immediately?

$$100\sqrt{22} = 475 = 50.\sqrt{t} \quad \text{(vol. excess } N_2 \text{ retained)}$$

$$\underline{t = 90} \text{ mins.}$$

or How long at 200 ft. sea water?

$$475 = 200\sqrt{t} \qquad \underline{t = 5\tfrac{1}{2}} \text{ mins.}$$

e.g. What is the depth of the first stop when 100 minutes have been spent at 200 ft. sea water?

$$\text{Arbitary units of nitrogen absorbed} = 200\sqrt{100}$$

$$= 2{,}000 \text{ (at atmospheric pressure)}$$

Arbitrary units of nitrogen absorbed = $200\sqrt{100}$

= 2,000 (at atmospheric pressure)

2,000 units at atmospheric pressure = 475 units at $\frac{2000}{475}$ atmospheres

pressure absolute = 4.21 atmospheres.

First stop is at 3.21 atmospheres gauge

pressure = 106 ft. sea water (110 ft. in practice)

These examples could be continued indefinitely, but the method of calculation is obvious and will not be laboured.

It can be seen that at 30 ft. this method of calculation sets a limit of 4 hours to the time allowed before stops become necessary. At this depth, of course, a diver can stay indefinitely and surface immediately without trouble. This sort of finding was predicted earlier as a result of the non-consideration of the finite width of the tissue. From a practical point of view the complications to the calculations which would have to be introduced in order to compensate for this slight defect are not worthwhile. Most diving is of an order of time where the square root basis is quite accurately obeyed.

The effect of exercise in reducing the time which can be spent at depth is well known. In this theory for inert gas exchange the effect of exercise is to increase the area of the blood-tissue interface and to decrease the effective width of the tissue. This means that the number of units allotted to the responsible tissue will be less and that the square root law for the diffusion times will not hold for as long a period as in a resting subject. However, the figures given above are for exercising human subjects and hence remain valid.

The calculation of the lengths of time to stay at various stops after a long dive at depth is quite difficult due to the distortions of the diffusion gradient in the tissue introduced by successive drops in the blood gas partial pressure. Part (B) of this report suggests a method of overcoming these difficulties.

ACKNOWLEDGMENTS.

Dr. H.J. Taylor, Surgeon Commander W.M. Davidson and Surgeon Lieutenant Commander W.E. Crocker for many fruitful discussions.

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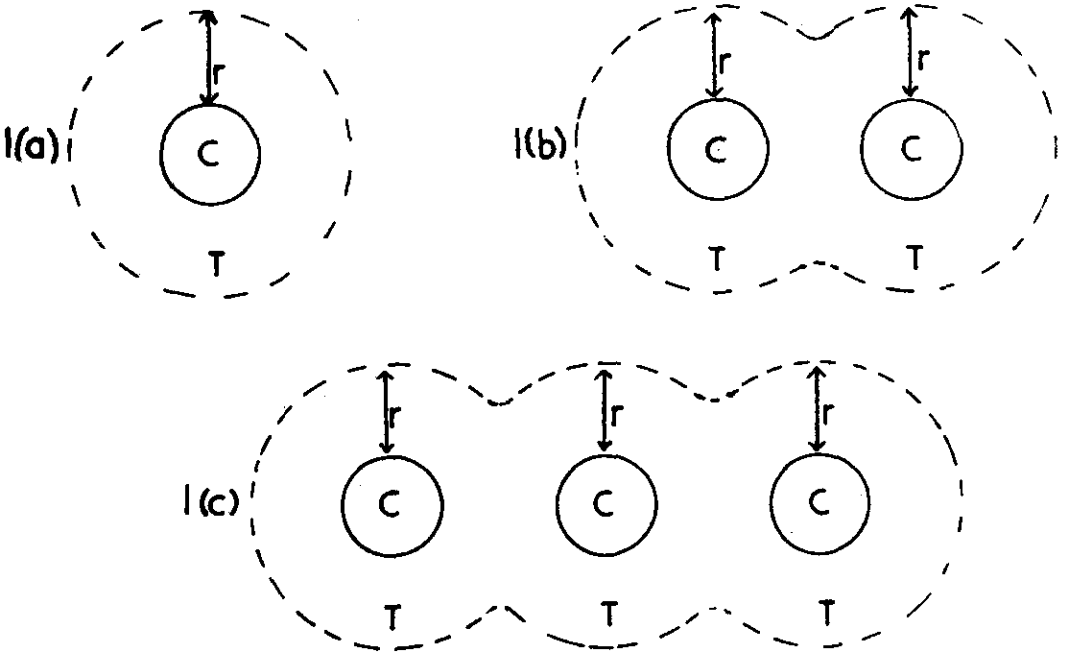
FIGURES 1a, 1b & 1c



T— TISSUE.

C— CROSS SECTION OF CAPILLARY SATURATED WITH NITROGEN.

r— RADIUS OF DIFFUSION FRONT AFTER TIME t.

Underwater Physiology

PROCEEDINGS OF THE THIRD SYMPOSIUM ON UNDERWATER PHYSIOLOGY SPONSORED BY THE COMMITTEE ON UNDERSEA WARFARE OF THE NATIONAL ACADEMY OF SCIENCES—NATIONAL RESEARCH COUNCIL AND THE OFFICE OF NAVAL RESEARCH, IN WASHINGTON, D. C., 23, 24, and 25 MARCH 1966.

C. J. LAMBERTSEN / Editor

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23 | H. V. HEMPLEMAN

Decompression Procedures for Deep, Open Sea Operations

The experiments to be described were designed both to provide further facts regarding the etiology of decompression sickness, and also to enable safe decompression procedures to be devised for deep dives in the open sea.

The first point to be established is how quickly, from the point of view of decompression sickness, does helium saturate the body tissues. Estimates have been made, but no sufficiently sound data are available. Some experiments by Duffner (1) suggest that the time to saturate the body tissues, as measured by the no-stop dive curve, is in the order of 12 hours, and hardly distinguishable from nitrogen. Looking at the solubility of helium in body tissues this result is somewhat surprising.

Assuming perfusion factors do not alter and taking as true the observations of Jones (2), then if the exponential exponent of the major slow component, assumed to be fat, is $K\alpha$ where α is the partition coefficient for the gas concerned between blood and fat tissue and K is the tissue perfusion factor, the ratio of the exponential exponents changing from nitrogen to helium will be $K\alpha_1/K\alpha_2$ i.e. α_1/α_2 where α_1 is the partition coefficient (water/tissue) for nitrogen and α_2 that for helium. Using the accepted values of $\alpha_1 = 1/5.2$ and $\alpha_2 = 1/1.7$ then $\alpha_1/\alpha_2 = 1/3$ very nearly. This means that the very slow fat component seen when breathing nitrogen will be altered when breathing helium to a tissue with a half-time 3 times smaller. Taking 60 minutes to 120 minutes as an appropriate range of values for the half-times on nitrogen one would expect the corresponding half times on helium to range between 20 minutes and 40 minutes. The effective saturation time would then be 2 hours to 4 hours.

Alternately one may suppose that in decompression sickness all the mechanisms are diffusion limited and in this case the speed of saturation would be expected to vary nearly in accordance with Graham's Law, with helium saturating the relevant tissues 2.65 times as rapidly as nitrogen. In

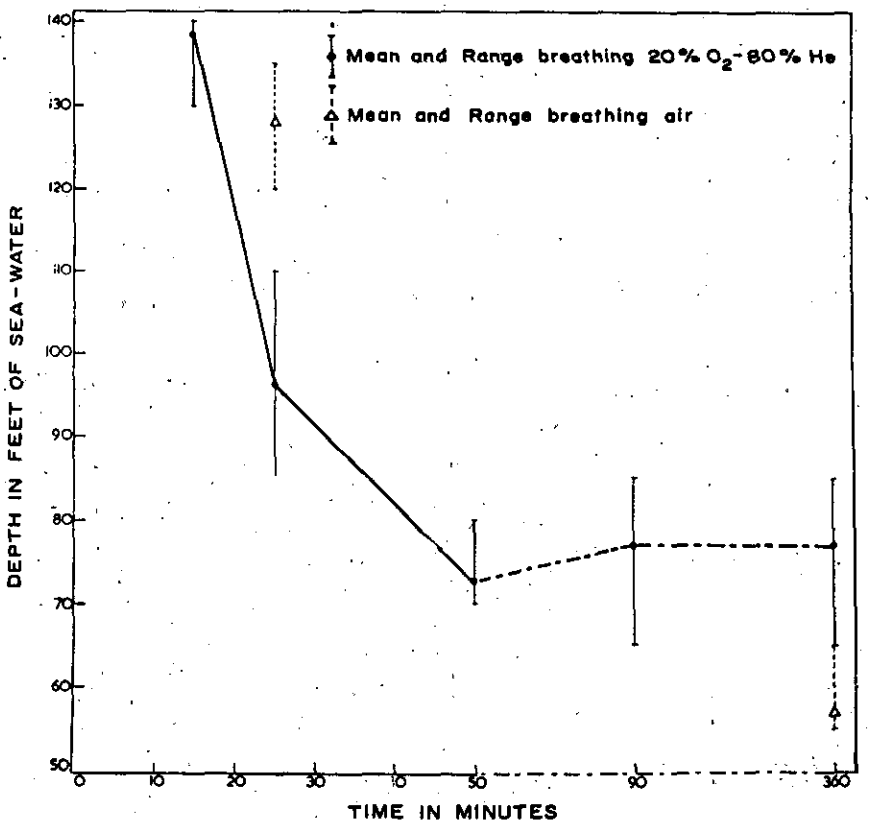

FIG. 70. Oxy-helium "No-stop" curve from data on six goats

practice, without vast numbers of experiments, this will be indistinguishable from the expectations of the perfusion limited ideas.

The first set of experiments was performed using female goats. The animal was placed in the pressure chamber and the door closed. All air inside was replaced by displacement with 80% He-20% O_2 while the animal was kept at atmospheric pressure. This took 3 or 4 minutes. Then the pressure inside was raised using 80% He-20% O_2 at a rate of 60 feet per minute to the desired level. After a certain time at this constant raised pressure the animal was decompressed at a uniform rate in 2.5 minutes back to atmospheric pressure. The door was opened and the animal brought out into air and watched for signs of decompression sickness.

The spread of results at various fixed times is displayed in Figure 70. The animals show no detectable difference in their threshold values for decompression sickness after a 50 minutes exposure. Reference to a similar curve of results on goats established using air as the breathing medium will

reveal that there is a just detectable difference between a 3 hour and a 4 hour exposure (6). Accurate comparison is difficult to make because only 6 animals were used to obtain the helium results whereas over 50 animals were used to obtain the air results. Within the limits imposed by relatively small numbers and also by the fact that searching for decompression sickness thresholds is performed using 5 feet increments, it is possible to state with confidence that goats effectively saturate with helium in not less than 40 minutes and not more than 90 minutes. Taking 65 minutes as being the average for most normal animals one would expect from both the perfusion and diffusion theories a saturation on air time of approximately 3 hours, which accords well with the practical findings.

An attempt was made to define the problem similarly using six men. The times of exposure chosen were 16 minutes, 120 minutes and 240 minutes. The procedure adopted was as follows.

Two men entered the pressure chamber and the door was closed. One man seated himself on a rowing machine, the other on a chair. They were compressed on air at 100 feet per minute. At the 35 feet level the men put on noseclips and commenced breathing 90 % He-10 % O_2 via a demand valve from a bank of high pressure cylinders on the outside of the pressure chamber. Once the desired pressure had been reached the man on the rowing machine commenced a two minute period of vigorous rowing. Upon completion of this work the men changed places, and these alternate periods of work and rest continued throughout the dive time. On decompression the men took a lung full of oxygen at either 50 feet, or just before leaving the depth, depending which was the shallower and were brought back to atmospheric pressure at a uniform rate of 50 feet per minute. The outline results are displayed in Figure 71. Certain resemblances to the goat results are immediately apparent. For short dives of 16 minutes duration there are cases of decompression sickness on helium at levels below the accepted normal practice on air.

On the other hand for the dives of 4 hours duration it seems that the helium performance is better than the air one. Using such small numbers it is impossible to state this with any certainty. The situation, particularly for the prolonged dives, is further complicated by the possibility that men can acclimatise themselves. This may be illustrated by the following observations. When the 2 hour exposures were commenced all 6 men completed a 40 ft. depth without incident. Two days later a 45 feet exposure yielded very minor fleeting pains in some of the men. This was interpreted to mean that they were near more serious troubles and therefore only 3 feet increments in pressure were now employed. The experiments continued therefore with exposures of 48 feet, 51 feet, 54 feet etc. up to 72 feet. Throughout these experiments transient post-decompression pains (niggles) were en-

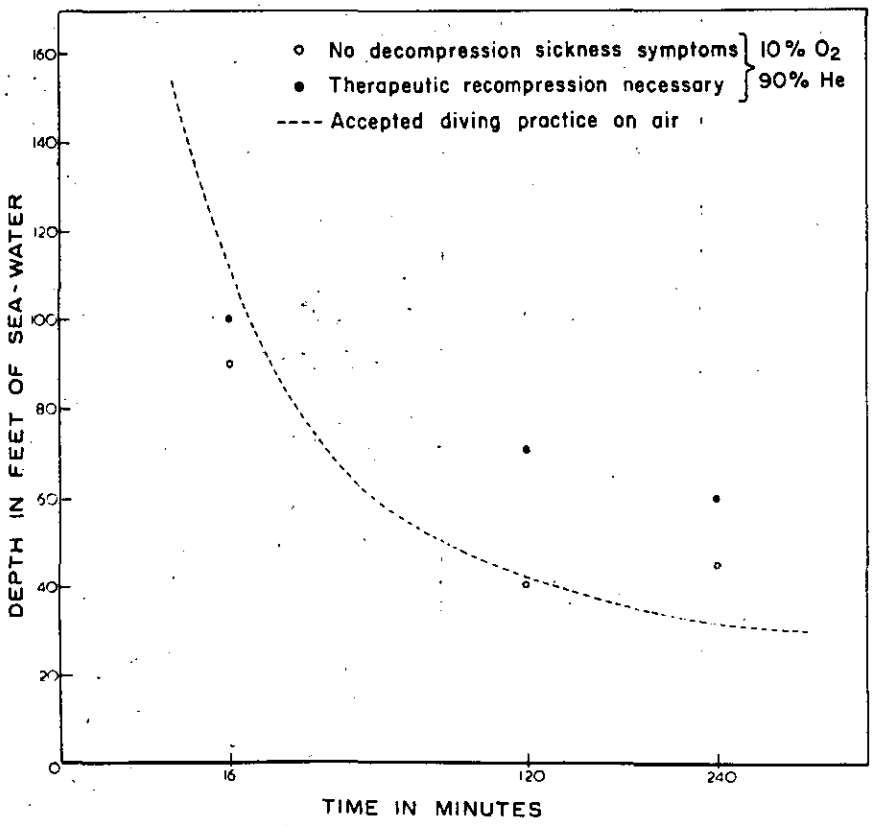

FIG. 71. Oxy-helium "No-stop" curve for men

countered at 51 feet, 57 feet, 60 feet, and 69 feet. These niggles were such a low level of trouble that it was not thought worth recompressing the man concerned. There were no itches or rashes accompanying any of these niggles. At 72 feet however, one man of a pair had a severe attack of decompression sickness almost immediately after reaching atmospheric pressure. This was considered the threshold for this group. It is of interest to note that 3 of the divers completed 2 hrs. at 75 feet without any ill effects whatsoever and that one of these three had complained of a mild transient pain after the 45 feet exposure very early in the series. Next these same men carried out 4 hour exposures. At 55 feet all men completed a trouble-free exposure, but at 60 feet two bends occurred. The position was now that 6 men had completed 2 hour dives, with minor aches and pains occurring sporadically at all pressures greater than 45 feet, but 72 feet seemed to be the upper limit for these transient post-decompression events. For 4 hour

exposures no troubles were encountered at 55 feet, but 60 feet seemed to be too much for a no-stop dive. After these 6 men had been carried through the first series of exposures, a second series not shown in Figure 71 was started with a group of 4 men. These men were given an initial exposure of 2 hours at 55 feet. One man had to be recompressed and two others had attacks of niggles. The man who had to be recompressed and one of his companions who had an attack of niggles were together tried at a later date on a dive of 4 hours at 45 feet which gave them no troubles at all.

Three facts are apparent from the results to-date.

a) The spread of pressure covering all forms of decompression sickness is very great. For the two hour exposures at least from 45 feet to 80 feet and for 16 minutes exposure at least from 85 feet to 130 feet.

b) It is possible to acclimatise to helium decompression, just as has been found amongst caisson and tunnel workers breathing compressed air (3). New starters, or men who have not dived for several weeks display lower decompression sickness thresholds. A suitable work-up period will lead to much more resistant individuals.

c) Insufficient data is available for assessing the true relative performances at 2 hours and 4 hours but it may be seen that at 4 hours the performance of a group of men on 90% He-10% O_2 is better than standard practice on 79% N_2-21% O_2 (air). Aso the preformance at 16 minutes is significantly worse on the oxy-helium than on air, even allowing for the altered oxygen percentage. These results bear a great resemblance to those obtained on the goats, and one would say by analogy that the saturation time of men would, as with goats, be much less on helium than on nitrogen, and lie between 3 hours and 6 hours.

Goats were first used to assess the following hypothesis. After a saturation exposure to pressure P_1 it is possible to ascend rapidly and safely to a pressure P_2 and that there is some simple relationship between P_1 and P_2 such that $P_1/P_2 = r$ (constant) or $P_1 - P_2 = K$ (constant). In the first instance this was tried on air, using a 6 hour exposure at P_1 followed by ascent in 2½ minutes to P_2..

The P_1/P_2 value which just gave a mild attack of the bends is obtained for each goat for a representative set of values of P_1. These threshold ratios are plotted versus the initial pressure of exposure in Figure 72. The ratio diminishes with increase of pressure and this decrease is most marked in the first 140 feet (absolute) pressure. From 140 feet to 230 feet absolute the ratio is nearly constant and these observations agree qualitatively with the power function curves expressing the relationship between pressure and ratio used in the calculation of the U. S. Navy air decompression tables (4). It is of interest to note that some of the results shown in Figure 72 were obtained by changing from greater than atmospheric pressure to sub-atmos-

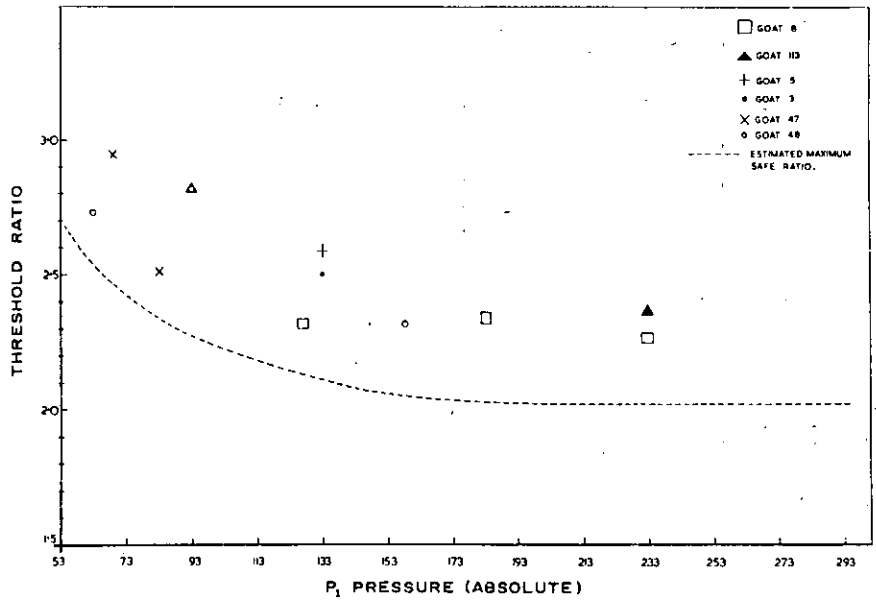

FIG. 72. Threshold ratio vs. pressure for goats breathing air

TABLE 37

Variation of Threshold Ratio following a Long Exposure to Oxy-Helium Gas

PRESSURE (GAUGE)		RATIO	
FEET SEA WATER	PSI	GOATS	MEN
45	17.8	—	2.67
66	29.4	3.0	—
350	155.9	2.09	—
600	267.2	2.00	—
800	356.3	—	1.59

pheric pressures. Similar threshold values are being obtained using helium-oxygen as the breathing medium. In Table 37 the threshold ratios for saturation or near-saturation dives on goats and men are given. On all these occasions a relatively mild attack of decompression sickness has been taken as indicating the threshold. The cut-back in the critical ratio on the goats breathing helium has the same features as on air. In the pressure range of 350 feet to 600 feet there seems to be a definite but relatively small change in the critical ratio, whereas from 350 feet to 66 feet there is a large change. With men the critical data are not well established but it has been shown that in addition to the data in Table 37 a 2 hour exposure at 500

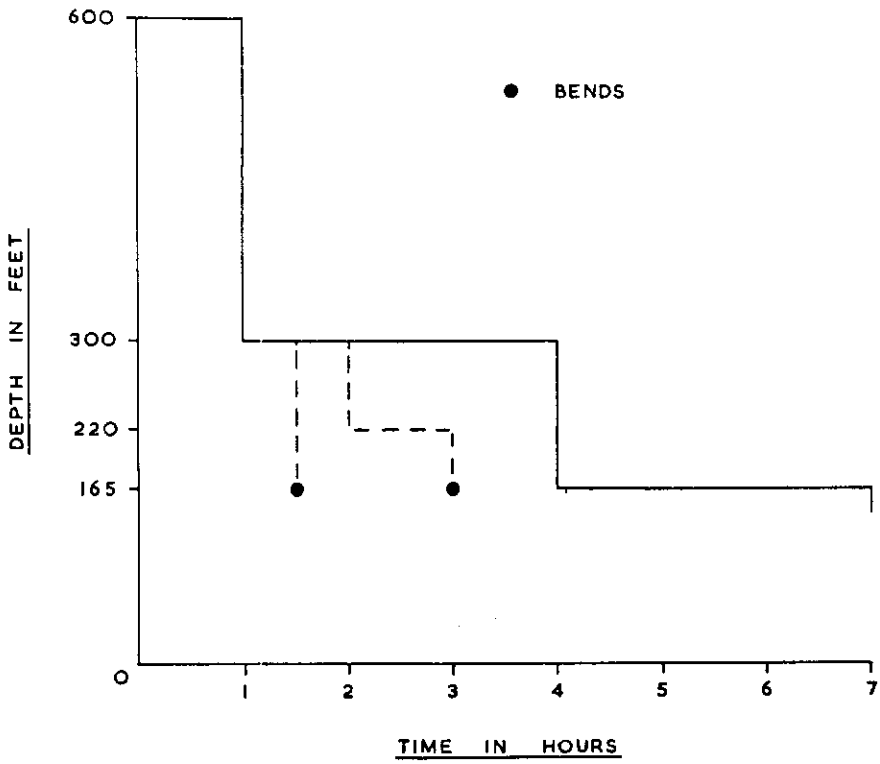

FIG. 73. Stage decompression of goats following a 50-minute dive at 600 feet breathing 10% O_2-90% He.

feet may safely be followed by a rapid ascent to 290 feet (ratio 1.65) and using 12 men, 4 hours at 300 feet may safely be followed by rapid ascent to 170 feet (1.64 ratio). The rule has now been reached that for dives at depths greater than 250 feet a 1.6 ratio or a drop in pressure of 200 feet, which ever involves the least pressure change is quite safe to establish the pressure value of the first stop following dives to depths as great as 800 feet for bottom times as long as 4 hours.

The goats were next used to establish the form of safe decompression schedules using only oxy-helium as the breathing medium. Figure 73 shows a series of attempts to reach 165 feet following a dive of 50 minutes at 600 feet by a single stage at 300 feet. A duration at 300 feet of 30 minutes was grossly inadequate to allow ascent to 165 feet, i.e. a ratio change of only 1.68 following a first ratio change of 1.9. A one hour stay at 300 feet followed by an intermediate stay of 1 hour at 220 feet was still inadequate to permit safe ascent to 165 feet. Eventually a 3 hour stay at 300 feet was found necessary to ensure trouble-free ascent to 165 feet. This served to emphasize

findings similar to those found on air (5). The rate of loss of the risk of decompression sickness is not the same as the rate of acquisition of this risk. No difference could be detected in the decompression requirements of a dive of 50 minutes duration and one of 6 hours. However when decompressing from such a dive a 50 minutes duration at a stage is certainly not equally as effective as 3 hours. This irreversibility was seen during the subsequent 3 hours stops from 165 feet to the surface. Pressure changes corresponding to a ratio of 1.3 were performed after a stage (stop) duration of 3 hours. This procedure met with complete success, but an attempt to repeat a 1.6 ratio following a 3 hours stay met with failure at the 60 feet level. Such a finding demonstrates that even after 3 hours the tissues of the animal are nowhere near returned to normal, otherwise immediate return to atmospheric pressure would have been possible, giving a ratio change of 2.82. To achieve such a ratio change would clearly require many hours in excess of the three already tested. Viewing this as a reflection of tissue half times it is possible to state that the half-times necessary to explain the tissue desaturation data in the decompression procedures are many times greater than the tissue half-times necessary to explain the saturation data.

At this juncture it may be concluded that the use of large and sudden pressure changes in the stage method of decompression creates a dangerous situation in the tissues, closely approximating an attack of decompression sickness. The possibility exists that if smaller pressure changes were made then there would be a more rapid pressure-time course back to atmospheric pressure. This hypothesis was tested a number of times on male human volunteers. Three representative sets of results are plotted in Figure 74. An exposure of 4 hours duration at 300 feet pressure, breathing 10 % oxygen-90 % helium, and using unacclimatised exercising subjects, was followed in many cases by rapid ascent to 170 feet with a period of 2 hours at this stage, and then rapid ascent to 120 feet with a 2 hour's pause here. These long duration stops and large pressure drops can give a successful but lengthy decompression. Several attempts were made to drop the pressure rapidly only to 220 feet and then follow in 10 feet stages a relatively smooth decompression back to atmospheric pressure. This procedure clearly did not offer any great advantages in time. In order to avoid the bends it was necessary to re-shape the pressure-time course so that the total decompression time was not significantly different from the previous technique of adopting long duration stops followed by relatively large pressure changes. There is a third possibility for achieving a shorter decompression schedule. If it is possible to ascend rapidly to a stop value which would normally be expected to give a severe attack of the bends, then there is a latent period for the appearance of decompression sickness. The situation is entirely analogous to the man at atmospheric pressure in the first phase of a surface decom-

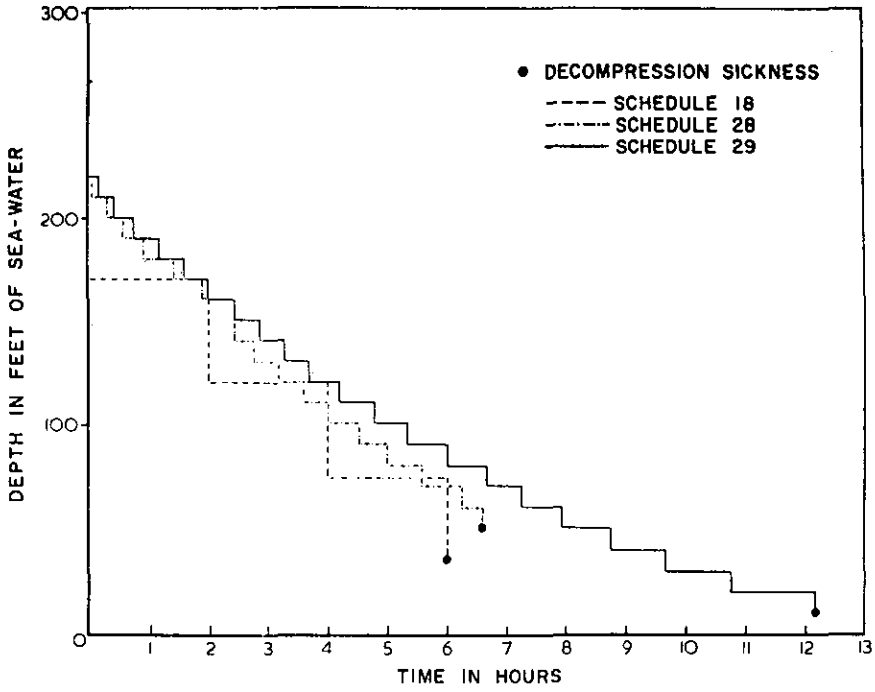

FIG. 74. Decompression from dives of 4 hours duration at 300 feet. Relative effectiveness of different pressure-time courses in preventing decompression sickness in men.

pression dive. In this latent period it is possible to change the composition of the breathing mixture and attempt to avert the impending attack. Several successful dives of this nature were attempted where the breathing medium was changed from oxy-helium to air during the latent period, with the result that very short decompression times were successfully accomplished by a team of men both in the chamber and in the sea. Unfortunately it was found that when this procedure failed to work there was a very serious form of decompression sickness, and it was decided not to pursue this technique any further.

As well as finding that the decompression pressure-time course when breathing oxy-helium was quite flexible, there were a number of puzzling observations on the role of oxygen in diving. A dive of 16 minutes to 400 feet breathing 90% He-10% O_2 gave 2 bends out of 4 attempts. When exactly the same dive, with the same decompression schedule was attempted breathing 87% He-13% O_2 then 10 trouble-free dives in the sea were performed. This confirmed the generally held view that oxygen-rich mixtures are advantageous to the diver, and agrees with previous work (6).

TABLE 38

Example of Dive Using Oxygen for Decompression from a Deep Prolonged Dive

Depth (feet)...	300	170	120	80	55	35	20	10
Time (hours)..	4	3	3	3	3	3	3	3
Breathing gas mixture.....	90% N_2-10% O_2	80% He-20% O_2			40% He-60% O_2			100% O_2

However when oxygen rich mixtures were used in the later stages of many of the lengthy decompressions necessary from deep prolonged dives they did not give any noticeable benefit. This is borne out by the following observations. The schedule to be discussed is shown in Table 38. Here the divers breathe 90% He-10% O_2 at 300 feet and 80% He-20% O_2 from 170 feet to 80 feet, 40% He-60% O_2 from 55 feet to 20 feet and oxygen for 1 hour at 10 feet. This is a reasonably successful procedure on unacclimatised men and in fact gave two transient niggles at the first attempt by a pair of divers. In one man these transient attacks were noted from 55 feet to the surface, re-occurring at every pressure stage and disappearing in a minute or two. The other diver had similar effects but only on reaching atmospheric pressure. This was considered marginally safe, but in order to test whether oxygen made any really worthwhile contribution it was decided to breathe 80% He-20% O_2 from 170 feet to 20 feet and then to change to 60% He-40% O_2 at 20 feet and 10 feet. No oxygen breathing was performed. This in theory should render the schedule alarmingly unsafe if oxygen has the role usually attributed to it. In fact 6 men attempted this dive and only one man had a transient niggle during the decompression. Far from being rendered more unsafe it was the impression that the dive was made safer. Following these dives, a number of dives of 1 hour duration at 300 feet were also tried using schedules involving oxygen breathing from 50 feet to the surface. In order to avoid bends in the last 50 feet of the schedule it became clear that it would be necessary to breathe pure oxygen for times in excess of 2 hours and such prolonged breathing of oxygen was considered undesirable. A change was made to oxy-helium mixtures without any noticeable increase in the time requirements for a safe ascent. It is now considered that breathing of oxygen during the decompression may cause vasoconstriction giving a lowered inert gas elimination rate and that this effect can offset any benefit derived from the lack of inert gas pressure in the arterial blood. Breathing oxygen or oxygen rich mixtures during the time on the bottom, or even just prior to the dive, is of course very beneficial for exactly the same reasons operating in reverse.

The main principles are now established for calculating schedules, as follows:

1) The body tissues effectively saturate in 4 hours.
2) It is possible to extend the general ideas of calculating air tables i.e. stage decompression, ratio cut-back.
3) There is an irreversibility in the uptake and elimination of the gas responsible for decompression sickness.
4) Oxygen and oxygen rich mixtures do not confer the benefit expected when breathed during the decompression.

In addition to these general principles there are several necessary controls which must be maintained on the diver, his activities and his environment. For example,

1) It is necessary to test schedules on either acclimatised men or completely unacclimatised men.
2) Hard work while on the bottom is essential to give a severe test to a schedule.
3) Work during the decompression must be reduced to the minimum.
4) Pressure measurements at sea can never follow the same pattern as in the laboratory. This is due to wave motion and sea swell as well as the fact that in any real situation the diver alters his position in the water from time to time. At depths of 600 feet for instance a variation of 15 feet may well be encountered.
5) During the dive and decompression the diver must be kept warm. In laboratory experiments the temperature ranged between 80° F and 90° F, whereas at sea in our recent trials the temperatures varied between 55° F and 60° F. The divers were very cold during the dive and for the first part of the decompression, and this was thought to be influencing the outcome of the decompression.
6) Atmosphere control must ensure accurate breathing mixtures, and carbon dioxide must not rise above a partial pressure of 1% of 1 atmosphere.
7) A schedule is not considered successful unless 10 trouble free dives are performed by 10 different divers.

Helium diving at sea has always produced more decompression sickness than in the laboratory. At present the possible contributing effects of cold and raised carbon dioxide pressures are being tested on small animals.

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Relevant phase conditions for predicting occurrence of decompression sickness

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HILLS, B. A. *Relevant phase conditions for predicting occurrence of decompression sickness.* J. Appl. Physiol. 25(3): 310–315. 1968.—An experiment has been designed to determine whether phase equilibration or limited supersaturation is the relevant thermodynamic state of the critical tissue type to be considered in predicting the occurrence of decompression sickness. The total decompression times of five goats have been titrated individually for direct surfacing from pressures equivalent to 10, 20, and 30 ft, apart from two of the animals which developed symptoms on reaching 10 ft by the standard schedule employed. For the others it was found that time spent at the normal 10-ft last stop of a conventional decompression format, based on the concept of limited supersaturation, can be employed more effectively if allotted to the 20-ft stop. This would indicate that the gas phase is present during the popular Haldanian type of decompression so that the mathematical basis of such calculation methods would then be inconsistent with the physics of the system.

cavitation in vivo; metastable limit; phase equilibration; random nucleation; supersaturation of tissue

MANY CALCULATION METHODS have been proposed for predicting the occurrence of decompression sickness. Most are semiempirical in origin and tend to deviate significantly from experience for dives exceeding 100 ft in depth or 60 min exposure time (9). However, in deriving the necessary mathematical expressions for approaches based on fundamental physiological and physical parameters, it is essential to know the phases present in the critical tissue type(s) during decompression. It is vital to know whether gas has separated from solution in tissue since only gas in true physical solution can contribute to a concentration gradient, or differential, which is the driving force for the exchange of inert substances between blood and tissue. This applies whether the rate-limiting process is blood perfusion (15), bulk diffusion (11), or diffusion across the specific barriers required to give a linear transport response (14). Thus, when the same time functions are used to estimate both the uptake and elimination of inert gas by a tissue type, there is the inherent assumption that there has been no separation of gas from solution in the tissue during decompression. This is embodied in the original Haldanian approach (1) and its many empirical modifications (4, 7, 23, 24) where the criterion for safety is taken as a critical degree of supersaturation, i.e., a metastable limit beyond which the gas phase can appear and subsequently become manifest as symptoms. The theme for the decompression format to which this assumption leads is well illustrated by Schreiner's statement (18) that "the required reduction in pressure must be carried out in a manner that will not permit the formation of inert gas bubbles in the tissues of the diver."

However, appreciable evidence has been collected (10) to show that the gas phase can be present, in small amounts, in many tissues without symptoms of decompression sickness becoming apparent. This includes a summary (5) of X-ray data and of volume changes in cerebrospinal fluid with decreasing pressure. Moreover, it is likely (12) that nucleation of the gas phase in tissue is a random process no different from cavitation in vitro, or from any other aspect of the general phenomenon of suppressed transformation.

Even so, this concept of the metastable limit could still apply in the critical tissue type which has not been identified positively. If it does not apply, there is still the problem of whether the relevant case for analysis is the statistical average or the "worst possible" tissue regions which would be those sufficiently nucleated to be in phase equilibrium with the surroundings. A microregion of tissue in such a thermodynamic state would be the "worst possible" from the standpoint of achieving a pain-provoking threshold for two reasons. First, it represents the maximum quantity of gas which can separate from solution and, second, by virtue of this phase change there is the minimum driving force for eliminating this gas via capillary blood.

Hence in analyzing dives, or in calculating decompression procedures, it is essential to know when the gas phase is present. Thus, a crucial experiment is required to differentiate between supersaturation and equilibrium states within the critical tissue type(s).

One method has been the measurement of the wash-

out of total body nitrogen by oxygen breathing with and without decompression (22). It was concluded that the body essentially retained its supersaturation since the elimination rate was not reduced to a constant value by simultaneous decompression, as anticipated for a fully equilibrated system. However, there was a significant decrease in nitrogen washout indicating that the individual behavior of any fully nucleated regions may have been masked by the others, since the over-all washout must reflect the behavior of the statistical average. Moreover, these measurements referred to the whole body.

METHODS

To avoid the above objection it is necessary to ensure that one is dealing with the tissue type(s) responsible for marginal cases of decompression sickness. One safe method is to use the occurrence of symptoms as the outward indication of any means used to differentiate between the possible thermodynamic states of the critical tissue(s).

The principle adopted here is that of exploiting the difference in gas transport properties between a supersaturated and a phase-equilibrated tissue region.

Conventional "staging" procedures are based on the former concept. Thus, the diver is given a large initial decompression (19) with the intention of establishing the maximum tissue-blood gas tension differential, and hence obtaining the maximum driving force for tissue desaturation from the start of decompression. On this basis the subject is kept at the shallowest depth permitted by the relevant decompression ratio until he surfaces, 10 ft being taken as the last stop in most tables.

However, if the gas phase is present, then a greater driving force should be obtained at greater depth. This tension differential (ΔP_{N_2}) for the elimination of nitrogen has been derived theoretically (11) as

$$\Delta P_{N_2} = P(1 - \mu) - 133 + 47\mu \text{ mm Hg} \qquad (1)$$

where P is the absolute pressure and μ is the mole fraction of nitrogen in the breathing mixture composed of N_2 and O_2.

Equation 1 is consistent with experimental determinations of total tissue tension measured in constant volume cavities implanted in dogs breathing air at normal atmospheric pressure (16), and in rabbits breathing a variety of gas mixtures at various pressures (11). It is also compatible with data for the reabsorption of gas injected subcutaneously into rabbits (3) and rats (20).

In *equation 1* it can be seen that ΔP_{N_2} should increase with P for a breathing mixture of constant composition. Hence, the decompression time normally spent at 10 ft should be more effective if deployed at 20 ft, provided the gas phase is present. If not, then the converse must be true.

This provides a simple means of determining the relevant thermodynamic state of the critical tissue by titrating, to a bends point, the time spent at last stops of 10, 20, and 30 ft before surfacing directly.

If the total decompression time required is less when surfacing from 10 ft than from 20 ft, and less from 20 ft than from 30 ft, then this confirms the general assumption, that gas remains in true physical solution during safe decompressions, and that the conventional concept of limited supersaturation is correct. If, however, less time is required when surfacing directly from 20 ft than from 10 ft, then the gas phase must have been present during the decompression whether symptoms appear or not.

In this case, depths greater than 20 ft could prove more effective as the last stop. The limit would then be set by the tolerance of the critical tissue type for the increasing quantities of gas separating from solution during longer last "pulls" to the surface. Thus, titration of a 30-ft last stop has been included in the experimental program despite the difficulty of interpreting results if the gas phase is otherwise confirmed as present.

RESULTS

Large female goats have been used as the subjects since one can readily detect symptoms in these animals. They lift a hoof if they experience bends pain in that limb (6). This very simple subjective test has proved quite adequate, and has indicated that these animals are comparable with men in susceptibility to decompression sickness (9) as well as in body mass and percentage of blood volume (1).

Each goat was compressed individually, at least 2 days elapsing between successive trials. The animals were placed in separate pressure chambers intermittently ventilated with air to keep the CO_2 partial pressure below 3 mm Hg. As soon as any definite symptoms were noted, that goat would be recompressed by the addition of 100% O_2 to attain a tank gauge pressure of 60 ft, held there for 60 min, and then slowly decompressed to normal atmospheric pressure over a period of 2 hr. This cured all cases and did not appear to influence the next trial with that animal beyond normal acclimatization.

The dive selected was an exposure of 60 min at 160 ft, followed by the standard decompression schedule advocated in United States Navy tables (19) which are based on conventional theories of limited supersaturation. The following modifications have been made to the later stages to implement the method of detecting the gas phase: *1)* The standard 10-ft stop is changed by large time intervals (about 32 min) until two points are reached—one at which direct surfacing gives bends and another at which no bends develop within 24 hr of decompression. The interval of 32 min is then halved in successive trials until bends and no-bends cases are separated by periods of 4 min or less for that particular animal. *2)* The same procedure is repeated with the exception that the standard 20-ft stop is prolonged, and the time for direct surfacing from this depth titrated

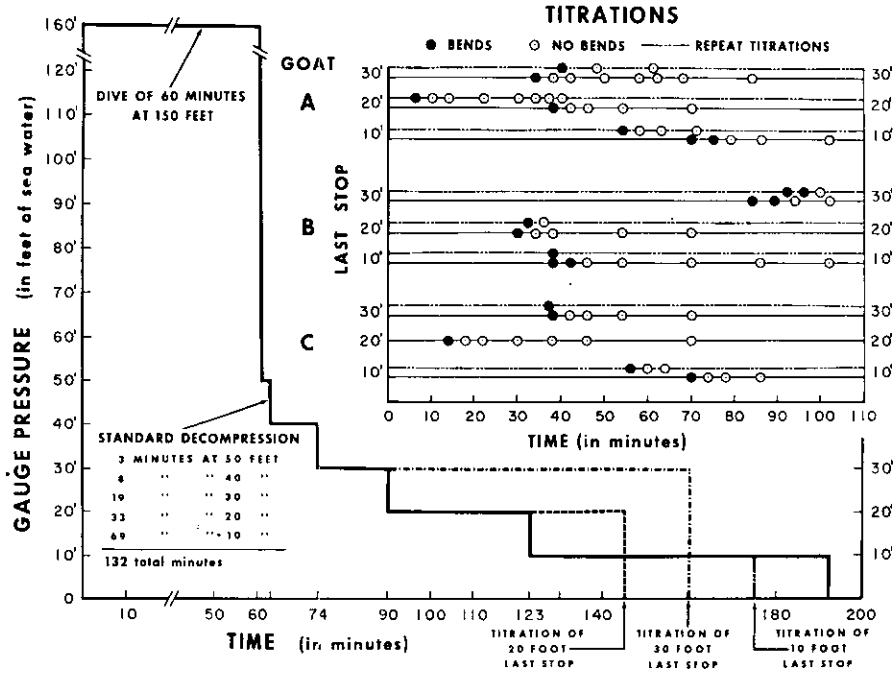

FIG. 1. Titration of total decompression time when the last stop of an otherwise standard decompression schedule (19) is 10, 20, or 30 ft. Zero of time scale for the linear illustrations of titrations is the point at which the formats first diverge.

as above. *3*) The same titration is performed with direct surfacing from the extended 30-ft stop.

These procedures are illustrated in Fig. 1. A total of 85 individual decompressions were performed on five large female goats of various breeds. These were weighed at monthly intervals during the trials, all of them keeping within the range 97–115 lb., apart from *goat A*. This animal weighed from 75 to 82 lb.

The first titration on any given animal was always repeated to account for any increase of tolerance with successive dives. Acclimatization has been noted in caisson workers (21). Where the change was found to be sufficient to influence the scores between 10-, 20-, and 30-ft series, other titrations were also repeated. In practice it was difficult to detect any difference in the reaction of the animal to decompression time differentials of 2 min or less.

The results are listed in Table 1, together with the nature of symptoms, their time of onset, and the number of days since that animal was first used in this program. The titration of *goats A*, *B*, and *C* are displayed diagrammatically in Fig. 1. Those of *D* and *E* are omitted since they developed symptoms on reaching the 10-ft stop by the normal procedure.

A comparison of the decompression times obtained for *goats A*, *B*, and *C* is given in Table 2

Note that the reduction in total decompression time between first and repeat runs is greater for "shallower" last stops, the largest being observed when "surfacing" from 10 ft. This pressure corresponds to that used in decompressing the caisson workers among whom Walder (21) found marked acclimatization.

By all methods of scoring, a quantitative comparison of the efficiencies of 10-, 20-, and 30-ft stops shows that total decompression time is less for a 20-ft than for a 10-ft last stop. Taking a simple average, the mean decompression time for all three goats is given in Table 2—exclusive and inclusive of repeat titrations. The same order of performance is obtained, in comparing 10- and 20-ft values, whether one takes the shortest decompression times for each titration, worst values, repeat titrations only, or any combination.

DISCUSSION

The total decompression times for all titrations of the *goats A*, *B*, and *C* lie well within the 132 min allowed in standard United States Navy tables (19). Hence the constants used in computing this conventional schedule must be safe for those animals performing that particular dive. Thus, the initial stops must be safe according to the conventional assumption, so they cannot invalidate the interpretations to be drawn from titration of the later stops.

This cannot be said for *goats D* and *E* which developed symptoms upon reaching the 10-ft stop, so these animals were omitted from further trials. However, it was surprising that standard tables, with no modification, should give three cases of bends—particularly when applied to a species generally regarded as less susceptible to decompression sickness than man.

The variation in susceptibility between individuals is demonstrated by the range of *absolute decompression* times shown in Fig. 1, and can account for the differ-

TABLE 1. *Titrated 10-, 20-, and 30-ft stops for a dive of 60 min at 160 ft*

Dive No.	Goat	Time Since First Dive, days	Last Stop, ft	Total Decompression Time, min	T,* min	Symptoms† Observed	Onset Time‡ min
1	A	0	10	100	70	Bend R hind	0
2	A	2	10	102	102	Nil	
3	A	4	10	116	86	Nil	
4	A	7	10	109	79	Nil	
5	A	9	10	105	75	Mild bend L hind	14
6	A	11	30	114	84	Nil	
7	A	14	30	98	68	Nil	
8	A	16	30	92	62	Nil	
9	A	18	30	88	58	Nil	
10	A	21	30	80	50	Nil	
11	A	25	30	72	42	Nil	
12	A	28	30	64	34	Bend L hind	3
13	A	30	30	68	38	Nil	
14	A	35	20	100	70	Nil	
15	A	37	20	84	54	Nil	
16	A	42	20	76	46	Nil	
17	A	44	20	68	38	Mild bend R fore	12
18	A	47	20	72	42	Nil	
19	A	50	30	91	61	Nil	
20	A	52	10	101	71	Nil	
21	A	57	10	93	63	Nil	
22	A	59	10	84	54	Bend R hind	1
23	A	64	10	88	58	Nil	
24	A	71	20	70	40	Nil	
25	A	78	20	67	37	Nil	
26	A	80	20	64	34	Nil	
27	A	84	20	60	30	Nil	
28	A	86	20	52	22	Nil	
29	A	99	20	44	14	Nil	
30	A	101	20	40	10	Nil	
31	A	105	20	36	6	Bend R hind	5
32	A	129	30	70	40	Bend R hind	11
33	A	131	30	78	38	Nil	
34	B	0	30	114	84	CNS	5
35	B	2	30	132	102	Nil	
36	B	5	30	124	94	Nil	
37	B	7	30	119	89	Bend R fore	12
38	B	9	10	132	102	Nil	
39	B	12	10	116	86	Nil	
40	B	15	10	100	70	Nil	
41	B	18	10	84	54	Nil	
42	B	20	10	68	38	Bend L hind	27
43	B	25	10	76	46	Nil	
44	B	27	10	72	42	Bend L hind	35
45	B	32	20	100	70	Nil	
46	B	34	20	84	54	Nil	

TABLE 1—*Continued*

Dive No.	Goat	Time Since First Dive, days	Last Stop, ft	Total Decompression Time, min	T,* min	Symptoms† Observed	Onset Time‡ min
47	B	37	20	68	38	Nil	
48	B	46	20	60	30	Bend R fore	0
49	B	49	20	64	34	Nil	
50	B	53	10	68	38	Mild bend	64
51	B	55	30	122	92	Bend R hind	19
52	B	60	30	126	96	Bend R fore	8
53	B	67	30	130	100	Nil	
54	B	84	20	66	36	Nil	
55	B	86	20	62	32	Bend R fore	2
56	C	0	10	100	70	Bend R fore	?
57	C	2	10	116	86	Nil	
58	C	7	10	108	78	Nil	
59	C	9	10	104	74	Nil	
60	C	12	30	100	70	Nil	
61	C	15	20	100	70	Nil	
62	C	17	30	84	54	Nil	
63	C	2	30	68	38	Bend L fore	43
64	C	24	30	76	46	Nil	
65	C	29	30	72	42	Nil	
66	C	36	30	67	37	Nil	
67	C	38	20	76	46	Nil	
68	C	45	20	68	38	Nil	
69	C	49	20	60	30	Nil	
70	C	57	20	52	22	Nil	
71	C	64	20	44	14	Both hind legs	10
72	C	66	20	48	18	Nil	
73	C	70	10	86	56	Bend R hind	21
74	C	94	10	94	64	Nil	
75	C	96	10	90	60	Nil	
76	D	0	30	100	70	Bend R hind	7
77	D	2	30	132	102	Nil	
78	D	4	30	114	84	Bend L hind	7
79	D	7	30	123	93	Nil	
80	D	9	30	107	77	Mild bend	12
81	D	11	10	116	86	Nil	
82	D	13	Bend in R foreleg on reaching 10-ft stage				
83	D	15	10	116	86	Nil	
84	D	20	Bend in L hindleg on reaching 10-ft stage				
85	E	0	Bend in L foreleg on reaching 20-ft stage				

CNS denotes symptom indicating involvement of the central nervous system. * T is time after normal 30-ft stop (see Fig. 1). † R fore = right foreleg, L fore = left foreleg, R hind = right hindleg, L hind = left hindleg. ‡ Time of onset after surfacing.

TABLE 2. *Comparison of total decompression time for 10-, 20-, and 30-ft last stops*

	Subj	10-Ft Last Stop		20-Ft Last Stop		30-Ft Last Stop		Order of Effectiveness of Last Stop, ft
		Max time for bends	Min time for no bends	Max time for bends	Min time for no bends	Max time for bends	Min time for no bends	
1	Goat	105	109	68	72	64	68	30,20,10
2	(Repeat)	(84)	(88)	(36)	(40)	(70)	(78)	20,30,10
3	Avg	94.5	98.5	52	56	67	73	20,30,10
4	Goat B	72	76	60	64	119	124	20,10,30
5	(Repeat)	(68)		(62)	(66)	(122)	(126)	20,10,30
6	Avg	70	76	61	65	120.5	125	20,10,30
7	Goat C	100	104	44	48	68	72	20,30,10
8	(Repeat)	(86)	(90)			(68)		
9	Avg	93	97	44	48	68	72	20,30,10
10	Mean of lines 1, 4, 7	92.3	96.3	57.3	61.3	83.7	88	20,30,10
11	Mean of lines 3, 6, 9	85.8	90.5	52.3	56.3	85.2	90.0	20,30,10
Mean of bends and no bends								
	Line 10	94.2		59.3		85.9		20,30,10
	Line 11	88.2		54.3		87.6		20,30,10

Data from Fig. 1. All times given in minutes.

ence in the relative scores between titrated 10-ft and 30-ft last stops. Thirty feet has proven more effective than ten feet for *goats A* and *C* whereas the reverse is true for *B*. This indicates that the gas phase was present in *A* and *C*, and could even have been present in *B* during the initial stages of decompression if it had dissolved before the end of the 30-ft stage. At that point the gas elimination rate would have decreased significantly. This could result in a less favorable balance than attained at 10 ft between the duration of the faster elimination rate (*equation 1*) and the worse equilibrium position which the system must approach after dissolution of all gas. The final "pull" to the surface would then result in a larger volume of gas separating from solution in the critical tissue type(s), the relative merits of 30-ft and 10-ft last stops depending on the tolerance of the individual.

The best compromise for most subjects should lie closer to an intermediate last stop of 20 ft if the gas phase is present from the start of a conventional decompression. Thus the most significant feature of the titrations is that time can be spent more effectively at a last stop of 20 ft than at 10 ft. This observation has been recorded for all three animals shown in Fig. 1, irrespective of the method of scoring.

This must mean that the gas phase is present in the critical tissue type during the last stop at least, unless other physiological changes occur within the critical tissue type between depths of 20 and 10 ft for air inhalation. This is most unlikely since: *1)* The slightly greater blood nitrogen tension of 20 ft, compared with 10 ft, should have a slightly greater narcotic action, if any. This should have the effect of reducing, and not increasing, blood-tissue exchange as required to explain the experimental results on a supersaturation basis. *2)* The greater arterial oxygen tension at 20 ft should cause vasoconstriction rather than the vasodilatation which would be necessary to explain the more effective exchange of gas between blood and tissue at that depth if the tissue were supersaturated.

This simple experiment can thus be claimed as strong evidence in favor of the postulation that the gas phase is present in the critical tissue type during decompressions based on the conventional calculation methods. In this case, such schedules must, in reality, represent a therapeutic treatment for separated gas which does not become manifest as symptoms by virtue of its compression to below pain-provoking dimensions by the hydrostatic staging pressure (Boyle's law).

While this may seem too simple a conclusion to warrant such an arduous series of chamber trials, in all calculations it is imperative to know whether the gas phase is present at all stages of the decompression. Only gas in true physical solution can contribute to a concentration gradient, or differential, for blood-tissue exchange. Consequently, there would be great differences in both the driving force and the boundary conditions which must be reflected in totally different mathematical expressions for the two cases. This would provide a sound physical basis for the practical experience that gas uptake is faster than its elimination during conventional decompression (8).

If the gas phase is present, *equation 1* would indicate a decompression format in which the diver should be kept at depths appreciably greater than advocated by conventional theories, followed by direct surfacing from 20 to 25 ft. Dives optimized on this assumption (13) have resulted in savings of 30–35% in total decompression time. The findings of this paper are also consistent with the empirically derived techniques of Okinawan pearl divers (17) who employ stops deeper than advocated in standard Navy tables, and yet surface directly from 25 to 35 ft in appreciably shorter total decompression times.

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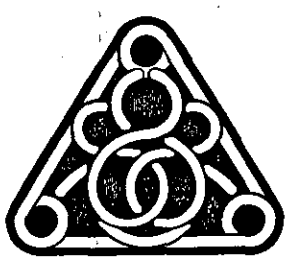

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A QUANTITATIVE CORRELATION OF CONDITIONS FOR THE OCCURRENCE OF DECOMPRESSION SICKNESS FOR AERIAL AND UNDERWATER EXPOSURES

B.A. HILLS *

Any equation derived for predicting the occurrence of decompression sickness must express the imminence of marginal symptoms as a function of at least two variables. One of these must be time, while the other can be any parameter(s) indicative of the inherent susceptibility of the individual as determined by the constitution of his critical tissue type(s).

In order to isolate the effects of the second of these variables, it is convenient to select cases where the subject has been inhaling a breathing mixture of constant composition and pressure (P_1) prior to decompression. A particularly relevant example is that of the pilot undergoing aerial ascent without pre-oxygenation. For the rapid decompression of such subjects to a lower absolute pressure (P_2), the occurrence of decompression sickness should be independent of time.

Thus the first, and still most widely accepted, index of individual susceptibility is the decompression ratio (R)—as introduced by Boycott et al. (1) in 1908. This is defined as:—

$$R = P_1/P_2$$

This classical approach has been modified empirically by many later workers (2,3) who have attributed slightly different values of R to each of Haldane's theoretical tissues. In addition, modifications of the response times have been advocated by others (4,5) until, ultimately, a computer (6) has been used to test all combinations—but with little improvement.

For many years the concept of the decompression ratio has been questioned on the grounds of the difference in numerical values required to correlate aerial and underwater data for the time-independent case described above. If one considers a pre-selected diver, with a minimum bends depth of 38 feet (7), or 876 mm Hg (gauge), as equivalent to a pre-selected pilot with a minimum bends altitude (8) of 25,000 feet (273 mm Hg absolute), then $P_1/P_2=(876+760)/760=2.15$ for the diver compared with $P_1/P_2=760/273=2.79$ for the pilot. Similarly, if one considers a weak diver for whom 30 feet (1,451 mm Hg absolute pressure) is a reasonable minimum bends depth (9) as comparable with a "weak" pilot whose minimum bends altitude (8) is 22,000 feet (321 mm Hg absolute for P_2), then $P_1/P_2=1,451/760=1.91$ for the diver compared with $P_1/P_2=760/321=2.37$ for the pilot.

In view of the doubt which such calculations cast upon the ratio concept, Hempleman (10) has undertaken a painstaking series of trials upon goats at higher pressures (P_1 in the range 50-240 feet). Keeping the animals at P_1 upon air for twelve hours, he has titrated the absolute pressure P_2 to which rapid decompression will give marginal symptoms. His results show that a constant ratio offers quite a good correlation at these high pressures. However a re-analysis of this data upon a plot of P_1 versus P_2 (Fig. 1 p. 250), has shown that the "bends" and "no bends" cases can be separated completely by a straight line not concurrent with the origin. P_1 would thus seem to be a linear function of P_2 having a positive intercept upon the P_1 axis rather than directly proportional to P_2—as implied by a constant decompression ratio.

Thus it would be most desirable to derive an expression for the above linear relationship between P_1 and P_2 from fundamental physico-chemical and physiological reasoning, and to test the result upon the data quoted above, together with that for many other conditions—e.g. helium breathing.

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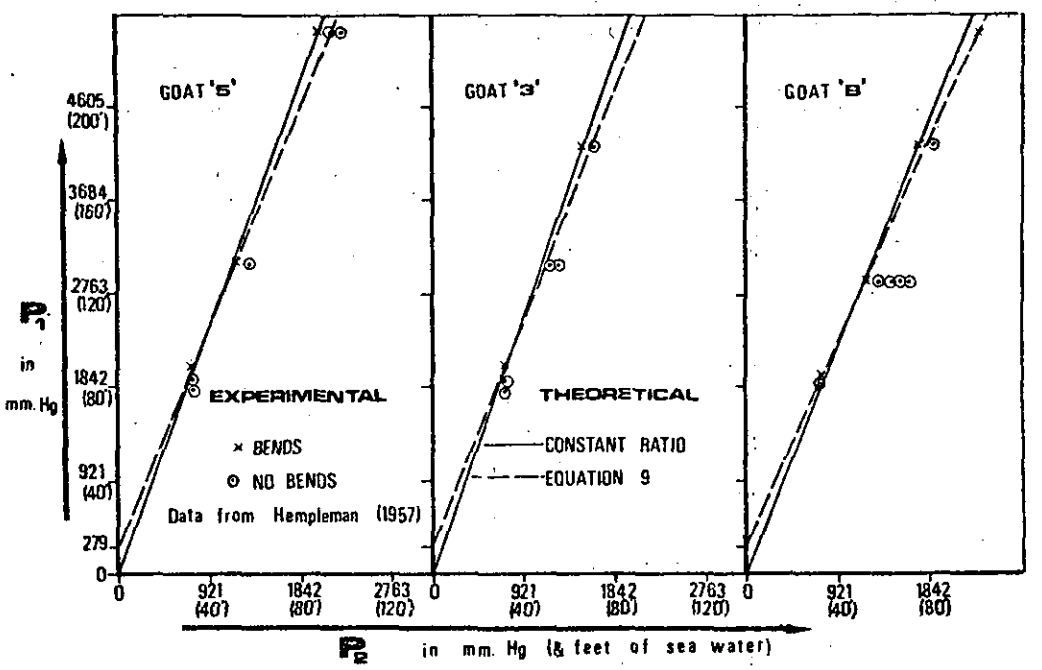

FIG. 1. — A comparison of a constant ratio with a linear relationship based upon phase equilibration (equation 9) in correlating the occurrence of symptoms in goats (10) decompressed to an absolute pressure P_2 following an effectively infinite exposure to an absolute pressure P_1.

THE MODEL

Most workers in the field of decompression sickness tend to imply that the mere presence of the gas phase in tissue is sufficient to precipitate symptoms. In a very recent paper discussing decompression procedures, the above assumption is well illustrated by Schreiner's (11) initial statement that "the required reduction in pressure must be carried out in a manner that will not permit the formation of inert gas bubbles in the tissues of the diver".

Others have not ruled out the possibility that the ratio which is so frequently interpreted as defining a critical degree of supersaturation may, in reality, be an index of the degree of embolism which body tissues can tolerate. Notable among these were Haldane's group (1) and Behnke (7). The latter interpretation of the ratio has been placed upon a simple quantitative basis by Piccard (12). He has pointed out that any solution, saturated with a gas at an absolute pressure P_1 will liberate the same volume of that gas when re-equilibrated to a new pressure P_2 — IF P_1/P_2 is constant.

This holds whatever value one takes for P_1, provided the solution obeys Henry's law.

Although Haldane and others left the explanation of the ratio as an open question, by their use of the same transport equation for estimating both the uptake and elimination of gas from the same tissue, they are effectively assuming supersaturation. Only gas in true physical solution can contribute to a driving force for its exchange between blood and any tissue type—whether the rate-limiting process is blood perfusion (13), bulk diffusion (14) or permeation of an unspecified resistance (15). If the gas phase is present, then the physics of the system is different, and the mathematics must be changed accordingly.

A considerable amount of evidence has been amassed (16) from the qualitative literature upon the syndrome to show that the gas phase can be present, in small amounts, in many tissues without any symptoms of decompression sickness becoming apparent. Moreover there appeared to be a good correlation between the occurrence of bends and bubble size according to a summary of X-ray data (17).

Previous studies (18) of cavitation *in vitro*, in systems designed to simulate the case *in vivo*, have indicated that nucleation of the gas phase is random and that there are no metastable limits to supersaturation—at least, not of the order of magnitude implied by the popular decompression ratios. In the absence of any such threshold, the largest bubble should form from the largest local volume of gas separated from solution. This should occur in any region where the distribution of nuclei has permitted phase equilibration. Hence the state of this worst possible site determines the model for quantitative analysis.

ANALYSIS

Let us consider the case of a subject who has been inhaling a mixture of oxygen and inert gas at an absolute pressure P_s for an effectively infinite period. If μ is the mole fraction of inert gas in the breathing mixture, then the tension of inert gas (p_i) throughout the blood is given by:

$$p_i = \mu(P_s - 47) \text{ mm Hg} \quad (1)$$

allowing for alveolar dilution by water vapour.

If the subject is now rapidly compressed or decompressed, upon the same breathing mixture, to an absolute pressure P_1, then the new tension of inert gas in capillary blood is $\mu(P_1 - 47)$ mm Hg since it has been shown (17) that venous tension of inert gas rapidly asymptotes towards the arterial value.

For this step in the inert gas tension of blood, defined mathematically as $p_i = \mu(P_s - 47)$ for $t \leqslant 0$ to $p_i = \mu(P_1 - 47)$ for $t > 0$ the mean tissue tension ($\bar{p}_i$) after an exposure time (τ) should be given by:

$$\bar{p}_i = \mu\,[(P_s - 47) + (P_1 - P_s).\,\emptyset(\tau))] \text{ mm Hg} \quad (2)$$

where $\emptyset(t)$ is the time function for inert gas uptake.

The total quantity of inert gas in a volume (V) of the critical tissue type, at the end of the exposure (τ), is thus $VS\bar{p}_i.\,\emptyset(\tau)$ where S is the net solubility of the inert gas in the tissue expressed as the volume of gas, measured at body temperature and standard pressure (P_o), which will dissolve in unit volume of tissue for a unit increase in partial pressure.

Let the part of this inert gas eliminated from the volume (V) of tissue during any staging be (GVS) in reaching the absolute pressure P_a. The problem is therefore one of determining whether sufficient gas could separate from solution to cause symptoms if the subject remained at this pressure.

MASS BALANCE FOR INERT GAS

If the partial pressure of inert gas in that separated from solution at pressure P is p'_i, then this must also be its tension in the adjacent tissue. Hence the quantity of inert gas remaining in true physical solution in volume (V) soon after reaching P is VSp'_i. Let us apply an inert gas balance to the system, when the volume of gas (u), reduced to body temperature and standard pressure (P_o), in equilibrium with a volume (V) of tissue is given by:

$$u = VS\,(p_i - G - p'_i) \quad (3)$$

where p'_i is determined by equilibrium conditions.

EQUILIBRIUM CONDITIONS

The gas separated from solution in tissue must be in both mechanical and chemical equilibrium with its surroundings, thus:

$$p'_i + p_{co_2} + p_{o_2} + p_w = P + 2\gamma/r + \delta \quad (4)$$

where δ is the pressure contributed by elastic deformation of tissue, γ is its interfacial tension with the gas that has been coalesced into bubbles of radius (r). p_{co_2}, p_{o_2} and p_w are the partial pressures of CO_2, O_2 and water vapour respectively in the separated gas. Analysis of subcutaneous gas bubbles (19, 20) have shown that CO_2, O_2 and H_2O partial pressures rapidly revert to venous values after a change of external pressure. Moreover the total venous value of these gases changes little by comparison with normal diving pressures. Hence there is negligible error in taking normal venous values of 40 mm Hg for O_2, 46 mm Hg for CO_2 and 47 mm Hg for water vapour.

$$\text{Thus } p_{o_2} + p_{co_2} + p_w = 133 \text{ mm Hg} \quad (5)$$

Taking values of $\gamma = 17.9$ dynes cm^{-1}, $r = 1.41$ microns and $\delta = 10$ mm Hg, considered relevant at the onset or marginal symptoms (16), then

$$2\gamma/r + \delta = 264 \text{ mm Hg} \quad (6)$$

Substituting in equation 4 the numerical values given in equations 5 and 6, we derive the partial pressure of inert gas in the bubble as:

$$p_i = P + 131 \text{ mm Hg} \quad (7)$$

Substituting for p_i and p'_i according to equations 2 and 7 respectively, equation 3 gives the partial molar volume of inert gas at body temperature, and reduced to pressure (P_o), as

$$u = VS\,[\mu(P_s - 47) + \mu(P_1 - P_s).\,\emptyset(\tau) - P - 131 - G] \quad (8)$$

The total volume, reduced to standard pressure (P_o), of gas separated from solution in tissue $= \mu$(total gas pressure in bubble)/(partial pressure of inert gas) $= u(P + 2\gamma/r + \delta)/p'_i$

However we are interested in the total volume of gas (v) separating from solution at the ambient pressure (P)

Hence

$$v = u \cdot \frac{(P + 2\gamma/r + \delta)}{p'_i} \cdot \frac{P_o}{(P + 2\gamma/r + \delta)} = \frac{u.P_o}{p'_i}$$

Substituting for p'_i and u according to equations 7 and 8 respectively, we can express the mechanical strain (f) in the tissue as the total volume of gas (v) actually separated from solution in the equilibrated volume of tissue (V) by: $f = v/V$, or

$$f = \frac{[\mu(P_s - 47) + \mu(P_1 - P_s).\,\emptyset(\tau) - P - 131 - G]\,SP_o}{(P + 131)}$$

If this mechanical strain (f) exceeds a critical value (f') then it is reasonable to assume that a nerve ending can be bent, or otherwise distorted beyond a threshold for pain, i.e. bends can occur if:

$$f = \frac{[\mu(P_s - 47) + \mu(P_1 - P_s).\,\emptyset(\tau) - P - 131 - G]\,SP_o}{(P + 131)} > f' \quad (9)$$

Individual Susceptibility	"Weakest" individuals			"Pre-selected" pilots and divers	
Nature of exposure Breathing mixture	aerial air	underwater air	underwater He : O_2	aerial air	underwater air
Fraction of inert gas (μ)	0.8	0.8	0.8	0.8	0.8
P_1 (in mm Hg)	760	1,451	1,612	760	1,636
P_2 (in mm Hg)	321	760	760	273	760
Ratio (P_1/P_2)	2.37	1.91	2.09	2.79	2.15
(f'/SP_n) from equation 9	0.261	0.260	0.426	0.412	0.427

TABLE 1. — Analyses of conditions for the occurrence of decompression sickness based upon both the ratio concept and the equilibrium concept (equation 9).

in which all pressures are expressed in mm Hg.

This expression can now be used to analyze practical data.

"SATURATION" DIVES WITH NO-STAGE DECOMPRESSION

For the "saturation" no-stage decompressions cited earlier as a test of the ratio:

$G=O$ for no staging

$\emptyset(\tau)=1$ for saturation

and $P=P_2$ (the final pressure)

Thus equation 9 reduces to:

$$(f/SP_n)=\frac{\mu\,(P_1-47)-P_2-131}{(P_2+131)} \geq (f'/SP_n) \qquad (10)$$

This expression has been used to correlate the aerial and air-diving data quoted earlier, and to compare with data published for helium diving (21) from which it is possible to extract a fairly clear value of 37 feet as the minimum bends depth for a "weak" diver breathing 80% He+20% O_2. The correlation is given in table 1 *ci-dessus*.

LINEAR RELATIONSHIP

Equation 10 may be re-written as:

$$P_1=\left[\frac{(f'/SP_n+1)}{\mu}\right]P_2+\left[\frac{131\,(f'/SP_n+1)}{\mu}+47\right]$$

μ and (f'/SP_n) are constants for a given breathing mixture. Thus P_1 displays a linear relationship with respect to P_2 as required to separate the "bends" and "no bends" cases in Hempleman's data. Moreover, for $P_2=0$, $P_1=279$ mm Hg which intercept lies on a straight line which can separate all safe and unsafe cases as shown in *Fig.* 1. The foregoing value of the intercept was calculated using a value of (f'/SP_n)=0.42—as derived for pre-selected divers from table 1.

DISCUSSION

The improved correlation of aerial and underwater data is illustrated in table 1. For "weak" individuals breathing air, there is a 37% discrepancy in decompression ratio compared with less than 1% for the variation in the dimensionless group of constants (f'/SP_n). Moreover the value *for nitrogen (0.260) corresponds exactly* with that for helium (0.426) if the net solubilities (S) of these gases in the critical tissue type(s) are in the ratio 1.64:1. This would be the case for a tissue containing approximately 3% lipid according to solubility data quoted for water and for fat (7).

Such a value would give the net solubility of nitrogen in the tissue in the dimensionless form $SP_n=0.0142$, when $f'=0.0034$. This would suggest that symptoms can occur in any region of the critical tissue type(s) where the fraction of space occupied by the gas phase exceeds 0.34% of the volume from which it has separated from solution. However this gas would probably need to be partially coalesced, or congregated by some means, before the local mechanical strain can be concentrated to give the stress which could exceed the threshold value for pain. In pursuit of this simple mechanical mechanism for bends, it is interesting to *note* that exercise following decompression reduces onset time considerably (8). Exercise should produce a motion particularly conducive to the coalescence of gas deposited in a critical tissue type known to be closely associated with the locomotor system (17).

Since such tissues are predominantly aqueous, 3% would seem a reasonable value for the lipid content. It is highly likely that some lipid is present since it has been known for many years (1, 27) that more obese men, and fatter animals, are more susceptible to decompression sickness.

Comparing pilots and divers naturally pre-selected for their tolerance, table 1 shows a discrepancy in the decompression ratio of 30% compared with just under 4% in (f'/SP_n). Moreover (f'/SP_n) is a more "sensitive" parameter since it is calculated as a difference rather than a ratio, $1+(f'/SP_n)$ giving a truer reflection in comparing errors.

Hence it would seem fair to claim that equation 9 offers a better correlation of data independent of time than that afforded by the popular concept of a decompression ratio. This is further exemplified upon the classical data of Hempleman (10). This is shown in *Fig.* 1 for three out of the four goats titrated to bends following an effectively infinite exposure at pressure P_1. Results for the fourth goat are omitted since they show only one bends point, so almost any equation would fit. In *Fig.* 1 it can be seen that a constant ratio fails to correlate one case of bends out of three for goat "5". Both lines satisfy the data for goat "3". The ratio fails to correlate two "bends" and one "no bends" out of four titrations for goat "B". On the other hand, equation 10 would appear to separate "bends" from "no bends" cases in all instances.

The above correlations of practical data would cast serious doubt upon the popular concept of a critical threshold to supersaturation in tissue. It would favour one of random nucleation in tissue (16) where isolated regions were sufficiently seeded to be in phase equilibrium.

If the above reasoning is essentially correct, and the gas phase can be present for decompressions which are known to be safe, then conventional decompression tables are essentially a therapeutic treatment for "silent bubbles" which do not become manifest as symptoms by virtue of their compression, as expressed quantitatively by Boyle's Law.

The concept of phase equilibration in randomly-scattered tissue regions implies that the physics of the system for inert gas uptake is very different to that for its elimination from these areas during decompression. Moreover, the successful correlation of time-independent data would favour equation 9 as a sound basis for estimating the uptake and elimination response functions free from any superimposed doubts in accounting for susceptibility.

SUMMARY

A QUANTITATIVE CORRELATION OF CONDITIONS FOR THE OCCURRENCE OF DECOMPRESSION SICKNESS FOR AERIAL AND UNDERWATER EXPOSURES

B.A. HILLS

Expressions of conditions for the occurrence of decompression sickness are derived from basic physico-chemical principles which provide a correlation of aerial and underwater exposures appreciably better than any obtainable by the popular concept of a decompression ratio. The relative magnitude of errors is shown to be of the order of 30% by latter compared with 3% by the thermodynamic approach. This improvement is based upon the concept that one must consider the worst possible occurrence in the critical tissue type(s) when estimating the imminence of symptoms of decompression sickness. In a system where nucleation of the gas phase is a random process, the relevant case is one where the fully-nucleated zones are in phase equilibrium with the tissue. The experimental data analyzed has been selected to isolate the problem of finding a realistic method of expressing individual susceptibility quantatively from that of providing suitable transient functions to represent gas transport.

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RESUME

CORRELATIONS QUANTITATIVES DES CONDITIONS QUI PRESIDENT A L'INCIDENCE DE LA MALADIE DE DECOMPRESSION D'ORIGINE AERIENNE ET SUBAQUATIQUE

B.A. HILLS

Les conditions qui président à l'incidence de la maladie de décompression s'appuient sur des principes physico-chimiques fondamentaux qui fournissent, par l'étude de l'exposition aérienne et subaquatique, une appréciation beaucoup plus valable que celle obtenue par les données classiques du taux de décompression. Les erreurs relatives sont de l'ordre de 30 % pour cette dernière méthode alors qu'elles ne sont que de 3 % lorsque le problème est abordé par une approche thermodynamique. Cette amélioration tient au peu d'importance qu'il convient d'attacher au facteur tissulaire devant l'imminence des symptômes de la maladie de décompression. Dans un système où la « nucléation » des gaz est un processus de par hasard, il s'agit d'une situation où les zones pleinement « nuclées » sont en équilibre avec les tissus. Grâce aux données expérimentales ainsi analysées, le problème qui donne une expression quantitative des susceptibilités individuelles pourra être séparé de celui qui fournit des fonctions transitoires pour la représentation des transports gazeux.

(Rev. Phys. Subaq. Méd. Hyperb., T. I, 1969, N° 4, p. 249-254.

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UNSATURATION IN LIVING TISSUE RELATIVE TO THE PRESSURE AND COMPOSITION OF INHALED GAS AND ITS SIGNIFICANCE IN DECOMPRESSION THEORY

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SUMMARY

1. An experimental investigation has been undertaken to test theoretical predictions of the variation in the total gas tension in tissue with respect to the pressure and composition of the inhaled atmosphere.

2. The total gas tension has been measured as the pressure attained in constant volume cavities equilibrated with the adjacent tissue. This has been achieved in rabbits using fine-bore plastic tubing permeable to all physiological gases.

3. After reaching steady-state conditions, the total gas tension was invariably found to be lower than the pressure of the breathing mixture. This deficit, or 'inherent unsaturation', was found to: (a) increase linearly with respect to the absolute pressure of a breathing mixture of constant composition, and (b) decrease linearly with respect to the mole fraction of inert gas in an atmosphere inhaled at constant pressure.

These findings are discussed in relation to their implications in the avoidance and treatment of decompression sickness.

In an analysis of diving techniques current in the Torres Strait in 1960 (LeMessurier & Hills, 1965) methods of decompression for deep long dives (200–280 ft for 35–60 min) showed marked differences from recognized schedules (e.g. U.S.N. Diving Manual, 1943). With the realization that no current theory could explain these anomalies, a thermodynamic analysis of gas absorption and excretion from tissue was undertaken by Hills (1966) who proposed a theory which differed widely from conventional approaches to diving. One of the more controversial aspects of this work was the suggestion that there is no significant metastable limit to the supersaturation of tissue by a gas, but rather that nucleation of the gas phase is random. This implies no tension threshold to the formation of bubbles in tissue so that this process can occur for any gas concentration in excess of equilibrium. Thus it was argued that a state of phase equilibrium would represent the 'worst possible' occurrence, and therefore the safest condition on which to base the programming of decompressions or the analysis of dives.

However, if one dispenses with the popular concept of supersaturation, then what can be the true driving force for the known elimination of gas from tissue during decompression? Hence

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it was further postulated that the major source of the driving force for this elimination is an unsaturation of tissue with respect to the atmosphere arising by virtue of metabolism. Moreover it was predicted, on the basis of the thermodynamic analysis, that this inherent unsaturation should increase linearly with respect to rises in the absolute pressure and the mole fraction of oxygen in the breathing mixture. However, such theoretical predictions need experimental verification. Now it has been known for some time that the sum of the tensions of all gases measured directly in blood (Asknes & Rahn, 1957), and indirectly in living tissues (Van Liew, 1962), does not attain the absolute pressure of the inhaled atmosphere in which the subject has been living continuously. If this deficit, or 'inherent unsaturation', is in truth the major source of the driving force for the elimination of inert gas from tissues during the decompression of a diver, then it is very pertinent to obtain more direct measurement of its magnitude and variation with the factors likely to influence it during diving.

The original work of Campbell (1924), who analysed the contents of subcutaneous gas pockets in rabbits breathing air at normal atmospheric pressure, has been considerably extended by Van Liew *et al.* (1965). They have employed a similar technique upon rats breathing various gas mixtures at different pressures.

However, gas in subcutaneous pockets is essentially at constant pressure—if its absorption causes negligible variations in the surface tension and tissue elasticity. Hence, in extracting values for the unsaturation, Van Liew *et al.* (1965) needed to assume that O_2, CO_2 and H_2O tensions have reached a steady-state condition in a system which is essentially transient by virtue of the continuous decrease in bubble size. Moreover, in estimating the rate of gas absorption, they assume that the cavity maintains geometric similarity in applying their correction for the reduction in surface area available for gas exchange.

Individually the above assumptions would not appear serious, but they can be avoided by using a constant volume method in which total tissue tension is measured as the total pressure of gases in a rigid cavity equilibrated with the tissue. One such device has been used by Lategola (1964) who recorded an 'inherent unsaturation' of 41–48 mmHg in dogs breathing air at normal atmospheric pressure. Equilibration times of 2–3 days were found necessary.

However, in order to investigate a range of pressure and a variety of breathing mixtures, it was considered advisable to reduce the equilibration time by a design of cavity with more rapid response.

Moreover, it was considered essential to prove that the membrane used was permeable to all physiological gases, since failure of any one gas to equilibrate with the tissue would invalidate the principle of estimating the 'inherent unsaturation' as simply the difference between the external and final cavity pressures.

The design of such a subcutaneous probe has been undertaken and the device used to measure the 'inherent unsaturation' with change of pressure using air, and change of the composition of the breathing mixture at constant pressure.

MATERIALS AND METHODS

Constant volume and membrane permeability tests in vitro

The cavity selected was a 49 cm length of polyvinyl chloride tubing of fine bore (0·4 mm I.D. and 0·8 mm O.D.), these dimensions giving a large membrane surface relative to the

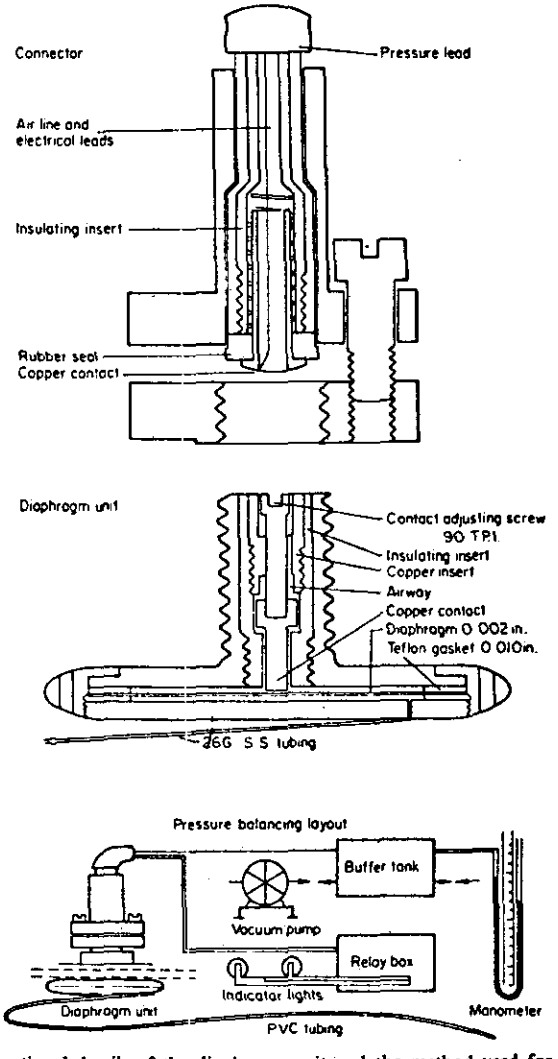

FIG. 1. Constructional details of the diaphragm unit and the method used for measuring the 'inherent unsaturation' by balancing the pressure across the diaphragm. The 'inherent unsaturation' is the tension deficit between the tissues and the inhaled atmosphere after an effectively infinite exposure.

enclosed volume. One end was sealed by fusion and the other closed by means of a diaphragm unit (shown in Fig. 1).

Preliminary tests *in vitro* showed that the cavity volume decreased by less than 0·1% when the pressure differential across the tubing was increased by 1 atm.

To test permeability, a similar length of the same tubing was flushed with O_2, then heat-sealed at one end and finally closed by a pellet of clean dry mercury at the other. This end was then kept at atmospheric pressure while the pressure upon the outside of the tubing was reduced to less than 5 mmHg absolute. The rate of travel of the mercury pellet within the tubing was then recorded. It reached the half-way point within 35 min for each of the two runs. Repeating the procedure for the initial inclusion of N_2 and CO_2, the corresponding times were 74 and 12 min, respectively, at 17°. The above times are consistent with values of diffusion coefficients for the above gases in plasticized PVC quoted by Brubaker & Kammermayer (1953).

Permeability to water vapour was demonstrated by immersing in water the external surface of a length of tubing of the same material in which a near Torricellian vacuum had been formed. The mercury level fell by the water vapour pressure.

The above experiments, performed *in vitro*, showed that the PVC tubing selected provided an effectively constant volume cavity whose walls were permeable to all physiological gases.

The diaphragm unit

This was designed of suitable external dimensions to be deposited subcutaneously with the tubing attached, so permitting an animal unrestricted movement during the period of time required for equilibration.

The resulting unit was 1 in. in diameter, $\frac{1}{8}$ in. thick and weighed 12 g. The threaded connection ($\frac{1}{16}$ in. diameter) for attaching the pressure lead protruded $\frac{1}{2}$ in. from the casing.

The cavity pressure was measured by applying a variable pressure to the external side of the diaphragm, and sensing its balance by electrical continuity between the diaphragm and a carefully-adjusted contact. The balance could be obtained within 1 min, during which time the displacement of the diaphragm caused negligible change in the quantity of gas in the sealed cavity.

The electrical leads for sensing pressure balance were connected to a transistorized bridge circuit incorporating a relay for operating indicator lights. This provided a maximum current of 5 mA and a 'break' potential of 100 mV between the diaphragm and contact—so eliminating arcing. The balancing pressure (P^1) could be measured to within $\pm 1{\cdot}0$ mmHg if the contact in the diaphragm unit was well adjusted. This could be performed during an experiment, since the screw adjustment is located on the side of the diaphragm remote from the equilibrating cavity. However, this was seldom found necessary after eliminating corrosion by rhodium plating the contact surfaces.

Implantation of the unit

The diaphragm unit and tubing were externally sterilized in absolute alcohol for 4 hr and were introduced, under aseptic conditions, into a rabbit anaesthetized by paraldehyde (1 g/kg) by stomach tube. Supplementary anaesthesia was provided by ether inhalation following atropine sulphate intravenously (1 mg/kg).

The folded plastic tubing was drawn into a stainless steel tube (33 cm × 2·5 mm O.D.) with a cotton thread until the attached diaphragm unit came in contact with one end. The other end was then closed with a stainless steel point. This trochar was gently passed through the subcutaneous areolar tissue from an incision in the skin of the upper thoracic region to the level of the pelvic girdle, where another smaller incision allowed the tip of the trochar to emerge. By gently withdrawing the trochar the loop of tubing was automatically deposited subcutaneously, and the diaphragm unit drawn into the original opening. Four loose stitches through holes in the edge of the diaphragm unit served to secure it to the overlaying skin. The skin wound was closed, effectively burying the diaphragm unit leaving the threaded portion protruding. It was finally located in position by tying off the loose stitches. Two Teflon washers were placed, one internally between capsule and the skin, and the second externally between the skin and a nut lightly screwed down over the protruding threaded portion. These washers acted as a sandwich-board reinforcing the sutures and preventing sloughing of the skin by contact with the metal diaphragm unit.

Finally, a dose of 300 000 I.U. of penicillin was given intramuscularly at the time of operation and repeated daily for 2 days.

The diaphragm unit and tubing remained in position for 2–3 months. The stainless steel, despite Teflon spray-coating, provoked some tissue reaction but the polyvinyl chloride tubing was practically inert. Stainless steel was chosen for the diaphragm casing to withstand both positive and negative pressure changes without distortion or change of volume.

Experimental programme in vivo

The investigation was designed to determine the variation of the 'inherent unsaturation with the pressure and composition of the inspired gas mixture. The experimental procedure took the form of measuring the pressure (P^1) required to balance the diaphragm after 24 hr exposure of the animal to a particular set of conditions. To separate variables, P^1 was measured for:

(1) A range of 0–0·8 in the mole fraction of nitrogen (x) in a mixture of N_2 and O_2 inspired at normal atmospheric pressure (P = 760 mmHg).

(2) A range of external pressure (P) of 480–1761 mmHg (absolute) using air as a breathing mixture of constant composition (x = 0·8).

All experiments were performed upon unanaesthetized animals. Hyperbaric studies were carried out in a positive-pressure chamber, low-pressure studies in a decompression chamber; ground level studies were performed in a polythene tent using pre-mixed gas mixtures perfused at a rate of 2 l/min. The pre-mixed gas was checked for nitrogen content on a Lundin Nitrogen Meter.

Access to the animal when at pressure in the high pressure chamber was not possible, but repeated measurements following 'descent' from the altitude chamber experiments showed no change in cavity pressure within 10 min of reaching ground level. It was assumed the same was true for high pressure exposures.

Three animals were used in the initial trials to show that the unsaturation trends were reproducible, to test tissue reaction to the implanted materials and in modifying the diaphragm unit to give the final design. This design gave consistent results and was used in a fourth rabbit to obtain the readings given in Table 1.

Although earlier readings indicated that the internal cavity pressure had attained 95% of its asymptotic value within 12 hr *in vivo*, final values were not recorded until the rabbit had been subjected to the particular set of conditions for 24 hr.

RESULTS

Table 1 gives values of the absolute pressure (P^1) found necessary to balance the diaphragm after an effectively infinite exposure of the animal to a nitrogen–oxygen mixture at an absolute pressure (P); x is the mole fraction of the inert gas.

The 'inherent unsaturation' (Δp) is somewhat less than ($P-P^1$) on account of volume displacement by the diaphragm in reaching a position of balance.

TABLE 1. Results are shown for 'inherent unsaturation' in an unanaesthetized rabbit exposed to atmospheres of various compositions at constant pressure and at various pressures for constant composition

Days following membrane insertion	Inhaled absolute pressure P (mmHg)	Balancing pressure (absolute) P^1 (mmHg)	Fraction of nitrogen in breathing mixture (x)	Inherent* unsaturation Δp (mmHg)
70	480	395	0·80	18
15	760	113	0	628
37	760	216	0·183	507
16	760	374	0·42	322
17	760	471	0·62	209
19	760	582	0·80	79
27	760	582	0·80	79
29	760	582	0·80	79
68	760	570	0·80	94
33	1116	811	0·80	166
28	1349	950	0·80	236
40	1761	1236	0·80	314

The number of days of the trial, following insertion of the diaphragm unit, are given in column 1.

* Calculated using equation (2).

Let V be the volume of the membrane plus that side of the diaphragm unit with the diaphragm pressed against the casing under the pressure differential developed by virtue of the 'inherent unsaturation'. If v is the volume change due to the diaphragm displacement in reaching a 'balance' position, then the application of Boyle's Law to the gas in the above compartment gives:

$$(P-\Delta p)V = P^1(V+v)$$

since the gas has been expanded by an amount v in reaching the balance pressure P^1

$$\text{Hence } \Delta p = P - P^1 - P^1(v/V) \qquad (1)$$

Calibration of the unit *in vitro* at 37° gave $v/V = 0{\cdot}17$.
Hence equation (1) becomes:

$$\Delta p = P - 1{\cdot}17\,P^1 \qquad (2)$$

The results of Table 1, interpreted according to equation (2) are plotted in Figs. 2 and 3. While the above results refer to the animal in a quiet condition, it was noted that readings of P^1 could fall rapidly if the animal exercised or became excited, Δp values rising by as much as 25 mmHg.

The results in Table 1 indicate that the sum of the gas tensions in the tissue immediately adjacent to the implanted membrane does not attain the absolute pressure of the inhaled

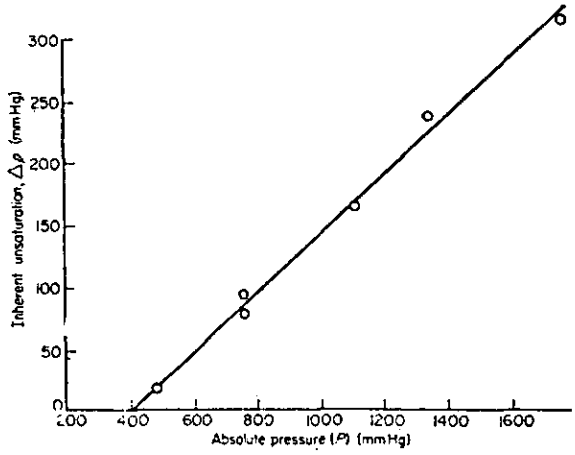

FIG. 2. The values of 'inherent unsaturation' measured after 24 hr exposure to air at pressures varying from 480 to 1760 mmHg absolute, i.e. equivalent to 12 500 ft aerially to 44 ft under water, show a linear increase with respect to absolute pressure. Constant composition of inhaled gas (x = 0·8).

atmosphere, despite an effectively infinite exposure. Moreover, this tension deficit, or 'inherent unsaturation' (Δp) would appear to:

(a) Increase linearly with respect to absolute pressure (P) for a breathing mixture of constant composition (Fig. 2).
(b) Decrease linearly with respect to the mole fraction (x) of the inert gas in the breathing mixture inhaled at constant pressure (Fig. 3).

Since both x and P determine the partial pressure of oxygen in the inspired air, both sets of results can be plotted in terms of the alveolar O_2 partial pressure (P_{A,O_2}) and seem consistent with each other—see Fig. 4.

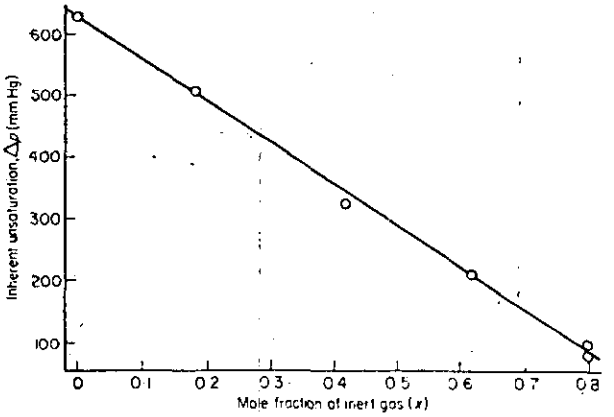

FIG. 3. The values of 'inherent unsaturation' measured after 24 hr exposure at 760 mmHg to varying mole fractions of inert gas (nitrogen), show a linear decrease with respect to the mole fraction. Constant pressure, $P = 760$ mmHg.

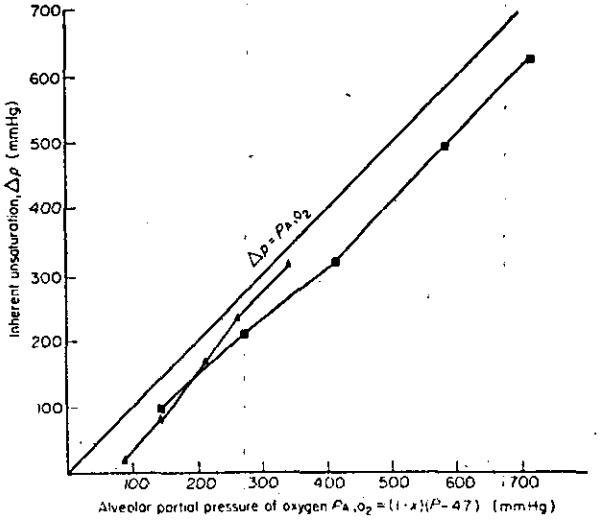

FIG. 4. The results in Table 1 plotted to show the variation in the inherent unsaturation with change of alveolar oxygen partial pressure. Δp can be seen to be less than P_{A,O_2} in all cases by an approximately constant value. ■, $P = 760$, $(1-x)$ varied; ▲, $(1-x) = 0{\cdot}2$, P varied.

DISCUSSION

The foregoing results are consistent with the principal equation of Van Liew *et al.* (1965) if venous values are assumed for the O_2 and CO_2 tensions (Pp,O_2 and Pp,CO_2 respectively) in subcutaneous pockets of gas:

$$\Delta P_{N_2}^{\frac{1}{2}} = (P_{A,O_2} - P_{p,O_2}) + (P_{A,CO_2} + P_{p,CO_2}) \quad (3)$$

where P_{AO_2} and P_{A,CO_2} are the alveolar partial pressures of O_2 and CO_2 respectively. $\Delta P_{N_2}^{\frac{1}{2}}$ is the alveolar to gas pocket tension differential and, by mechanical balance, must equal the 'inherent unsaturation' (Δp). At least this must be so if a minor correction is made to equation (3) to allow for surface tension and tissue elasticity.

However, P_{p,O_2} and P_{p,CO_2} are terms specific to gas pocket analyses and need to be related to ambient conditions to be of mathematical value in programming the decompression of divers or the prevention of decompression sickness in airmen.

More convenient for this purpose is the following expression relating 'tissue unsaturation' (Δp) to the parameters defining the environment—absolute pressure (P) and mole fraction (x) of inert gas in the breathing mixture:

$$(1-x)(P-46)-46 \geqslant \Delta p \geqslant (1-x)(P-46)-86 \quad (4)$$

where Δp is the difference between the absolute pressure and the sum of tissue tensions:

$$\text{i.e. } \Delta p = P-(P_{t,N_2}+P_{t,O_2}+P_{t,CO_2}+P_{t,H_2O})$$

where P_{t,N_2}, P_{t,O_2}, P_{t,CO_2} and P_{t,H_2O} are the tensions of inert gas, oxygen carbon dioxide and water vapour respectively.

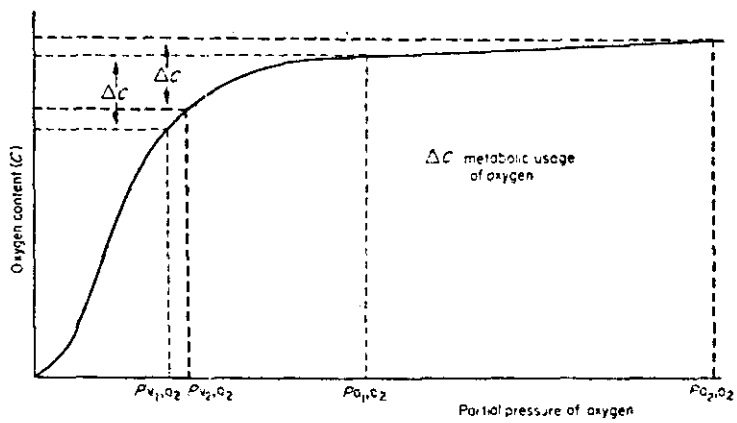

FIG. 5. The dissociation curve of oxygen from whole blood. For a constant metabolic usage (ΔC), it can be seen that widely differing arterial oxygen tensions (Pa_1O_2 and Pa_2O_2) should give similar venous tensions (Pv_1O_2 and Pv_2O_2 respectively).

Equation (4) has been derived (Hills, 1966) from a mathematical physico-chemical analysis in which the 'inherent unsaturation' can be attributed to metabolism by virtue of two principal factors. These are:

(1) The higher solubility of carbon dioxide in cellular material compared with that of oxygen particularly if this $CO_2:O_2$ solubility ratio is of the order of 24:1 quoted for water (Pigford & Colburn, 1950). Thus the only gaseous reagent (oxygen) involved in metabolism is being

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converted into a comparable number of molecules (respiratory quotient 0·71–1) of a gaseous product of far greater solubility. Thus the total tension of CO_2 and O_2 in a cell must be less than the corresponding extracellular total as long as there is active metabolism, i.e. gaseous equilibrium can only occur after death.

(2) The physico-chemical characteristics of the reaction of oxygen with haemoglobin, whereby very similar venous oxygen tensions (e.g. Pv_1,O_2 and Pv_2,O_2 in Fig. 5) can be obtained from widely differing arterial values (Pa_1,O_2 and Pa_2,O_2, respectively) for the same metabolic consumption of O_2.

While the first effect determines the deficit of total cellular gas tension with respect to the extracellular total, the second fixes the arteriovenous difference in total gas tensions. Hence Δp can be estimated as the difference between inspired air pressure and total cellular gas tension if it is assumed that venous blood leaves tissue in equilibrium with the extracellular fluid. This assumption is consistent with inert gas studies whether one assumes that the process limiting the rate of blood–tissue exchange is blood perfusion (Kety, 1948) or both circulation and bulk diffusion into cells of relatively low permeability (Hills, 1967). However, since it is difficult to estimate cellular oxygen tensions, equation (4) expresses the limits set by venous oxygen and carbon dioxide values on one hand and minimum cellular values on the other. The latter have been selected to correspond to the limit where every molecule of oxygen would be instantaneously assimilated by metabolism upon entering the cell.

Equation (4) is consistent with the experimental data given in Table 1 in so far as it predicts that Δp will display: (a) a linear increase with respect to absolute pressure when breathing a gas mixture of constant composition (Fig. 2), and (b) a linear decrease with respect to the mole fraction of inert gas for a constant total pressure (Fig. 3).

The experimental results from the constant volume method described here are in good agreement with those of the constant pressure method (Van Liew *et al.*, 1965). For air at normal atmospheric pressure, the latter authors have estimated $\Delta P_{N_2}^{\frac{1}{2}}$ from equation (3) as 70 mmHg in rats, while Table 1 gives Δp as 79 mmHg in rabbits. However, such values are significantly higher than those of Lategola (1964) (41–48 mmHg) for dogs. Asknes & Rahn (1957) measured Δp in dogs venous blood as 54 mmHg.

The value of 628 mmHg for the unsaturation when the animal was breathing 100% oxygen at normal atmospheric pressure is in good agreement with the value of 600 mmHg quoted by Rahn (1960).

While a comparison of absolute values appears to be influenced by the species selected, there seems little doubt from constant volume results, or from constant pressure results, that Δp and $\Delta P_{N_2}^{\frac{1}{2}}$ increase as the alveolar partial pressure of oxygen increases, whether it be by change of pressure or mole fraction or both. This is shown in Fig. 4 where the alveolar oxygen tension exceeds Δp by a relatively small, yet roughly constant, value over the whole range of O_2 partial pressures used. Thus it would appear that the inert gas came to equilibrium during all runs—or, at least, there would appear to be no evidence for such equilibrium not having been reached.

While the significance of the unsaturation in the treatment of symptoms of decompression sickness has been emphasized by Van Liew *et al.* (1965), it would appear to have a far wider application in the prevention of this syndrome. Besides determining the driving force for the elimination of any gas separated from solution in tissue, it also fixes the position of phase equilibrium.

While the decrease in Δp with x (Fig. 3) is consistent with the proven advantages (Goodman & Workman, 1965) of using oxygen to treat cases of decompression sickness, the results shown in Fig. 2 are probably more significant in diving theory. If the gas phase is present during a conventional decompression, as there is strong experimental evidence to believe (Hills, 1968), then the results would indicate that a greater driving force for inert gas elimination can be obtained by keeping the diver or caisson worker at greater pressure, i.e. decompression time can be employed more effectively at depths greater than advocated in standard schedules. This is the exact reverse of conventional practice (Boycott, Damant & Haldane, 1908) where the subject is kept at the lowest symptom-free pressure in the belief that the maximum extraction gradient for tissue gases is being attained. With the gas phase present this then represents the worst condition on the basis of equation (4) since smaller values of P give smaller values of Δp: Re-deployment of decompression time according to equation (4) has shown savings of up to 35% in total decompression time (Hills, 1966) for the same goats subjected to this approach and to that of the U.S.N. Diving Manual (1943).

ACKNOWLEDGMENTS

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Deep diving and short decompression by breathing mixed gases[1]

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KELLER, H., AND A. A. BÜHLMANN. *Deep diving and short decompression by breathing mixed gases.* J. Appl. Physiol. 20(6): 1267–1270. 1965.—A series of test dives carried out by 14 subjects in depths between 130 and 1,000 ft, for periods varying between 5 min and 2 hr revealed that changes of the inert gas in the breathing mixture permit a considerable shortening of the decompression time. The physical and physiological basis of the method is discussed.

physiological properties of He, N_2, and Ar related to molecular weight and solubility; differences in diffusion rate and saturation speed of He, N_2, and Ar

OXYGEN INTOXICATION in diving can be prevented by reducing the oxygen percentage of the breathing mixture and by a respective replacement with inert gases up to a total gas pressure which must be equal to the water pressure. Since any appreciable rise in ventilation of the lungs causes turbulent flow in the bronchial tree, and the flow resistance increases with rising pressures, it is most desirable to use light inert gases such as helium and hydrogen in order to reduce breathing resistance (2, 4, and others). Another reason for using light gases is the fact that inert gases have a certain narcotic effect which is related to their molecular weight. With nitrogen, light narcotic effects can sometimes be noticed as early as at 6 atm, severe effects and unconsciousness are seen over 15 atm. Deep diving is therefore only possible when the breathing mixtures contain a high proportion of helium or hydrogen. However, light gases diffuse into the body tissues when they are under pressure and out of the tissues when pressure is released more rapidly than heavy gases. This physical process carries an increased danger of bubble formation and entails a prolonged decompression. The advantage of reaching greater depths with light gases is burdened by unduly long decompression times. The present experiments demonstrate how it is possible to reduce decompression times by progressive replacement of the light gases used for diving with heavy gases in the process of decompression.

Two pilot experiments took place in the high-pressure laboratory of the French Navy at Toulon (GERS). These experiments showed that it is possible to reach pressures equal to a depth of 800 and 1,000 ft and to return to the surface without any harm. The decompression times were 47 min for the 800-ft dive and 61 min for the 1,000-ft dive. In another experiment it was possible to demonstrate that 10 min of hard work can be performed at 650 ft with a decompression of only 140 min. This experiment was performed both at Toulon and at the Experimental Diving Unit of the US Navy in Washington D.C. Extensive tests were performed in the high-pressure chamber of the Department of Internal Medicine in Zurich with 14 different subjects including three women at depths between 130 and 1,000 ft. In almost all cases we used semiclosed systems with fresh gas injection of about 20–50 liters (STPD)/min. Oxygen was used always in an open circuit employing a half-face mask. During the experiments in the chamber the gases of the expired mixture as well as the O_2 saturation, CO_2 content, and pH in the arterial and venous blood taken from an arm were analyzed. The nitrogen pressure in the mixture was always less than 4,800 mm Hg (6.4 atm) and the arterial P_{CO_2} below 40 mm Hg. The oxygen saturation of the venous blood varied between 90 and 95%. In some cases the decompression schedule derived from the experience of the fast dives was not adequate and difficulties with bends occurred. Two cases of shock due to hypovolemia secondary to extravascular plasma loss occurred in the chamber after dives with a bottom time of 20 min at 650 ft. Treatment with plasma was successful in both cases (1). In later experiments the decompression time was therefore prolonged and no major difficulties occurred with the corrected decompression schedule listed on Figs. 1–6. It must be mentioned that the calculations for decompression are influenced by variable factors. The decompression times were partly based on empirical data. The calculations can therefore only serve as a guide for the decompression pattern that has to be followed in each case (3).

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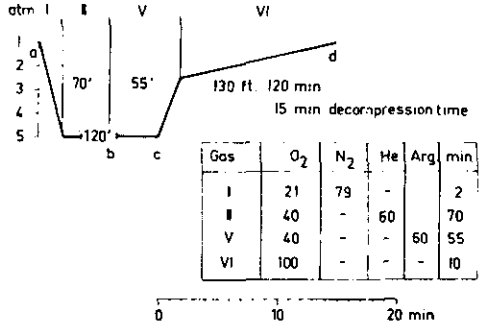
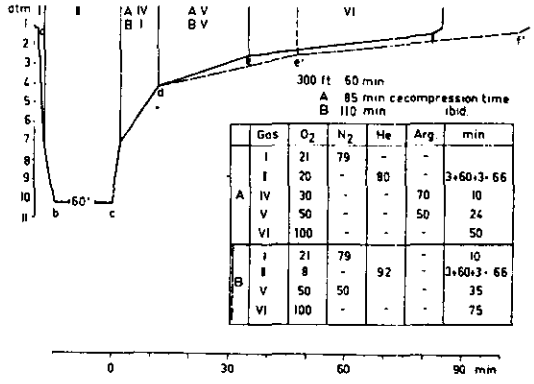


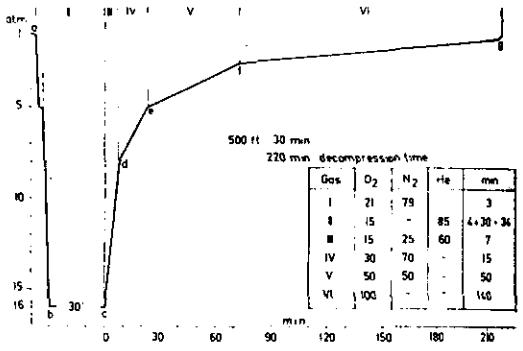
Gas	O_2	N_2	He	Arg	min
I	21	79	-		2
II	40	-	60		70
V	40	-	-	60	55
VI	100	-	-	-	10

FIG. 1. Seven subjects, 130-ft dive with 120 min bottom time.



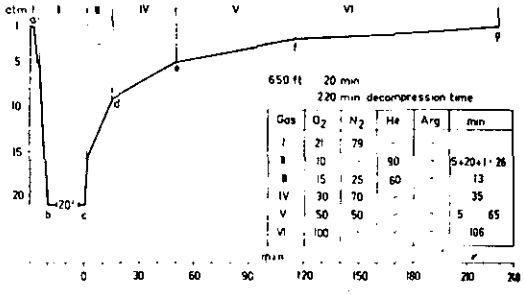
	Gas	O_2	N_2	He	Arg	min
A	I	21	79	-	-	
	II	20	-	80	-	3+60+3·66
	IV	30	-	-	70	10
	V	50	-	-	50	24
	VI	100	-	-	-	50
B	I	21	79	-	-	10
	II	8	-	92	-	3+60+3·66
	V	50	50		-	35
	VI	100	-	-	-	75

FIG. 2. Nine subjects, 300-ft dive with 60 min bottom time



Gas	O_2	N_2	He	min
I	21	79		3
II	15	-	85	4+30+36
III	15	25	60	7
IV	30	70	-	15
V	50	50	-	50
VI	100	-	-	140

FIG. 3. Six subjects, 500-ft dive with 30 min bottom time.



Gas	O_2	N_2	He	Arg	min
I	21	79	-	-	
II	10	-	90	-	5+20+1·26
III	15	25	60	-	13
IV	30	70	-	-	35
V	50	50	-	-	5 65
VI	100	-	-	-	106

FIG. 4. Five subjects, 650-ft dive with 20 min bottom time.

RESULTS

The 130-ft dive with 120 min bottom time was performed with seven different subjects (Fig. 1). At this depth no difficulty arose from breathing heavy gases. Therefore the change from helium to argon was made in the second half of the bottom time. During the argon-breathing period helium was eliminated. The diffusion of argon never led to a critical oversaturation. The last phase of decompression lasting 5 min was made with oxygen. The advantage of the new method with a decompression time of only 15 min is obvious. The same dive using air at the bottom and during decompression would require a decompression of about 210 min; if oxygen is used for decompression it would last 140 min. The determining factors of the short decompression are the change of inert gases and the partial oxygen pressure of 1.7 atm.

Two versions of the 300-ft dive with a bottom time of 60 min were performed with nine subjects (Fig. 2). In version A, during decompression a change was first made from helium to argon and later to oxygen. Total decompression time was 85 min. In version B, nitrogen was used in place of argon. Decompression time was 110 min. The difference is not significant, particularly since the helium concentration was slightly higher than in version A. When using compressed air the same dive requires a decompression time of 458 min. This example demonstrates how the decompression time from medium depth can be considerably shortened with the change of inert gases.

For a dive to 500 ft with a bottom time of 30 min helium was used as the inert gas at the bottom. The change to nitrogen was made in two steps with rising oxygen concentration. The decompression time was 220 min (Fig. 3). Without change of inert gases but with oxygen at 40 ft or less the decompression time would be approximately 260 min (value extrapolated from the table of the US Diving Manual).

The 650-ft dive turned out to be particularly difficult for decompression and was therefore performed with several subjects, 10 times altogether (Fig. 4). The decompression time of 220 min is greater than originally expected for this method. The reduced bottom time of 20 min can still be of practical importance.

The 800- and 1,000-ft dives, both performed with only two subjects, resulted in decompression times of 270 min, which are still acceptable (Figs. 5 and 6). The 1,000-ft dive was also performed in the sea and the diver (*HK*) was able to move freely for about 3 min at this maximal depth.

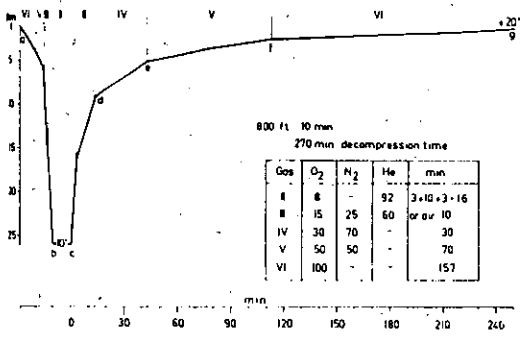


FIG. 5. Two subjects, 800-ft dive with 10 min bottom time.

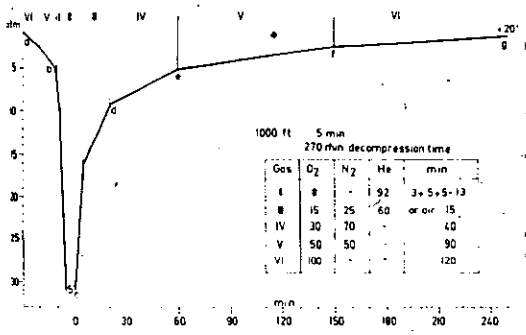


FIG. 6. Two subjects, 1,000-ft dive with 5 min bottom time.

DISCUSSION

The most important and determining factor for the uptake of an inert gas by the blood in the lung from the alveoli is its diffusion rate. The diffusion rate of a gas, i.e., the amount diffusing per unit of time through a membrane for a given pressure gradient, is proportional to the solubility of the gas in the medium and inversely proportional to the square root of the molecular weight of the gas. Table 1 shows the considerable differences of some inert gases in relation to nitrogen.

The saturation of the tissues depends on the saturation speed. The saturation speed of a gas diffusing in a medium is defined as the time elapsing from the moment a certain gas begins to diffuse into a medium free of it until the moment the quantity of gas absorbed is equal to half the quantity that would be absorbed after infinite time. For a given perfusion rate the saturation speed of a gas in a particular tissue is inversely proportional to the square root of the molecular weight of the gas and is independent of the solubility. The real saturation time of a certain tissue or organ is therefore a function of the rate of perfusion. The saturation speed and the perfusion rate are also determining factors during decompression. The desaturation speed is equal to the saturation speed for a given perfusion rate.

TABLE 1. *Physical parameters of various gases applied in diving*

	N_2	Ar	He	H_2	O_2
Atomic or molecular weight	28	40	4	2	32
Solubility in blood, ml/ml, 760 mm Hg, 37 C	0.012	0.026*	0.0088	0.0149	0.02356
Diffusion rate relative to N_2	1	1.81*	1.94	4.63	1.835
Saturation speed relative to N_2	1	0.84	2.65	3.74	0.94

* Approximate value.

The saturation speed for helium or hydrogen is considerably higher than for nitrogen or argon (Table 1). For short dives (bottom time up to 2 hr) the decompression schedule after and while breathing helium takes longer than with nitrogen because the helium saturates a greater proportion of the body tissues than nitrogen would do in the same time. Heavy gases have great advantages for decompression after short dives because of their slow saturation speed. For extremely long dives (over 3 hr) the body gets saturated with either heavy or light gases. The decompression time is proportional to the desaturation speed. The decompression after an extremely long dive with helium is therefore about 2.5 times faster than after a nitrogen dive of equal duration.

The new method applying different gas mixtures for shortening decompression time is based on the idea of using a light gas such as helium for the dive and of replacing it by a heavy gas such as nitrogen or argon during decompression. Since most of the decompression even after a deep dive takes place at relatively shallow depths, it is possible to breathe heavy gases such as nitrogen and argon at this level without the risk of significant tissue saturation and narcotic side effects. The light gas (helium) used at the bottom is rapidly eliminated during decompression because of the high desaturation speed and the large gradient between blood and alveolar gas tension. The amount of heavy gas absorbed by the body tissues at shallow depths is limited because of the small gradient between alveolar gas tension and blood; it is less than the amount of released helium because its diffusion rate is lower and its saturation speed slower than that of helium.

The most important factor for reducing the decompression period is the choice of time for changing from a light gas to a heavy gas. After switching gases the decompression effect increases to a maximum but decreases in function of time because the tissues take up heavy gases which will be subject to decompression as well. In the ideal situation the heavy gases may just reach the critical saturation limit at the end of decompression while the light gas should have been virtually eliminated. In shallow dives it is even possible to switch from helium to nitrogen at the

bottom; while the light gas is being rapidly eliminated at a high speed the heavy gases will only be absorbed at a low speed. In this case it is possible to obtain a desaturation of the body with a switch of gases without any change of the pressure (Fig. 1). For dives with medium bottom time (about 1 hr) it is particularly interesting that the tissues with poor circulation and only partial saturation decompress right from the beginning of the change of gases. Without changing gases a reasonable decompression effect of these tissues would begin in a much later phase of decompression at relatively shallow depths and a lot of time would be lost. The last period of decompression below a pressure of 2.5 atm is usually shortened by breathing pure oxygen.

The reported experiments have demonstrated the validity of the theoretical considerations which served as a basis for reaching greater diving depths and reduced decompression times.

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Calculations of decompression tables for nitrogen-oxygen and helium-oxygen dives. U.S. Navy Exp. Diving Unit

R. D. Workman

1. OBJECT

1.1 Objectives

(1) To detail the development of decompression calculation theory to include the method of Haldane and subsequently developed whole body gas exchange methods.

(2) To describe the modifications to the Haldane method used by the U.S. Navy and present the basis for these changes.

(3) To update the method presented by Dwyer by demonstrating the general case for decompression calculation rather than for air alone.

(4) To provide some textual material for use by student submarine medical officers.

1.2 Scope

1.2.1 This report considers several of the approaches to decompression calculations alternate to the "Haldane method" which have received attention in recent years.

1.2.2 The theoretical justification to the present form of the "Haldane method" as modified for use in the U.S. Navy is presented together with the control limits used for calculation of nitrogen-oxygen and helium-oxygen dives.

1.2.3 An attempt has been made to demonstrate the calculation procedure in step-wide fashion to implement the theory of exponential gas exchange.

2. DESCRIPTION

2.1 Development of the Haldane method

2.1.1 The first systematic study of decompression requirements following exposure of animals and man to increased ambient pressure of air was reported by Boycott, Damant and Haldane in 1908. As a result of numerous pressure exposures of small animals and goats, a rational basis for calculation of decompression schedules was derived. The basic tenets of their procedure, which has become known as the "Haldane method," relate to (1) the estimation of the percent of complete saturation or desaturation of the body tissues with nitrogen during any pressure exposure time-course, and (2) the amount of excess nitrogen pressure in the tissues related to hydrostatic pressure which is permissible without symptoms of decompression sickness resulting during or following the reduction of pressure to one atmosphere.

2.1.2 The processes of saturation and desaturation were considered in the following manner. The blood passing through the lungs of a man breathing compressed air becomes instantly saturated to the full extent with nitrogen at the existing partial pressure in the air. When this blood reaches the systemic capillaries, most of the excess nitrogen will diffuse out into the body tissues, and the blood return to the lungs for a fresh charge. This process is repeated until the tissues are equilibrated with nitrogen at the same partial pressure as in the air breathed. But the blood supply to different parts of the body varies greatly as does the capacity for dissolving nitrogen. It can be seen that the time taken for different parts of the body to become saturated with nitrogen will vary greatly.

2.1.3 Boycott, Damant and Haldane estimated that the whole body of a man weighing 70 kg. will take up about 1 liter of nitrogen for each atmosphere of excess air pressure, about 70% more nitrogen than an equal amount of blood would take up. With the weight of blood in man equal to 6.5% of the body weight, the amount of nitrogen held in solution in the completely saturated tissues would be about 170/6.5, or 26 times as great as the amount held in the blood alone. If the composition of the body were the same in all parts, and the blood distributed itself evenly to all tissues, the body would receive at one complete round of the blood after sudden exposure to increased pressure of air one twenty-sixth of the nitrogen corresponding to complete saturation. Each successive round would add one twenty-sixth of the remaining excess of nitrogen. Thus, it is seen that the body would be half-saturated in less than twenty rounds of circulation, or about ten minutes, and that complete saturation would be practically complete in an hour. The progress of saturation would follow an exponential curve, but it was considered a mistake that this rate of saturation and desaturation could be applied to the body as a whole. Actually the rate of saturation would vary widely in different parts of the body, but for any particular part the rate of saturation would follow a curve of this form, assuming that the circulation rate remained constant.

2.1.4 A variable rate of saturation and desaturation was considered to exist for different parts of the body, relating to the different perfusion rates of tissues with blood. This variable time-course of nitrogen uptake for various parts of the body was simulated by use of a family of discrete hypothetical half-time tissues (5, 10, 20, 40 and 75 minutes) to represent the physiologic processes of gas exchange in the whole body.

2.1.5 In their work with goats, the differences in respiratory exchange rate and cardiac output from man were considered. These were related to man as being two-thirds greater for the goat per kilo of body weight by direct measurement. Thus, a time of 3 hours was thought to be required for complete saturation for goats, while 5 hours was considered required for man. The 75 minutes of half-time would represent 7.5 hours time to 98.5 percent saturation. Therefore, it appears that an attempt was made toward conservatism or in considering that more time might be required for equilibration with nitrogen in some subjects.

Toward defining this, time of exposure to increased pressure was varied in animal experiments, the exposure pressure and decompression time remaining constant. It is not evident from the data reported that equilibration time was defined for man, as most exposures were not sufficiently long. This defect became apparent in the inadequacy of schedules for longer dives derived by this method until half-times of 120 to 240 minutes were used.

2.1.6 Perhaps more important than the estimation of uptake and elimination of nitrogen is the concept of stage decompression which developed from their studies. This makes the fullest use of the permissible difference in pressure between that of the tissue and blood nitrogen to hasten the elimination of nitrogen from the tissues. The limit applied to reduction of hydrostatic pressure was to never allow the computed nitrogen pressure in the tissues to be more than twice the ambient pressure. This 2 to 1 ratio actually assumed equilibration to the ambient pressure of the maximum depth, rather than to the nitrogen partial pressure. The absolute pressure of the maximum depth was then halved to determine the first decompression stop. A special case was assumed for air, for with its 79 percent nitrogen content, the actual ratio of nitrogen pressure upon equilibration to ambient pressure would be

$$\frac{2 \times 0.79}{1} = \frac{1.58}{1} \text{ in place of } \frac{2}{1}$$

2.1.7 It is true that this ignores the presence of oxygen in the breathing mixture as a factor in bubble formation. Extensive diving with nitrogen and helium mixtures enriched with oxygen in excess of 21 percent confirms the absence of significant effect of oxygen as part of the total pressure in decompression. It appears that if sufficient time is permitted for excess oxygen in tissues to be utilized during reduction of pressure, decompression sickness due to this factor is unlikely to occur.

2.1.8 The importance of the initial ascent to initiate the maximum safe gradient for inert gas elimination cannot be overemphasized. Prior to recognition of this concept, ascent to the surface was carried out at a constant rate which unnecessarily exposed the diver to pressure, resulting in further inert gas uptake in tissues which had not completely equilibrated. This increased the magnitude of decompression time required over that actually needed if the diver had achieved the initial decrease in depth compatible with safety. Only the special case of complete total body equilibration requires a continuous ascent at a constant rate to permit the use of a maximum safe gradient for inert gas elimination from the slowest half-time tissue controlling. Even this can follow an initial more rapid reduction of pressure of the order of one atmosphere.

2.1.9 Studies of permissible decrease in pressure considered the two cases of (1) reduction by some absolute value and (2) of that relative to ambient pressure. Haldane noted that goats decompressed from exposure at 6 atmospheres absolute to 2.6 atm had no symptoms. This is a 2.3 to 1 ratio of ambient pressure, with an absolute pressure change of 3.4 atmospheres. Goats were then similarly exposed at 4.4 atmospheres absolute pressure before being decompressed to 1 atmosphere. With the same 3.4 atmospheres absolute pressure change only 20 percent of the animals escaped symptoms.

2.1.10 Decompression schedules for man based on the 2 to 1 ratio concept have not proven to be safe for longer and deeper exposures. Haldane himself recognized this in his book "Respiration" by stating that for air dives exceeding 6 atmospheres absolute, some reduction of this ratio was required.

2.2 Further studies to define decompression limits

2.2.1 Studies by Hawkins, Shilling and Hansen and others by VanDerAue demonstrated that:

(1) the faster half-time tissues sometimes control deep stops even with high tissue ratios.

(2) tissue ratios must be reduced considerably for all components in longer and deeper dives.

(3) the surfacing ratios could be increased to the following values:

half-time (min)	tissue ratio	M(ft.)	M_{actual} (ft.)
5	3.8:1	125	99
10	3.4:1	112	88
20	2.8:1	92	73
40	2.27:1	75	59
75	2.06:1	68	54
120	2.00:1	66	52

The above values were used with slight modification to develop the present Standard Air Decompression Tables.

2.2.2 Ratios used at depth were projected from the surfacing values by using a tenth-power relationship between the tissue ratio at surface and at depth of decompression stop to fit existing data.

$$M = 33\left[\left(\frac{rs}{rd}\right)^{10} + rd - 1\right]$$

M = maximum final tissue pressure in feet of sea water

rs = surfacing ratio

rd = depth ratio at stop

2.2.3 Values for M in which only nitrogen is considered are derived by multiplying by 79 percent those developed with air considered as 100 percent nitrogen, or the absolute pressure of the exposure. With the values for slower half-time tissues required for longer and deeper exposures, the allowable surfacing values are:

half time (h)	5	10	20	40	80	120	160	240
M (ft)	104	88	72	56	54	52	51	50
$\Delta M/\Delta 10$ ft.	+18	+16	+15	+14	+13	+12	+11	+11

2.2.4 A linear projection of the M values to decompression stops at depth is described by a constant additive value listed as $\Delta M/\Delta 10$ ft. This projection is somewhat more conservative than values resulting from the tenth-power relationship described above. Deeper stops are required by this method, though reduction of gradient for elimination of nitrogen is not excessive. Dives calculated with these M values have been safe through a wide range of depth and time of exposure. The linear projection of M values is useful for computer programing as well.

2.2.5 The question as to why the faster half-time tissues permit greater inert gas tensions upon surfacing and at progressively deeper depths than the slower tissues must be faced. Graphical solution of the time-course of inert gas tension permitted for the various half-time tissues upon surfacing shows that within 16 minutes all inert gas tensions of half-time tissues are less than, or equal to, the value for the 120 minutes half-time tissue. Thus, the excess saturation time-course is brief for all except the slower half-time tissues. The same statement can be made for the inert gas tensions permitted at the various decompression stops. As there should be a time-concentration course of probability for bubble formation, a brief time-course of greater excess saturation may be as saf as a sustained time-course of lesser excess saturation. It is apparent from this hypothesis that the magnitude of permissible excess saturation time-course may vary appreciably between that which is sustain d during continuous ascent and that which is periodic with stage d[illegible]ression.

2.2.6 An important factor of difference in permissible tissue tension values for various half-time tissues may well be the greater molar concentration of inert gas for some slow tissues resulting from greater solubility of inert gas in these tissues. As molar concentration of inert gas increases in a tissue the probability for bubble formation would increase upon reduction of hydrostatic pressure as a greater number of gas molecules are available in excess of that held in solution at saturation. In some measure the permissible final tissue pressure values for the various half-time tissues will reflect this variable molar concentration as a time-concentration course permissible to avoid bubble formation in tissues of varying solubility for inert gas.

2.3 Further experiments in gas uptake and elimination

2.3.1 Subsequent experiments in uptake and elimination of nitrogen and other inert gases by Behnke and Shaw have yielded quantitative data to validate the gas exchange processes indicated by Boycott, Damant and Haldane. From data obtained in a series of studies on dogs and human subjects they concluded:

(1) that nitrogen absorption is proportional to the partial pressure of nitrogen in the lungs.

(2) that with the same pressure head, the rate of nitrogen absorption is equal to the rate of nitrogen elimination.

(3) that the time for complete nitrogen elimination, and percentage rate of nitrogen elimination for corresponding periods of time, are the same irrespective of the quantity of nitrogen absorbed by the body.

2.3.2 However, the precise end-point of nitrogen elimination could not be measured with accuracy, with the result that the slowest tissues to be considered in calculation of decompression schedules appeared to be those that were 98 $\pm$ 2% desaturated at the end of 6 hours. This led to the conclusion that it was unlikely that compressed air illness following long exposure to increased pressure resulted from an underestimation of the time required for nitrogen elimination. Experimental values for the nitrogen elimination curve gave further support to the multiple tissue theory of calculation developed by Haldane by demonstrating the variation in distribution of blood flow in relation to the distribution of nitrogen in the body.

2.4 Factors of difference in exchange of various inert gases

2.4.1 When trying to analyze the mechanism of gas uptake and elimination, there are at least two factors, assuming respiration and cardiac output to remain constant, which govern the saturation or desaturation half-time for non-reactive tissues:

(1) capacity of the tissue for storage of gas

(2) effectiveness of gas transport to and from the tissues.

It is obvious that if a tissue is continuously perfused by blood, supposing the gas to be carried away at a certain rate, the time required for elimination is longer the greater the gas content of the tissue. If different gases are compared for the same tissue, the storage capacity is proportional to the solubility coefficients for the gases in the tissue. At the same time, the period for gas equilibration between tissue and blood is shorter the better the gas transport.

2.4.2 From the body gas exchange curve

$$Pt = Po\ e^{-kt}$$

Where Pt = tension of gas after time t

Po = tension of gas at t = o

e = base of natural logarithm

k = constant of elimination

the value of k is found to not remain constant, but to decrease progressively, the shape of the curve thus differing from those of its hypothetical and exponential components each having its own constant k.

2.4.3 By definition, the half-time (h) is that time required to reduce Po to half its original value. For each discrete value of k, therefore

$$h = \frac{0.693}{k}$$

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

Where: c = a constant of proportionality

C = symbol of gas transport effectiveness

S = solubility coefficient for the gas in a tissue

Therefore, the desaturation half-time (h) is also proportional to the solubility coefficient of the gas in a particular tissue, and inversely proportional to the effectiveness of gas transport from the tissue.

$$h = \frac{1}{c} \times \frac{S}{C}$$

2.4.4 In highly vascularized tissues, the high blood-tissue perfusion rate may mask differences in diffusion rates of inert gases, half-time for different gases in the tissue varying only as determined by the solubility coefficients. For poorly vascularized tissues, equilibration half-times of different gases should vary as determined by solubility coefficients plus diffusion rates.

2.4.5 Theoretically, the body-exchange curve representing the rate of uptake and elimination of inert gas by the body as a whole is the sum of an infinite number of exponential curves with different half-times, each representing tissue regions with the same individual ratio of fat-fluid content to efficiency of gas transport. Helium having a low solubility in fat compared to nitrogen may yield a shorter half-time than nitrogen in a tissue rich in fat and having an efficient gas transport. The differentiation of an amount of tissue defined by a nitrogen half-time into several types of tissue having different half-times when another gas is substituted for nitrogen is in accordance with the results of Jones et. al., which support the principle that the varying decay terms of the component exponential expression (e^{-kt}) are not to be referred to as anatomically defined phases.

2.4.6 In fatty tissues the exchange rates differ from the blood-tissue perfusion rate by a factor of the ratio blood solubility/tissue solubility of the gas concerned. Thus, for helium, the final concentration in the fatty tissues will be less than for nitrogen when the exposure is to the same partial pressure of these gases due to the lower fat solubility of helium ($He/N_2 = 1/4.5$). However, some of the slow tissues may be characterized more by a poor blood-tissue perfusion rate than by high fat content, differences in fat solubility of the gases having less influence on the elimination time. Thus, the different kinds of arbitrary tissues within the same half-time class may well represent different fat-fluid ratios and blood-tissue perfusion rates, though the average of their ratios is constant. If helium is substituted for nitrogen, the classification, which is a physiological rather than an anatomical one, may cause new tissue combinations to arise with common half-time for this gas. Theoretically, the arrangement of different half-time groups will remain unchanged from one gas to another only for gases with the same fat-water solubility ratio, as for argon and nitrogen at 5.2/1. Thus, the half-time would be multiplied by the ratio of argon/nitrogen solubility coefficients in oil and water (2/1).

2.4.7 It has been determined experimentally that for helium diving somewhat deeper decompression stops are required to prevent bends than for air diving. Behnke considered this to be due to the rate of helium diffusion into the blood stream being more rapid than for nitrogen, thus making bubble formation more likely if the early stages of decompression are too rapid. However, comparison of the helium and nitrogen elimination curves for subjects demonstrates the quantity of helium eliminated to be one-third that of nitrogen for any comparable time period. Recent studies of bubble growth and resolution in water have indicated that the growth rate of helium bubbles in solutions of equal concentrations of the respective gases should be six times greater than for nitrogen bubbles. This is due to the lesser solubility and greater diffusibility of helium in either aqueous or fatty tissues.

2.5 Decompression studies based on the whole body gas exchange process

2.5.1 Several attempts have been made to develop decompression calculation procedures based upon the whole body uptake and elimination curves for nitrogen and helium. Behnke devised a method in which the quantity of excess nitrogen taken up during any depth-time exposure was related to the percent of whole body uptake of nitrogen with time on the whole body gas exchange curve. Decompression schedules prepared on the basis of this method were not reported.

2.5.2 Several workers at the Royal Naval Physiological Laboratory have been the most recent proponents of this method. Hempleman found a good correlation of the minimal decompression dives permissible when air is breathed, to a constant value as follows:

$$k = D\sqrt{T}$$

where: $k = 500$

D = depth in feet of sea water

T = exposure time in minutes

2.5.3 It was noted that this method did not accurately predict the depth of the permissible exposure in excess of 100 minutes. The form of the equation appeared to be similar to that for diffusion processes, so that further definition of this method has been in developing equations to simulate the diffusion gas exchange process.

2.5.4 Rashbass further expanded the development of the theory of the diffusion-limited gas exchange process using modifications of equations developed by A. V. Hill to explain diffusion of oxygen in various geometrical models of tissues. A limit of 30 feet of excess gas taken up was permitted at any ambient pressure. Dive schedules calculated by this method required deeper stops than conventional air schedules, and time spent at shallower stops tended to be of equal length. While shorter working dives in the dry chamber were reasonably safe, open-sea testing of these schedules produced a high incidence of bends.

2.5.5 Duffner applied a similar calculation procedure to that of Hempleman in deriving decompression schedules for helium-oxygen dives with mixed gas scuba. He developed the following power function equation to fit experimentally determined minimal decompression dives:

$$Q = DAt^x$$

Q = excess helium in feet of sea water = 37 ft..

D = exposure depth in feet of sea water

A = constant equal to the fraction of available excess helium in feet of sea water taken up when t = 1

t^x = time in minutes

x = 1

Values of At^x from 1 to 180 minutes were derived and presented in tabular form. The time to be spent at a decompression stop is determined by the following equation:

$$t = \left[\frac{Q - (37 + DNS)}{(Q - Ds)0.083}\right]$$

Ds = depth of present stop

DNS = depth of next stop

2.5.6 Decompression schedules calculated by this method either for air or helium-oxygen dives relate closely to those derived by the Rashbass method; that is, deeper stops are required, and the shallower stops for longer exposures tend to be of the same duration. A comparable result can be obtained by use of a single half-time tissue of 60 minutes with a 2 to 1 ratio limiting, when the Haldane method is employed. Thus, it is apparent that insufficient consideration of slower half-time tissues representing poorly perfused areas of the body is given by the diffusion-limited methods of calculation as presently constituted. Longer and deeper dive schedules calculated by these methods have proven to be grossly inadequate in providing safe decompression.

2.6 Definitions and symbols

2.6.1 Depth (D) is the vertical distance below the surface at any phase of the dive. The units of depth are feet of water.

2.6.2 Absolute depth (A) is the absolute pressure at any depth (D) expressed in feet of water. A is always 33 feet greater than D, except in the special condition of diving at other than sea level, as in a mountain lake.

2.6.3 The oxygen percentage decimal (X) expresses the oxygen content of the breathing medium during each phase of the dive.

2.6.4 The inert gas percentage decimal (G) expresses the inert gas content of the breathing medium during any phase of the dive. It is derived by substracting the breathing medium oxygen percentage decimal (X) from unity (1.00).

2.6.5 The inert gas partial pressure (N) represents the sum of the partial pressures of all gases in the breathing medium other than oxygen. N is derived by multiplying the absolute depth (A) by the inert gas percentage decimal (G). Special procedures may require handling several inert gases separately, as in the calculation of helium-oxygen decompression schedules.

2.6.6 The initial tissue pressure (P) is the partial pressure of inert gas in a tissue at the start of any particular time interval. When there has been no dive within 12 hours prior to the dive being considered, the initial tissue pressure for all tissues at the start of the dive is taken as that in air. For repetitive dives within a 12 hour period, the amount of inert gas remaining in tissues must be calculated during the time interval on the surface. For each step in the decompression calculation, the final tissue pressure (Q) of one step becomes the initial tissue pressure (P) of the next step.

2.6.7 The differential pressure (E) is the difference between the inert gas partial pressure (N) of the breathing medium and the initial tissue pressure (P). (E) represents the driving force for inert gas exchange, being positive (+) if (N) is greater than (P), indicating that the tissue gains inert gas. The value of E is negative (-) if (N) is less than (P), indicating that the tissue loses inert gas.

2.6.8 The tissue pressure change (S) is the increase or decrease of tissue pressure during a time interval, resulting from the existence of a differential pressure (E). It is derived by multiplying (E) by the time function (F) for the time interval. (S) is positive (+) or negative (-) according to the sign of (E).

2.6.9 The final tissue pressure (Q) is the partial pressure of inert gas in the tissue at the end of a time interval. (Q) is the sum of (P) and (S). (Q) for one interval becomes (P) for the next interval.

2.6.10 The time interval (T) is the duration in minutes of any specific phase of the dive considered. These phases are usually taken as (1) the exposure (2) the ascent (3) the first stop (4) each of the subsequent stops (5) in repetitive dives, the surface interval.

2.6.11 The exposure time interval includes both time of descent and time at depth. Unless descent is slower than the normal rate, there is no separate calculation for descent time.

2.6.12 The ascent time interval depends on the depth of the first stop and the rate of ascent. In standard diving practice the rate is 60 feet per minute or less.

2.6.13 The time interval (T) at each stop depends on the length of time required to desaturate the "controlling tissue" to a (Q) equal to or less than the maximum tissue pressure (M) permitted for the next stop.

2.6.14 The surface time interval must be considered when it is less than 12 hours to the next dive. The (Q) at the end of the surface interval is the (P) for the next exposure.

2.6.15 Saturation is the process of gaining inert gas during exposure to a positive differential pressure (E). The process is complete when (Q) equals (N) in the breathing medium.

2.6.16 Desaturation is the process of losing inert gas during exposure to a negative differential pressure (E). This is complete when (Q) equals (N) in air at the surface.

2.6.17 The tissue half-time (H) is the specific time interval (T) required to produce a tissue pressure change (S) equal to half of the differential pressure (E) acting at the beginning of the interval. In calculations, tissues are designated by their half-time. The body is probably composed of an infinite number of tissues with half-time from zero to 240 minutes or more. For calculations the range of tissues is sampled in a geometrical progression of half-times consisting of 5, 10, 20, 40, 80, 120, 160, 200 and 240 minutes. A 40 minute increment of half-time tissues is used in excess of 40 minutes half-time to insure adequate sampling of time obligation for decompression.

2.6.18 The time unit (U) is the number of half-times in a given time interval (T) for a tissue with a specific half-time (H). It is therefore the ratio (T/H) of the time interval to the half-time of the tissue, and is dimensionless. The time unit (U) is different for each tissue half-time (H) being considered for a given time interval (T). The time unit normally ranges from 0.000 to 6.000, and is related to the time function (F) as follows:

$$F = 1 - 1/2^{U}$$

Tables of time unit against time function, and time function against time intervals for specific half-times are used in calculations.

2.6.19 The time function (F) is the ratio of the amount of change (S) to the differential pressure (E). When a differential pressure(E) acts on a given half-time tissue, the initial tissue pressure (P) changes by a specific amount (S) in any given time interval (T). The total amount of change (S) increases with the time interval (T), so that the time function (F) also increases. The value varies from 0.000 to 1.000 in a special relation to the time unit.

2.6.20 Since F = S/E, then S = FE. Thus, the amount of change in tissue pressure for a specific time interval can be determined. During decompression a certain amount of tissue pressure change (S) must occur during the time interval (T) to reduce the final tissue pressure (Q) to within limiting values of (M), so that depth can be decreased by ten feet to the next stop. The time interval required is determined from the relationship F = S/E.

2.6.21 The maximum tissue pressure (M) is the greatest partial pressure of inert gas in a specific tissue which will not permit bubbles to form in the tissue at a given absolute pressure. The values of (M) for each half-time tissue and depth of decompression stop are tabulated for convenience in calculation. The final tissue pressure (Q) must fall to or below the values of (M) for the next stop before ascent to that stop.

2.6.22 Values of (M) are derived from safe minimal decompression exposures of variable depth and time to the inert gas mixture being considered, as air or helium-oxygen. From these exposures, the value of (Q) upon surfacing is calculated for each half-time tissue to derive the maximum permissible values of Q = M. As discussed previously, the values of (M) could not be safely projected for decompression stops on the basis of a constant ratio to ambient pressure as indicated by Haldane. Following a considerable amount of evaluation of experimental dives, a method of projecting (M) values to depth of stops with a constant factor of increase per 10 feet depth change has been developed. This relates closely to the tenth-power relationship of surface to depth ratio of Dwyer, but permits greater flexibility. The rate of change of values of (M) with absolute depth varies with the inert gas breathed, as also do the permissible surfacing values. Thus, values of (M) for air dives do not provide sufficient depth of decompression stops for helium dives (Tables N and H).

2.6.23 Supersaturation is an unstable state occurring when the initial tissue tension (P) exceeds a value of the inert gas partial pressure (N), which represents the maximum equilibration state of the gas in a tissue at the absolute pressure. The maximum tissue pressure (M) allowable at any given absolute depth is a value exceeding (N) such that the tissue will not release inert gas in the form of bubbles. The initial tissue pressure (P) is always greater than (N), such that the differential pressure (E) is algebraically negative, and the tissue will lose inert gas.

2.6.24 The controlling tissue for ascent is that which must stop at the greatest depth to avoid bubble formation, and for a given stop is that which requires the longest time to desaturate to the maximum tissue pressure (M) permitted at the next stop. At a given decompression stop some initial tissue pressures (P) will be greater than the corresponding maximum tissue pressures (M) permitted at the next stop. Each final tissue pressure (Q) must be equal to or less than the maximum tissue pressure (M) for the next stop before the tissue can ascend to that stop.

2.7 Theory of exponential saturation

2.7.1 The need for decompression arises when tissue saturation with inert gas reaches the point that the tissue can no longer surface directly without bubble formation. This is necessary for saturation dives on air exceeding 33 feet, and 37 feet when 80 - 20% HeO_2 is breathed.

2.7.2 Final tissue pressure (Q) at the end of any time interval (T) is the sum of the initial tissue pressure (P) and the tissue pressure change (S) during the interval.

$$Q = P + S$$

2.7.3 Initial tissue pressure (P) at the start of an interval is the final tissue pressure (Q) for the preceding interval.

$$P_2 = Q_1$$

2.7.4 Tissue pressure change (S) during an interval depends on the existence of a differential pressure (E) and the exponential function (F) of the time interval (T). The tissue pressure change (S) is the product of the time function (F) and the differential pressure (E).

$$S = (F)(E)$$

2.7.5 The differential pressure (E) is the difference between the inert gas partial pressure (N) to which the tissue is exposed and the initial tissue pressure (P) at the start of the exposure.

$$E = N - P$$

2.7.6 The time function (F) is a specific exponential function of the time unit (U).

$$F = 1 - 1/2^U$$

2.7.7 The time unit (U) is the ratio of the time interval (T) to the half time (H).

$$U = T/H$$

2.7.8 The entire theory of exponential tissue saturation can be expressed in a single equation as follows:

$$\begin{aligned} Q &= P + S \\ &= P + (F)(E) \\ &= P + (1 - 1/2^U)E \\ &= P + (1 - 1/2^U)\ (N - P) \\ &= P + (1 - 1/2^{\frac{T}{H}})\ (N - P) \end{aligned}$$

2.8 Theory of control of excess saturation of tissues

2.8.1 A tissue can hold some amount of dissolved inert gas in supersaturation. The amount depends on the absolute pressure around the tissue. Haldane considered the ratio of maximum tissue pressure (M) to absolute depth (A) to be a constant for all half-time tissues. Prior discussion has considered the application of a relative relationship of (M) >(A) dependent on (A) and the specific half-time tissue (H).

2.8.2 A tissue gains inert gas during a dive. At the end of the dive, the absolute depth to which the tissue can ascend is determined by the tissue pressure at the end of ascent. Values of maximum allowable tissue pressure (M) at 10 foot increments of stops are presented in tabular form for both nitrogen-oxygen and helium-oxygen dives. (Tables N and H).

2.8.3 At each decompression stop the controlling tissue determines the time interval (T) for the stop. The final tissue pressure (Q) must be equal to or less than the value of (M) for that tissue permitted at the next stop before all tissues may ascend to that stop.

$$Q \leq M$$

2.8.4 The minimum tissue pressure change (S_{min}) required at a stop is at least the difference between the initial tissue pressure (P) and the value of (M) at the next stop.

$$S_{min} = M - P$$

2.8.5 The differential pressure (E) for the controlling tissue is:

$$E = N - P$$

Both (S) and (E) are algebraically negative. The ratio (S/E) of the required tissue pressure change to the acting differential pressure is the least value of the time function for the controlling tissue at a given stop.

$$F \text{ min} = S \text{ min}/E$$

The least time function (F min) corresponds to some minimum time unit (U min) and to some minimum time interval (T min) for the controlling tissue half-time (H).

2.8.6 Control generally shifts from the faster to slower half-time tissues during decompression. During the deeper stops the slow tissues frequently have positive values of (E) and continue to gain gas at these stops. Subsequent requirement to lose gas places these slower tissues in control at the shallower stops.

2.8.7 Table U is a tabulation of time function (F) against time unit (U). Values of (F) are given to three decimal places, and (U) to two decimal places. The left-hand column shows the integer and the first decimal of the time unit. The other columns are headed by the second decimal of the time unit, and show the corresponding time function.

2.8.8 Table T is a tabulation of time interval (T) in minutes from 1 to 150 and time function (F) for the various half-time tissues.

2.9 Decompression calculation worksheet

2.9.1 Minimal calculation of decompression requires handling the several tissues simultaneously. This is aided by use of the worksheet on which the entire dive is divided into several steps (Figure 1).

(1) Exposure

(2) Trial first stop and ascent

(3) First stop

(4) Succeeding stops

(5) Surface interval

2.9.2 The top section is for ambient conditions for any phase of the dive, including D, A, N and T. The other sections are divided into U, F, E, P, S, Q, and M. A special section box (G) is provided, though this may vary with the breathing mixture during the dive. Box (H) provides for six different half-times to be considered (Figure 1).

3. PROCEDURE

3.1 Calculation of decompression schedules

3.1.1 The various components of the calculation required to derive the final tissue tension (Q) for each step of the dive have been defined in prior discussion.

3.1.2 Where

$$Q = P + S$$
$$P = N = G \times A$$

when there has been no previous pressure exposure for 24 hours. The inert gas partial pressure of the breathing medium (N) at each phase of the dive is derived similarly:

$$N = G \times A$$

3.1.3 The time function (F) is then determined for the exposure period time interval (T) from Table T, or Table U, if this exceeds 150 minutes.

3.1.4 E can then be determined from N - P, as these values are known.

3.1.5 S is then determined from FE, the algebraic sign being observed.

3.1.6 Q then equals P + S, added algebraically for each half-time tissue at each step of the dive.

3.1.7 Depth of first stop is determined for (Q) resulting from the time interval (T) accrued at 60 fpm ascent.

3.1.8 The value of (N) is determined as the mean value between that of the exposure depth and that of the first stop.

3.1.9 A trial first stop is evaluated by comparing values of (P) at beginning of ascent to values of (M) for the various half-time tissues.

3.1.10 The resulting (Q) values after ascent, as affected by change (S) = FE, must be equal to or less than the value of (M) for each half-time tissue, (Table N and H)

3.1.11 The time interval (T) required at each stop is determined from the expression F = S/E where S = P - M, the change in (P) required to reduce it to a value equal to or less than M permitted at the next stop ten feet shallower for all half-time tissues (H).

3.1.12 The time interval (T) is thus calculated for each subsequent decompression stop until the surfacing value of (M) is reached and ascent to the surface permitted.

3.1.13 Calculation of the surface time interval (T) is necessary in the analysis of repetitive dives, to determine the initial tissue pressure (P) at the start of succeeding dives. The procedure is identical to that described, with the initial tissue pressure (P) being the final tissue pressure (Q) upon surfacing from the preceding dive.

3.2 Calculation worksheet

3.2.1 A sample calculation worksheet is included as Figure 2 to demonstrate a sample calculation for a 180 foot-30 minute air dive. Values of M for nitrogen-oxygen dives from Table 1 are used.

3.2.2 Figure 3 demonstrates the calculation procedures used for a 200 foot 30 minute helium-oxygen dive in which 75 - 25% HeO_2 is breathed during the exposure and ascent to a depth of 50 feet, where oxygen decompression is begun until surfacing is permitted. Table 2 gives values of M for helium-oxygen dives.

3.3 Calculation of oxygen decompression

3.3.1 Oxygen decompression is usually considered to be 80% efficient due to leakage of air or helium into the mask. Thus, in deriving N = GA, G = 0.2 as the inert gas fraction. When oxygen is breathed at one or more atmospheres pressure for in excess of 30 minutes, some reduction in tissue perfusion occurs to effectively prolong the time required to eliminate inert gas from the tissue. Reduction of tissue perfusion by 25 percent will require 133 percent of the time to accomplish the same perfusion for each half-time tissue. This factor may be applied to the time interval (T) derived by the regular calculation procedure when oxygen breathing is sustained for 30 minutes or more.

3.4 Calculation of decompression for deeper working dives

3.4.1 It is also recognized that inert gas uptake during work will be greater than during rest due to increased cardiac output and tissue perfusion. Elimination of inert gas during rest periods will also be more prolonged than during work. Determination of M values for working dives does provide for the difference in inert gas uptake in some measure.

3.4.2 However, as the depth of the dive increases, the differential pressure (E) becomes greater than for minimal decompression dives for which surfacing M values are derived. It appears that for dives in excess of 200 feet, some factor must be multiplied by the time interval of the exposure to provide for the additional inert gas uptake with work. A factor of 1.5 provides well for many dives tested, though a factor of 2.0 was used in calculation of the helium-oxygen schedules in the present diving manual.

4. RESULTS

4.1 Decompression Schedules

4.1.1 Upon completion of the calculations for the ten foot stop, tabulate the data for the decompression schedules as follows:

Depth (ft)	Bottom time (min)	Time to first stop (min)	Decompression stop (min) (ft) 40	30	20	10	Total Ascent time (min)
200	30	2.7	2	9	22	37	73

Breathing mixture: air (79 - 21% Nitrogen-oxygen)

(1) For the dive exposure show the depth and time

(2) For the ascent show the time to the nearest tenth of a minute

(3) For the decompression stops show the depth in feet and time in minutes

(4) Show the total ascent time in minutes

(5) Show the breathing mixture percentage of inert gas and oxygen. If this changes during the exposure period or at decompression stops, this must be noted at these depth and times.

5. DISCUSSION

5.1 Other methods

5.1.1 Several other methods can be used to calculate decompression schedules. No attempt has been made to present all the possible methods or to assess these critically. All those based on Haldane's theories give similar results, varying only with the controlling limits of excess saturation permitted at various ambient pressures, when the same breathing mixtures are employed.

5.1.2 The necessity to consider longer half-time tissues for deeper and longer exposures has only recently become apparent. This has been necessary for helium-oxygen dives, as well as those in which nitrogen-oxygen mixtures are breathed. For the most part, dive exposures have not been of sufficient magnitude to test this requirement until recently. This is only a necessary modification to the basic method devised by Haldane.

5.1.3 Testing of dive schedules developed by the methods employing a diffusion-limited inert gas exchange formulation have been the only others considered adequate to permit a judgment. For the most part the results have not been as satisfactory as the schedules developed by the Haldane method, as modified for use by the U. S. Navy. It is possible that further effort with the former method may be more rewarding.

5.1.4 Continuous ascent decompression can be calculated by the method presented, as well as stage decompression. The mean absolute depth (A) and inert gas partial pressure (N) of the breathing medium is calculated for the increment of depth change considered. The time required for the controlling tissue to lose a sufficient amount of inert gas to ascend to the depth desired is then calculated. The procedure is followed until the surface is reached.

5.1.5 Control of continuous ascent is possible in the decompression chamber after transfer of the diver under pressure from the submersible decompression chamber. It is not possible in the water unless conditions are optimal for accurate depth keeping, which is seldom the situation in open sea diving.

5.1.6 There are several theoretical advantages of continuous ascent decompression over the stage method. First, the maximum safe gradient (E) for elimination of inert gas can be maintained to result in reduction of decompression time required for the same dive exposure. The greatest time saving occurs in decompression from saturation dives, where the slowest half-time tissue controls. Maintenance of the maximum safe gradient will permit elimination of the excess inert gas in about one-fourth the time required by the stage method under such conditions.

5.2 Inadequacies of decompression prediction

5.2.1 The present information concerning concentration of various inert gases at anatomical sites during the elimination time-course is quite inadequate. Whole body inert gas elimination studies of exhaled gas are not particularly helpful in further defining this information. Increasing refinements of this technique are also unlikely to produce information that is particularly helpful. Data needed can only be derived from inert gases which are tagged with radioactive tracers. Unfortunately, the gases of interest, nitrogen and helium, do not have isotopes of sufficient half-life to make this a useful method. Since the gases with longer isotope half-life as xenon and kryton have much greater solubility coefficients in tissues than nitrogen and helium, their tissue concentrations are not apt to be predictive of those of the respirable gases of interest. Thus, much dependence is still placed on design of decompression studies to attempt to define permissible inert gas time-concentration course in tissues during dive exposures.

5.2.2 Since quantitation of decompression adequacy is still dependent primarily on presence or absence of symptoms related to decompression sickness, definition is only relatively gross. Ultrasonic methods of bubble detection in vivo and in vitro are being explored to permit better definition of decompression adequacy, but this is still in its early stages. Observation of micro-circulation of the bulbar conjunctiva to detect changes in circulation, presence of intra-vascular agglutination, and possible presence of bubbles presents another possibility for quantitation, but this too is in an early stage of investigation.

5.2.3 Evaluation of decompression schedules is greatly complicated by marked intra and inter-individual differences in susceptibility to decompression sickness. Little is known of the mechanisms involved. A definite acclimatization occurs in caisson workers and divers through repeated exposure to pressure. Coincidental to these exposures may be a significant increase in physical conditioning with the work involved to improve cardiac output and tissue perfusion efficiency. An improvement of these factors should facilitate inert gas exchange efficiency, to thus reduce the excess saturation time-course of inert gas in tissues and decrease the probability for bubble formation. Excess fatigue and relative ill-health in divers has been observed to increase the risk of bends following schedules which have been safe on other occasions. Factors decreasing tissue perfusion such as exposure to cold or PO_2 of one atmosphere or more during the depth exposure and decompression, may also play an important part in prolonging the inert gas elimination such that prediction in the calculation procedure is grossly impaired. It is apparent that such variables impose severe constraints on any method of calculation to provide adequate decompression schedules.

5.3 Validity

5.3.1 The multiple tissue theory and the half-time exponential saturation theory have received criticism because the resultant decompression schedules are not always satisfactory. This is particular true of the schedules for long, deep dives. However, no other method has yet produced comparably satisfactory decompression schedules with such a low overall incidence of decompression sickness.

5.3.2 A recent review of air and helium dives in the U. S. Navy requiring decompression over a recent two year period gave an incidence of 0.69% and 0.83% bends, respectively. When it is considered that hundreds of no decompression dives were not included, and that not all the dive records were available, but that the reports of decompression sickness were available, this is a somewhat conservative estimate. Considering all the possible variables, it seems unlikely that very great improvement in the calculation procedure to provide safer schedules can be expected.

6. CONCLUSIONS

6.1 Conclusions

(1) This report provides background information on the development of the Haldane method of decompression calculation as modified for use by the U. S. Navy.

(2) Other methods of decompression calculation developed in recent years are reviewed and appraised in reference to that described above.

(3) The step by step procedure of calculation exployed is detailed as it implements the application of the theory. Examples of calculations of dive schedules are presented for both air and helium-oxygen dives.

6.2 Recommendations

(1) Computer programs have already been developed employing the basic format presented here. As the dive schedules calculated are tested, report the results of these evaluations with any modifications of the calculation procedure required to produce safe schedules.

(2) That this report be used for instruction to acquaint personnel with the theoretical basis of decompression calculations and to guide them in calculating dive schedules.

(3) That this report be revised or superceded as a text as this becomes necessary.

7. FIGURES AND APPENDICES

7.1 Figures

7.1.1 Figure 1 is a worksheet for the calculation of decompression schedules. The use of the worksheet and definition of symbols is described in the text.

7.1.2 Figure 2 is a sample decompression calculation of a 180 foot-30 minute dive on air using the worksheet in figure 1.

7.1.3 Figure 3 is a sample decompression calculation of a 200 foot-30 minute dive on 75-25% helium-oxygen using the worksheet in figure 1.

7.2 Appendices

7.2.1 Appendix A presents Table U, a tabulation of the time function against the time unit.

7.2.2 Appendix B presents Table I, a tabulation of the time function against the time interval for various tissue half-time.

7.2.3 Appendix C presents Table N, a compilation of maximum allowable tissue tensions (M) at decompression stops for nitrogen-oxygen dives.

7.2.4 Appendix D presents Table H, a compilation of maximum allowable tissue tensions (M) at decompression stops for helium-oxygen dives.

7.2.5 Appendix E presents Table D, a compilation of maximum allowable tissue tension (M) at decompression stops for air dives, based on a 10th power relationship of surface and depth ratios, used in calculation of the U. S. Navy Standard Air Decompression Tables.

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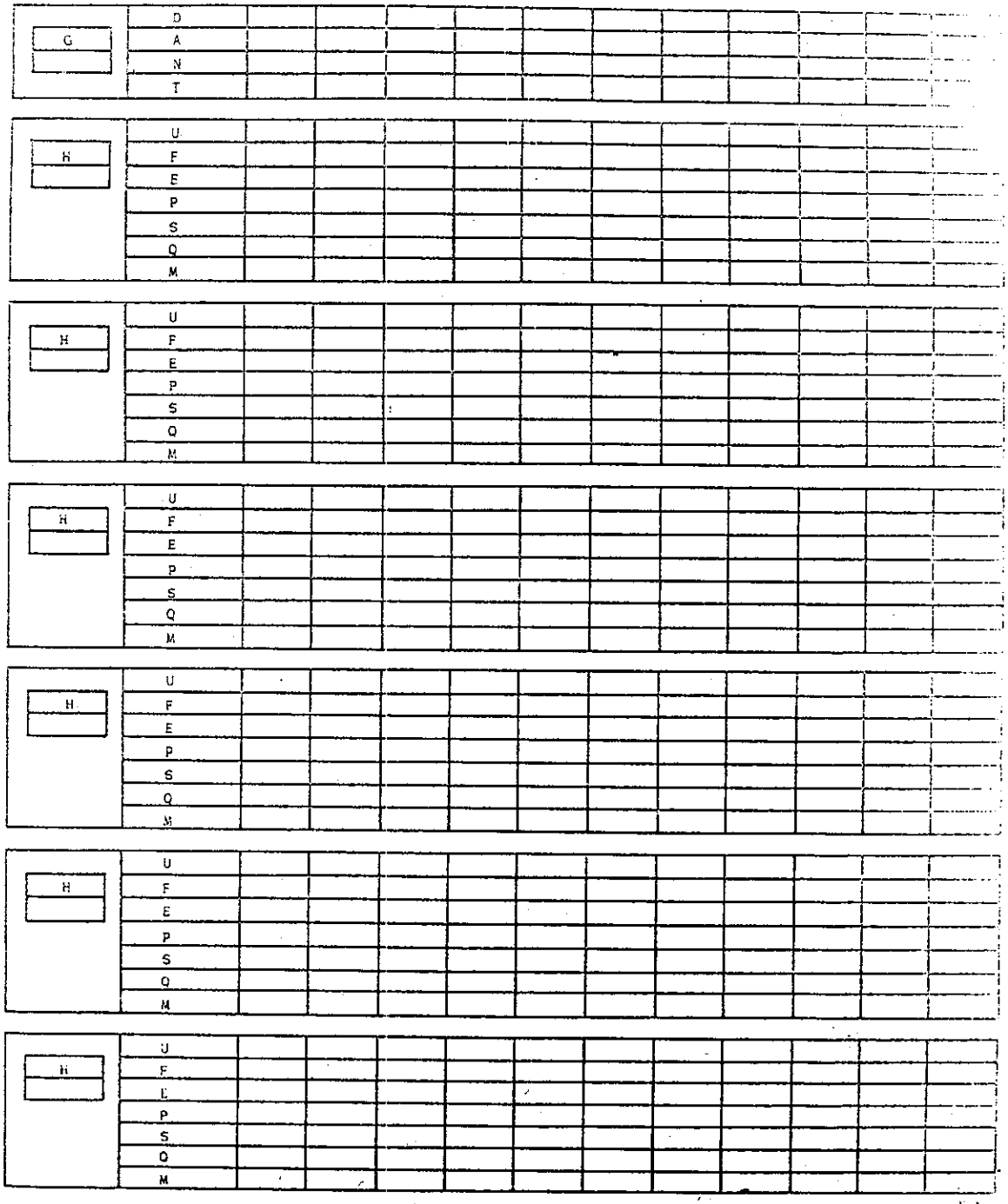

FIGURE 1 - WORKSHEET

	Air	Exp.	Asc.	1	2	3	4					
	D	100		40	30	20	10	0				
G	A	213		73	63	53	43	33				
.79	N	168	113	58	50	42	34					
	T	30	2.33	2	6	20	29					
	U		.467									
H	F	.985	.276	.242	.564	.937	.982					
5	E	+142	-53	-94	-80	-43	-11					
	P	26	166	152	130	85	45	35				
	S	+140	-14	-22	-45	-40	-10					
	Q	166	152	130	85	45	35					
	M		176	158	140	122	104					
	U		.233									
H	F	.875	.149	.129	.340	.750	.866					
10	E	+142	-37	-87	-84	-64	-24					
	P	26	150	145	134	106	58	38				
	S	+124	-5	-11	-28	-48	-20					
	Q	150	145	134	106	58	38					
	M		152	136	120	104	88					
	U		.117									
H	F	.646	.078	.066	.187	.500	.633					
20	E	+142	-5	-60	-64	-60	-38					
	P	26	118	118	114	102	72	48				
	S	+92	0	-4	-12	-30	-24					
	Q	118	118	114	102	72	48					
	M		132	117	102	87	72					
	U		.058									
H	F	.405	.040	.034	.098	.293	.395					
40	E	+142	+29	-27	-34	-39	-36					
	P	26	84	85	84	81	70	56				
	S	+58	+1	-1	-3	-11	-14					
	Q	84	85	84	81	70	56					
	M		112	98	84	70	56					
	U		.029									
H	F	.229	.020	.017	.050	.156	.222					
80	E	+142	+54	-2	-10	-18	-23					
	P	26	59	60	60	60	57	52				
	S	+33	+1	0	0	-3	-5					
	Q	59	60	60	60	57	52					
	M		106	93	80	67	54					
	U		.019									
H	F	.158	.013	.011	.034	.108	.154					
120	E	+142	+64	+8	0	-8	-16					
	P	26	49	50	50	50	50	48				
	S	+23	+1	0	0	0	-2					
	Q	49	50	50	0	50	48					
	M		100	88	76	64	52					

FIGURE 2 180' - 30 MINUTES AIR DIVE

				Oxygen O = 0.2								
	H_2O_2	Exp.	Acc.	1	2	3	4	5				
	D	200		60	50	40	30	20	0			
G	A	233		93	83	73	63	53	33			
.75	N	175	123	70	17	15	13	11				
	T	30	2.33	2	2	3	5	19				
	U		.467									
N	F	.605	.276	.242	.242	.360	.500	.927				
5	E	+149	-40	-92	-123	-95	-65	-35				
	P	26	173	162	140	110	78	46	14			
	S	+147	-11	-22	-30	-32	-32	-32				
	Q	173	162	140	110	78	46	14				
	M		176	161	146	131	116	86				
	U		.233									
N	F	.875	.149	.129	.129	.187	.293	.732				
10	E	+149	-34	-82	-126	-111	-93	-68				
	P	26	157	152	142	126	106	79	29			
	S	+130	-5	-10	-16	-20	-27	-50				
	Q	157	152	142	126	106	79	29				
	M		158	144	130	116	102	74				
	U		.117									
N	F	.646	.078	.066	.066	.098	.158	.482				
20	E	+149	+1	-52	-102	-98	-91	-79				
	P	26	122	122	119	113	104	90	52			
	S	+96	0	-3	-6	-9	-14	-38				
	Q	122	122	119	113	104	90	52				
	M		144	131	118	105	92	66				
	U		.058									
N	F	.405	.040	.034	.034	.050	.083	.280				
40	E	+149	+36	-19	-72	-72	-71	-67				
	P	26	87	89	89	87	84	78	60			
	S	+61	+2	0	-2	-3	-6	-18				
	Q	87	89	89	87	84	78	60				
	M		132	120	108	96	84	60				
	U		.029									
N	F	.229	.020	.017	.017	.026	.042	.152				
80	E	+149	+63	+9	-44	-46	-47	-47				
	P	26	60	61	61	61	60	58	51			
	S	+34	+1	0	0	-1	-2	-7				
	Q	60	61	61	61	60	58	51				
	M		128	116	104	92	80	56				
	U		.015									
N	F	.118	.013	.011	.011	.017	.028	.103				
120	E	+149	+73	+19	-34	-35	-38	-39				
	P	26	50	51	51	51	51	50	46			
	S	+24	+1	0	0	0	-1	-4				
	Q	50	51	51	51	51	50	46				
	M		126	114	102	90	78	54				

FIGURE 3 200' - 30 MINUTES 75-25% HELIUM-OXYGEN DIVE

TIME UNIT (Integer and one decimal place)	TIME UNIT (Second decimal place)										TIME FUNCTION (Three decimal places)
	.0	1	2	3	4	5	6	7	8	9	
0.0	----	.007	.014	.021	.027	.034	.041	.047	.054	.061	
0.1	.067	.073	.081	.086	.092	.099	.105	.111	.117	.123	
0.2	.129	.136	.141	.147	.153	.159	.165	.171	.176	.182	
0.3	.188	.193	.199	.204	.210	.215	.221	.226	.232	.237	
0.4	.242	.247	.253	.258	.263	.268	.273	.278	.283	.288	
0.5	.293	.298	.303	.307	.312	.317	.322	.326	.331	.336	
0.6	.340	.345	.349	.354	.358	.363	.367	.372	.376	.380	
0.7	.384	.389	.393	.397	.401	.405	.410	.414	.418	.422	
0.8	.426	.430	.434	.438	.441	.445	.449	.453	.457	.460	
0.9	.464	.468	.472	.475	.479	.482	.486	.490	.493	.496	
1.0	.500	.503	.507	.510	.514	.517	.520	.524	.527	.530	
1.1	.533	.537	.540	.543	.546	.549	.553	.556	.559	.562	
1.2	.565	.568	.571	.574	.577	.580	.583	.585	.588	.591	
1.3	.594	.597	.600	.602	.605	.608	.610	.613	.616	.618	
1.4	.621	.624	.626	.629	.632	.634	.637	.639	.642	.644	
1.5	.646	.649	.651	.654	.656	.659	.661	.663	.666	.668	
1.6	.670	.672	.675	.677	.679	.681	.684	.686	.688	.690	
1.7	.692	.694	.697	.699	.701	.703	.705	.707	.709	.711	
1.8	.713	.715	.717	.719	.721	.723	.725	.726	.728	.730	
1.9	.732	.734	.736	.738	.739	.741	.743	.745	.747	.748	
2.0	.750	.752	.754	.755	.757	.759	.760	.762	.764	.765	
2.1	.767	.768	.770	.772	.773	.775	.776	.778	.779	.781	
2.2	.782	.784	.785	.787	.788	.790	.791	.793	.794	.796	
2.3	.797	.798	.800	.801	.803	.804	.805	.807	.808	.809	
2.4	.811	.812	.813	.815	.816	.817	.818	.820	.821	.822	
2.5	.823	.824	.826	.827	.828	.829	.830	.832	.833	.834	
2.6	.835	.836	.837	.839	.840	.841	.842	.843	.844	.845	
2.7	.846	.847	.848	.849	.850	.851	.852	.853	.854	.855	
2.8	.856	.857	.858	.859	.860	.861	.862	.863	.864	.865	
2.9	.866	.867	.868	.869	.870	.871	.872	.872	.873	.874	
3.0	.875	.876	.877	.878	.878	.879	.880	.881	.882	.883	
3.1	.883	.884	.885	.886	.887	.887	.888	.889	.890	.890	
3.2	.891	.892	.893	.893	.894	.895	.896	.896	.897	.898	
3.3	.899	.899	.900	.901	.901	.902	.903	.903	.904	.905	
3.4	.905	.906	.907	.907	.908	.909	.909	.910	.910	.911	
3.5	.912	.912	.913	.913	.914	.915	.915	.916	.916	.917	
3.6	.918	.918	.919	.919	.920	.920	.921	.921	.922	.923	
3.7	.923	.924	.924	.925	.925	.926	.926	.927	.927	.928	
3.8	.928	.929	.929	.930	.930	.931	.931	.932	.932	.933	
3.9	.933	.934	.934	.934	.935	.935	.936	.936	.937	.937	
4.0	.938	.938	.938	.939	.939	.940	.940	.941	.941	.941	
4.1	.942	.942	.943	.943	.943	.944	.944	.944	.945	.945	
4.2	.946	.946	.946	.947	.947	.947	.948	.948	.949	.949	
4.3	.949	.950	.950	.950	.951	.951	.951	.952	.952	.952	
4.4	.953	.953	.953	.954	.954	.954	.955	.955	.955	.956	
4.5	.956	.956	.957	.957	.957	.957	.958	.958	.958	.959	
4.6	.959	.959	.959	.960	.960	.960	.960	.961	.961	.961	
4.7	.962	.962	.962	.962	.963	.963	.963	.963	.964	.964	
4.8	.964	.964	.965	.965	.965	.965	.966	.966	.966	.966	
4.9	.967	.967	.967	.967	.967	.968	.968	.968	.968	.969	
5.0	.969	.969	.969	.969	.970	.970	.970	.970	.970	.971	
5.1	.971	.971	.971	.971	.972	.972	.972	.972	.972	.973	
5.2	.973	.973	.973	.973	.974	.974	.974	.974	.974	.974	
5.3	.975	.975	.975	.975	.975	.976	.976	.976	.976	.976	
5.4	.976	.977	.977	.977	.977	.977	.977	.977	.978	.978	
5.5	.978	.978	.978	.978	.979	.979	.979	.979	.979	.979	
5.6	.979	.980	.980	.980	.980	.980	.980	.980	.981	.981	
5.7	.981	.981	.981	.981	.981	.981	.982	.982	.982	.982	
5.8	.982	.982	.982	.982	.983	.983	.983	.983	.983	.983	
5.9	.983	.983	.984	.984	.984	.984	.984	.984	.984	.984	

APPENDIX A
TABLE U
THREE-PLACE TIME FUNCTIONS
FOR TIME UNITS FROM 0.00 TO 5.99

TIME FUNCTIONS
(PERCENTAGE DECIMAL)

FOR DETERMINATION OF TISSUE PRESSURE IN 5, 10, 20, 40, 80, 120, 160, 200 AND 240 – MINUTE TISSUES DURING EXPOSURES UP TO 150 MINUTES.

EXPOSURE TIME MINUTES	TISSUE HALF TIME (Minutes)								
	5	10	20	40	80	120	160	200	240
1	.129	.066	.034	.017	.009	.004	.004	.002	.002
2	.242	.129	.066	.034	.017	.011	.009	.007	.004
3	.340	.187	.098	.050	.026	.017	.013	.011	.009
4	.425	.242	.129	.066	.034	.022	.017	.014	.011
5	.500	.293	.158	.083	.042	.023	.022	.018	.014
6	.564	.340	.187	.098	.050	.034	.025	.021	.017
7	.621	.384	.215	.114	.059	.039	.030	.024	.020
8	.669	.425	.242	.129	.067	.045	.034	.027	.022
9	.712	.463	.268	.144	.075	.050	.037	.031	.025
10	.750	.500	.293	.158	.083	.055	.042	.034	.028
11	.782	.533	.317	.173	.091	.061	.045	.038	.031
12	.811	.564	.340	.187	.099	.066	.050	.041	.034
13	.835	.593	.362	.201	.107	.072	.055	.044	.036
14	.857	.621	.384	.215	.114	.078	.059	.047	.039
15	.875	.646	.405	.229	.122	.083	.063	.051	.042
16	.892	.669	.425	.242	.129	.088	.067	.054	.045
17	.906	.692	.445	.254	.137	.093	.071	.057	.047
18	.918	.712	.463	.268	.144	.096	.074	.061	.050
19	.927	.732	.482	.280	.152	.103	.078	.064	.053
20	.937	.750	.500	.293	.158	.108	.084	.067	.055
21	.945	.766	.516	.304	.165	.114	.087	.070	.059
22	.953	.782	.533	.317	.173	.119	.090	.073	.061
23	.959	.797	.548	.328	.181	.124	.094	.077	.064
24	.963	.811	.564	.340	.187	.129	.099	.081	.066
25	.967	.824	.579	.351	.196	.134	.102	.083	.069
26	.972	.835	.593	.362	.201	.139	.107	.086	.072
27	.977	.847	.607	.373	.209	.143	.110	.089	.075
28	.980	.857	.621	.384	.215	.149	.114	.092	.078
29	.982	.866	.633	.395	.222	.154	.118	.096	.081
30	.985	.875	.646	.405	.229	.158	.122	.099	.083
31		.884	.657	.415	.235	.162	.125	.102	.085
32		.892	.669	.425	.242	.168	.129	.105	.088
33		.899	.681	.435	.249	.173	.132	.108	.090
34		.906	.692	.445	.255	.178	.137	.111	.093
35		.912	.702	.454	.262	.183	.141	.114	.095
36		.918	.712	.463	.268	.187	.144	.117	.098
37		.922	.722	.473	.275	.192	.148	.120	.101
38		.927	.732	.482	.280	.197	.151	.123	.103
39		.932	.741	.491	.287	.201	.154	.126	.106
40		.937	.750	.500	.293	.206	.159	.129	.108
41		.941	.758	.508	.299	.210	.162	.133	.111
42		.945	.766	.516	.304	.215	.166	.136	.114
43		.949	.774	.525	.311	.219	.169	.139	.116
44		.953	.782	.533	.317	.224	.173	.141	.119
45		.956	.790	.541	.323	.228	.177	.144	.121
46		.959	.797	.548	.328	.233	.180	.147	.124
47		.960	.804	.556	.335	.237	.184	.150	.126
48		.963	.811	.564	.340	.242	.188	.153	.129
49		.965	.817	.572	.346	.248	.192	.156	.131
50		.967	.824	.579	.351	.250	.195	.159	.134
51		.970	.830	.586	.357	.255	.198	.162	.137
52		.972	.835	.593	.362	.259	.201	.165	.139
53		.974	.841	.600	.369	.264	.205	.168	.141
54		.977	.847	.607	.373	.268	.208	.171	.143
55		.978	.852	.614	.379	.272	.211	.174	.146
56		.980	.857	.621	.384	.277	.215	.176	.149
57		.981	.862	.627	.390	.281	.218	.179	.151
58		.982	.866	.633	.395	.285	.222	.182	.154
59		.984	.871	.639	.400	.289	.226	.185	.156
60		.985	.874	.646	.405	.293	.229	.188	.159
61			.880	.652	.411	.297	.235	.191	.161
62			.884	.657	.415	.300	.238	.193	.164
63			.888	.664	.421	.304	.238	.196	.166
64			.892	.669	.425	.309	.242	.199	.169
65			.895	.675	.431	.313	.244	.201	.171
66			.899	.681	.435	.317	.248	.204	.173
67			.902	.686	.440	.321	.251	.207	.175
68			.906	.692	.445	.324	.255	.210	.178
69			.909	.697	.450	.328	.259	.213	.180
70			.912	.702	.455	.332	.262	.215	.183
71			.915	.707	.459	.336	.264	.218	.185
72			.918	.712	.464	.340	.268	.221	.187
73			.920	.717	.469	.342	.271	.224	.190
74			.922	.722	.473	.347	.274	.226	.192
75			.925	.727	.478	.352	.276	.229	.194

TABLE T

EXPOSURE TIME MINUTES	TISSUE HALF TIME (Minutes)						
	20	40	80	120	160	200	240
76	.927	.732	.482	.354	.280	.232	.197
77	.930	.736	.487	.359	.284	.235	.199
78	.932	.741	.491	.362	.287	.237	.201
79	.934	.745	.495	.368	.289	.240	.203
80	.937	.750	.500	.373	.293	.242	.206
81	.939	.754	.505	.374	.296	.245	.208
82	.941	.756	.508	.377	.299	.247	.210
83	.943	.760	.512	.381	.302	.250	.212
84	.945	.766	.516	.384	.305	.253	.215
85	.947	.770	.521	.387	.308	.256	.217
86	.949	.774	.524	.391	.310	.258	.219
87	.951	.778	.528	.395	.313	.261	.222
88	.953	.782	.533	.399	.317	.263	.224
89	.955	.786	.537	.402	.319	.266	.226
90	.956	.790	.541	.405	.323	.268	.228
91	.957	.794	.545	.408	.325	.271	.231
92	.959	.797	.550	.411	.328	.273	.233
93	.959	.797	.554	.415	.332	.275	.235
94	.960	.804	.557	.419	.334	.278	.237
95	.962	.807	.561	.423	.337	.281	.239
96	.963	.811	.565	.425	.340	.283	.242
97	.964	.814	.569	.428	.342	.285	.245
98	.965	.817	.573	.431	.346	.288	.248
99	.966	.820	.576	.435	.348	.291	.249
100	.967	.824	.580	.439	.352	.293	.250
101	.968	.826	.584	.442	.355	.295	.253
102	.970	.830	.587	.445	.357	.298	.255
103	.971	.832	.591	.448	.359	.301	.257
104	.972	.835	.594	.451	.363	.303	.259
105	.973	.838	.597	.455	.365	.305	.262
106	.974	.841	.601	.458	.368	.307	.264
107	.976	.844	.605	.461	.371	.310	.266
108	.977	.847	.608	.463	.374	.312	.269
109	.977	.849	.611	.466	.377	.314	.270
110	.978	.852	.615	.469	.379	.317	.272
111	.979	.854	.618	.472	.381	.320	.274
112	.980	.857	.622	.476	.384	.322	.277
113	.980	.859	.625	.479	.386	.324	.279
114	.981	.862	.628	.482	.390	.326	.281
115	.982	.864	.631	.484	.392	.329	.283
116	.982	.866	.634	.487	.395	.331	.285
117	.983	.868	.637	.491	.398	.333	.287
118	.984	.870	.640	.494	.400	.336	.289
119	.984	.873	.644	.497	.403	.338	.291
120	.985	.875	.647	.500	.405	.340	.293
121		.877	.650	.503	.407	.343	.295
122		.880	.653	.505	.411	.345	.297
123		.882	.656	.509	.413	.347	.299
124		.884	.659	.512	.416	.349	.300
125		.886	.662	.515	.418	.351	.302
126		.888	.665	.517	.421	.354	.304
127		.890	.668	.520	.424	.356	.306
128		.892	.670	.523	.426	.358	.309
129		.894	.673	.525	.428	.361	.311
130		.895	.676	.528	.431	.363	.313
131		.898	.679	.531	.433	.365	.315
132		.899	.682	.533	.436	.367	.317
133		.900	.685	.536	.438	.370	.319
134		.902	.687	.540	.440	.372	.321
135		.904	.690	.542	.443	.374	.323
136		.906	.693	.545	.445	.376	.324
137		.908	.695	.547	.447	.378	.326
138		.909	.698	.550	.450	.380	.328
139		.910	.701	.552	.452	.382	.330
140		.912	.703	.555	.455	.384	.332
141		.913	.705	.557	.457	.387	.334
142		.915	.708	.560	.459	.389	.335
143		.916	.711	.562	.462	.391	.338
144		.918	.713	.565	.464	.393	.340
145		.919	.715	.567	.466	.395	.342
146		.920	.718	.570	.469	.397	.344
147		.920	.720	.572	.471	.399	.346
148		.922	.723	.575	.474	.401	.347
149		.924	.725	.577	.476	.403	.349
150		.925	.726	.580	.478	.405	.350

APPENDIX B

Table of Maximum Allowable Tissue Tensions (M) of Nitrogen for Various Half-time Tissues

	Depth of decompression stop									
D (ft)	10	20	30	40	50	60	70	80	90	100
A (ft)	43	53	63	73	83	93	103	113	123	133
t (min)	(M) (Feet of sea water equivalent)									
5	104	122	140	158	176	194	212	230	248	266
10	88	104	120	136	152	168	184	200	216	232
20	72	87	102	117	132	147	162	177	192	207
40	56	70	84	98	112	126	140	154	168	182
80	54	67	80	93	106	119	132	145	158	171
120	52	64	76	88	100	112	124	136	148	160
160	51	63	74	86	97	109	120	132	143	155
200	51	62	73	84	95	106	117	128	139	150
240	50	61	72	83	94	105	116	127	138	149

	ΔM/Δ10 feet depth								
(min)	5	10	20	40	80	120	160	200	240
M(ft)	18	16	15	14	13	12	11.5	11	11

TABLE N APPENDIX C

Table of Maximum Allowable Tissue Tension (M) of Helium for Various Half-time Tissues

Depth of decompression stop

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

$\Delta M/\Delta 10$ feet depth

H (min)	5	10	20	40	80	120	160	200	240
ΔM (ft)	15	14	13	12	12	12	11	10	10

TABLE H APPENDIX D

Table of Maximum Allowable Tissue Tensions (M) of Inert Gas for Various Half Time Tissue (H) for Air Dives

D (ft)	10	20	30	40	50	60	70	80
A (ft)	43	53	63	73	83	93	103	113
h (min)	(M) (Feet of sea water equivalent)							
5	104	126	150	174	195	220	242	263
10	88	107	128	148	167	189	208	228
20	72	90	106	124	141	158	174	192
40	58	72	87	99	113	128	141	156
80	52	65	78	90	103	115	128	142
120	51	64	76	88	101	114	126	140

$M = 33 \left[(J) + r - 1.25\right]$

$J = (S/r)^{10} = M/33 - (r - 1.25)$

S = Surfacing tissue ratio

r = Depth tissue ratio at stops

TABLE D APPENDIX E